

# 2011 ANNUAL REPORT

## CIBERDEM

Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas  
Spanish Biomedical Research Centre in Diabetes and Associated Metabolic Disorders

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# Prologue

# Letter from the Scientific Director

It is not easy for researchers to carry out their tasks in times of economic crisis, but no more difficult than it is for the rest of the population, who have to adapt to a period not of growth, but of recession. At all times in history, there have been difficult moments for scientific investigation, although this has never prevented talented researchers from bringing new knowledge to humanity; even in the dark days of war.

At Ciberdem, our researchers have battled on with their projects and have made significant achievements even though they have been obliged to restructure or downsize their teams or be much more sparing in their use of materials. It was extraordinary and highly stimulating to see how, year after year, we were able to debate new proposals and, in the majority of them, give a positive answer. However, countries with a solid scientific tradition show us that now is the time to make better use of our scientific structures, to put a little extra effort into our labours, be more rigorous in our priorities and sharpen our wits in order to take the best advantage of the results we have obtained. It is also a time to look outside our frontiers to Europe and try to obtain funding from beyond our own borders.

We are pleased to be able to say that, as this annual report shows, we have made significant advances which are of great importance to our health system, such as the Di@bet.es Study, which provides us with accurate information on the prevalence of diabetes in the Spanish population, and the results obtained by researchers using the Metabolomics Platform. I single these out because they are collective achievements, a general effort on the part of all our researchers. I should also like to highlight the fact that several of the collaborative programmes we encouraged are leading to the appearance of high-level publications.

Even at times like this, when we must demand more of ourselves, Ciberdem's achievements put it in a highly commendable position in certain prestigious international indicators, as the SCImago Institutions Rankings (SIR 2011) attest. We are at the start of a journey; we believe that support for Ciberdem programmes is essential if we are to continue to consolidate what we have achieved and, of course, to improve them. Our research system is fragile and needs time to get the most out of the investments which have been initiated. We know that this view is shared by the Instituto de Salud Carlos III (ISCIII), which continues to provide financial support despite the great economic difficulties the country is experiencing. We are sure that its efforts and determination will be rewarded with the best possible biomedical science on the part of all of us in the community of researchers who make up Ciberdem.

Ramon Gomis  
Ciberdem Scientific Director

# Management report

In its fourth year of existence, Ciberdem has consolidated its status as a State Public Research Consortium and has managed to achieve all the goals laid out in its annual plan of action. In particular, it has achieved all the aims set out in the first strategic objective as regards fostering competitive translational research. It has also increased its participation in Europe, continued to develop and gain access to competitive platforms and maintained its training programme.

In 2011 it has signed knowledge-transfer and cooperation agreements with several companies and has been successful with its campaign to capture private funding for research projects. We must draw special attention to the fact that researchers contracted by Ciberdem have secured competitive projects within Spain, which means that the organization's own structure has brought in additional resources.

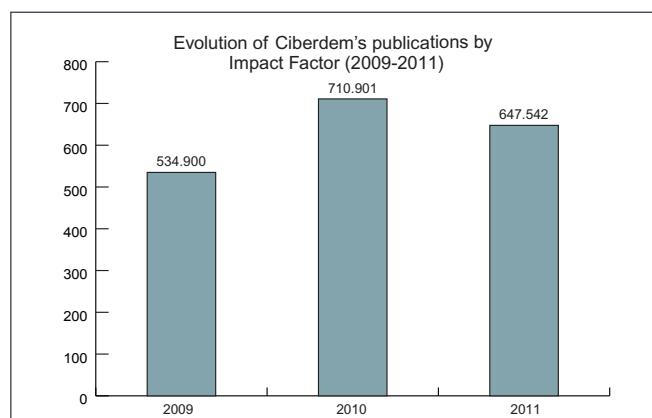
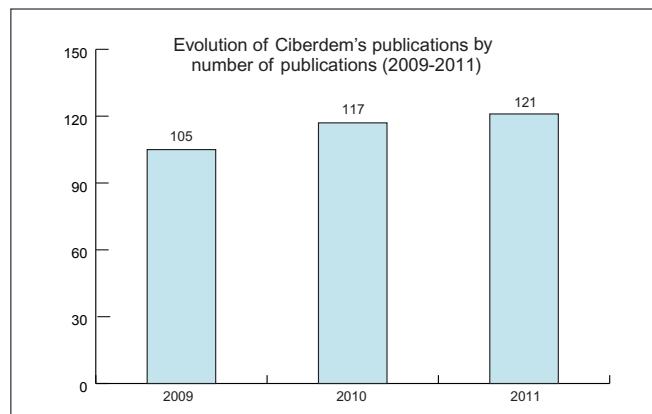
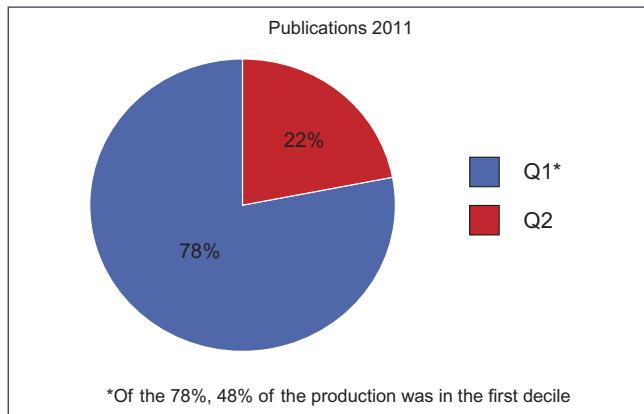
Ciberdem has been able to adapt to the spending cuts occasioned by the world recession. With a noticeably reduced budget in comparison with previous years, it has been obliged to redirect its scientific and human-resources strategies. In spite of the cuts made, scientific output has increased and levels of synergy between our groups and international collaboration have been consolidated.

Our challenges for the future involve a reorientation of our strategic efforts in order to guarantee budgetary stability, optimize available resources and boost our rate of success in obtaining outside funding, thus allowing our groups to continue to carry out research of excellence.

Ana Bosch  
Ciberdem Managing Director

# Research results

Publications\*: 121  
Impact Factor: 647.542  
Impact Factor average: 5.352  
Q1 indicator (High Quality Publications)\*\*: 80.5%  
First decile: 45  
Q1: 49  
Q2: 27  
IntraCIBER: 15  
InterCIBER: 31  
International: 45  
Research grants\*\*\*: 176  
National: 127  
International: 27  
Private funds: 22  
Clinical trials: 47  
Clinical practice guidelines: 8  
PhD theses: 22  
Patents: 1  
Spin-offs: 1  
Awards: 8



## Publications

In 2011, Ciberdem published a total of 121 scientific articles in the first and second quartiles of their speciality. It is worth noting that the total number of articles published was higher, but here we refer, for reasons of scientific excellence, only to those in the first and second quartiles.

Of these 121 articles, 78% (94) were in the first quartile and of these, 48% (45) were in the first decile of their specialist category.

The total impact factor was 647.542 (source: ISI Web of Knowledge), which gives an average impact factor of 5.352. If we take into account the fact that the average impact factor in the endocrinology and metabolism category in the ISI Web of Knowledge is 2.796, the quality of the scientific work done by Ciberdem becomes apparent.

Another factor to note is the increase in the number of scientific collaborations with other Cibers, which in 2011 grew by 16% as compared to 2010. International collaborations also increased steadily.

In conclusion, Ciberdem consolidated its scientific production and maintained the same levels of quantity, excellence and quality, both in general terms and in terms of every one of its scientific programmes.

## Projects

As a consortium, in 2011, Ciberdem presented 11 applications for funding in response to public calls in Spain and 8 in response to European calls. Here are the details of the successful applications:

### European calls

DIATRAIN. DIAbetes Trans-national Research Advancement for INvestigators.

People programme, 7th Framework Programme, Marie Curie

\* Only those published in 2011, with Ciberdem listed among the affiliations, which are related to Ciberdem's field of research and are located in the first or second quartile of their subject category are included. Sources: JCR 2010 and PubMed.

\*\* Ratio of publications that an institution publishes in the most influential scholarly journals of the world. Journals considered for this indicator are those ranked in the first quartile (25%) in their categories as ordered by SJR indicator. Source: SIR World Report 2011, SCImago.

\*\*\* Through Associate Institutions.

Actions-COFUND Call, European Union

Coordinator: Ciberdem

Budget: 443,038.00 €

Duration: 4 years

Current Status (June 2012): Implemented

MEDIGENE. Genetic and environmental factors of insulin resistance syndrome and its long-term complications in immigrant Mediterranean populations.

Health Programme, 7th Framework Programme, European Union.

Partner (Deputy Coordinator): Ciberdem

Budget: 371,381.00 €

Duration: 4 years

Current status (June 2012): Granted

#### **National calls**

Subprogramme Miguel Servet for the hiring of a Postdoctoral researcher for three years –Strategic Action in Health- (ISCIII-MICINN)

Characterization of the lipin family in human adipocytes.

Principal Investigator: Mercedes Miranda

Budget: 243,000.00 €

Duration: 3 years

Reference: CP11/00021

Current status (June 2012): Granted / Implemented

National Programme for Non-directed Fundamental Research Projects (Ministry of Economy and Competitiveness and the European Regional Development Fund (ERDF).

Identification of metabolic pathways in retinal neurodegeneration induced by hyperglycaemia and ischaemia using a metabolomic and proteomic approach.

Principal Investigator: Oscar Yanes

Budget: 157,300.00 €

Duration: 3 years

Reference: SAF2011-30578

Current status (June 2012): Granted / Implemented

Salvador de Madariaga grant. Subprogramme of the Ministry of Education for the stay of Spanish professors and researchers in foreign research and higher education centres.

Principal Investigator: Mercedes Miranda

Budget: 19,400.00 €

Duration: 6 months

Reference: PR2011-0584

Current status (June 2012): Finished

#### **Transfer of Knowledge and Innovation**

##### **Patents**

New in 2011:

Empleo de anticuerpos anti-beta-lactoglobulina en el diagnóstico y seguimiento de la celiaquía

Patent application number: P201131979

Inventors: Franz Martín, Bernat Soria, María Ángeles Ortega

Fundación Progreso y Salud-Universidad Pablo de Olavide

Active in 2011:

Gene therapy composition for use in diabetes treatment

Patent application number: EP10169309.1

Inventors: F Bosch, E Ayuso, D Callejas

Universitat Autònoma de Barcelona

Telomerase reverse transcriptase for protection against ageing

Patent application number: EP10168341.5

Inventors: MA Blasco, B Bernardes, F Bosch, E Ayuso

Universitat Autònoma de Barcelona and Centro Nacional de Investigaciones Oncológicas

Composition comprising an androgen receptor blocker and an insulin sensitizing agent and use thereof for treatment of polycystic ovary syndrome

Patent application number: PCT/BE 02/00052

Inventors: F de Zegher, L Ibáñez

University of Leuven and University of Barcelona

Uso de la proinsulina para la elaboración de una composición farmacéutica neuroprotectora, composición terapéutica que la contiene y sus aplicaciones

Patent application number: ES2331342B1

Inventors: EJ de la Rosa Cano, F de Pablo Dávila, P Boya Tremoleda, S Corrochano Sánchez, P de la Villa Polo, R Barhoum Tannous and F Bosch Tubert

CIB-CSIC, Universitat Autònoma de Barcelona and Universidad de Alcalá de Henares

Salicylate Conjugates Useful for Treating Metabolic Disorders

Patent application number: US 2009/0298923A1

Inventors: Mayoux E, Martí L, García-Vicente S, Serrano M, Mian A, Zorzano A

Genmedica Therapeutics

Marcadores genéticos del riesgo de sufrir reestenosis

Patent application number: 200900507

Inventors: Andrés V, Silvestre C, Fernández P, Sánchez PL, Fernández-Avilés F, Chaves FJ

Fina Biotech, SLU

Formulación tópica oftálmica de péptidos

Patent application number: P200931242

Inventors: R Simó, C Hernández, J Fernández, M Gómez, R Jordana, J Farrera, B Bonsati

Institut de Recerca Hospital Universitari Vall d'Hebron and BCN Peptides SA

Composiciones de terapia génica para prevenir y/o tratar enfermedades autoinmunes

Patent application number: P200930442

Inventors: Xavier Anguela, Sabrina Tafuro, Fátima Bosch

Universidad Autònoma de Barcelona

Composition for prevention or treatment of Diabetes Mellitus

Patent application number: P200900829

Inventors: Francisco Javier Navarro, Franz Martín, Patricia Moreno, Verónica Rivero, Elvira León  
UPO-Fundación Progreso y Salud

Stem cells of the islets of Langerhans and their use in treating diabetes mellitus

Patent application number: 11/410412, US 7544510

Inventors: Habener J, Abraham E, Zulewski H, Thomas MK, Vallejo M

The General Hospital Corporation (Massachusetts General Hospital, Boston)

Stem cells and their use in transplantation

Patent application number: 10/984645, US 7438902

Inventors: Habener JF, Zulewski H, Abraham E, Vallejo M, Faustman D, Thomas M

The General Hospital Corporation (Massachusetts General Hospital, Boston)

Method of pre-inducing a state of immune tolerance before organ transplantation

Patent application number: US 6923959

Inventors: Habener JF, Zulewski H, Abraham E, Vallejo M, Faustman D, Thomas M

The General Hospital Corporation (Massachusetts General Hospital, Boston)

Method of transplanting in a mammal and treating diabetes mellitus by administering a pseudo-islet like aggregate differentiated from a nestin-positive pancreatic stem cell

Patent application number: US 6866843

Inventors: Habener J.F, Zulewski H, Abraham E, Vallejo M, Faustman DL, Thomas MK

Viacell, Inc Charlestown, MA

Alimento funcional con efectos en la prevención de enfermedades cardiovasculares

Patent application number: 20080487

Inventors: Ramírez B, Anglès MN, Reguant J, Solà R, Godàs G

#### **Clinical practice guidelines**

Insulinas: Nuevas opciones para optimizar el tratamiento de la Diabetes Mellitus

Aguilera E, Gatzambide S, Aguiló E, Gonzalo MA, Calvo F, Lara JI, Conget I, Puig M, Duran S, Rovira A, Tinahones FJ, Faure E, Vázquez F, Fernández-García JC

Diabetomecum, ed Permanyer, ISBN 9788499262529 (2011)

ESC/EAS Guidelines for the management of dyslipidaemias: the Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

European Association for Cardiovascular Prevention & Rehabilitation, Reiner Z, Catapano AL, De Backer G, Graham

I, Taskinen MR, Wiklund O, Agewall S, Alegria E, Chapman MJ, Durrington P, Erdine S, Halcox J, Hobbs R, Kjekshus J, Filardi PP, Riccardi G, Storey RF, Wood D; ESC Committee for Practice Guidelines (CPG) 2008-2010 and 2010-2012 Committees, Bax J, Vahanian A, Auricchio A, Baumgartner H, Ceconi C, Dean V, Deaton C, Fagard R, Filippatos G, Funck-Brentano C, Hasdai D, Hobbs R, Hoes A, Kearney P, Knuuti J, Kohl P, McDonagh T, Moulin C, Poldermans D, Popescu BA, Reiner Z, Sechtem U, Sirnes PA, Tendera M, Torbicki A, Vardas P, Widimsky P, Windecker S, Funck-Brentano C, Poldermans D, Berkenboom G, De Graaf J, Descamps O, Gotcheva N, Griffith K, Guida GF, Gulec S, Henkin Y, Huber K, Kesaniemi YA, Lekakis J, Manolis AJ, Marques-Vidal P, Masana L et al.

Eur Heart J, 32, 1769-1818 (2011)

Triglyceride-rich lipoproteins and high-density lipoprotein cholesterol in patients at high risk of cardiovascular disease: evidence and guidance for management

Chapman MJ, Ginsberg HN, Amarenco P, Andreotti F, Borén J, Catapano AL, Descamps OS, Fisher E, Kovanen PT, Kuivenhoven JA, Lesnik P, Masana L, Nordestgaard BG, Ray KK, Reiner Z, Taskinen MR, Tokgözoglu L, Tybjærg-Hansen A, Watts GF; European Atherosclerosis Society Consensus Panel  
Eur Heart J, 32, 1345-1361 (2011)

Urgencias Pediátricas: Diagnóstico y Tratamiento

FJ Benito y cols

5th edition, p 611-622, ISBN 9788498353563 (2011)

Protocolos de Endocrinología y Nutrición

Real JT, Ampudia-Blasco J, Ascaso JF (editors)

Servicio de Endocrinología y Nutrición, HCU, Valencia, ed Menta, p 1-397, DL V-3007-2011 (2011)

Protocolo de tratamiento de la diabetes tipo 2

Grup de treball de Diabetes Tipus 2 Barcelona Dreta Consorci Sanitari de Barcelona, p 1-8 (2011)

Follow-up of the small-for-gestational-age child: clinical guidelines

López ID, Muñoz Ade A, Muñoz JB, Rodríguez PC, Gómez EG, Ollero MJ, Rodríguez JM, Dehlia AC, Estrada RC, Toda LI An Pediatr (Barc), 76, 104.e1-7 (2012). Epub 2011 Oct 19

Epidemiology, diagnosis and management of hirsutism: a consensus statement by the Androgen Excess and Polycystic Ovary Syndrome Society

Escobar-Morreale HF, Carmina E, Dewailly D, Gambineri A, Kelestimur F, Moghetti P, Pugeat M, Qiao J, Wijeyaratne CN, Witchel SF, Norman RJ

Hum Reprod Update, 18, 146-170 (2012). Epub 2011 Nov 6

#### **Spin-off**

Beyond Food SL

Description: Support to industry for the validation of functional food  
Researchers: L Masana, R Solà, JC Vallvé, J Ribalta, J Girona, C Prats  
Collaborating institution: Universitat Rovira i Virgili

#### ***Transfer agreements***

Ciberdem:

Object of the contract: Search for compounds modulating exocytosis with applications in the treatment of type 2 diabetes

Company: BRAINco Biopharma SL

Budget: 107,011.19 €

Ciberdem Groups: Joan Vendrell, Anna Maria Gómez-Foix and Anna Novials

In 2011, the groups worked on different lines of research, but the work continued until April 2012.

Through Associate Institutions:

Object of the contract: Development of a metabolomics platform for the study of metabolic disorders caused by obesity

Company: Bioorganic Research and Services, SL (Bionaturis)

Budget: 65,000.00 €

PI Xavier Correig

Object of the contract: Characterization of diabetic retinopathy models and evaluation of the possible therapeutic effects of proinsulin

Company: Proretina Therapeutics SL

Budget: 19,752.00 €

PI Flora de Pablo

Object of the contract: Development of monoclonal antibodies

Company: Fundación Progreso y Salud, Junta de Andalucía

Budget: 103.400,00 €

PI Franz Martín

Object of the contract: Technical and nutritional advice for sportspeople

Company: Gesalus-Real Betis Balompie

Budget: 15,733.33 €

PI Franz Martín

Object of the contract: Transfer of human material within the nPOD program (network Pancreas Organ Donation)

Company: University of Florida

Budget: 57,000.00 €

PI Eduard Montanya

#### ***Innovation***

Ciberdem:

Name of project: Diabetes a la carta (see [page 15](#) for more)

Description: Therapeutic education programme for people with type 2 diabetes mellitus

Type of activity: Technical

PIs Anna Novials and Ramon Gomis

Through Associate Institutions:

Name of project: Preparation for the molecular diagnosis of MODY1, MODY5 and hereditary renal glycosuria

Description: PCR and gene HNF4 alfa, HNF1 beta y SLC2A2 sequencing study

Type of activity: Technical

PI Francisco Blanco Vaca

Name of project: Autoanticuerpos anti transportador de Zn

Description: New autoimmunity marker, characteristic of type 1 diabetes

Type of activity: Technical

PI Luis Castaño

Name of project: Design and development of a study of the AIRE gene (chr21q22.3)

Description: Preparation and molecular analysis of the AIRE gene for application in the study of autoimmune diabetes associated with autoimmune polyglandular syndrome type 1

Type of activity: Technical

PI Luis Castaño

Name of project: Methodology for the isolation of pancreatic islets

Description: A comparison of different methods for the isolation of murine pancreatic islets

Type of activity: Procedure

PI Luis Castaño

# Project management

## Introduction

The Spanish Biomedical Research Centre in Diabetes and Associated Metabolic Disorders (Ciberdem) works hard to obtain additional competitive funding to develop research into diabetes and associated metabolic disorders.

Currently, Ciberdem's project management department is involved in all project phases, giving support to our researchers in the preparation and presentation of proposals, and also the submission, implementation and justification of funded projects.

Ciberdem aims to expand its presence in the worldwide scientific community in its specific research field. The strengthening of national, international and intersectorial collaboration in research will help us to obtain more and better scientific outcomes with high translational impact.

## Objectives

To achieve excellence, to obtain competitive funding and to monitor projects from implementation to justification.

To give support in the preparation of proposals by researchers in the consortium.

To internationalize Spanish biomedical research, in particular as regards Ciberdem's main lines of research into diabetes and associated metabolic disorders.

To encourage and motivate researchers to participate in calls and seize opportunities to take part in different kinds of programmes through the newsletter.

## Coordination

Gemma Pascual and Francesc Martí, Ciberdem Project Managers.

## Achievements in 2011

### *Ciberdem's own actions*

These are transversal initiatives implemented by members of the consortium and in some cases with the collaboration of external personnel. These translational projects try to answer complex questions which could not be resolved by one group working alone and will prove of benefit to diabetic patients and the healthcare system in general.

In 2011, 14 research actions were underway, although some of these had been implemented in previous years. They were:

- 1) the Di@bet.es Study, which is the first national epidemiological study that will provide the Spanish health authorities with real figures relating to the prevalence of type 2 diabetes (diagnosed as such or not) in addition to other relevant parameters. For more information see [page 21](#).
- 2) ten Ciberdem projects defined as translational initiatives resulting from internal collaborative work: NEURORET-DIAB,

INGENFRED, MODIAB, DIASOBS, GIDIPRED, ANTIBECELL, METADIAB, ENDODIAB, IODURE and STEMOP. For more information see [page 23](#).

3) Telemed-diabetes Study, designed to evaluate the impact on costs and efficacy of a telematic control system. For more information see [page 26](#).

4) Amicus Canis and Pilchardus, two privately funded projects which took their first steps during 2011 and are continuing in 2012. For more information see [page 15](#).

### *National grants obtained*

During 2011, a proposal submitted under the Miguel Servet subprogramme of the Strategic Health Action Call of the Spanish Ministry of Science and Innovation and the Carlos III Health Institute, received a grant. This project (Characterization of the Lipin family in human adipocytes) is directed by Dr Mercedes Miranda and is funded for 3 years. Dr Miranda was also awarded a Salvador de Madariaga grant, subprogramme of the Ministry of Education, for Spanish professors and researchers to stay in foreign research and higher education centres.

Another proposal (Identification of metabolic pathways in retinal neurodegeneration induced by hyperglycaemia and ischaemia using a metabolomic and proteomic approach) submitted under the National Programme for Non-directed Fundamental Research Projects of the Ministry of Economy and Competitiveness and the European Regional Development Fund (ERDF) was granted to Dr Oscar Yanes and will be funded for 3 years.

### *National grants implemented*

In 2010, two projects, one directed by Dr Mercedes Miranda (Phosphatidate phosphatases regulation of cellular functions by controlling phospholipid biosynthesis and its relation with obesity) and another by Dr Josep Julve (HDL functionality in diabetes mellitus and hyperhomocysteinaemia: studies in patients and animal models) received grants from the National Scientific Research, Development and Technological Innovation Plan of the Spanish Ministry of Science and Innovation and the Carlos III Health Institute. These two projects were implemented during 2011 and produced several high level publications:

The stress-activated protein kinase Hog1 develops a critical role after resting state

Escoté X, **Miranda M**, Rodríguez-Porrata B, Mas A, Cordero R, Posas F, Vendrell J

Mol Microbiol, 80, 423-435 (2011)

[PMID 21371138](#)

ATP-binding cassette G5/G8 deficiency causes hypertriglyceridemia by affecting multiple metabolic pathways

Méndez-González J, **Julve J**, Rotllan N, Llaverias G, Blanco-Vaca F, Escolà-Gil JC

Biochim Biophys Acta, 1811, 1186-1193 (2011)

PMID 21855652

The cholesterol content of Western diets plays a major role in the paradoxical increase in high-density lipoprotein cholesterol and upregulates the macrophage reverse cholesterol transport pathway

Escolà-Gil JC, Llaverias G, **Julve J**, Jauhainen M, Méndez-González J, Blanco-Vaca F

Arterioscler Thromb Vasc Biol, 31, 2493-2499 (2011)

PMID 21885848

#### ***International grants obtained***

MEDIGENE (Genetic and environmental factors of insulin resistance syndrome and its long-term complications in immigrant Mediterranean populations), a Cooperation Programme with several other European institutions, was granted after negotiations under the FP7 Health Call during 2011 and was implemented at the beginning of 2012.

#### ***International grants implemented***

In 2011, our DIATRAIN project (DIAbetes Trans-national Research Advancement for Investigators), a Marie Curie-COFUND programme cofunded by Ciberdem and the European Commission, concluded negotiations and implementation started in September 2011. This programme involves two post-doctoral mobility schemes, one incoming and one outgoing, and is led by Dr Ramon Gomis. The first call for fellowships closed at the end of 2011 and the first fellows started working in Ciberdem and travelling abroad at the beginning of 2012.

#### **Future challenges**

The Project Management Department wants to establish stronger interactivity with all the groups in Ciberdem and also to increase their participation in national and international calls to obtain additional funding for our projects and in this way enrich the scientific outcomes of the consortium.

Our principal goals are to increase the rate of success of our proposals in competitive calls and also to attract investment from the private sector to fund and sponsor our own projects such as the previously mentioned Pilchardus and Amicus Canis. Obtaining this funding will allow Ciberdem to increase its research efforts, which as always will continue to be into the prevention, treatment and cure of diabetes and its associated metabolic disorders.

# Training programme

## Introduction

The training of research staff was envisaged right from the start of Ciberdem and has been at the very centre of strategic action plan design ever since, especially the training of predoctoral staff and specialists with tenure. The aim of the teaching programme is to encourage the acquisition and transfer of knowledge, both basic and clinical, among the research staff under training in the groups which make up Ciberdem in order to achieve the general research objectives as defined, while at the same time making better use of the resources available. The teaching programme represents an investment in our younger staff and in the future of the consortium itself.

## Objectives

Our objectives are to create and implement a research staff training programme aimed especially at predoctoral researchers which will help participants to consolidate their investigative career, improve their future prospects and bring added value to the groups to which they belong; to enhance the methodological, technical, communicative and organizational skills of the younger members of the research staff and improve their scientific capacity in general; and to increase mobility, communication and the transfer of scientific knowledge between the groups which make up Ciberdem in order to develop their scientific proficiency, both basic and clinical.

## Coordination

Fàtima Bosch, Ciberdem Principal Investigator.

## Achievements in 2011

### *Renewal of contracts for predoctoral research staff*

Objective: A commitment to support young researchers so that they can carry out their work in the field of diabetes in a group of excellence linked to Ciberdem. In 2011 Ciberdem renewed the contracts of predoctoral grant holders as shown below:

Name: Eleazar Rubio Martín

Activity: The role of adipose tissue and adipokines in the development of type 2 diabetes. A population cohort study

Name: Verónica Moreno Viedma

Activity: The function of IRS-2 in the differentiation of embryonic stem cells from insulin-producing cells

### *The organization of an annual training course in translational matters with special emphasis on clinical research, aimed at Ciberdem's predoctoral researchers*

Objective: Regular ongoing training for predoctoral researchers (under contract or attached) covering subjects

of translational interest given by experienced Ciberdem specialists or outside speakers. Ciberdem organized the following training course:

Title: Physiological Techniques Applied to Islets of Langerhans

Date: 20-21 January, 2011

Venue: Elx (Alicante)

Hours of classes: 9 hours of classes divided between theoretical and practical sessions:

a. Theory: 8 sessions of 45 minutes each

b. Practicals: 3 hours

Number of presentations: 8 oral presentations

Participants: 40 Ciberdem researchers

### *II Clinical Symposium on Research into Diabetes and Associated Metabolic Disorders*

The second Clinical Symposium organized jointly with the MSD pharmaceutical company. Aimed at professional clinicians.

Objective: To create an environment for the dissemination and exchange of research results.

Papers were given by international speakers as well as speakers from Spain and members of Ciberdem.

Date: 30th September - 1st October, 2011

Venue: Barcelona

Hours of classes: 6 hours of classes, divided into 5 sessions

Number of presentations: 10 oral presentations

Participants: 185 attendees, including 34 Ciberdem researchers

### *First Symposium on Epigenetics*

A symposium attended by speakers working in epigenetics.

Organized by CBATEG with the collaboration of Ciberdem

Date: 3rd June, 2011

Venue: Barcelona

Number of presentations: 11 oral presentations divided into 4 sessions and a scientific poster session

Participants: 100 researchers, including 24 members of Ciberdem

### *Training periods*

Objective: For junior and senior researchers to spend short periods (a maximum of three months) in other laboratories to broaden their scientific knowledge in specific techniques, collaborate with other groups and develop joint experiments. In 2011, 3 training periods of this type were made possible thanks to Ciberdem.

### *Theses defended and directed by researchers attached to Ciberdem*

In 2011, a total of 22 doctoral theses were read.

***CBATEG Seminars (UAB-Ciberdem)***

Organized by the Transgenic animal models and gene therapy approaches for diabetes group (PI Fàtima Bosch) during 2011 at the UAB, Bellaterra, Spain.

March 15: The role of adipocyte glutamine synthesis in the development of obesity-induced inflammation. Presentation by Dr. Malcolm Watford, Rutgers University, New Brunswick NJ, USA.

March 17: Gene therapy approaches for protecting beta cells in type 1 diabetes and transplanted islets. Presentation by Prof. Bruce Verchere, Head, Diabetes Research Program, Child & Family Research Institute, University of British Columbia, Vancouver, Canada.

April 1: Identifying suppressors of Mecp2 symptoms in the mouse. A genetic approach to therapeutic intervention. Presentation by Dr. Monica Justice, Depts. of Molecular and Human Genetics and Molecular Physiology and Biophysics, Baylor College of Medicine, Houston, USA.

May 4: Modulation of the inflammatory response by bioactive lipids. Presentation by Dr. Lisardo Boscá, Instituto de Investigaciones Biomédicas Alberto Sols, Centro Mixto CSIC-UAM, Madrid, Spain.

June 30: Emerging roles of microRNAs in the control of pancreatic beta cell functions. Presentation by Dr. Romano Regazzi, Faculty of Biology and Medicine, University of Lausanne, Switzerland.

September 6: Novel role for a transcriptional coregulator, TRIP-Br2, in adipocytes metabolism. Presentation by Dr. Liew Chong Wee, Joslin Diabetes Center, Harvard Medical School, Boston, USA.

December 16: Insulin regulation of proinsulin processing in pancreatic beta cells. Presentation by Prof. Rohit Kulkarni, Joslin Diabetes Center, Boston, USA.

***Diabetes and Obesity Research Lab Seminars (Idibaps-Ciberdem)***

Organized by the Metabolic and molecular disturbances in diabetes group (PI Anna Novials) during 2011 in CEK, Barcelona, Spain.

March 3: Role of IRS proteins in diabetes mellitus. Presentation by Dr. Deborah Burks from Centro de Investigación Príncipe Felipe, Valencia, and Ciberdem, Spain.

April 28: Adipose tissue, lipotoxicity and the metabolic syndrome. Presentation by Antonio Vidal-Puig, MD PhD FRCP, Professor of Molecular Nutrition and Metabolism, Scientific

Director of Cambridge Phenomics Centre, University of Cambridge Metabolic Research Laboratories, UK.

May 12: Alx3, folic acid and oxidative stress. Implications for the prevention of congenital malformations induced by hyperglycaemia. Presentation by Dr. Mario Vallejo of the Instituto de Investigaciones Biomédicas Alberto Sols-CSIC, Madrid, and Ciberdem, Spain.

May 16: Regulation of AMPK activity plays a critical role in glucose-induced insulin secretion. Presentation by Dr. Pascual Sanz, CSIC Research Professor and Director of the Instituto de Biomedicina de Valencia, Spain.

June 9: Alternative splicing, a novel mechanism modifying diabetes risk. Presentation by Dr. Jussi Pihlajamäki, Department of Medicine, University of Eastern Finland and Kuopio University Hospital, Kuopio, Finland.

# Fundraising

[www.investigaladiabetes.org](http://www.investigaladiabetes.org)

## Introduction

In its effort to continue supporting the work of its research groups, Ciberdem has designed and implemented since 2010 a plan a strategic fundraising plan with two clearly defined lines of action: on the one hand, actions aimed at private individuals, and on the other, those aimed at the business community.

## Objectives

To raise the level of awareness of the problem of diabetes in Spain to obtain the active participation of key sectors of society in order to raise funds for research into diabetes.

To involve diabetics and their families in actions which allow them to support research into diabetes.

To inform people of what Ciberdem research groups are doing.

To build and strengthen alliances with our stakeholders.

In order to achieve these objectives, Ciberdem continues to implement its "Investiga la diabetes" initiative, which is non-profit-making and aims to promote research projects to help prevent, treat and cure diabetes.

## Coordination

Johanna Rivera, Ciberdem Fundraising & Marketing.

## Achievements in 2011

### Fundraising Conferences

Ten talks were held in cities such as Barcelona, Cartagena, Castellón, Madrid and Valencia to inform people of what Ciberdem research groups are doing.

Speakers: Ramon Gomis, Rafael Carmena, Franz Martín, Flora de Pablo, José Real Collado, Serafín Murillo, Daria Roca, Margarida Jansà and Pere Santamaría.

Target audience: Patients' associations on a national level and the public in general.

An example of two of the actions which took place in 2011: "¡Deja huella!" (Leave your mark!), a charity event in aid of Ciberdem

Date: 10th April, 2011

Activities: a group of children and young people performed dances and figure skating, among other things, to raise funds for the consortium's research activities

Attendance: 350 people

"Soñar con los pies en la tierra: Lo último en investigación de la diabetes" (Dreaming with your feet on the ground: the



Investiga la diabetes Logo.



Ciberdem Fundraising Events.

latest research into diabetes)

Date: 26th November, 2011

Venue: La Pedrera, Barcelona, Spain

Attendance: 150 people

Ciberdem firmly believes in and is committed to the popularization of science, this is why since it was first set up, every November (the month of World Diabetes Day), it has held a public awareness event for diabetics, their families, friends and the public in general (see page 16 for more).

### **Research projects**

"Pilchardus" is a study to test the hypothesis that a diet rich in sardine (*pilchardus*) protein can improve metabolic control in patients with type 2 diabetes mellitus as compared to a control diet without sardines. It is innovative because few projects have tackled the role of proteins in the diet in regulating insulin sensitivity and glucose homeostasis. There is evidence that this study will also provide information on changes in other parameters such as inflammation, changes in the composition of microbiota, blood pressure, weight and the distribution of body fat, among others.



In 2011, a funding agreement for the sum of 60,000 € was signed with CatalunyaCaixa and an agreement was also reached with Conservas Cerqueira, the company which will supply all the sardines needed for the study.

"Amicus Canis" aims to demonstrate whether dogs are efficient at detecting a hypoglycaemic crisis. This opens up



new possibilities for the health and way of life of diabetics with type 1 diabetes mellitus via the presence of a dog in the household. The dog is a key element in social and family cohesion which can not only help to reduce the fear and anguish which these crises cause, but also play a key role in optimizing the patient's metabolic control.

In 2011, work was done on the design of the study and a fundraising plan was made to launch the project. Several companies expressed an interest in participating; the nature of their collaboration is to be defined in 2012.

### **An education and innovation project**

"Diabetes a la carta". A therapeutic education project which puts forward a new alternative for the prevention



and treatment of diabetes. The aim of this initiative is to provide new tools for people with type 2 diabetes, their families and friends, to manage their daily food intake in a more balanced, enjoyable and healthy way.

One of the partners in the initiative is the Fundación Alícia, Alimentación y Ciencia, a centre researching into food whose president is the chef, Ferran Adrià. Thanks to this contribution, there is a multidisciplinary group of researchers, dieticians, cooks, educators and designers, among others.

In order to implement and publicize these actions, we are able to count on the help of Esteve, a laboratory which is committed to research leading to better quality of life for diabetics.

In 2011, various materials were produced, which were presented on World Diabetes Day; of these, we would like to mention the website [www.diabetesalacarta.org](http://www.diabetesalacarta.org) which, in its first month of operation, clocked up over 9,000 visits with an average duration of 4'55".

Ciberdem groups: Dr Anna Novials and Dr Ramon Gomis, Institut d'Investigacions Biomèdiques August Pi i Sunyer.

### **Future challenges**

The Department of Fundraising & Marketing will seek to establish and consolidate strategic alliances with Ciberdem's stakeholders with the aim of promoting our groups' research. It will also promote the development of innovative initiatives to involve the business sector and improve the health and quality of life of diabetes sufferers.

# Outreach activities

## 4th Public Awareness Event

The 4th Ciberdem Public Awareness Event “Investiga la diabetes’11” was held at the Paraninfo of the Universidad del País Vasco (UPV/EHU) in Bilbao, on November 12, 2011. The programme included exhibitions and interactive activities with the aim of showing the general public the latest advances in diabetes research. More than 300 people attended the event and took part in the different activities, including the lecture given by Dr Bernat Soria, researcher and president of Fundación de la Sociedad Española de Diabetes, on the research being done in diabetes. Also, researchers and members of Ciberdem participated in the creation and development of scientific workshops which opened up the world of science to all who attended. This event also motivated people to take part and give their support to diabetes research.

Partners: Asociación Vizcaína de Diabetes, Universidad del País Vasco, Escuela Universitaria de Enfermería de Leioa, Fundació Alícia and Sociedad Española de Diabetes.

Sponsors: Bilbao Bizkaia Kutxa (Caja de Ahorros de Bilbao y Vizcaya), Lifescan – Johnson & Johnson, Laboratorios Esteve and AXA Seguros.

[www.investigaladiabetes.org](http://www.investigaladiabetes.org)



4th Ciberdem Public Awareness Event.

## 4th Annual Meeting

More than 123 Ciberdem researchers and staff members met to attend the 4th Ciberdem Annual Meeting, held in Vall de Boí (Lleida, Spain) on October 23, 24, 25 and 26, 2011. This scientific meeting allowed research groups to share information on methods and the results of research projects with one another by means of 49 posters and 40 oral communications divided into 6 different sessions. The meeting was received with great enthusiasm and members were able to interact with one another and prepare the way for future collaborations.

[www.annualmeeting.ciberdem.org](http://www.annualmeeting.ciberdem.org)



## 4th ANNUAL MEETING

Boí Taüll, October 23-26, 2011

### CIBERDEM

Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas  
Spanish Biomedical Research Centre in Diabetes and Associated Metabolic Disorders



4th Ciberdem Annual Meeting.

## The 9 CIBERs in Science Week

In the context of the 2011 Science Week, the 9 Spanish Biomedical Research Centres for excellence (CIBERs) offered two round tables on translational research. Dr Flora de Pablo, PI of Ciberdem, represented the consortium in the Madrid round table and Dr Ramon Gomis, Scientific Director of Ciberdem, did so at the Barcelona round table. Both events were moderated by Teresa Bomboi of the Subdirección General de Redes y Centros de Investigación Cooperativa del Instituto de Salud Carlos III (ISCIII).

### ***CECA, Madrid, November 15, 2011***

Ciber-bbn: Margarita Calonge

Ciberdem: Flora de Pablo

Ciberehd: Javier Vaquero

Ciberer: Javier Benítez

Ciberes: Germán Peces-Barba

Ciberesp: Marina Pollán

Ciberned: José Ramón Naranjo

Ciberobn: José Antonio Fernández

Cibersam: Juan Carlos Leza

### ***CEK, Barcelona, November 24, 2011***

Ciber-bbn: Simó Schwartz

Ciberdem: Ramon Gomis

Ciberehd: Jordi Bruix

Ciberer: Francesc Cardellach

Ciberes: Ramon Farré

Ciberesp: Ángela Domínguez

Ciberned: Alberto Lleó

Ciberobn: Fernando Fernández Aranda

Cibersam: Miquel Bernardo

[www.vimeo.com/ciber](http://www.vimeo.com/ciber)



2011 Madrid Science Week.

# More about Ciberdem

## Introduction

The Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (Ciberdem) is a public research consortium which was founded on December 3rd 2007 and is financed by the Instituto de Salud Carlos III (ISCIII) and the Ministerio de Ciencia e Innovación (MICINN). Ciberdem is made up of 31 research groups based in different hospitals, universities and research centres throughout Spain. The main aim of Ciberdem is to promote research into diabetes and associated metabolic disorders, identifying the genes which predispose to these diseases and the environmental factors which contribute to their development; to discover the molecular mechanisms involved in the alteration of insulin secretion and signalling; to determine the molecular and cellular mechanisms involved in the formation and destruction of pancreatic beta cells; to study strategies for substitution of this cell mass; and to investigate the signals which link obesity and diabetes. Of special interest is research into the complications of diabetes and associated metabolic disorders.

Ciberdem is divided into 4 Research Programmes:

Programme 1. Molecular and physiological determinants of lifestyle in diabetes/obesity. Population studies for genetic/epigenetic association analysis in type 2 diabetes mellitus and related traits

Programme 2. Mechanisms promoting the development of diabetes and its vascular complications. Associated disorders and co-morbidities. Strategies for prevention and treatment

Programme 3. Impact of beta cell dysfunction and plasticity on the natural history of diabetes. Development of novel treatment strategies

Programme 4. Use of biomedical approach systems to develop personalized therapies for diabetes

## Management Committee

### President

José J. Navas, Director of the Instituto de Salud Carlos III (ISCIII)

### Vice President

Joaquín Arenas, Subdirector General de Redes y Centros de Investigación Cooperativa (ISCIII)

### Members

Dolores González, Consejo Superior de Investigaciones Científicas (CSIC)

Rubén Moreno, Fundación Centro de Investigación Príncipe Felipe

Dolores Iglesias, Fundación Hospital Clínico Universitario de Valencia

Emilià Pola, Fundación IDIBELL

Francesc Vidal, Fundació Institut d'Investigació Sanitària Pere Virgili

José Luis de Sancho, Fundació Institut de Recerca Hospital Universitari Vall d'Hebron

José Francisco Cañón, Fundación Instituto Mediterráneo para el Avance de la Biotecnología Sanitaria

Emili Bargalló, Fundación para la Investigación y Docencia Sant Joan de Déu

Carmen Ayuso, Fundación Jiménez Díaz

Jorge Domínguez, Fundació Privada Institut de Recerca Biomèdica

Carmen Garaizar, Fundación Vasca de Innovación e Investigación Sanitarias

Jaume Kulisevsky, Institut de Recerca Hospital de la Santa Creu i Sant Pau

Mª Carmen Fernández, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS)

Elena Andradas, Servicio Madrileño de Salud

Anna Ripoll, Universitat Autònoma de Barcelona

Xavier Meneses, Universitat de Barcelona

Joaquín Plumet, Universidad Complutense de Madrid

Fernando Borrás, Universidad Miguel Hernández

José Manuel Rosado, Universidad Pablo de Olavide

### Secretary

Ana Bosch, Ciberdem Managing Director

## Permanent Commission

### President

Joaquín Arenas, Subdirector General de Redes y Centros de Investigación Cooperativa (ISCIII)

### Members

Elena Andradas, Servicio Madrileño de Salud

José Francisco Cañón, Fundación Instituto Mediterráneo para el Avance de la Biotecnología Sanitaria

Rubén Moreno, Fundación Centro de Investigación Príncipe Felipe

Joan Xavier Comella, Fundació Institut de Recerca Hospital Universitari Vall d'Hebron

### Secretary

Ana Bosch, Ciberdem Managing Director

## Steering Committee

Ramon Gomis, Scientific Director and President of the Steering Committee

Anna Novials, Adjunct Scientific Director and Coordinator Programme 3

Rafael Carmena, Coordinator Programme 1

Manuel Benito, Coordinator Programme 2

Antonio Zorzano, Coordinator Programme 4  
 Fàtima Bosch, Training Programme Coordinator  
 Ana Bosch, Managing Director and Secretary of the Steering Committee

### External Scientific Committee

#### President

José M Ordovás, Tufts University, Boston (USA)

#### Members

Francesc Xavier Pi-Sunyer, Columbia University, New York (USA)  
 Decio Eizirik, Université libre de Bruxelles (Belgium)  
 Antonio Vidal-Puig, University of Cambridge (UK)  
 Ele Ferrannini, Università di Pisa (Italy)

### Research Groups

#### Madrid

PIs Carmen Álvarez (Univ. Complutense), Manuel Benito (Univ. Complutense), Enrique Blázquez (Univ. Complutense), Héctor F Escobar Morreale (Hospital Ramón y Cajal), Flora de Pablo (CSIC Research Centre), Manuel Serrano Ríos (Hospital Clínico), Mario Vallejo (CSIC Research Centre), María Luisa Villanueva Peñacarrillo (Fundación Jiménez Díaz), Ángela Martínez Valverde (Univ. Complutense)

#### Valladolid

PI Jesús Balsinde (CSIC Research Centre)

#### Vizcaya

PI Luis Castaño (Hospital de Cruces)

#### Barcelona

PIs Francisco Blanco Vaca (Hospital Sant Pau), Fàtima Bosch (CBATEG Research Centre), Anna Novials (IDIBAPS Research Centre), Jorge Ferrer (IDIBAPS Research Centre), Ramon Gomis (IDIBAPS Research Centre), Manuel Vázquez Carrera (Univ. Barcelona), Anna M Gómez Foix (Univ. Barcelona), Joan J Guinovart (IRB Research Centre), Antonio Zorzano (IRB Research Centre), Eduard Montanya (Hospital Bellvitge), Rafael Simó (Hospital Vall d'Hebron), Lourdes Ibáñez (Hospital Sant Joan de Déu)

#### Tarragona

PIs Xavier Correig (Metabolomics Platform), Joan J Vendrell (Hospital Joan XXIII), Lluís Masana (Hospital Sant Joan Reus)

#### Valencia

PIs Rafael Carmena (Hospital Clínico), Deborah Burks (Príncipe Felipe Research Centre)

#### Alicante

PI Angel Nadal (Univ. Miguel Hernández)

#### Málaga

PI Federico Soriguer (Hospital Carlos Haya)

#### Sevilla

PI Franz Martín (CABIMER Research Centre)

### Management Office

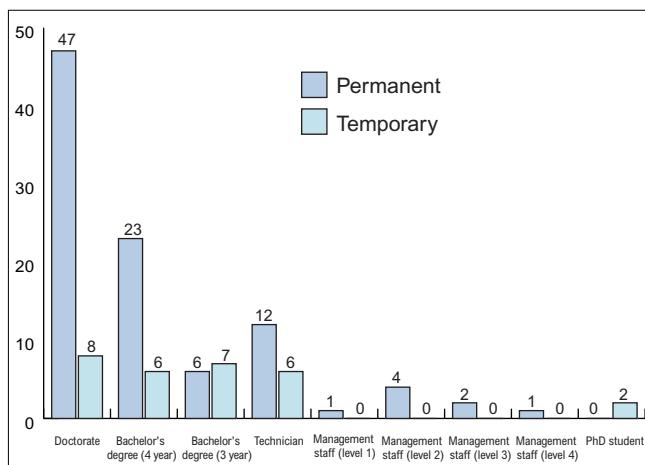
Ana Bosch, Managing Director

Tania Fernández, Executive Secretary

Gemma Pascual and Francesc Martí, Project Management  
 Marta Vidal, Knowledge Management and Communication  
 Johanna Rivera, Fundraising and Marketing  
 Libertad Montaño, Human Resources and Legal Manager  
 Antonio Santaliestra, Accounting Agent  
 María Rosa Vázquez, Administrative Assistant

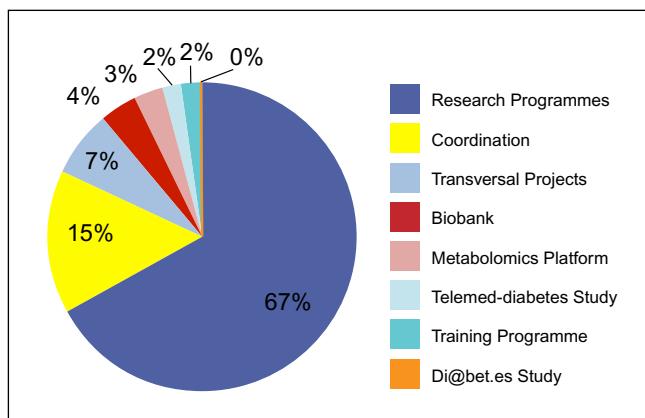
### Human Resources

In 2011, Ciberdem had a total of 413 researchers; of which 125 belonged to Ciberdem's own staff (including the Management Office) and 288 were attached staff. The following graph shows a breakdown of Ciberdem's own staff by category and type of contract.



### Financial Highlights

In 2011 Ciberdem expended a total of 4,521,326.55 € \*:  
 Research Programmes 3,059,247.84 €  
 Biobank 183,926.90 €  
 Metabolomics Platform 128,476.85 €  
 Transversal Projects 308,911.55 €  
 Telemed-diabetes Study 77,323.18 €  
 Di@bet.es Study 6,056.62 €  
 Training Programme 63,786.79 €  
 Coordination 693,596.82 €



\* Private funds 129,276.20 €.

# Research

# Di@bet.es Study

[www.ciberdem.org/estudiodiabetes](http://www.ciberdem.org/estudiodiabetes)

## Introduction

Attempts to halt the growing presence of diabetes in Spanish society, a cause of concern for both public and private healthcare systems, require reliable and accurate data on the incidence of diabetes in different groups within the Spanish population. Di@bet.es, a joint initiative of the Spanish Diabetes Federation (FED), the Spanish Diabetes Society (SED) and Ciberdem, was born with the goal of providing improved knowledge of the epidemiology of diabetes in Spain.

Ciberdem, primary funding organization of Di@bet.es, believes firmly in the importance of the epidemiological information that the study will provide as a point of reference for measuring the success of its programmes. The results of this study will assist Ciberdem groups in focusing their research on relevant pursuits and will allow public and private institutions to formulate more efficient and effective strategies for diabetes prevention, diagnosis, treatment and research.

## Objectives

To determine the overall incidence (known and unknown) of type 2 diabetes mellitus in a representative sample of the Spanish population.

To determine the relationship between the incidence of type 2 diabetes mellitus and the nutritional habits and physical activity of the individuals within the sample, as well as relevant information regarding their demographic and genetic characteristics.

To provide a scientific tool for assessing institutional health strategies.

To determine the incidence of impaired fasting glucose and impaired glucose tolerance, insulin-resistance, hypertension, dyslipidaemia, obesity, and metabolic syndrome in a representative sample of the Spanish population.

To determine the relationship between the incidence of these disorders and the nutritional habits and physical activity of the individuals within the sample.

To provide a collection of human serum samples for carrying out studies on the analysis of gene-environment interaction in the pathogenesis of diabetes.

## Steering Committee

**Direction** Federico Soriguer (Hospital Carlos Haya-IMABIS, Málaga, and Ciberdem)

**Coordination** Gemma Pascual (Ciberdem Management Office) and Gemma Rojo (Hospital Carlos Haya- IMABIS, Málaga, and Ciberdem)



Field work regions.

**Northern region** Field work coordination and Management: Luis Castaño (Hospital de Cruces, Bilbao, and Ciberdem)  
Field work: Alicia Cobo, Ana María Megido

**Northeastern region** Field work coordination: Albert Goday (Hospital del Mar de Barcelona) Management: Ramon Gomis (Hospital Clínic de Barcelona, IDIBAPS, and Ciberdem) Field work: Alba Arocas, Laura Esquius, Rosario Suarep, María Dolores Zomeño

**Eastern region** Field work coordination: Miguel Catalá (Hospital Clínico de Valencia and Ciberdem) Management: Rafael Carmena (Hospital Clínico de Valencia and Ciberdem)  
Field work: Clara Bixquert, Nieves Brito

**Central region** Field work coordination: Alfonso Calle (Hospital San Carlos de Madrid) Management: Manuel Serrano Ríos (Hospital San Carlos de Madrid and Ciberdem) Field work: Isabel Alonso, Enrique Mañas

**Southern region** Field work coordination: Gemma Rojo (Hospital Carlos Haya-IMABIS, Málaga, and Ciberdem)  
Management: Federico Soriguer (Hospital Carlos Haya- IMABIS, Málaga, and Ciberdem) Field work: Rocío Badía, Isabel Guillén

**Other Steering Committee members** Alfonso López Alba (Hospital Universitario de Canarias, Tenerife), Elena Bordiu (Hospital San Carlos de Madrid), Roser Casamitjana (Hospital Clínic de Barcelona, IDIBAPS, and Ciberdem), Conxa Castell (Consell Assessor sobre la Diabetis, Direcció General de Salut Pública, Generalitat de Catalunya, Barcelona), Elias Delgado (Hospital General de Asturias), Edelmiro Menéndez (Hospital

Universitario Central de Asturias), Josep Franch (Centre d'Atenció Primària Raval Sud, Barcelona), José A Vázquez (Hospital de Cruces, Bilbao), Sonia Gaztambide (Hospital de Cruces, Bilbao, and Ciberdem), Juan Girbés (Hospital Arnau de Vilanova de Valencia), María Teresa Martínez Larrad (Hospital San Carlos de Madrid and Ciberdem), Emilio Ortega (Hospital Clínic de Barcelona, IDIBAPS, and Ciberdem), Inmaculada Mora (Hospital Universitario de Canarias, Tenerife), Sergio Valdés (Hospital Carlos Haya-IMABIS, Málaga, and Ciberdem), and Joan J Vendrell (Hospital Joan XXIII de Tarragona and Ciberdem)

### Achievements in 2011

The Di@bet.es Study has allowed us to know for the first time the real situation in Spain as regards the total prevalence of type 2 diabetes and other cardiometabolic risk factors such as obesity, metabolic syndrome, hypertension and so on and the relationship between them. It has also provided information about the degree of adherence of patients to health programmes (this being an important part in the treatment of diabetes and obesity, as well as other chronic diseases) and confirms once again the close association between preventable risks and modifiable habits (diet, exercise, obesity, etc) and cardiometabolic risk.

The study also confirms the positive effects, previously observed in other studies, of olive oil on patients' health.

The results of this study will change our understanding of the national prevalence of some of the cardiovascular risk factors, which will have consequences not only in planning, but also in the precision of many of the diagnostic tests carried out by clinicians.

### Publications

Prevalence of diabetes mellitus and impaired glucose regulation in Spain: the Di@bet.es Study

Soriguer F, Goday A, Bosch-Comas A, Bordiu E, Calle-Pascual A, Carmena R, Casamitjana R, Castaño L, Castell C, Catalá M, Delgado E, Franch J, Gaztambide S, Girbés J, Gomis R, Gutiérrez G, López-Alba A, Martínez-Larrad MT, Menéndez E, Mora-Peces I, Ortega E, Pascual-Manich G, Rojo-Martínez G, Serrano-Rios M, Valdés S, Vázquez JA, Vendrell J

Diabetologia, doi 10.1007/s00125-011-2336-9

PMID 21987347

### Future challenges

The utilization of the information obtained in this field study will contribute in the future to new knowledge on diabetes and other biomedical problems studied. These results will allow us to carry out collaborations with other national and international projects with similar objectives and also to reassess resources according to the magnitude of the problem and make further progress in the design of prevention strategies, therapeutic educational programmes and study the need to carry out a screening of the population to detect so far unnoticed T2D.

Some of our future goals include: the request for public and private projects to provide us with the necessary resources to exploit the "seroteca" and "DNAteca"; the design of a project to reevaluate a study subsample to assess the risks and incidence of T2D; the design of a project for the prevention of T2D incidence through a virtual programme of intervention and also collaboration with similar international databases.

# Ciberdem Projects

[www.ciberdem.org/projects](http://www.ciberdem.org/projects)

## Introduction

Ciberdem seeks to achieve scientific excellence in research and encourage bench-to-bed as well as bed-to-bench transition (see figures 1 and 2).

In order to achieve these goals it promotes collaboration between basic and clinical research groups to prioritize translational research in the network. To this end, 14 initiatives based mainly on diabetes and its complications were implemented during 2009-2010 and 10 of them continued through 2011.

Ciberdem forges synergies between its members and launches initiatives that can offer an attractive opportunity to build up collaborations with other centres outside the consortium, whether national or international, because these projects can be seen as a pool of scientific knowledge that involves several Spanish research groups of excellence in diabetes at the same time.

## Objectives

To develop scientific actions focused on diabetes and its metabolic disorders with a high impact on research.

To improve collaboration among researchers, mainly among clinical and basic research groups, with a minimum participation of 3 research groups and a maximum of 8 at any one time and at least one of them being a clinical group.

To forge alliances between researchers through joint work on the design and implementation of the projects.

To demonstrate the competitiveness of researchers and the innovation of their collaborative projects.

To establish initiatives that a single research group can not embark upon alone.

## Achievements in 2011

The original 14 Ciberdem projects officially ended on the 31<sup>st</sup> of December, 2010. However, due to the good results of these collaborations, the projects were evaluated by analysing their accomplished objectives and justification reports and it was decided to continue funding 10 of them during 2011.

Ciberdem Projects were presented to the wider national and international scientific community; oral presentations were made at several congresses worldwide and many original articles were published in international peer review journals such as the American Journal of Physiology Endocrinology and Metabolism, Peptides, PLoS ONE, European Journal of Clinical Investigation, Diabetologia and so on.

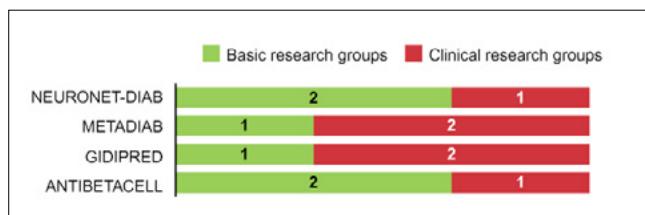


Figure 1. Ciberdem bench to bed projects (NEURONET-DIAB, METADIAB, GIDIPRED, ANTIBECCELL) showing the number of research groups participating in each project (in green, the groups with a basic profile; in red, those with a clinical profile).

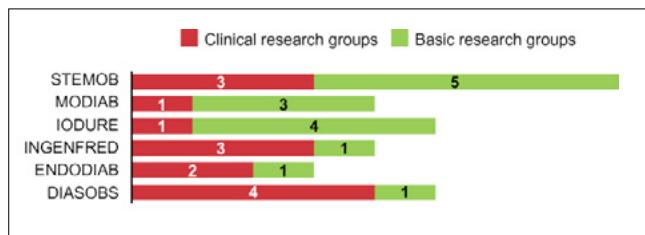


Figure 2. Ciberdem bed to bench projects (STEMOB, MODIAB, IODURE, INGENFRED, ENDODIAB, DIASOBS) showing the number of research groups participating in each project (in red, the groups with a clinical profile; in green, those with a basic profile).

## Publications

Alx3-deficient mice exhibit decreased insulin in beta cells, altered glucose homeostasis and increased apoptosis in pancreatic islets

Mirasierra M, Fernández-Pérez A, Díaz-Prieto N, Vallejo M  
Diabetologia, 54, 403-414 (2011)  
[PMID 21104068](#)

Amylin effect in extrapancreatic tissues participating in glucose homeostasis, in normal, insulin-resistant and type 2 diabetic state

Moreno P, Acitores A, Gutiérrez-Rojas I, Nuche-Berenguer B, El Assar M, Rodriguez-Mañas L, Gomis R, Valverde I, Visa M, Malaisse WJ, Novials A, González N, Villanueva-Peña Carrillo ML  
Peptides, 32, 2077-2085 (2011)

[PMID 21939703](#)

ELOVL6 genetic variation is related to insulin sensitivity: a new candidate gene in energy metabolism

Morcillo S, Martín-Núñez GM, Rojo-Martínez G, Almaraz MC, García-Escobar E, Mansego ML, de Marco G, Chaves FJ, Soriguer F  
PLoS ONE, 6, e21198 (2011)  
[PMID 21701577](#)

Erythropoietin protects retinal pigment epithelial cells against the increase of permeability induced by diabetic conditions: essential role of JAK2/ PI3K signaling  
Garcia-Ramírez M, Hernández C, Ruiz-Meana M, Villarroel M, Corraliza L, García-Dorado D, Simó R  
Cell Signal, 23, 1596-1602 (2011)  
PMID 21620963

Fenofibric acid reduces fibronectin and collagen type IV overexpression in human retinal pigment epithelial cells grown in conditions mimicking the diabetic milieu: functional implications in retinal permeability

Trudeau K, Roy S, Guo W, Hernández C, Villarroel M, Simó R, Roy S  
Invest Ophthalmol Vis Sci, 52, 6348-6354 (2011)  
PMID 21715349

Measuring permeability in human retinal epithelial cells (ARPE-19): implications for the study of diabetic retinopathy  
Garcia-Ramírez M, Villarroel M, Corraliza L, Hernández C, Simó R

Methods Mol Biol, 763, 179-194 (2011)  
PMID 21874452

New gene targets for glucagon-like peptide-1 during embryonic development and in undifferentiated pluripotent cells

Sanz C, Blázquez E  
Am J Physiol Endocrinol Metab, 301, E494-503 (2011)  
PMID 21712536

Plasma PTX3 protein levels inversely correlate with insulin secretion and obesity, whereas visceral adipose tissue PTX3 gene expression is increased in obesity

Osorio-Conles O, Guitart M, Chacón MR, Maymo-Masip E, Moreno-Navarrete JM, Montori-Grau M, Näf S, Fernandez-Real JM, Vendrell J, Gómez-Foix AM  
Am J Physiol Endocrinol Metab, 301, E1254-1261 (2011)  
PMID 21900125

Polymorphisms of the UCP2 gene are associated with body fat distribution and risk of abdominal obesity in Spanish population

Martinez-Hervas S, Mansego ML, de Marco G, Martinez F, Alonso MP, Morcillo S, Rojo-Martinez G, Real JT, Ascaso JF, Redon J, Martin Escudero JC, Soriguer F, Chaves FJ  
Eur J Clin Invest, doi: 10.1111/j.1365-2362.2011.02570.x  
PMID 21883184

Stromal stem cells from adipose tissue and bone marrow of age-matched female donors display distinct immunophenotypic profiles

Pachón-Peña G, Yu G, Tucker A, Wu X, Vendrell J, Bunnell BA, Gimble JM  
J Cell Physiol, 226, 843-851 (2011)  
PMID 20857424

## Future challenges

The funding of the projects concluded at the end of 2011, but the results of this initiative will continue over the coming years. New publications are in preparation and different sources of funding are being sought to continue with research in all projects.

## The 10 CiberDEM Projects

### *Identification of neurodegenerative mechanisms that promote the development of diabetic retinopathy: the role of insulin signalling and apoptosis. NEURONET-DIAB*

The molecular mechanisms which mediate the development of diabetic retinopathy (DR) remain unknown. Insulin and IGF-I signalling play important roles in the development and survival of retinal cells. Our hypothesis is that resistance to insulin/IGF-I in the retina disables the molecular mechanisms which protect retinal cells against stress and apoptosis, thereby triggering neurodegeneration and DR. The results will provide a rational basis for developing novel strategies to detect, prevent and treat DR in its earliest stages.

Groups: Deborah Burks, Ángela Martínez Valverde, Rafael Simó. Project coordinator: Deborah Burks

### *Cooperative population and database studies for genetic association analysis in T2DM and related traits. INGENFRED*

Type 2 diabetes mellitus (T2DM) is a complex disease resulting from the interaction of environmental and genetic factors. The genetics of several functional systems in T2DM have not been dissected. The project aims to develop genetic T2DM studies, integrating different populations and databases, considering the interaction between genetic and environmental factors with the aim of developing future projects that will ultimately lead to clinical applications.

Groups: Rafael Carmena, Francisco Blanco Vaca, Manuel Serrano Ríos, Federico Soriguer. Project coordinator: Felipe Javier Chaves

### *Clinical, genetic and functional characterization of monogenic diabetes: from the bench to the bedside. MODIAB*

Monogenic diabetes (MD) accounts for 1-2% of diabetes cases and is often misdiagnosed. Knowledge of the genetic aetiology of diabetes enables better treatment, prediction, disease progression, screening of relatives and genetic counselling. The project aims to determine aspects such as new genetic causes of MD, novel functional information for pancreatic beta cells and the importance of new regulatory sequences through the discovery of mutations in known genes.

Groups: Luis Castaño, Enrique Blázquez, Jorge Ferrer, Mario Vallejo. Project coordinator: Luis Castaño

### *Determinants of insulin resistance and glucose tolerance disorders (including diabetes) in severe obesity and their changes after bariatric surgery-induced weight loss. DIASOBS*

Obese patients submitted to bariatric surgery present a marked weight loss that frequently normalizes abnormalities in glucose tolerance because obesity is the major risk factor for this kind of disorder. This project focuses on the identification of risk factors for insulin resistance, abnormal glucose tolerance and diabetes in severely obese patients, as well as on the identification of the determinants of the resolution of these disorders following the marked and sustained weight loss usually attained after bariatric surgery. Groups: Héctor F Escobar Morreale, Xavier Correig, Eduard Montanya, Rafael Simó, Joan J Vendrell. Project coordinator: Héctor F Escobar Morreale

**Glycogen-induced dysfunctions in the pancreas and retina and their involvement in the ethiogenesis of diabetes mellitus. GIDIPRED**

The project is based on the idea that, contrary to the general belief which considered glycogen to be beneficial for cells, the deposition of glycogen may be deleterious for certain cell types. The aim is to study the alterations induced by this abnormal accumulation in pancreatic beta cells, neurons, and retinal cells. The working hypothesis is that the accumulation of this polysaccharide in these cell types contributes to the induction of apoptosis and therefore the pathological consequences associated with diabetes mellitus, namely reduced insulin secretion and retinopathy.

Groups: Joan J Guinovart, Ramon Gomis, Rafael Simó. Project coordinator: Joan J Guinovart

**The production of monoclonal antibodies which selectively react with cell surface molecules on human pancreatic beta cells. ANTIBECELL**

So far, it has not been possible to obtain an antibody that recognizes human beta cells, although the identification of these pancreatic cells in vitro and in vivo is highly desired. In this project we propose a novel immunization strategy making it possible to obtain immune response against antigens expressed poorly and to search for antibodies against receptors on the cell surface of pancreatic beta cells. The objective achievement opens new perspectives for studies in regeneration, development and cell therapy using islets.

Groups: Franz Martín, Eduard Montanya, Angel Nadal. Project coordinator: Juan Tejedo

**Comparative metabolomic analysis for the detection of biomarkers in diabetes. METADIAB**

In METADIAB, metabolomics is used to determine, thanks to the information provided by the endogenous metabolite profile, which metabolites are altered in diabetes. The changes that we aim to study are the consequences produced by high concentrations of glucose and lipids (glucolipotoxicity) in the islet pancreatic metabolome. Another aspect in which we are interested is the evaluation of the metabolomic effects induced by physical exercise in both type 1 and 2 diabetes

mellitus. As a result, we will improve our knowledge in these situations and discover candidate biomarkers of the disease. Groups: Xavier Correig, Ramon Gomis, Anna Novials. Project coordinator: Xavier Correig

**Mechanisms of endothelial dysfunction in diabetes: the role of amylin and circulating endothelial cells. ENDODIAB**

The main aetiology for death and for a high percentage of morbidity in patients with diabetes is vascular disease. Thus, this project aims to investigate circulating endothelial cells (CECs) as markers of endothelial dysfunction in diabetic patients; to determine the role of amylin in endothelial function; and to investigate the presence of preclinical atherosclerosis by assessing endothelial function in patients with type 1 diabetes mellitus, type 2 diabetes mellitus and obesity.

Groups: Anna Novials, Ramon Gomis, María Luisa Villanueva Peñacarrillo. Project coordinator: Anna Novials

**The impact of overnutrition, diabetes-obesity and undernutrition on the regulation of energy homeostasis in the central nervous system. From animal models to humans. IODURE**

Increasing evidence suggests that the central nervous system plays a crucial role in regulating energy homeostasis through crosstalk with adipose tissue and the endocrine pancreas. The objective of the project is to investigate how the brain reacts to metabolic challenges associated with overnutrition, diabetes-obesity and undernutrition. It is expected that novel mechanisms responsible for the dysregulation of energy homeostasis which leads to obesity and diabetes will be identified.

Groups: Manuel Serrano Ríos, Carmen Álvarez, Enrique Blázquez, Deborah Burks, Mario Vallejo. Project coordinator: Manuel Serrano Ríos

**Adult adipose tissue-derived progenitor cells: the influence of the clinical phenotype and adipose depot origin in their biological properties. STEMOP**

The objective of this project is to test for differential behaviour in adult pre-adipocytes and adipocytes derived from adipose tissue mesenchymal stem cells (ad-MSC) obtained from lean and obese subjects and also to characterize adipose derived cells from a molecular and lipidomic perspective. The expected result is the identification of the differences in adMSC (from subcutaneous and visceral depots) that exist between lean and obese subjects.

Groups: Joan J Vendrell, Jesús Balsinde, Anna María Gómez Foix, Eduard Montanya, Rafael Simó, Manuel Vázquez Carrera, Antonio Zorzano. Project coordinator: Joan J Vendrell

# Telemed-diabetes Study

[www.ciberdem.org/telemed-diabetes](http://www.ciberdem.org/telemed-diabetes)

## Introduction

The costs associated with type 1 diabetes mellitus are high, for both patient and family, as well as for the healthcare system: a) Healthcare costs – hospital days, visits, medication and care. b) Other costs not included in healthcare expenses – reduction or loss of productivity due to high morbidity and premature mortality. c) Intangibles – life expectancy and quality of life. Different programmes of healthcare quality have been designed to cope with this reality by promoting basic research, clinical education in healthcare and the social integration of patients. As previous studies have shown, in order to prevent or delay chronic complications it is optimal to obtain good metabolic control through a system of intensified treatment when results of glycated haemoglobin are higher than recommended. Telemed-diabetes Study is crucial for comparing cost and efficiency parameters of two control optimization programmes through face-to-face healthcare visits and by replacing some of these visits with a telematic communication system. It is a multicentre study developed by Ciberdem and the five participating centres are the Hospital Clínic de Barcelona, the Hospital Carlos Haya in Málaga, the Hospital Clínico de Madrid, the Hospital de Cruces in Barakaldo and the Hospital Clínico de Valencia.

## Objectives

The main objective is to assess the impact of the Medical Guard Diabetes® (MGD) system on the efficiency of the clinical and economic management of the human resources and materials allocated to a programme of optimization of metabolic control in patients with type 1 diabetes mellitus, with particular reference to the degree of metabolic control and quality of life of the patients. This telematic communication system conveys the results of capillary blood glucose, insulin dose, carbohydrate intake during meals and other events, from the patient's home or elsewhere to the medical team through a web server.

Telemed-diabetes is a multicentre, randomized, prospective, comparative, open study which it is hoped will reveal the effectiveness and utility of the telematic communication program through the assessment and comparison of the two groups of patients in respect of the following results:

- Metabolic control of diabetes: results of glycated haemoglobin and frequency of hypoglycaemic and hyperglycaemic crisis.
- Costs of visits considering the time needed for the patient, expenses of travel to the hospital and impossibility of performing usual activities (school, work) due to face-to-face healthcare visits in the hospital, compared with the costs of medical visits carried out remotely, with the help of the telematic communication system used.

## Steering Committee

**Coordinator** Enric Esmatjes (Hospital Clínic de Barcelona and Ciberdem)

**Expert collaborator** Oriol Solà Morales (Agència d'Informació, Avaluació i Qualitat en Salut)

**Organizations involved** Insight Consulting & Research (Monitorization and follow-up of the study) and Pulso Ediciones SL (Telematic communication system Medical Guard Diabetes®)

**Promotor** Spanish Biomedical Research Centre in Diabetes and Associated Metabolic Disorders (Ciberdem) - Instituto de Salud Carlos III, Spanish Ministry of Economy and Competitiveness (ISCIII, MEC)

## Participating centres:

Enric Esmatjes, Margarita Jansà and Daria Roca (Hospital Clínic de Barcelona and Ciberdem)

Marisol Ruiz de Adana, Francisca Linares and Mercedes Guerrero (Hospital Carlos Haya-IMABIS, Málaga and Ciberdem)

Federico Vázquez and Anibal Aguayo (Hospital de Cruces, Bilbao, and Ciberdem)

Sergio Martínez-Hervás and Nieves Brito (Hospital Clínico de Valencia and Ciberdem)

Natalia Pérez-Ferrer and Laura del Valle (Hospital San Carlos de Madrid and Ciberdem)

## Achievements in 2011

Patients were recruited to the study between May and October of 2011. A total of 160 patients were divided in two groups, one of them a control group (hospital visits) and the other an intervention group (hospital visits substituted by telemedicine).

The evolution of the metabolic control data and the corresponding economic costs of monitoring the patients have been studied.

## Future challenges

The first six months of patient monitoring will finish in 2012 and the database will be completed and the results ready for analysis.

# Biobank

[www.clinicbiobanc.org](http://www.clinicbiobanc.org)

## Introduction and objectives

The Ciberdem Biobank is a scientific and technological platform which coordinates the collection, processing, storage and retrieval of biological samples in the field of diabetes and other metabolic diseases, which may then be utilized by the consortium's research groups and by other scientific institutions in their experiments and projects. The Biobank, thanks to its experience and expertise in this field, holds one of the most important collections of samples of metabolic disorders in southern Europe, bringing great added value to the biomedical research conducted by Ciberdem. Structured into nodes with multiple collection and processing sites, the Biobank allows for the immediate storage of samples following blood extraction in order to ensure the highest quality possible. Through the centralized coordination of sample management, the Biobank also ensures the traceability of its samples, as required by the recently passed Biomedical Research Act. The coordinating node of the Ciberdem Biobank obtained the ISO9001 quality certification in December 2009.

## Scientific services

The main services provided by the Biobank consist of the following:

Design and management of a large metabolic disorder sample collection, involving donor recruitment; data registration; informed consent management; serum and plasma storage; DNA purification and storage; lymphocyte isolation and immortalization; and quality management. Assurance of traceability.

Quality control of the stored samples.

Organization of an internal database for the analysis of samples and data.

Management of sample request proposals through the coordination of the Scientific External Committee and the Ethics Committee.

Personalized assistance in sample management.

## Coordinating node

IDIBAPS (Barcelona, Spain): **Principal investigator** Ramon Gomis, Anna Novials **Coordinator** Anna Bosch **Associate researcher** Laura Brugnara **Lab technician** Anna Morales **Lab manager** Albert Davins **Lab technician and quality control manager** Roser Mas **Nurse** Laura Tugores

## Nodes

Hospital Joan XXIII (Tarragona, Spain): **Principal investigator** Joan Vendrell **Research assistant** Lluís Gallart **Lab technician** Miriam Campos



The Biobank Logo

Hospital Sant Joan (Reus, Spain): **Principal investigator** Lluís Masana **Research assistant** Jordina Saladié, Jordi Merino **Lab technician** Carme Buixadera

Hospital de Cruces (Barakaldo, Spain): **Principal investigator** Luis Castaño **Research assistant and lab manager** Inés Urrutia **Research assistant and dietician** Teba González

Hospital Clínico San Carlos (Madrid, Spain): **Principal investigator** Manuel Serrano Ríos **PhD student** Carina Zabena **Lab technician** Ainara González Pereña

Hospital Carlos Haya (Málaga, Spain): **Principal investigator** Federico Sorriquer **Associate researcher** Gemma Rojo **Research assistant** Francisca Linares **Nurse** Mª José Moreno

Hospital Clínico (Valencia, Spain): **Principal investigator** Rafael Carmena **Associate researcher** Javier Chaves **Research assistant** Esther Benito **Lab technician** Verónica González

Hospital de Sant Pau (Barcelona, Spain): **Principal investigator** Francesc Blanco Vaca **Associate researcher** Jesús Martín **Lab technician and Nurse** Cristina Martín

## Facilities

The Coordinating Node of the Biobank centralizes the organization of Biobank sample management and is therefore endowed with the most advanced technology available for this purpose: automated DNA extraction platform (Chemagen system, magnetic beads); liquid handling station (Tecan EVO150), cell immortalization facility (P2 level safety lab); liquid nitrogen tanks; continuous monitoring of environmental conditions from storage systems; -150 °C freezers; bar-code

readers and printers; nanodrop spectrophotometer; and nitrogen and cryogen free controlled rate freezers.

The Biobank is equipped with the following facilities within each node, permitting the immediate storage of samples taken: -80 °C freezers; micronic system for the storage of the samples in standardized aliquots; and web-based IT infrastructure.

### Achievements in 2011

During 2011, the Biobank collected samples from more than 800 new donors affected by the most widespread metabolic diseases in Spain: type 1 diabetes; type 2 diabetes; dyslipidaemias; obesity; and morbid obesity. As previously established, all of the donors completed an extensive questionnaire with personal clinical data, demographic information, and exercise and eating habits, which have been entered into the Biobank clinical database. These data, together with the corresponding samples, represent one of the most exhaustive collections available for the study of metabolic disorders. Overall, the Biobank freezers and tanks stored more than 150,000 aliquots, which were coded and registered in a specially designed database. As the sample and data repository has achieved a considerable size, several groups from Ciberdem have decided to request samples for their research projects. Most of them used DNA, but serum, plasma and PBMCs were also supplied. The projects which have used samples from the Ciberdem Biobank during 2011 are as follows:

- Biochemical, metabolic and genetic characterization of hypertriglyceridaemia associated with high cardiovascular risk. PI Lluís Masana
- Clock gene implication in obesity and T2DM physiopathology. PI Ramon Gomis
- New lipid target identification (IDL, RLP) against micro and macrovascular complication in diabetic patients, and its differential effect in T1DM and T2DM. PI Lluís Masana
- Epigenetic study of DNA methylation differences in T2DM, obesity and controls. PI Ramon Gomis
- Replication in the Di@bet.es Study of the genotype-phenotype correlations found in the Ingene study. PI Gemma Rojo
- Identification of exome gene variants associated with T2DM. PI Javier Chaves
- Cooperative population and database studies for genetic association analysis in T2DM and related traits. PI Javier Chaves
- Organic damage in T2DM and prediabetes: risk factors and Ras and NO pathway interactions - oxidative stress. PI Javier Chaves

All the available samples from the Ciberdem Biobank have an extended set of associated data, physically located in the BCGene database. This database, physically located in the IDIBAPS servers, hosts demographic, clinical, and analytical data associated with the Biobank samples, and has been uploaded in its entirety during 2011. The web-based architecture of the database offers secure access to all the Biobank nodes, guarantees donor confidentiality and ensures sample traceability. Data access is provided by the data manager once a request has been made to the Biobank Committees and approved.

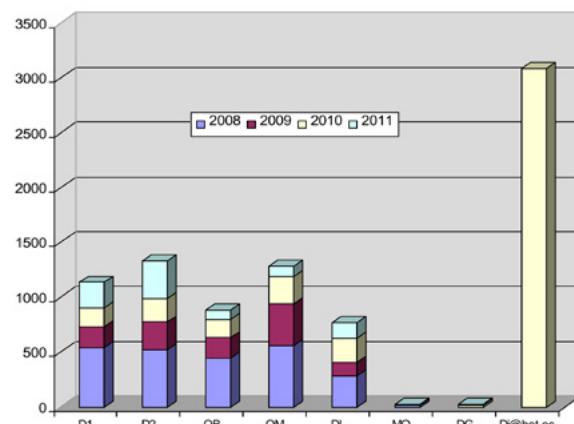
Another great achievement of 2011 has been the performance of Whole Genome Amplification from all the DNA samples included in the Di@bet.es Epidemiological Project, thus obtaining large amounts of genomic DNA to be provided for different research projects. These samples are especially valuable due to the quality of the associated data.

### Future challenges

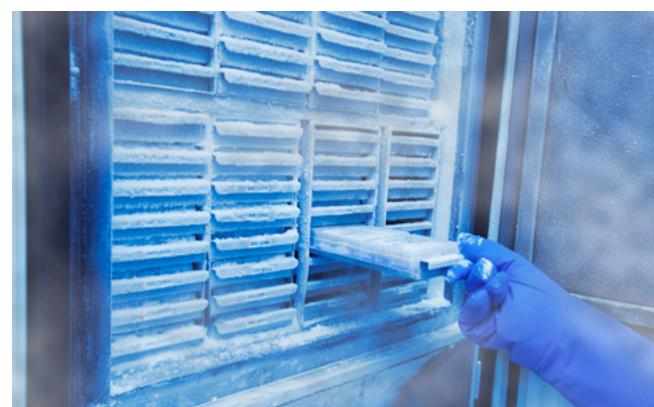
Now that the Biobank is established and consolidated, the main goal for the coming years is to continue to provide as many samples as possible in order to facilitate projects of outstanding quality which could not be carried out without the collaboration of different sample providers.

Another great objective for the coming years will be the establishment of an ancient DNA bank for the ancient population of the Roman city of Tarraco, in the framework of the MEDIGENE project funded by the EU with 3 M €. This DNA bank will be unique in the world and will provide a basis for studying the origin and evolution of many diseases.

Finally, the last big challenge for the Ciberdem Biobank will be to include prospective cohorts of people affected by metabolic disorders in its sample catalogue.



Available cases from the Ciberdem Biobank, 2008-2011. Left to right: Diabetes Type 1, Diabetes Type 2, Obesity, Morbid Obesity, Dyslipidaemia, MODY Diabetes, Gestational Diabetes, Di@bet.es Study.



Marc Vergés © HUBc.

# Metabolomics Platform

[www.metabolomicsplatform.com](http://www.metabolomicsplatform.com)

## Introduction and objectives

The Metabolomics Platform is a joint research facility created by the URV (Universitat Rovira i Virgili, Tarragona, Spain) and Ciberdem. The mission of the Metabolomics Platform is to offer metabolomic services to the biomedical and clinical research community of both Ciberdem and the URV. The main objective of the Metabolomics Platform is to work as an integrative facility and act as a consulting site which becomes fully involved in the metabolomics-related experiments proposed by the groups.

Our collaboration starts with the defining of goals, dimension and characteristics of the sample set, as well as experiment design. Later on, the raw data is processed by our team and we are involved in the interpretation of the results, delivering sound, significant and useful clinical conclusions for the different research groups.

The equipment currently available in high field NMR, GC-MS and LC-MS allows high throughput analytical measurements of body fluids (i.e. serum and urine) as well as tissues or biopsies from humans and/or animal models (rats, mice, etc). The use of advanced statistical, chemometric, multivariate and artificial-intelligence algorithms allows us to turn large measurement datasets into metabolic fingerprinting or profiling results, and ultimately into useful clinical information.

Our goal is to introduce metabolomics as a potential tool for clinical diagnostics and elucidate unknown mechanisms associated with disease. The Metabolomics Platform is particularly addressed to the needs of Ciberdem and URV groups, however, its services and potential scientific collaborations are available to other biomedical research groups in Spain and worldwide.

## Coordination

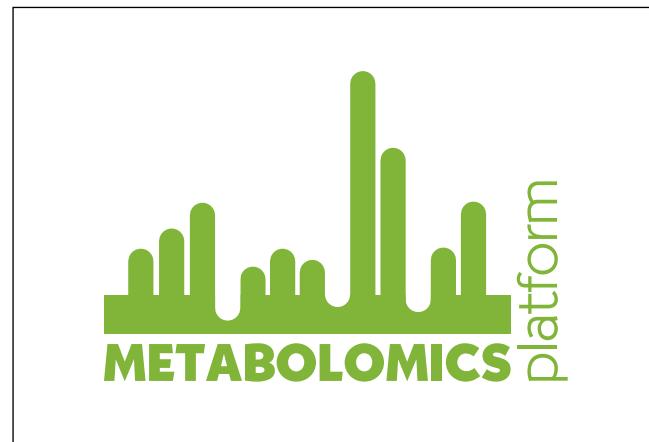
**Principal Investigator** Xavier Correig **Scientific Coordinator** Oscar Yanes **Associate researchers** Jesús Brezmes, Nicolau Cañellas **Research assistants** Miguel Ángel Rodríguez, María Vinaixa, Antoni Beltran

## Scientific equipment

The Platform currently manages and has full access to the following NMR technology:

600 MHz Bruker Avance III + cryoprobe + ScanJet  
500 MHz Bruker Avance III + HR-MAS probe

The Rovira i Virgili University shares three mass spectrometers with the Metabolomics Platform.



The Metabolomics Platform Logo.

## Scientific Services

Name	Principle	Application
1H-NMR rat/mouse liver profiling	Identification and (relative) quantification of up to 52 metabolites from aqueous and lipid extracts	Phenotyping of genetically-modified animals. Drug toxicity and pre-clinical drug candidate safety assessment. Biomarker discovery. Clinical studies (diagnosis and therapeutic efficacy). Monitoring of diet-related health phenotyping
1H-NMR rat/mouse brain profiling	Identification and (relative) quantification of 64 metabolites from aqueous and lipid extracts	Drug neurotoxicity and pre-clinical drug candidate safety. Neurotoxicity studies
1H-NMR serum/plasma extract profiling	Identification and (relative) quantification of up to 47 metabolites from serum/plasma extracts of human/animal models	Biomarker discovery. Clinical studies (diagnosis and therapeutic efficacy). Monitoring of diet-related health phenotyping
1H-NMR urine extract profiling	Identification and (relative) quantification of up to 46 metabolites in human/animal model urine	Biomarker discovery. Assessment of diet or drug intervention. Drug toxicology studies. Clinical studies (diagnosis and therapeutic efficacy)

Name	Principle	Application
HR-MAS 1H-NMR of biopsies, tissues or cell cultures	Metabolic fingerprinting and profiling of intact non-solid/non-liquid biological samples	Clinical diagnostic. Biomarker discovery
GC-MS untargeted metabolomics on serum, urine or tissue extract samples	Identification of features that are differently expressed in cases vs. control experiments and identification of key metabolites	Biomarker discovery. Clinical studies (diagnosis and therapeutic efficacy). Assessment of diet interventions
LC-MS untargeted metabolomics on serum, urine or tissue extract samples	Identification of features that are differently expressed in cases vs. control experiments and identification of key metabolites	Biomarker discovery. Clinical studies (diagnosis and therapeutic efficacy). Assessment of diet interventions
Targeted LC-MS metabolomics	Detection and quantification of predetermined metabolites in biofluids or sample extracts	Phenotypic and physiological effects. Pre-clinical drug-candidate safety assessment. Pharmaco-metabolomics. Disease diagnosis and therapeutic efficacy
Statistics and multivariate analysis	Programming and implementation of supervised and unsupervised multivariate algorithms in metabolomics datasets	Basic univariate statistical tests. Using advanced multivariate and artificial intelligence algorithms for metabolomics data sets and turning them into useful clinical information (PCA, PLS-DA, ANNs). Identifying metabolic relationships, mechanisms, functions and pathways in experimental data and mapping of relevant pathways

-NMR: the existing spectrometers will be complemented with new probes to measure 19F, 13C, 31P and 15N.

-Mass Spectrometry:

2 LC-Q-TOF

2 LC-QqQ

1 GC-TOF

1 GC-QqQ

1 GC-QTOF

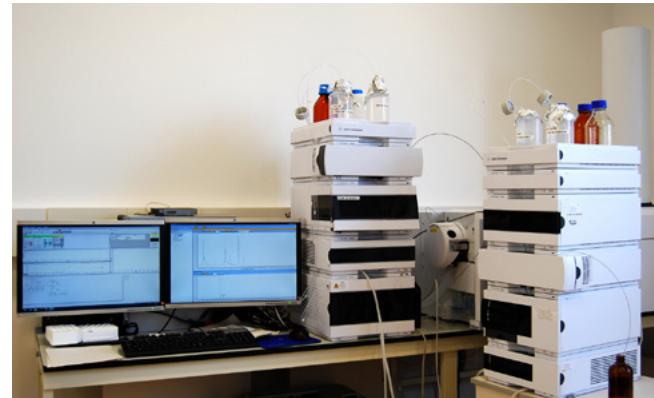
1 LTQ Orbitrap Velos Pro + ETD

1 MALDI-TOF/TOF

2 liquid handling systems

The integration of the Metabolomics Platform in the Centre for Omic Sciences, will represent an excellent opportunity to combine the results from several omic experiments (genomics, transcriptomics, proteomics and metabolomics) and integrate the data from a systems biology approach.

For more information see [page 63](#).



LC-Q-TOF/MS (Agilent 6530 Q-TOF, LC/MS).

## Achievements in 2011

The Metabolomics Platform, inaugurated in June 2008, is now able to offer a complete set of NMR- and MS-based metabolomic services to Ciberdem groups. During 2011, the Metabolomics Platform worked on 5 intramural Ciberdem collaborations in the areas of diabetic dyslipidaemias, insulin resistance related to polycystic ovarian syndrome, and diabetes and exercise. In 2011, the Platform began 14 projects with Ciberdem groups and other institutions in the areas of nutrition and health, metabolomic experiments with cell cultures, phenotyping of animal models, and so on. The number of serum samples processed was over 3000, comprising serum/plasma, urine, tissue extracts and cell cultures.

## Future challenges

In 2012, the Metabolomics Platform will join the Centre for Omic Sciences, located in Reus, and will increase the quantity and quality of its NMR and MS equipment, incorporating the following state-of-the-art technology:

# Programme 1

Molecular and physiological determinants of lifestyle in diabetes/obesity. Population studies for genetic/epigenetic association analysis in type 2 diabetes mellitus and related traits

---

Publications\*: 34

Impact Factor: 165.670

Impact Factor average: 4.873

First decile: 9

Q1: 13

Q2: 12

IntraCIBER: 2

InterCIBER: 15

International: 11

Research grants\*\*: 36

National: 25

International: 6

Private funds: 5

Clinical trials: 9

Clinical practice guidelines: 1

PhD theses: 2

Spin-offs: 1

Awards: 2

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## Letter from the Scientific Programme Coordinator

The year 2011 saw the assignation of research groups to the different programmes defined for Ciberdem activities. Programme 1 includes two areas of research: molecular and physiological determinants of lifestyle in diabetes/obesity; and population studies for genetic-epigenetic association analysis in type 2 diabetes mellitus and related traits. This programme incorporates the activities of nine research groups, both basic and clinical investigators. The activity during this period comprises thirty-six research projects, twenty-five of them funded by national competitive research grants, and six from international sources. As will be expected, our aim was to generate translational collaborative research, ranging from epidemiological studies, and a global therapeutic approach to diabetes and its complications, reaching into the area of genetic and epigenetic studies.

As a direct outcome of the work performed by the different groups during 2011, a total of thirty-four scientific papers were published. Nine of them in journals in the first decile of the speciality and thirteen in journals in the first quartile. The accumulated impact factor for this period was 165.670, with an average impact factor per article of 4.873. Furthermore, two of the papers were collaborative efforts between Ciberdem groups, fifteen with research groups from other CIBERs and eleven were international collaborations.

Regarding other scientific activities of Programme 1 during 2011, two doctoral theses directed by Ciberdem researchers were defended, nine clinical research trials were conducted and one spin-off was generated as a result of the research activity. Moreover, the results of research activities were transferred to clinical practice with the publication by one of the groups of a new edition of "Protocols for the Diagnosis and Treatment of Diabetes and Endocrine Diseases".

Rafael Carmena

\* Only those published in 2011, with Ciberdem listed among the affiliations, which are related to Ciberdem's field of research and are located in the first or second quartile of their subject category are included. Sources: JCR 2010 and PubMed.

\*\* Through Associate Institutions.

## **Objectives**

- Strategies for generating nutritional guidelines in lifestyle studies and in diabetes/obesity prevention.
- The impact of overnutrition, diabetes-obesity and undernutrition on the regulation of energy homeostasis in the central nervous system. From animal models to humans.
- Body fat amount and distribution in childhood and predisposition to type 2 diabetes.
- Environment, genes and prevalence of diabetes mellitus in Spain. Di@bet.es Study.
- Cooperative-population and database studies for genetic association analysis in type 2 diabetes mellitus and related traits.
- Genetic and environmental factors of the insulin resistance syndrome and its long-term complications in immigrant Mediterranean populations.
- Characterization of low HDL syndrome in type 2 diabetes.

## **Groups**

Endocrinology and metabolism PI Carmen Álvarez

Brain glucose sensor, satiety control, insulin resistance and type 2 diabetes PI Enrique Blázquez

Dyslipidaemia, inflammation and endothelial dysfunction PI Rafael Carmena

Metabolomics Platform PI Xavier Correig

Lipids and Arteriosclerosis Research Unit PI Lluís Masana

Metabolic and molecular disturbances in diabetes PI Anna Novials

Diabetobe PI Manuel Serrano Ríos

Endocrinology and Nutrition Service PI Federico Soriguer

# Programme 2

Mechanisms promoting the development of diabetes and its vascular complications. Associated disorders and co-morbidities. Strategies for prevention and treatment

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Publications\*: 38

Impact Factor: 192.004

Impact Factor average: 5.053

First decile: 14

Q1: 13

Q2: 11

IntraCIBER: 9

InterCIBER: 11

International: 11

Research grants\*\*: 46

National: 30

International: 4

Private funds: 12

Clinical trials: 25

Clinical practice guidelines: 3

PhD theses: 5

Awards: 1

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## Letter from the Scientific Programme Coordinator

Among our achievements in 2011, we have ascertained that protein-tyrosine phosphatase 1B (PTP1B) negatively regulates insulin action, promoting attenuation of the insulin signalling pathway. The production of this phosphatase is enhanced in insulin-resistant states, such as obesity and type 2 diabetes, where high levels of proinflammatory cytokines (TNF- $\alpha$ , IL-6) are found. Glycogen deposition is impaired in diabetes, thus contributing to the development of hyperglycaemia. The restoration of liver glycogen ameliorated diabetes and is therefore considered a potential strategy for the treatment of this disease. Amylin is co-secreted with insulin, responds to the same stimuli, is anorectic, lowers body weight by reducing fat mass, and is proposed for diabetes treatment. This suggests that the beneficial effect of amylin in states running with altered glucose homeostasis could occur by partially acting on the hexose metabolism of the liver and mainly on that of the adipose tissue.

Our new data provides direct evidence of the crucial role of dietary cholesterol signalling through liver ABCG5/G8 upregulation in the HFHC diet-mediated induction of macrophage-specific RCT. We also carried out a retrospective analysis of the electrocardiograms (ECGs) recorded at baseline and after 2 years for the first 1,004 type 2 diabetic individuals to be randomized in the Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycaemia in Diabetes (RECORD) study. HDL cholesterol and apolipoprotein A1 levels had a strong, positive correlation with small artery reactive hyperaemia, whereas smoking, waist circumference and triglyceride levels were inversely associated. HDL cholesterol was the main determinant of RHI in small peripheral resistance arteries.

On the other hand, the outer blood-retinal barrier is formed by retinal pigment epithelial (RPE) cells and its disruption significantly contributes to the development of diabetic macular oedema (DME). Epo treatment was able to prevent, but not to restore, the increase of permeability induced by high glucose plus IL-1 $\beta$ . We conclude that RPE disruption induced by high glucose plus IL-1 $\beta$  is prevented by Epo through the downstream signalling of JAK2 and PI3K/AKT pathways. Finally, no differences in cbAdiponectin concentration or its multimeric forms were observed in the offspring of diabetic mothers as compared with NGT mothers. In the multivariate analysis, maternal multimeric forms of adiponectin emerged as independent predictors of cbAdiponectin, its multimers, and their distribution.

Manuel Benito

\* Only those published in 2011, with Ciberdem listed among the affiliations, which are related to Ciberdem's field of research and are located in the first or second quartile of their subject category are included. Sources: JCR 2010 and PubMed.

\*\* Through Associate Institutions.

## **Objectives**

- The identification of neurodegenerative mechanisms which promote the development of diabetic retinopathy: the role of insulin signalling and apoptosis.
- Glycogen-induced dysfunctions in the pancreas and retina and their involvement in the ethiopathogenesis of diabetes mellitus.
- Mechanisms of endothelial dysfunction in diabetes: the role of amylin and circulating endothelial cells.
- The influence of insulin resistance and the compensatory response of the endocrine pancreas on endothelial/vascular damage.

## **Groups**

[Diabetes and cardiovascular](#) PI Manuel Benito

[Metabolic disease and cardiovascular risk](#) PI Francisco Blanco Vaca

[Proinsulin and tyrosine hydroxylase/dopamine effects in cardiac development](#) PI Flora de Pablo

[Diabetes and obesity: biopathology and cellular plasticity](#) PI Ramon Gomis

[Metabolic engineering and diabetes therapy](#) PI Joan J Guinovart

[Lipids and Arteriosclerosis Research Unit](#) PI Lluís Masana

[Diabetes and Metabolism Research Group](#) PI Rafael Simó

[Molecular mechanisms of insulin resistance and sensitivity in peripheral tissues](#) PI Ángela Martínez Valverde

[Diabetes and Metabolic Associated Diseases Research Group](#) PI Joan J Vendrell

[Molecular characteristics, and action of incretins, the physiopathology of glucose, lipids and bone metabolism](#) PI María Luisa Villanueva Peñacarrillo

# Programme 3

**Impact of beta cell dysfunction and plasticity on the natural history of diabetes. Development of novel treatment strategies**

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Publications\*: 23

Impact Factor: 150.722

Impact Factor average: 6.553

First decile: 12

Q1: 7

Q2: 4

IntraCIBER: 1

InterCIBER: 2

International: 9

Research grants\*\*: 56

National: 43

International: 11

Private funds: 2

Clinical trials: 9

Clinical practice guidelines: 2

PhD theses: 9

Patents: 1

Awards: 3

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## Letter from the Scientific Programme Coordinator

Programme 3 of Ciberdem consists of ten groups of researchers dedicated to the study of the effects of beta cell alterations on the natural history of diabetes, as well as the development of novel strategies for treatment and prevention. Its scientific production during 2011 reflects a high level of impact and quality. Of twenty-three original publications, just over 50% are found in the first decile, with the remainder in the first and second quartiles. International collaborations involving our groups have brought added value to the overall results, while collaborative projects among the groups have consolidated the development of the programme.

In clinical research, clinical trials related to intervention studies on the type 1 diabetic population, along with the phenotypic and genetic characterization of monogenic diabetes, are currently in progress and are expected to produce significant results. In basic research, the development of new gene therapy strategies (such as *in vivo* pancreatic virus transduction or RNA silencing), efforts to differentiate stem cells or other cell-sources into insulin-producing cells, and the understanding of molecular mechanisms that induce pancreatic damage and regeneration, in addition to the cross-talk of islets with other key tissues, in particular, adipose tissue, represent important research lines that have reinforced the programme with excellent published results.

The field of epigenetics, the complexity of genomic programming and the transcriptional networks implicated in beta cell functioning appear as new forces highlighting great promise for our research. Another interest of our programme is the impact of environmental pollutants on beta cell function. Results have already had a high impact not only on the scientific community, but also on social networks. Finally, Programme 3 promotes our young investigators, who have successfully defended nine doctoral theses over the past year.

In conclusion, we consider that the efforts of all investigators included in Programme 3 have led to excellent results, as we hoped and expected.

Anna Novials

\* Only those published in 2011, with Ciberdem listed among the affiliations, which are related to Ciberdem's field of research and are located in the first or second quartile of their subject category are included. Sources: JCR 2010 and PubMed.

\*\* Through Associate Institutions.

## **Objectives**

- Recovery of functionally impaired metabolic tissues.
- Clinical, genetic and functional characterization of monogenic diabetes: from bench to bedside.
- Production of monoclonal antibodies which selectively react with cell-surface molecules in human pancreatic beta cells.
- Comparative metabolomic analysis for the detection of biomarkers in diabetes.

## **Groups**

Transgenic animal models and gene therapy approaches for diabetes PI Fàtima Bosch

Laboratory of Molecular Endocrinology PI Deborah Burks

Hospital Universitario Cruces Diabetes Research Group PI Luis Castaño

Genomic programming of beta cells PI Jorge Ferrer

Diabetes and obesity: biopathology and cellular plasticity PI Ramon Gomis

Islet cell and stem cell physiology PI Franz Martín

Group of Research into Diabetes and Metabolism PI Eduard Montanya

Unit of Cell Physiology and Nutrition IB-UMH PI Angel Nadal

Metabolic and molecular disturbances in diabetes PI Anna Novials

Transcriptional mechanisms of pancreatic function PI Mario Vallejo

# Programme 4

## Use of biomedical approach systems to develop personalized therapies for diabetes

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Publications\*: 26

Impact Factor: 139.146

Impact Factor average: 5.352

First decile: 10

Q1: 16

IntraCIBER: 3

InterCIBER: 3

International: 14

Research grants\*\*: 38

National: 29

International: 6

Private funds: 3

Clinical trials: 4

Clinical practice guidelines: 2

PhD theses: 6

Awards: 2

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### Letter from the Scientific Programme Coordinator

The research activity of Programme 4 centres on the use of systems biology approaches and other state-of-the-art biomedical methods designed to understand the pathophysiological mechanisms altered in diabetes, and to develop personalized therapies for diabetes and its chronic complications. The programme comprises a total of 10 research groups and includes both basic and clinical researchers. A priority of the programme is to propitiate the development of translational collaborative research.

During the year 2011, the groups included in Programme 4 published a total of twenty-six scientific articles, ten of them published in journals in the first decile of the speciality. The accumulated Impact Factor (IF) for this period was 139. Projects developed by the Principal Investigators of the Programme were funded by thirty-eight grants, six of them international. In addition, a total of four clinical research trials were conducted, six doctoral theses supervised by investigators in the Programme were defended, two new clinical guidelines were published, and two awards were received.

Relevant scientific achievements performed by members of the Programme are, among others, the following: a) identification of the role of decreased circulating hepcidin concentrations in the iron excess of women with the polycystic ovary syndrome; b) demonstration that early metformin therapy in girls with precocious pubarche reduces hirsutism, androgen excess and oligomenorrhoea in adolescence; c) documentation that fenofibrate prevents retinal pigment epithelium disruption induced by interleukin-1 $\beta$ ; d) identification that CD14 modulates inflammation-driven insulin resistance; and e) demonstration that activation of peroxisome proliferator-activated receptor- $\beta$ /- $\delta$  ameliorates insulin signalling by inhibiting STAT3 in interleukin-6-stimulated adipocytes.

Antonio Zorzano

\* Only those published in 2011, with Ciberdem listed among the affiliations, which are related to Ciberdem's field of research and are located in the first or second quartile of their subject category are included. Sources: JCR 2010 and PubMed.

\*\* Through Associate Institutions.

## **Objectives**

- Determinants of insulin resistance and glucose tolerance disorders (including diabetes) in severe obesity and their changes after bariatric-surgery-induced weight loss.
- Adult adipose-tissue-derived progenitor cells: the influence of the clinical phenotype and adipose depot origin on their biological properties.

## **Groups**

The Eicosanoid Research Division PI Jesús Balsinde

Diabetes, Obesity and Human Reproduction PI Héctor F Escobar Morreale

Genomic programming of beta cells PI Jorge Ferrer

Mechanisms of control of glucose and fatty acid metabolism in skeletal muscle cells and metabolic impairment in atrophy  
PI Anna Maria Gómez Foix

Prenatal growth restriction and subsequent risks for type 2 diabetes and cardiovascular disease PI Lourdes Ibáñez

Group of Research into Diabetes and Metabolism PI Eduard Montanya

Diabetes and Metabolism Research Group PI Rafael Simó

Pharmacological targets in inflammation and metabolic diseases PI Manuel Vázquez Carrera

Diabetes and Metabolic Associated Diseases Research Group PI Joan J Vendrell

Heterogenic and polygenic diseases. Genexartis PI Antonio Zorzano

# Endocrinology and metabolism

Departamento de Bioquímica y Biología Molecular II, Facultad de Farmacia, Universidad Complutense de Madrid  
[www.ucm.es/info/biomol2](http://www.ucm.es/info/biomol2)



**Principal Investigator** Carmen Álvarez [c.alvarez@farm.ucm.es](mailto:c.alvarez@farm.ucm.es) **Associate researchers** Fernando Escrivá, María Ángeles Martín **Postdoctoral fellow** Elisa Fernández **PhD students** Juan de Toro, Esther Lizárraga

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Publications: 1

Q2: 1

Research grants: 2

National projects: 1

Autonomous Community projects: 1

Scientific collaborations within Ciberdem: 1

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## Programmes

Programme 1. Molecular and physiological determinants of lifestyle in diabetes/obesity. Population studies for genetic-epigenetic association analysis in type 2 diabetes mellitus and related traits.

## Keywords

Islet degeneration and damage. Beta-cell signal transduction. Insulin action. Insulin sensitivity and resistance. Gastro-entero pancreatic factors.

## Main lines of research

The identification of the cellular and molecular mechanisms that link poor perinatal growth and increased risk of metabolic syndrome and type 2 diabetes in adult life through the use of animal models of nutritional manipulation: maternal undernutrition followed or not by overnutrition. To this end we have focused on:

- a) the effect of nutrients on the growth, death and function of pancreatic alfa and beta cells: involvement of different growth factors.
- b) the potential role of incretins (GLP-1 and GIP) in the relationship between intrauterine growth restriction and the development of type 2 diabetes in adulthood: study of the entero-insular axis.
- c) changes in insulin/glucagon plasma levels and liver sensitivity associated with early undernutrition which could alter the available substrates for the growing brain.

- d) impact of early undernutrition on the insulin and leptin hypothalamic responses and the hypothalamic expression of orexigenic and anorexigenic factors (NPY, POMC).  
e) the effect of early undernutrition followed by an overcaloric diet on the obesity risk and the white adipose tissue metabolism.

## Publications

Effect of PLGA hydrophilicity on the drug release and the hypoglycemic activity of different insulin-loaded PLGA microspheres

Presmanes C, de Miguel L, Espada R, Alvarez C, Morales E, Torrado JJ

J Microencapsul, 28, 791-798 (2011)

PMID 21967461. Q2. IF 1.515. Programme 1

## Research grants

Mecanismos moleculares que regulan el crecimiento y muerte de las células beta pancreáticas y las acciones insulínicas en el SNC: estudio en ratas subnutridas y diabéticas

Ministerio de Ciencia e Innovación, BFU 2008-02930: 2009-2011

Principal Investigator: Carmen Álvarez

*National project. Programme 1*

Mecanismos moleculares implicados en el desarrollo y crecimiento de las células beta pancreáticas y en las acciones de la insulina en el SNC: estudio en ratas subnutridas

Grupos de Investigación Santander-UCM. Ref. 950610: 2011

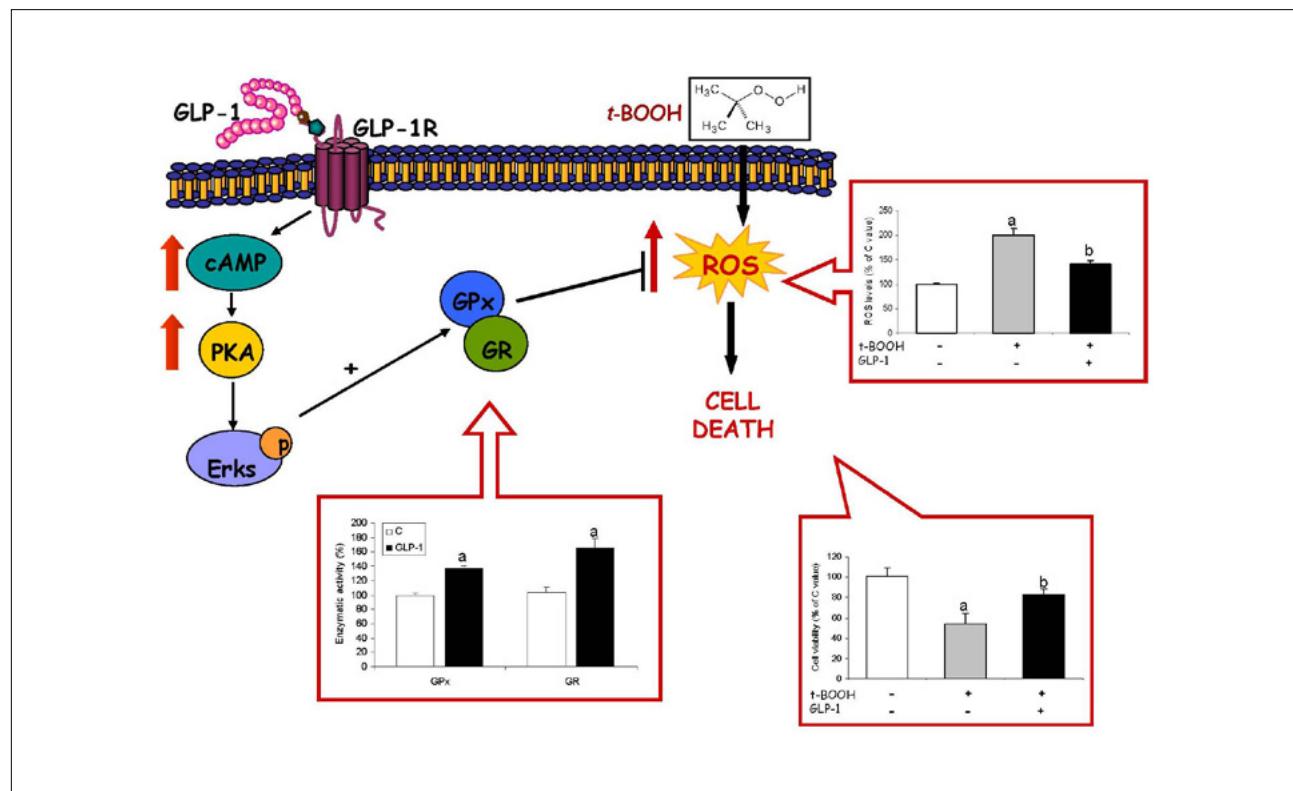
Principal Investigator: Fernando Escrivá  
*Autonomous Community project. Programme 1*

## Scientific collaborations within Ciberdem

The impact of overnutrition, diabetes-obesity, and undernutrition on the regulation of energy homeostasis in the central nervous system. From animal models to humans IODURE: 2009-2011

Coordinator: Manuel Serrano Ríos

Ciberdem groups: Alvarez C, Serrano-Ríos M, Blázquez E, Burks D, Vallejo M ■



Glucagon-like peptide-1 improves beta-cell antioxidant capacity by increasing the activity of glutathione-related enzymes (GPx and GR) via a mechanism that involves activation of Erks in a PKA-dependent manner.

# The Eicosanoid Research Division

Instituto de Biología y Genética Molecular, Consejo Superior de Investigaciones Científicas, Valladolid  
[www.balsinde.org](http://www.balsinde.org)



**Principal Investigator** Jesús Balsinde [jbalsinde@ibgm.uva.es](mailto:jbalsinde@ibgm.uva.es) **Associate researchers** María Ángeles Balboa, Olimpio Montero **Postdoctoral fellows** Clara Meana, Julio Rubio, Alma Astudillo, Juan Pablo Rodríguez **PhD students** Esperanza Esquinas, Luis Gil de Gómez, Lucía Peña, Martín Valdearcos, Carlos Guijas, Gema Lordén **Lab manager** Montserrat Duque

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Publications: 5

First decile: 1

Q1: 4

With other Ciberdem groups: 1

With other CIBERs: 1

With other international groups: 1

Research grants: 3

National projects: 2

Autonomous Community projects: 1

Scientific collaborations within Ciberdem: 1

PhD theses: 2

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## Programmes

Programme 4. Use of biomedical approach systems to develop personalized therapies for diabetes.

## Keywords

Cytokines. Lipid metabolism. Lipid signalling. Phospholipases.

## Main lines of research

- Lipid metabolic pathways in obesity and inflammation: roles of lipins and phospholipases A2.
- Lipid profiling by mass spectrometry; lipidomic and metabolipidomic approaches.
- The molecular cell biology of lipid droplets.
- Cell regulation of ω-6 and ω-3 fatty acid availability.

## Publications

Altered arachidonate distribution in macrophages from caveolin-1 null mice leading to reduced eicosanoid synthesis  
Astudillo AM, Pérez-Chacón G, Meana C, Balgoma D, Pol A, Del Pozo MA, Balboa MA, Balsinde J  
J Biol Chem, 286, 35299-35307 (2011)  
[PMID 21852231](https://pubmed.ncbi.nlm.nih.gov/21852231/). Q1. IF 5.328. Programme 4

Caveolin-1 deficiency causes cholesterol-dependent mitochondrial dysfunction and apoptotic susceptibility

Bosch M, Marí M, Herms A, Fernández A, Fajardo A, Kassan A, Giralt A, Colell A, Balgoma D, Barbero E, González-Moreno E, Matías N, Tebar F, Balsinde J, Camps M, Enrich C, Gross SP, García-Ruiz C, Pérez-Navarro E, Fernández-Checa JC, Pol A  
*Curr Biol*, 21, 681-686 (2011)

PMID 21497090. 1st decile. IF 10.026. With other CIBERS: Cibernet. With other international groups. Programme 4

Influence of cellular arachidonic acid levels on phospholipid remodeling and CoA-independent transacylase activity in human monocytes and U937 cells

Astudillo AM, Pérez-Chacón G, Balgoma D, Gil-de-Gómez L, Ruipérez V, Guijas C, Balboa MA, Balsinde J

*Biochim Biophys Acta*, 1811, 97-103 (2011)

PMID 21145415. Q1. IF 5.084. Programme 4

Subcellular localization and role of lipin-1 in human macrophages

Valdearcos M, Esquinas E, Meana C, Gil-de-Gómez L, Guijas C, Balsinde J, Balboa MA

*J Immunol*, 186, 6004-6013 (2011)

PMID 21478406. Q1. IF 5.745. Programme 4

The PPAR $\beta/\delta$  activator GW501516 prevents the down-regulation of AMPK caused by a high-fat diet in liver and amplifies the PGC-1 $\alpha$ -Lipin 1-PPAR $\alpha$  pathway leading to

increased fatty acid oxidation

Barroso E, Rodríguez-Calvo R, Serrano-Marco L, Astudillo AM, Balsinde J, Palomer X, Vázquez-Carrera M  
*Endocrinology*, 152, 1848-1859 (2011)  
PMID 21363937. Q1. IF 4.993. With other Ciberdem groups: Vázquez-Carrera M. Programme 4

### Research grants

Estudio por espectrometria de masas del perfil lipidómico de macrófagos humanos polarizados

Ministerio de Educación y Ciencia, BFU2010-18826/BMC: 2011-2013

Principal Investigator: J Balsinde

National project. Programme 4

Regulación de los procesos inflamatorios por lipina: papel en la transducción de señal en macrófagos humanos

Ministerio de Ciencia e Innovación, SAF2010-18831: 2011-2012

Principal Investigator: MA Balboa

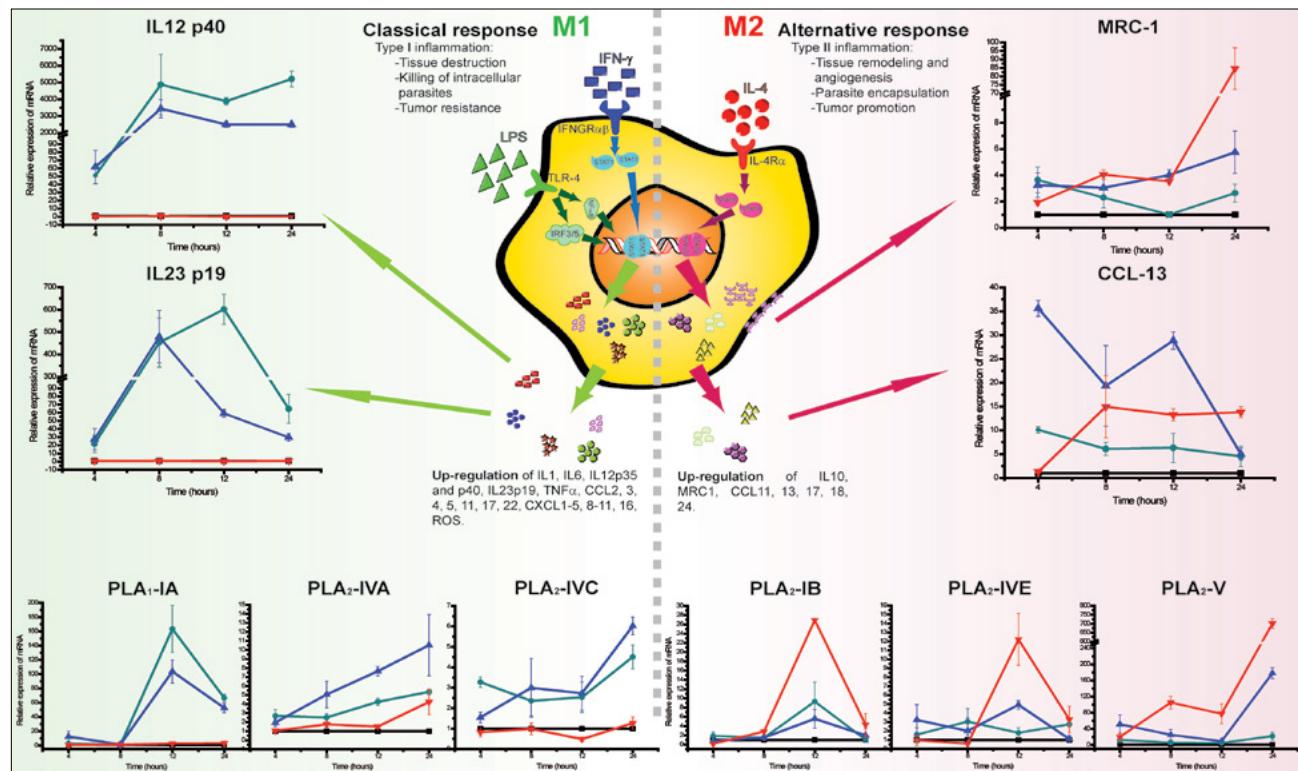
National project. Programme 4

The regulation of inflammation by lipin, an enzyme involved in obesity

Junta de Castilla y León, BIO39/VA04/10: 2010-2011

Principal Investigator: MA Balboa

Autonomous Community project. Programme 4



Expression of phospholipases A2 in human macrophage polarization.

### **Scientific collaborations within Ciberdem**

Adult adipose tissue-derived progenitor cells: the influence of the clinical phenotype and adipose depot origin on their biological properties

STEMOB: 2009-2011

Coordinator: Joan J Vendrell

Ciberdem groups: Balsinde J, Vendrell J, Zorzano A, Gómez-Foix AM, Montanya E, Simó R, Vázquez-Carrera M

### **PhD theses**

Regulación de la respuesta inflamatoria inducida por ácidos grasos en macrófagos: papel de la lipina-2

Author: Martín Valdearcos Contreras

Thesis advisor: Jesús Balsinde

University: Universidad de Valladolid

Thesis defense date: April 15, 2011

Programme 4

Mecanismos de control de los niveles de ácido araquidónico en monocitos y macrófagos

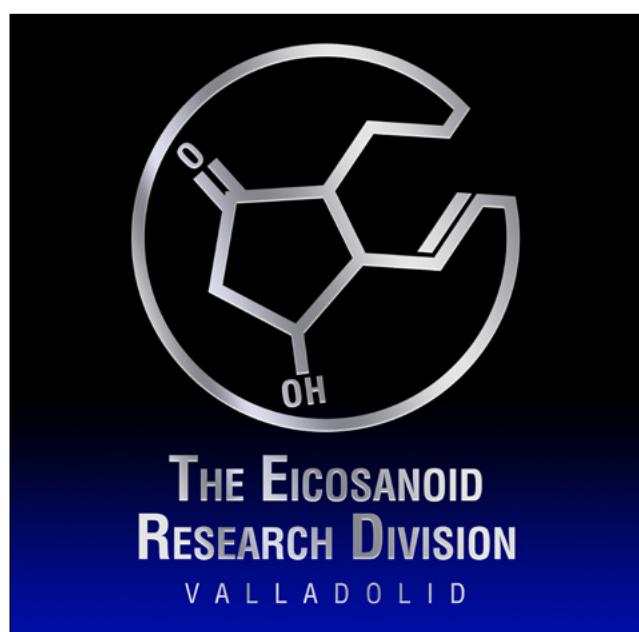
Author: Alma Astudillo del Valle

Thesis advisor: Jesús Balsinde

University: Universidad de Valladolid

Thesis defense date: July 29, 2011

Programme 4 ■



The Eicosanoid Research Division Logo.

# Diabetes and cardiovascular

Facultad de Farmacia, Universidad Complutense de Madrid  
[www.ucm.es/info/biomol2](http://www.ucm.es/info/biomol2)



**Principal Investigator** Manuel Benito [benito@farm.ucm.es](mailto:benito@farm.ucm.es) **Associate researchers** Óscar Escribano, Almudena Gómez, Carlos Guillén **Postdoctoral fellows** Iria Nieto, Beatriz Gozalbo **PhD students** Alberto Bartolomé, Liliana Perdomo, Yolanda Fernández **Post-graduate students** Beatriz Martínez, Selene Barros, Ana García **Lab manager** Gema García **Lab technician** Silvia Fernández **Administrative staff** Elena González

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Publications: 2

First decile: 1

Q2: 1

With other Ciberdem groups: 1

Research grants: 2

National projects: 1

Autonomous Community projects: 1

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## Programmes

Programme 2. Mechanisms promoting the development of diabetes and its vascular complications. Associated disorders and co-morbidities. Strategies for prevention and treatment.

## Keywords

Beta-cell signal transduction. Insulin sensitivity and resistance. Macrovascular disease.

## Main lines of research

- Compensatory mechanism to hepatic insulin resistance:
- The role of the liver-pancreas endocrine axis in triggering beta-cell hyperplasia.
- The role of autophagy and ER stress in the regulation of beta-cell pancreatic mass *in vivo*.
- The role of TSC1/TSC2 and m-TOR1 in the regulation of ER-stress and autophagy in pancreatic cell lines.
- New mouse models to study energy balance and body weight regulation: Brown adipose tissue-specific knockout of IGF-1R and DKO IGF-1R/IR.
- BATIRKO/apoE -/- DKO mice:
  - The role of the compensatory mechanisms of insulin resistance in the aggravation/attenuation of inflammation, oxidative stress and vascular lesion in the aorta.
  - Molecular mechanisms of insulin resistance:
    - The role of IR isoforms in cardiomyocytes and aortic

endothelial cells and vascular smooth muscle cells.

### Publications

New emerging role of protein-tyrosine phosphatase 1B in the regulation of glycogen metabolism in basal and TNF- $\alpha$ -induced insulin-resistant conditions in an immortalised muscle cell line isolated from mice

Alonso-Chamorro M, Nieto-Vazquez I, Montori-Grau M, Gomez-Foix AM, Fernandez-Veledo S, Lorenzo M

Diabetologia, 54, 1157-1168 (2011)

PMID 21311858. 1st decile. IF 6.973. With other Ciberdem groups: Gómez-Foix AM, Vendrell J. Programme 2

Tissue specificity on insulin action and resistance: past to recent mechanisms

Benito M

Acta Physiol, 201, 297-312 (2011)

PMID 21040498. Q2. IF 3.138. Programme 2

### Research grants

Modelos animales y celulares de resistencia a la insulina: daño cardiovascular

Ministerio de Ciencia e Innovación, SAF2008-00031: 2009-2011

Principal Investigator: Manuel Benito

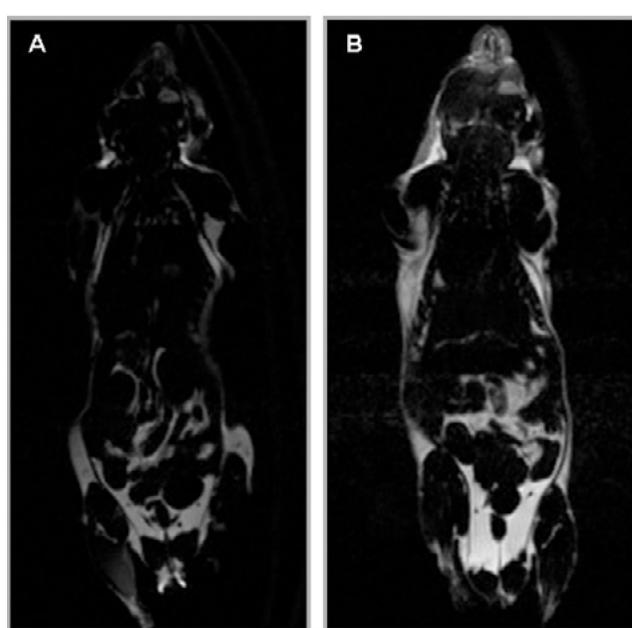
National project. Programme 2

Diabetes y cardiovascular (grupo 920384)

CAM-UCM GR35/10-A: 2010-2011

Principal Investigator: Manuel Benito

Autonomous Community project. Programme 2 ■



Magnetic resonance images of 52-week-old Control (A) and BAT-IRKO (B) mice. In these animals, the brown fat lipodystrophy and increased visceral adiposity through a concerted adipocytokines overexpression induces vascular insulin resistance and dysfunction.

# Metabolic disease and cardiovascular risk

Hospital de la Santa Creu i Sant Pau, Servei de Bioquímica i Endocrinologia, Barcelona  
[www.santpau.cat](http://www.santpau.cat)



**Principal Investigator** Francisco Blanco Vaca [fblancova@santpau.cat](mailto:fblancova@santpau.cat) **Associate researchers** Joan Carles Escolà, Jesús María Martín, Antonio Pérez, Josep Julve **Postdoctoral fellow** Juan Antonio Sánchez **Lab technicians** Carme Mayoral, Rosa Roig, David Santos

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Publications: 6

First decile: 2

Q1: 2

Q2: 2

With other Ciberdem groups: 2

With other international groups: 3

Research grants: 8

European projects: 1

National projects: 4

Autonomous Community projects: 1

Private funds: 2

Scientific collaborations within Ciberdem: 2

Clinical trials: 1

Clinical practice guidelines: 1

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## Programmes

Programme 2. Mechanisms promoting the development of diabetes and its vascular complications. Associated

disorders and co-morbidities. Strategies for prevention and treatment.

## Keywords

Lipid metabolism. Metabolic syndrome. Genetics type 2 diabetes.

## Main lines of research

-HDL: modulation by diet and role of diabetes mellitus and atherothrombotic cardiovascular disease development.

-Genetics of dyslipidaemia, type 2 diabetes and hyperhomocysteinaemia.

-Development of experimental-biochemistry and molecular biology techniques and their application to clinical laboratory practice (innovation).

## Publications

ATP-binding cassette G5/G8 deficiency causes

<p>hypertriglyceridemia by affecting multiple metabolic pathways</p> <p>Méndez-González J, Julve J, Rotllan N, Llaverias G, Blanco-Vaca F, Escolà-Gil JC</p> <p>Biochim Biophys Acta, 1811, 1186-1193 (2011)</p> <p><u>PMID 21855652.</u> Q1. IF 5.084. Programme 2</p>	<p>D, Chroni A, Jauhainen M, Savolainen M, von Eckardstein A, Kortsch A, Staels B, Shunkert H, Nofer JR, Calabresi L, Bernini F, Kuivenhoven JA, Karlsson H</p> <p><i>European project. Programme 2</i></p>
<p>Differential effects of gemfibrozil and fenofibrate on reverse cholesterol transport from macrophages to feces in vivo</p> <p>Rotllan N, Llaverias G, Julve J, Jauhainen M, Calpe-Berdiel L, Hernández C, Simó R, Blanco-Vaca F, Escolà-Gil JC</p> <p>Biochim Biophys Acta, 1811, 104-110 (2011)</p> <p><u>PMID 21126601.</u> Q1. IF 5.084. With other Ciberdem groups: Simó R. With other international groups. Programme 2</p>	<p>Papel de las lipasas que intervienen en el metabolismo lipoproteico en la modulación de las propiedades antiaterogénicas de las HDL (transporte reverso de colesterol específico de macrófagos y capacidad antioxidante)</p> <p>ISCIII, PI08/1147: 2009-2011</p> <p>Principal Investigator: Blanco Vaca F</p> <p>Associate investigators: Llaverias G, Roig R</p> <p><i>National project. Programme 2</i></p>
<p>Effect of atorvastatin on lipoprotein (a) and interleukin-10: a randomized placebo-controlled trial</p> <p>Hernández C, Francisco G, Ciudin A, Chacón P, Montoro B, Llaverias G, Blanco-Vaca F, Simó R</p> <p>Diabetes Metab, 37, 124-130 (2011)</p> <p><u>PMID 21131223.</u> Q2. IF 3.033. With other Ciberdem groups: Simó R. Programme 2</p>	<p>Efectos sistémicos del síndrome de las apneas durante el sueño. Análisis mediante modelos animales y estudios en humanos</p> <p>ISCIII, PI08/1211: 2009-2012</p> <p>Principal Investigator: Mayos M</p> <p>Associate investigator: Pérez A</p> <p><i>National project. Programme 2</i></p>
<p>Mast cell activation in vivo impairs the macrophage reverse cholesterol transport pathway in the mouse</p> <p>Lee-Rueckert M, Silvennoinen R, Rotllan N, Judström I, Blanco-Vaca F, Metso J, Jauhainen M, Kovánen PT, Escolà-Gil JC</p> <p>Arterioscler Thromb Vasc Biol, 31, 520-527 (2011)</p> <p><u>PMID 21212401.</u> 1st decile. IF 7.215. With other international groups. Programme 2</p>	<p>Funcionalidad de HDL en diabetes mellitus e hiperhomocisteinemia</p> <p>ISCIII, PI1000277: 2011-2013</p> <p>Principal Investigator: Julve J</p> <p><i>National project. Programme 2</i></p>
<p>Seeking novel targets for improving in vivo macrophage-specific reverse cholesterol transport: translating basic science into new therapies for the prevention and treatment of atherosclerosis</p> <p>Julve J, Llaverias G, Blanco-Vaca F, Escolà-Gil JC</p> <p>Curr Vasc Pharmacol, 9, 220-237 (2011)</p> <p><u>PMID 21143175.</u> Q2. IF 3.184. Programme 2</p>	<p>Análisis funcional de las propiedades antiaterogénicas de las HDL (transporte reverso de colesterol específico de macrófagos in vivo y capacidad antioxidante) en modelos animales de diabetes mellitus y arteriosclerosis</p> <p>ISCIII, PI09/00178: 2010-2012</p> <p>Principal Investigator: Escolà Gil JC</p> <p>Associate investigators: Roig R, Santos D, Méndez J</p> <p><i>National project. Programme 2</i></p>
<p>The cholesterol content of Western diets plays a major role in the paradoxical increase in high-density lipoprotein cholesterol and upregulates the macrophage reverse cholesterol transport pathway</p> <p>Escolà-Gil JC, Llaverias G, Julve J, Jauhainen M, Méndez-González J, Blanco-Vaca F</p> <p>Arterioscler Thromb Vasc Biol, 31, 2493-2499 (2011)</p> <p><u>PMID 21885848.</u> 1st decile. IF 7.215. With other international groups. Programme 2</p>	<p>Grup de recerca d'estructura de lipoproteïnes, dislipèmies i altres factors de risc cardiovascular</p> <p>AGAUR, Generalitat de Catalunya, 2009SGR1205: 2009-2014</p> <p>Principal Investigator: Ordóñez Llanos J</p> <p>Associate investigators: Blanco Vaca F, Julve J, Escolà Gil JC, Benítez S, Sánchez Quesada JL</p> <p><i>Autonomous Community project. Programme 2</i></p>
<p><b>Research grants</b></p> <p>HDL: from biological understanding to clinical exploitation</p> <p>COST Actions, European Union, BM0904: 2010-2014</p> <p>Principal Investigator: Kardassis D</p> <p>Associate investigators: Blanco Vaca F, Gómez-Coronado</p>	<p>Propiedades antiaterogénicas de las HDL en presencia de hiperhomocisteinemia: análisis y búsqueda de biomarcadores mediante técnicas proteómicas</p> <p>Fundación Española de Arteriosclerosis, Beca SEA/FEA Almirall: 2010-2012</p> <p>Principal Investigator: Blanco Vaca F</p> <p>Associate investigator: Julve J</p> <p><i>Private funds. Programme 2</i></p>

Efecto de la apolipoproteína A-II en el metabolismo de los triglicéridos en ratones transgénicos y sujetos normolipémicos

Sociedad/Fundación Española de Arteriosclerosis: 2009-2011

Principal Investigator: Escolà Gil JC

Private funds. Programme 2

### Scientific collaborations within Ciberdem

Cooperative population and database studies for genetic association analysis in T2DM and related traits

INGENFRED: 2009-2011

Coordinator: Felipe Javier Chaves

Ciberdem groups: Blanco-Vaca F, Carmena R, Serrano-Ríos M, Soriguer F

Ciberdem Biobank

Coordinator: Anna Novials

Ciberdem Biobank nodes: Blanco-Vaca F, Gomis R, Novials A, Vendrell J, Masana L, Castaño L, Serrano-Ríos M, Soriguer F, Carmena R

### Clinical trials

Estudio epidemiológico transversal y multicéntrico para conocer el grado de control de la hemoglobina glicosilada en pacientes con diabetes mellitus tipo 2 atendidos en atención primaria (estudio Diabcontrol)

DMM-01 SIT 11: 2011-2012

Coordinator: A Pérez

Programme 2

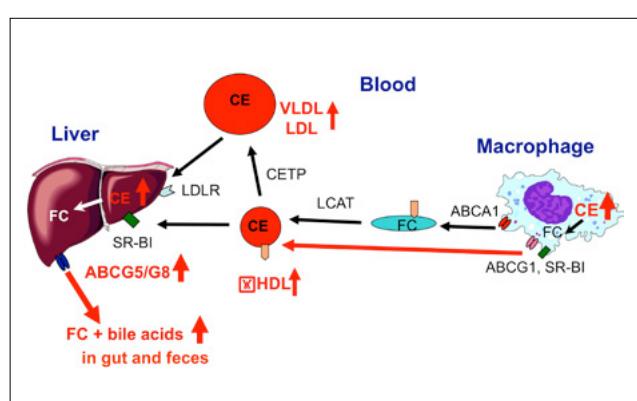
### Clinical practice guidelines

Protocolo de tratamiento de la diabetes tipo 2

Grup de treball de Diabetes Tipus 2 Barcelona Dreta

Consorci Sanitari de Barcelona, p 1-8 (2011)

Programme 2 ■



The cholesterol content of a typical high-fat diet increases HDL-cholesterol and macrophage-reverse cholesterol transport through LXR signalling in an unsuccessful, compensatory mechanism against atherosclerosis.

# Brain glucose sensor, satiety control, insulin resistance and type 2 diabetes

Universidad Complutense de Madrid

[www.ucm.es](http://www.ucm.es)



**Principal Investigator** Enrique Blázquez [ebiazquez@med.ucm.es](mailto:ebiazquez@med.ucm.es) **Associate researchers** Elvira Álvarez, María Ángeles Navas, Isabel Roncero, Juan Miguel Ruiz Albusac, María del Carmen Sanz, Esther Velázquez **PhD student** Carmen García Herrero **Lab manager** Verónica Hurtado Carneiro

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Publications: 2

Q1: 2

Research grants: 6

National projects: 3

Autonomous Community projects: 1

Private funds: 2

Scientific collaborations within Ciberdem: 2

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## Programmes

Programme 1. Molecular and physiological determinants of lifestyle in diabetes/obesity. Population studies for genetic-epigenetic association analysis in type 2 diabetes mellitus and related traits.

## Keywords

Genetics type 2 diabetes. Incretins. Obesity. Insulin sensitivity

and resistance. Insulin action. Carbohydrate metabolism. Biomarkers and imaging.

## Main lines of research

- Modifications of cerebral glucose metabolism in pathophysiological states related to feeding behaviour.
- The effects of GLP-1 and GLP-2 on the expression and activity of hypothalamic metabolic sensors and characterization of the neuroprotective role of these peptides.
- The effect of GLP-2 on the proliferation of cultured rat astrocytes.
- Signalling and the biological effects of GLP-1 on mesenchymal stem cells of human bone marrow and mouse embryonic stem cells - its effect on cell differentiation.
- Molecular diagnosis of monogenic diabetes (MODY) and the functional characterization of MODY mutations.

## Publications

Differential effects of HNF-1 $\alpha$  mutations associated with familial young-onset diabetes on target gene regulation  
Galán M, García-Herrero CM, Azriel S, Gargallo M, Durán M, Gorgojo JJ, Andía VM, Navas MA  
*Mol Med*, 17, 256-265 (2011)  
*PMID 21170474. Q1. IF 5.908. Programme 1*

New gene targets for glucagon-like peptide-1 during embryonic development and in undifferentiated pluripotent cells  
Sanz C, Blázquez E  
*Am J Physiol Endocrinol Metab*, 301, E494-503 (2011)  
*PMID 21712536. Q1. IF 4.686. Programme 1*

## Research grants

Efectos de los péptidos semejantes al glucagon GLP-1 y GLP-2 y otros péptidos anorexigénicos y orexigénicos sobre el metabolismo de la glucosa y el contenido de serotonina y su relector 1A en cerebro de rata  
Ministerio de Ciencia e Innovación, SAF2009-11297: 2010-2012  
Principal Investigator: Enrique Blázquez  
Associate investigators: M del Carmen Sanz Miguel, José Antonio Zueco Alegre, Luís García García, Pedro A Barrio Caballero  
*National project. Programme 1*

Programa de creación y consolidación de Grupos de Investigación UCM-Santander. Grupo Sensores cerebrales de glucosa, control de la saciedad, obesidad y diabetes tipo 2  
UCM-Santander, GR35/10A: 2011-2012  
Principal Investigator: Elvira Álvarez  
*National project. Programme 1*

Análisis de los mecanismos de regulación de la glucoquinasa y su implicación en diabetes  
PI10/00424  
Principal Investigator: María Ángeles Navas Hernández  
*National project. Programme 1*

Análisis de los mecanismos moleculares de regulación de proteínas implicadas en diabetes monogénicas  
Universidad Complutense-Comunidad de Madrid, CCG10-UCM/BIO-4728  
Principal Investigator: María Ángeles Navas Hernández  
*Autonomous Community project. Programme 1*

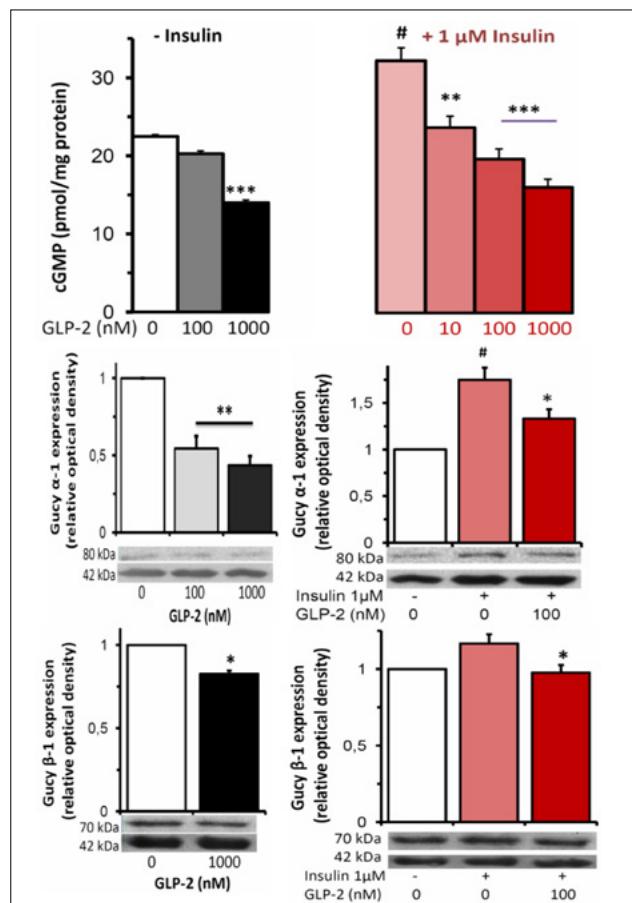
Caracterización del mecanismo neuroprotector de GLP-1 y GLP-2 en cerebro. Potencial aplicación de estos péptidos en enfermedades neurodegenerativas  
Fundación Médica Mutua Madrileña: 2008-2011  
Principal Investigator: Elvira Álvarez  
Associate investigators: E Blázquez, I Roncero, MC Sanz, E Velázquez, JM Ruiz, JA Zueco  
*Private funds. Programme 1*

Papel de peptidos anorexígenos sobre el metabolismo cerebral de glucosa y del receptor IA de serotonina en pacientes con anorexia y bulimia nerviosa u obesidad por atracón  
Fundación Médica Mutua Madrileña: 2007-2011  
Principal Investigator: Enrique Blázquez  
*Private funds. Programme 1*

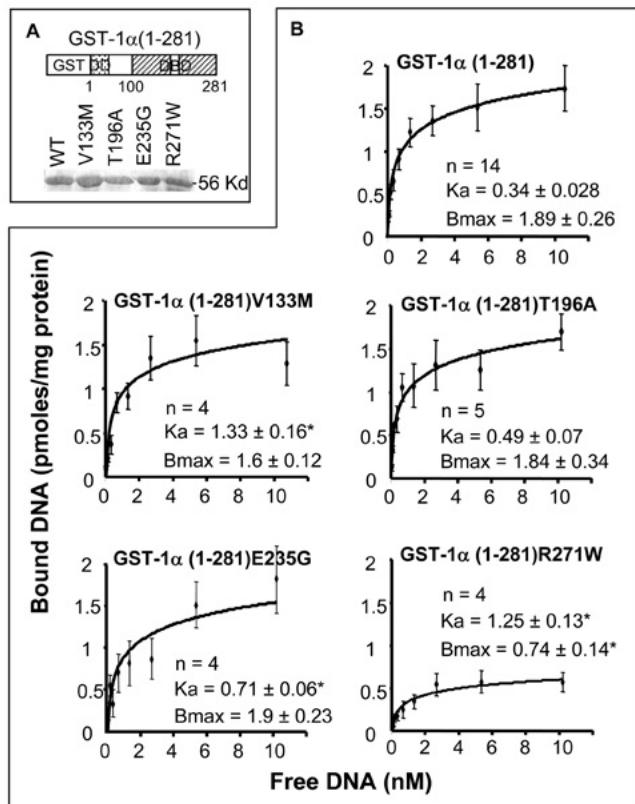
## Scientific collaborations within Ciberdem

The impact of overnutrition, diabetes-obesity, and undernutrition on the regulation of energy homeostasis in the central nervous system. From animal models to humans  
IODURE: 2009-2011  
Coordinator: Manuel Serrano Ríos  
Ciberdem groups: Blázquez E, Alvarez C, Serrano-Ríos M, Burks D, Vallejo M

Clinical, genetic and functional characterization of monogenic diabetes: from the bench to the bedside  
MODIAB: 2009-2011  
Coordinator: Luis Castaño  
Ciberdem groups: Blázquez E, Castaño L, Ferrer J, Vallejo M ■



The effect of GLP-2, insulin and insulin plus GLP-2 on cGMP production and on the expression of α1 and β1 subunits of the soluble guanylyl cyclase in cultured rat astrocytes.



The effect of HNF-1 $\alpha$ -MODY mutations on DNA binding: (A) Schematic representation of the GST fusion proteins containing mouse HNF-1 $\alpha$  amino acids 1 to 281 and SDS-PAGE of purified proteins. (B) Binding site titration experiments using GST fusion proteins GST-1 $\alpha$  (1-281) and specific radiolabelled probe. 2 ng of purified GST-1 $\alpha$  (1-281) proteins were incubated with a varying amount of radiolabelled oligonucleotide. GST-1 $\alpha$  (1-281)/DNA complexes were assayed by EMSA and quantified in a phosphorimager. Relative binding affinities ( $K_a$ ) and maximal binding ( $B_{max}$ ) for the mutant and wild type GST-1 $\alpha$  (1-281) proteins were calculated by using the Scatchard plot. Data indicate mean  $\pm$  SEM.  $K_a$  is given in nM;  $B_{max}$  is given in pmoles of DNA bound/mg of protein. N indicates number of independent experiments. (\*)  $p < 0.05$ .

# Transgenic animal models and gene therapy approaches for diabetes

Centre de Biotecnologia Animal i Teràpia Gènica, Universitat Autònoma de Barcelona  
<http://cbateg.uab.cat>



**Principal Investigator** Fàtima Bosch [fatima.bosch@uab.cat](mailto:fatima.bosch@uab.cat) **Associate researchers** Ana Carretero, Tura Ferré, Sylvie Franckhauser, Miquel García, Xavier Leon, Maria Molas, Sergio Antonio Muñoz, Víctor Nacher, Marc Navarro, Pedro José Otaegui, Anna Pujol, Martí Pumarola, Efren Riu, Jesús Ruberte, Virginia Haurigot **Postdoctoral fellows** Eduard Ayuso, Alba Casellas, Laia Vilà, Ricardo Lage, Ivet Elias, Verónica Jiménez **PhD students** David Callejas, Albert Ribera, Carles Roca, Pilar Villacampa, Meritxell Morró, Cristina Mallol, Iris Grifoll, Sara Marcó **Lab technician** Jennifer Barrero, Marta Moya, Mireia Zaguirre **Administrative staff** Montse Bellido

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Publications: 2

First decile: 1

Q1: 1

With other international groups: 1

Research grants: 13

European projects: 5

National projects: 7

Autonomous Community projects: 1

PhD theses: 1

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## Programmes

Programme 3. Impact of beta cell dysfunction and plasticity on the natural history of diabetes. Development of novel treatment strategies.

## Keywords

Beta-cell signal transduction. Gene therapy. Insulin sensitivity and resistance. Retinopathy.

## Main lines of research

- The study of the causes and pathophysiological mechanisms of diabetes mellitus using transgenic animal models.
- Analysis of the role of metabolic pathways in the development of insulin resistance and obesity, and the investigation of the molecular mechanisms involved in secondary complications (retinopathy, neuropathy).
- The development of new gene-therapy approaches for the treatment of diabetes mellitus based on:
  - a) the manipulation of skeletal muscle and the liver to

increase glucose uptake and  
b) engineering the endocrine pancreas in vivo to regenerate beta-cell mass.

### Publications

In vivo genetic engineering of murine pancreatic beta cells mediated by single-stranded adeno-associated viral vectors of serotypes 6, 8 and 9  
Jimenez V, Ayuso E, Mallol C, Agudo J, Casellas A, Obach M, Muñoz S, Salavert A, Bosch F  
*Diabetologia*, 54, 1075-1086 (2011)  
*PMID 21311856*. 1st decile. IF 6.973. Programme 3

Protein kinase C delta (PKC $\delta$ ) affects proliferation of insulin-secreting cells by promoting nuclear extrusion of the cell cycle inhibitor p21Cip1/WAF1  
Ranta F, Leveringhaus J, Theilig D, Schulz-Raffelt G, Hennige AM, Hildebrand DG, Handrick R, Jendrossek V, Bosch F, Schulze-Osthoff K, Häring HU, Ullrich S  
*PLoS ONE*, 6, e28828 (2011)  
*PMID 22216119*. Q1. IF 4.411. With other international groups. Programme 3

### Research grants

Identification of the genes regulated by the SIRT1 histone deacetylase and their contribution in the pathogenesis of type 2 diabetes and obesity  
EU, Marie Curie International Reintegration Grant, MIRGCT-2007-207745: 2008-2012  
Principal Investigator: Efrén Riu  
*European project. Programme 3*

Analysis of a new pathway to import iron into the retina: role of ferritin as iron carrier and implications in radical detoxification  
FCT Fundação para a ciéncia e a tecnologia. Ministério da ciéncia, tecnologia e ensino superior Portugal, PTDC/SAU-ORG/110856/2009: 2011-2014  
Principal Investigator: Jesús Ruberte  
*European project. Programme 3*

INFRAFRONTIER. The European Infrastructure for phenotyping, archiving and dissemination of disease models  
EU, European Strategy Forum on Research Infrastructures, FP7-INFRA-STRUCTURES-2007-1: 2008-2011  
Principal Investigator: Fàtima Bosch  
Coordinator: Martin Hrabé d'Angelis  
*European project. Programme 3*

EUMODIC. The European Mouse Disease Clinic. A distributed phenotyping resource for studying human disease  
EU, Integrated Project FP6-2005-LIFESCIHEALTH-6, LSHGCT-2006-037188: 2007-2011

Principal Investigator: Fàtima Bosch  
Coordinator: Steve Brown  
*European project. Programme 3*

CLINIGENE. European Network for the Advancement of Clinical Gene Transfer and Therapy  
EU, Network of Excellence, FP6-2004-LIFESCIHEALTH-5, LSHB-CT-2006-018933: 2006-2011  
Principal Investigator: Fàtima Bosch  
Coordinator: Odile Cohen-Haguenauer  
*European project. Programme 3*

Atlas morfológico para el fenotipado de ratones mutantes  
Ministerio de Ciencia e Innovación, SAF2008-0581-E: 2009-2011  
Principal Investigator: Jesús Ruberte  
*National project. Programme 3*

Estudio del efecto de la deacetilación de cromatina por miembros de la familia de las sirtuinas en la patogénesis de la resistencia a la insulina y diabetes tipo 2  
Ministerio de Ciencia e Innovación, SAF2008- 03083: 2009-2011  
Principal Investigator: Efrén Riu  
*National project. Programme 3*

Estudio del papel de los factores de crecimiento similares a la insulina en la regeneración de la célula  $\beta$  pancreática  
Ministerio de Educación y Ciencia, SAF2008-00962: 2009-2011  
Principal Investigator: Fàtima Bosch  
*National project. Programme 3*

Desarrollo de vectores adeno-asociados (AAV) para la terapia neuroprotectora en enfermedades degenerativas de la retina  
Proyectos TRACER, Ministerio de Ciencia e Innovación en colaboración con ProRetina Therapeutics SL, PET2008\_0282\_02: 2009-2011  
Principal Investigators: Enrique de la Rosa, Fàtima Bosch  
*National project. With other CIBERs: Ciberer. Programme 3*

Senescencia celular en los vasos sanguíneos de la retina: implicaciones de P16 en el cross-linking enzimático del colágeno de la membrana basal durante el envejecimiento  
ISCIII, PS09/01152: 2010-2013  
Principal Investigator: Jesús Ruberte  
*National project. Programme 3*

Generación de una librería AAV-CRE para la obtención de ratones mutantes condicionales  
Ministerio de Educación y Ciencia, SAF2010-10507-E: 2011-2012

Principal Investigator: Fàtima Bosch  
*National project. Programme 3*

Equipamiento para la producción de vectores de terapia  
génica a gran escala

Ministerio de Educación y Ciencia, Infraestructura  
Científico-Tecnológica, UNAB10-4E-156: 2011-2013

Principal Investigator: Fàtima Bosch  
*National project. Programme 3*

Ajut per a grups de recerca consolidats

Agència de Gestió d'Ajuts Universitaris i de Recerca  
(AGAUR), Generalitat de Catalunya, SGR 224: 2009-2013

Principal Investigator: Fàtima Bosch  
*Autonomous Community project. Programme 3*

#### PhD theses

AAV-mediated genetic engineering of the pancreas and  
adipose tissue for the study and treatment of diabetes  
and obesity

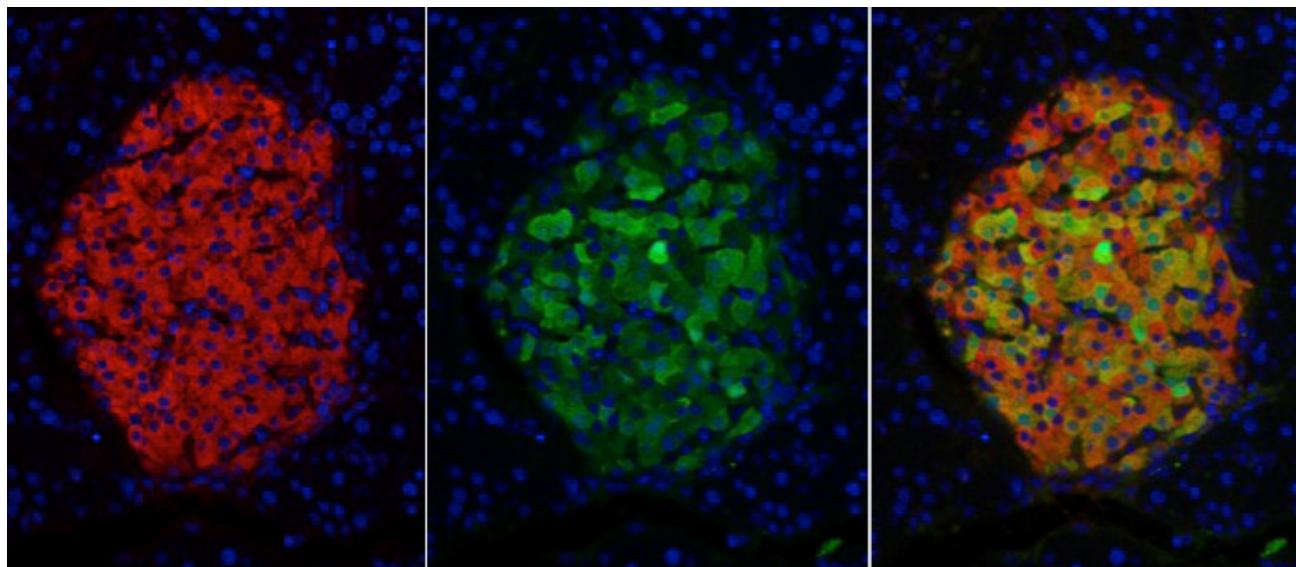
Author: Verónica Jiménez Cenzano

Thesis advisor: Fàtima Bosch

University: Universitat Autònoma de Barcelona

Thesis defense date: December 15, 2011

*Programme 3 ■*



Transduction of beta cells by AAV vectors delivered intraductally: Immunohistochemical analysis of insulin (A), GFP (B) and merged (C) in islets of mice injected intraductally with  $3 \times 10^{12}$  vg of AAV8 encoding the GFP reporter gene driven by the CAG ubiquitous promoter. Animals were analysed 1 month after injection. Original magnification 400x.

# Laboratory of Molecular Endocrinology

Centro de Investigación Príncipe Felipe, Valencia  
[www.cipf.es](http://www.cipf.es)



**Principal Investigator** Deborah Burks [dburks@cipf.es](mailto:dburks@cipf.es) **Postdoctoral fellows** Silvia Sanz, Carlos Acosta, Luke Noon, Cristina Fuente **PhD students** Juan Martín Aldana, Verónica Moreno, Richard Griffeth **Lab technician** Arantxa Leal

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Publications: 1

First decile: 1

Research grants: 4

European projects: 2

National projects: 2

Scientific collaborations within Ciberdem: 2

PhD theses: 1

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## Programmes

Programme 3. Impact of beta cell dysfunction and plasticity on the natural history of diabetes. Development of novel treatment strategies.

## Keywords

Beta-cell signal transduction. Insulin sensitivity and resistance. Islet degeneration and damage. Retinopathy. Obesity.

## Main lines of research

- Regulation of the cell-cycle in pancreatic beta cells.
- The role of IRS-2 signals in the differentiation of human pluripotent stem cells to progenitors of pancreas and liver.
- IRS-2 signalling in the regulation of neuronal function.
- The role of insulin/IGF-I signalling in diabetic retinopathy.
- The role of IRS2 in adipocyte progenitors and development of obesity.

## Publications

Differential sensitivity to adrenergic stimulation underlies the sexual dimorphism in the development of diabetes caused by Irs-2 deficiency

Garcia-Barrado MJ, Iglesias-Osma MC, Moreno-Viedma V, Pastor Mansilla MF, Gonzalez SS, Carretero J, Moratinos J, Burks DJ  
Biochem Pharmacol, 81, 279-288 (2011)  
[PMID 20959116. 1st decile. IF 4.889. Programme 3](https://pubmed.ncbi.nlm.nih.gov/20959116/)

### **Research grants**

LIVES: Development of culture conditions for the differentiation of hES cells to hepatocytes  
European Commission, Seventh Framework Programme,  
FP7-HEALTH-2007-B: 2009-2011  
Principal Investigator: Deborah Burks  
Coordinator: Anne Weber  
*European project. Programme 3*

Innovative strategies to generate human hepatocytes  
FP7, InnovaLIV: 2011-2014  
Principal Investigator: Deborah Burks  
*European project. Programme 3*

Análisis de la vía de señalización insulina/IRS-2 como un link molecular entre metabolismo diabético y neurodegeneración  
Ministerio de Educación y Ciencia, SAF2008-00011:  
2009-2011  
Principal Investigator: Deborah Burks  
*National project. Programme 3*

El papel de IRS-2 en la regeneración del páncreas endocrino  
ISCIII, Programa de Estabilización del Grupo EMER07/012:  
2007-2011  
Principal Investigator: Deborah Burks  
*National project. Programme 3*

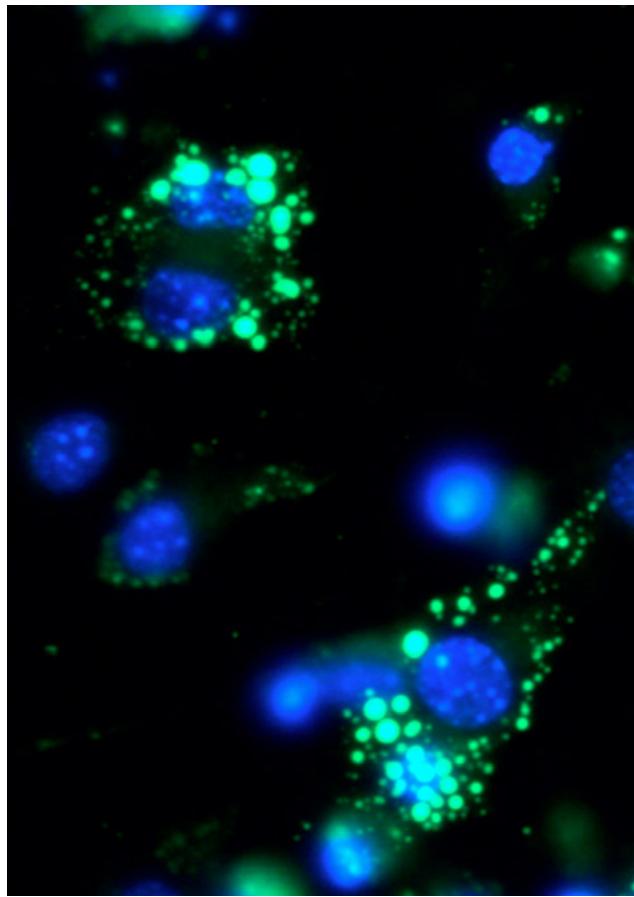
### **Scientific collaborations within Ciberdem**

Identification of neurodegenerative mechanisms that promote the development of diabetic retinopathy: the role of insulin signalling and apoptosis  
NEURONET-DIAB: 2009-2011  
Coordinator: Deborah Burks  
*Ciberdem groups: Burks D, Valverde AM, Simó R*

The impact of overnutrition, diabetes-obesity, and undernutrition on the regulation of energy homeostasis in the central nervous system. From animal models to humans  
IODURE: 2009-2011  
Coordinator: Manuel Serrano Ríos  
*Ciberdem groups: Burks D, Alvarez C, Blázquez E, Serrano-Ríos M, Vallejo M*

### **PhD theses**

Relación entre la señalización por insulina/IGF-1 vía IRS2 y la respuesta al daño en el ADN  
Author: Juan Martín Aldana  
Thesis advisor: Deborah Burks  
University: Universidad de Valencia  
Thesis defense date: December 16, 2011  
*Programme 3 ■*



Adipocyte progenitors in early stages (day 4) of differentiation as revealed by the accumulation of lipids. Nuclei are marked with DAPI (blue) and lipid droplets with BODIPY (green).

# Dyslipidaemia, inflammation and endothelial dysfunction

Servicio de Endocrinología y Nutrición, Fundación Investigación Hospital Clínico Universitario de Valencia  
[www.incliva.es](http://www.incliva.es)



**Principal Investigator** Rafael Carmena [rafael.carmena@uv.es](mailto:rafael.carmena@uv.es) **Associate researchers** Juan Francisco Ascaso, Miguel Catalá, Felipe Javier Chaves, Sergio Martínez Hervás, José Tomás Real **Postdoctoral fellows** Ana Bárbara García, Marta Peiró **Lab manager** Sebastián Blesa **Lab technicians** Esther Benito, Nieves Brito

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Publications: 6

Q1: 4

Q2: 2

With other Ciberdem groups: 2

With other CIBERs: 5

Research grants: 6

European projects: 1

National projects: 1

Autonomous Community projects: 2

Private funds: 2

Scientific collaborations within Ciberdem: 4

Clinical trials: 1

Clinical practice guidelines: 1

PhD theses: 1

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## Programmes

Programme 1. Molecular and physiological determinants of lifestyle in diabetes/obesity. Population studies for genetic-

epigenetic association analysis in type 2 diabetes mellitus and related traits.

## Keywords

Insulin sensitivity and resistance. Lipid metabolism. Macrovascular disease. Metabolic syndrome.

## Main lines of research

The degree of arterial damage and age of onset of arteriosclerosis varies in patients with primary dyslipidaemias or diabetes, indicating the existence of other contributing factors. We have investigated the role of oxidative stress (OS), inflammation, insulin resistance, and prediabetic states as possible candidates.

Our research lines include: primary hyperlipidaemias-genetic diagnosis and cardiovascular risk; primary mixed hyperlipidaemias-insulin resistance and diabetes mellitus; postprandial lipidaemia and arteriosclerosis in insulin-

resistant states; insulin resistance, inflammation and oxidative stress; diabetic foot – diagnosis, prevention and treatment; and genetic factors regulating BMI and abdominal obesity.

## Publications

Dietary polyunsaturated fatty acids may increase plasma LDL-cholesterol and plasma cholesterol concentrations in carriers of an ABCG1 gene single nucleotide polymorphism: study in two Spanish populations  
Abellán R, Mansego ML, Martínez-Hervás S, Morcillo S, Pineda-Alonso M, Carmena R, Real JT, Redon J, Rojo-Martínez G, Martín-Escudero JC, Chaves FJ  
*Atherosclerosis*, 219, 900-906 (2011)

PMID 21978921. Q1. IF 4.086. With other Ciberdem groups:  
Soriguer F. With other CIBERs: Ciberobn. Programme 1

Different impacts of cardiovascular risk factors on oxidative stress

Mansego ML, Redon J, Martínez-Hervás S, Real JT, Martínez F, Blesa S, González-Albert V, Saez GT, Carmena R, Chaves FJ  
*Int J Mol Sci*, 12, 6146-6163 (2011)

PMID 22016650. Q2. IF 2.279. With other CIBERs: Ciberobn. Programme 1

ELOVL6 genetic variation is related to insulin sensitivity: a new candidate gene in energy metabolism

Morcillo S, Martín-Núñez GM, Rojo-Martínez G, Almaraz MC, García-Escobar E, Mansego ML, de Marco G, Chaves FJ, Soriguer F  
*PLoS ONE*, 6, e21198 (2011)

PMID 21701577. Q1. IF 4.411. With other Ciberdem groups:  
Soriguer F. Programme 1

Inefficient arterial hypertension control in patients with metabolic syndrome and its link to renin-angiotensin-aldosterone system polymorphisms

Morales-Suárez-Varela MM, Mansego ML, Vicedo-Cabrera AM, Pineda-Alonso M, Llopis-González A, Martín-Moreno JM, Martín-Escudero JC, Chaves FJ  
*Hypertens Res*, 34, 758-766 (2011)

PMID 21471972. Q2. IF 2.353. With other CIBERs: Ciberesp, Ciberobn. Programme 1

Polymorphisms of antioxidant enzymes, blood pressure and risk of hypertension

Mansego ML, Solar Gde M, Alonso MP, Martínez F, Sáez GT, Escudero JC, Redón J, Chaves FJ  
*J Hypertens*, 29, 492-500 (2011)

PMID 21178785. Q1. IF 3.980. With other CIBERs: Ciberobn. Programme 1

Reduced penetrance of autosomal dominant hypercholesterolemia in a high percentage of families:

importance of genetic testing in the entire family  
García-García AB, Ivorra C, Martínez-Hervás S, Blesa S, Fuentes MJ, Puig O, Martín-de-Llano JJ, Carmena R, Real JT, Chaves FJ  
*Atherosclerosis*, 218, 423-430 (2011)  
PMID 21868016. Q1. IF 4.086. With other CIBERs: Ciberobn. Programme 1

## Research grants

Markers for Subclinical CArdiovascular Risk Assessment HEALTH 2011.2.4.2-2, EU-MASCARA: 2011-2015  
Principal Investigator: Josep Redon i Mas  
European project. Programme 1

Perfil de expresión de ARN en linfomonocitos tras sobrecarga oral con grasa insaturada en dos modelos con resistencia a la insulina: obesidad abdominal y diabetes tipo 2  
ISCIII, PI10/00511: 2011-2013  
Principal Investigator: Juan F. Ascaso  
National project. Programme 1

Mutaciones en SREBP2 como posible causa de diabetes mellitus: identificación, estudio poblacional y funcional  
Conselleria de Sanidad de la Generalitat Valenciana, AP-091/11: 2011  
Principal Investigator: Felipe Javier Chaves  
Autonomous Community project. Programme 1

Estudio de los factores implicados en el desarrollo de enfermedades de alto riesgo cardiovascular y sus complicaciones  
Conselleria de Educación de la Generalitat Valenciana, PROMETEO 2009/029: 2009-2012  
Principal Investigator: Rafael Carmena  
Autonomous Community project. Programme 1

Implicación funcional de SREBP2 en el metabolismo de la glucosa  
Fundación Incliva: 2011-2012  
Principal Investigator: Ana Bárbara García  
Private funds. Programme 1

Asociación de los niveles plasmáticos de vitamina D con el desarrollo de arteriosclerosis, y su modulación por polimorfismos en el gen del receptor de la vitamina D  
Fundación Incliva: 2011-2012  
Principal Investigator: Sergio Martínez Hervás  
Private funds. Programme 1

## Scientific collaborations within Ciberdem

Cooperative population and database studies for genetic association analysis in T2DM and related traits  
INGENFRED: 2009-2011  
Coordinator: Felipe Javier Chaves

*Ciberdem groups: Carmena R, Blanco-Vaca F, Serrano-Ríos M, Soriguer F*

*Di@bet.es Study: 1st epidemiological study of the prevalence of type 2 diabetes in Spain*

*Coordinator: Federico Soriguer*

*Ciberdem groups: Carmena R, Soriguer F, Castaño L, Gomis R, Serrano-Ríos M, Vendrell J*

*Telemed-diabetes Study*

*Coordinator: Enric Esmatjes*

*Ciberdem groups: Carmena R, Gomis R, Serrano-Ríos M, Soriguer F, Castaño L*

*Ciberdem Biobank*

*Coordinator: Anna Novials*

*Ciberdem Biobank nodes: Carmena R, Gomis R, Novials A, Vendrell J, Masana L, Castaño L, Serrano-Ríos M, Soriguer F, Blanco-Vaca F*

### **Clinical trials**

*Cardiovascular Fixed CombinationPill ASR: Ensayo Clínico farmacodinámico de la combinación de dosis fijas de ácido*

acetilsalicílico, simvastatina y ramipril (Cardiovascular Polypill). Colesterol LDL

2010-019720-32: 2011

*Coordinator: Juan F Ascaso  
Programme 1*

### **Clinical practice guidelines**

*Protocolos de Endocrinología y Nutrición*

*Real JT, Ampudia-Blasco J, Ascaso JF (editors)*

*Servicio de Endocrinología y Nutrición, HCU, Valencia, ed Menta, p 1-397, DL V-3007-2011 (2011)*

*Programme 1*

### **PhD theses**

Efecto de la sobrecarga oral con grasa insaturada sobre los marcadores de estrés oxidativo e inflamación. Estudios de lipemia postprandial en sujetos con hipercolesterolemia familiar heterocigota

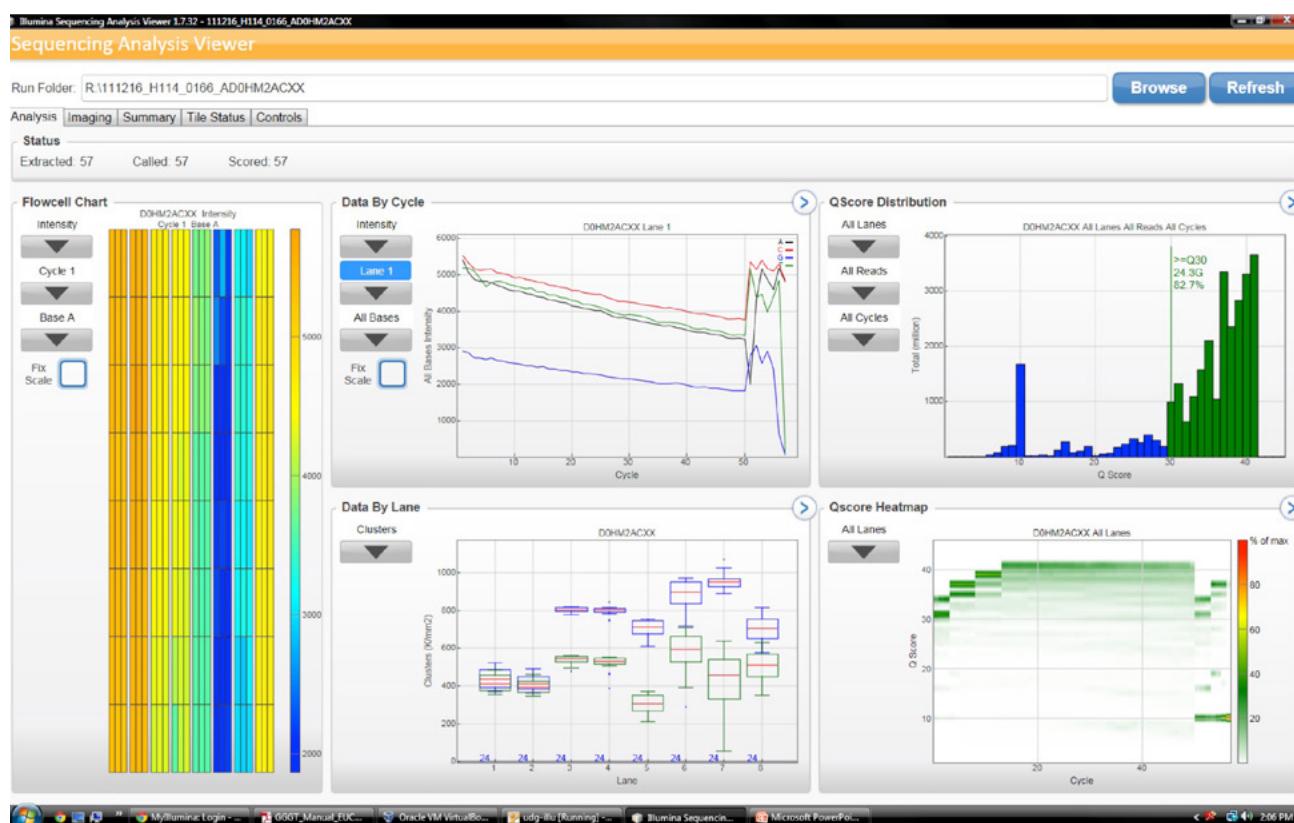
*Author: Teresa Pedro Font*

*Thesis advisor: Rafael Carmena*

*University: Universidad de Valencia*

*Thesis defense date: November 21, 2011*

*Programme 1 ■*



Preliminary sequencing experiments with HiScanSQ (Illumina) including different kinds of libraries and samples (microRNAs, mRNAs and exomes).

# Hospital Universitario Cruces Diabetes Research Group

Hospital Universitario Cruces, UPV-EHU, Barakaldo  
[www.hospitalcruces.com](http://www.hospitalcruces.com)



**Principal Investigator** Luis Castaño [lcastano@osakidetza.net](mailto:lcastano@osakidetza.net) **Associate researchers** María Ángeles Añel Quiroga, José Ramón Bilbao, María Ángeles Busturia, Alicia Cortázar, Sonia Gaztambide, Itxaso Rica, Federico Vázquez, Amaia Vela **Postdoctoral fellows** Rosa María Martínez, Miriam Ramírez, Sonsoles Morcillo, Anibal Aguayo **Research assistant** Inés María Urrutia **PhD students** Oihana Belar, Teba González, Tamara López, Leticia Plaza, Nora Fernández, Jesús Pérez Cámara **Lab managers** Galder Gutiérrez, Gustavo Pérez de Nanclares **Nurse** Alicia Cobo, Javier Rioja **Administrative staff** Sorkunde Rivero

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Publications: 1

First decile: 1

With other international groups: 1

Research grants: 7

International projects: 1

National projects: 2

Autonomous Community projects: 4

Scientific collaborations within Ciberdem: 4

Clinical trials: 5

Clinical practice guidelines: 2

PhD theses: 2

Awards: 2

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## Programmes

Programme 3. Impact of beta cell dysfunction and plasticity

on the natural history of diabetes. Development of novel treatment strategies.

## Keywords

Clinical diabetes. Genetics type 1 diabetes. Monogenic diabetes. Oral pharmacological agents. Prediction/prevention of type 1 diabetes.

## Main lines of research

-The identification of additional genetic susceptibility markers for type 1 diabetes and related autoimmune disorders in the extended MHC (6p21) and other regions using high throughput genotyping.

-The study of immune mediators of disease development, characterization of novel autoantigens/antibodies and cell populations in patients: Th1, Th2 and Th17 responses.

- The identification of new genes responsible for monogenic diabetes by genome wide analysis (both CGI and CGH approaches).
- The molecular and clinical characterization of monogenic diabetes and new therapeutic strategies for KATP channel alterations.
- The prediction and prevention of type 1 diabetes.
- The control of diabetes complications.
- The epidemiology of diabetes.

## Publications

The Trial to Reduce IDDM in the Genetically at Risk (TRIGR) study: recruitment, intervention and follow-up  
 TRIGR Study Group, Akerblom HK, Krischer J, Virtanen SM, Berseth C, Becker D, Dupré J, Ilonen J, Trucco M, Savilahti E, Koski K, Pajakkala E, Fransiscus M, Lough G, Bradley B, Koski M, Knip M  
*Diabetologia*, 54, 627-633 (2011)  
[PMID 21153533](#). 1st decile. IF 6.973. With other international groups. Programme 3

## Research grants

Trial to reduce IDDM in children at genetic risk. TRIGR  
 National Institutes of Health, 5U01HD040364-08: 2007-2011  
 Principal Investigator: Castaño L  
 Coordinator: Akerblom H  
 Associate investigators: Martul P, Bilbao JR, Rica I  
*International project. With other Ciberdem groups: Serrano-Ríos M. Programme 3*

Diabetes Neonatal y de comienzo precoz: Caracterización molecular y fenotipo  
 Ministerio de Sanidad y Consumo-ISCIII, PS09/01492: 2010-2012  
 Principal Investigator: Castaño L  
 Associate investigators: Fernández Ramos C, Busturia MA, Rica I, Martínez R, Rodríguez A, Blarduni E, Chueca M, Oyarzabal M  
*National project. Programme 3*

Biología de sistemas de la autoinmunidad: la Enfermedad Celíaca como modelo  
 ISCIII, PI10/00310: 2011-2014  
 Principal Investigator: Bilbao JR  
*National project. Programme 3*

Etiopatogenia de los trastornos autoinmunes: Diabetes mellitus tipo 1 y Enfermedad Celíaca  
 Departamento de Educación - Gobierno Vasco, IT-472-07: 2007-2012  
 Principal Investigator: Castaño L  
 Associate investigators: Vitoria JC, Gaztambide S, Bilbao JR  
*Autonomous Community project. Programme 3*

Detección precoz y cribado poblacional de Diabetes en el

Pais Vasco. Prevalencia de Diabetes en Euskadi  
 Departamento de Sanidad y Consumo. Gobierno Vasco, 2010111058: 2011-2014  
 Principal Investigator: Gaztambide S  
*Autonomous Community project. Programme 3*

Epidemiología de la Diabetes en el País Vasco  
 Departamento de Sanidad y Consumo. Gobierno Vasco, 2009COM11: 2009-2011  
 Principal Investigator: Castaño L  
*Autonomous Community project. Programme 3*

Caracterización clínica y molecular de la diabetes monogénica (neonatal y de comienzo precoz).  
 Implicaciones terapéuticas  
 Departamento de Sanidad y Consumo. Gobierno Vasco, 2010111185: 2011-2014  
 Principal Investigator: Castaño L  
*Autonomous Community project. Programme 3*

## Scientific collaborations within Ciberdem

Clinical, genetic and functional characterization of monogenic diabetes: from the bench to the bedside  
 MODIAB: 2009-2011  
 Coordinator: Luis Castaño  
*Ciberdem groups: Castaño L, Blázquez E, Ferrer J, Vallejo M*

Di@bet.es Study: 1st epidemiological study of the prevalence of type 2 diabetes in Spain  
 Coordinator: Federico Soriguer  
*Ciberdem groups: Castaño L, Soriguer F, Carmena R, Gomis R, Serrano-Ríos M, Vendrell J*

## Telemed-diabetes Study

Coordinator: Enric Esmatjes  
*Ciberdem groups: Castaño L, Carmena R, Gomis R, Serrano-Ríos M, Soriguer F*

## Ciberdem Biobank

Coordinator: Anna Novials  
*Ciberdem Biobank nodes: Castaño L, Gomis R, Novials A, Vendrell J, Masana L, Serrano-Ríos M, Soriguer F, Carmena R, Blanco-Vaca F*

## Clinical trials

Estudio aleatorizado, controlado frente a placebo, doble ciego, paralelo y multicéntrico para evaluar antagonistas de IL-1 en sujetos con diabetes tipo 1 de reciente diagnóstico  
 EudraCT 2007-007146-34: 2009-2011  
 Coordinator: Sonia Gaztambide  
*Programme 3*

Impacto en el control glucémico de intensificar la terapia insulínica como propone el consenso ADA/EASD, con insulina glargina como insulina basal mas una dosis diaria

de insulina glulisina en la comida principal: Estrategia Basal Plus en la vida real  
APIDR\_L\_05094: 2010-2011  
Coordinator: Sonia Gaztambide  
*Programme 3*

Estudio multicéntrico, doble ciego, aleatorizado, controlado con placebo y de grupos paralelos, para evaluar los eventos cardiovasculares durante el tratamiento con lixisenatide en pacientes con diabetes tipo 2 después de un Síndrome Coronario Agudo. Estudio ELIXA  
NCT01147250: 2011-2016  
Coordinator: Sonia Gaztambide  
*Programme 3*

A phase III 3 arm randomized double-blind placebo controlled multicenter study to investigate the impact of Diamyd on the progression of diabetes in patients newly diagnosed with type 1 diabetes mellitus  
D/P3/07/4: 2008-2011  
Coordinators: Luis Castaño (Spain), J Ludvigsson (International)  
*Programme 3*

Estudio multicéntrico, internacional, aleatorizado y de diseño factorial 2x2, para evaluar los efectos de lantus (insulina glargina) frente al tratamiento estándar, y de los ácidos grasos omega3 frente a placebo, en la reducción de la morbilidad y la mortalidad cardiovascular en sujetos de alto riesgo con alteración de la glucosa en ayunas, disminución de la tolerancia a la glucosa o diabetes mellitus de tipo 2 en fase inicial. Ensayo ORIGIN  
HOE9901/4032ORIGIN: 2004-2011  
Coordinator: Sonia Gaztambide  
*Programme 3*

#### Clinical practice guidelines

Urgencias Pediátricas: Diagnóstico y Tratamiento  
FJ Benito y cols  
5th edition, p 611-622, ISBN 9788498353563 (2011)  
*Programme 3*

Insulinas: Nuevas opciones para optimizar el tratamiento de la Diabetes Mellitus  
Aguilera E, Gaztambide S, Agullo E, Gonzalo MA, Calvo F, Lara JI, Conget I, Puig M, Duran S, Rovira A, Tinahones FJ, Faure E, Vázquez F, Fernández-García JC  
Diabetomecum, ed Permanyer, ISBN 9788499262529 (2011)  
*Programme 3*

#### PhD theses

Búsqueda de nuevos genes implicados en la Diabetes Monogénica  
Author: Intza Garin Elcoro

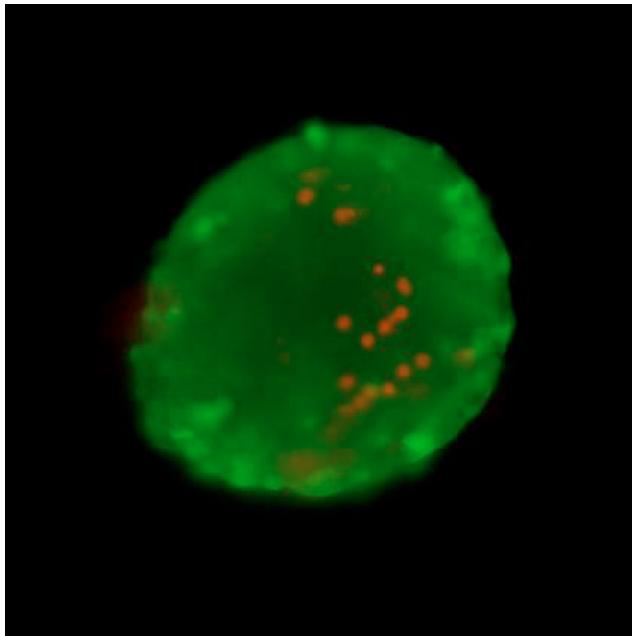
Thesis advisor: Guiomar Pérez de Nanclares  
University: UPV/EHU  
Thesis defense date: January 17, 2011  
*Programme 3*

Prevalencia del Síndrome Metabólico en una población de niños obesos en el País Vasco. Su relación con la resistencia a la Insulina, las Adipoquinas y Ghrelina  
Author: Anibal Agustín Aguayo Calcena  
Thesis advisor: Amaia Vela  
University: UPV/EHU  
Thesis defense date: March 4, 2011  
*Programme 3*

#### Awards

Premio a la Mejor Comunicación Clínica XIV Congreso SEDyNE (Sociedad de Endocrinología, Diabetes y Nutrición de Euskadi) (2011)  
Awardee: Luis Castaño  
*Programme 3*

Primer Premio en la III Edición Premios Osakidetza a la Innovación en Gestión (2011)  
Awardee: Luis Castaño  
*Programme 3* ■



Estimation of viability of mouse pancreatic islets isolated by hand-picking by inclusion and exclusion dyes. Green cells are viable cells dyed with FDA. Red cells stained with PI are dead cells. The picture was taken at 20x by a Fluorescence Inverted Microscope.

# Metabolomics Platform

Universitat Rovira i Virgili, Institut d'Investigació Sanitària Pere Virgili, Tarragona  
[www.metabolomicsplatform.com](http://www.metabolomicsplatform.com)



**Principal Investigator** Xavier Correig [xavier.correig@urv.cat](mailto:xavier.correig@urv.cat) **Coordinator** Oscar Yanes **Associate researchers** Jesús Brezmes, Nicolau Cañellas **Research assistants** Miguel Ángel Rodríguez, Maria Vinaixa, Antoni Beltran **PhD students** Roger Mallol, Sara Samino, Núria Amigó, Josep Gómez **Administrative staff** Serena Pujol

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Publications: 4

First decile: 2

Q1: 1

Q2: 1

With other Ciberdem groups: 3

With other international groups: 1

Research grants: 3

National projects: 3

Scientific collaborations within Ciberdem: 2

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## Programmes

Programme 1. Molecular and physiological determinants of lifestyle in diabetes/obesity. Population studies for genetic-epigenetic association analysis in type 2 diabetes mellitus and related traits.

## Keywords

Metabolomics. Retinopathy. Biomarkers and imaging.

## Main lines of research

- NMR lipoprotein characterization for the study of dyslipidaemias.
- A serum profiling method for the study of insulin resistance and diabetes in population studies.
- The development and study of advanced statistical, chemometric, multivariate and artificial intelligence algorithms which will allow large measurement datasets.
- Non-radioactive isotopomers for the study of metabolic profiling and its flux in cultured cells and animal models.
- The study of diabetic retinopathy.
- The study of tissue imaging with NIMS (Nanostructure Initiator Mass Spectrometry).

## Publications

AStream: an R package for annotating LC/MS metabolomic data  
Alonso A, Julià A, Beltran A, Vinaixa M, Díaz M, Ibañez L,

Correig X, Marsal S

Bioinformatics, 27, 1339-1340 (2011)

PMID 21414990. 1st decile. IF 4.877. With other Ciberdem groups: Ibáñez L. Programme 4

Expanding coverage of the metabolome for global metabolite profiling

Yanes O, Tautenhahn R, Patti GJ, Siuzdak G

Anal Chem, 83, 2152-2161 (2011)

PMID 21329365. 1st decile. IF 5.874. With other international groups. Programme 1

Metabolomics reveals reduction of metabolic oxidation in women with polycystic ovary syndrome after pioglitazone-flutamide-metformin polytherapy

Vinaixa M, Rodriguez MA, Samino S, Diaz M, Beltran A,

Mallol R, Bladé C, Ibáñez L, Correig X, Yanes O

PLoS ONE, 6, e29052 (2011)

PMID 22194988. Q1. IF 4.411. With other Ciberdem groups:

Ibáñez L. Programme 4

Surface fitting of 2D diffusion-edited  $^1\text{H}$  NMR spectroscopy data for the characterisation of human plasma lipoproteins

Mallol R, Rodríguez MA, Heras M, Vinaixa M, Cañellas N,

Brezmes J, Plana N, Masana L, Correig X

Metabolomics, 7, 572-582 (2011)

DOI 10.1007/s11306-011-0273-8. Q2. IF 3.608. With other Ciberdem groups: Masana L. Programme 2

### Research grants

Neurodegeneración en la patogénesis de la retinopatía diabética incipiente. Estudio de los mecanismos implicados a través de un abordaje integrado de biología de sistemas

Ministerio de Ciencia e Innovación, SAF 2009-07408: 2009-2011

Principal Investigator: Rafael Simó

Associate investigator: Miguel Ángel Rodríguez

National project. With other Ciberdem groups: Simó R.  
Programme 2

Dislipemia aterógena de la obesidad, síndrome metabólico y diabetes tipo 2: caracterización metabólica y mecanismos patogénicos

FIS, PI081409: 2009-2012

Principal Investigator: Lluís Masana

Associate investigator: Jesús Brezmes

National project. With other Ciberdem groups: Masana L.  
Programme 2

Caracterización bioquímica, metabólica y genética de la hipertrigliceridemia asociada a alto riesgo cardiovascular

FIS, PI081579: 2009-2012

Principal Investigator: Josep Ribalta

Associate investigator: Nicolau Cañellas

National project. With other Ciberdem groups: Masana L.  
Programme 2

### Scientific collaborations within Ciberdem

Determinants of insulin resistance and glucose tolerance disorders, including diabetes, in severe obesity and their changes after bariatric surgery-induced weight loss

DIASOBS: 2009-2011

Coordinator: Héctor F Escobar Morreale

Ciberdem groups: Correig X, Montaña E, Escobar-Morreale HF, Simó R, Vendrell J

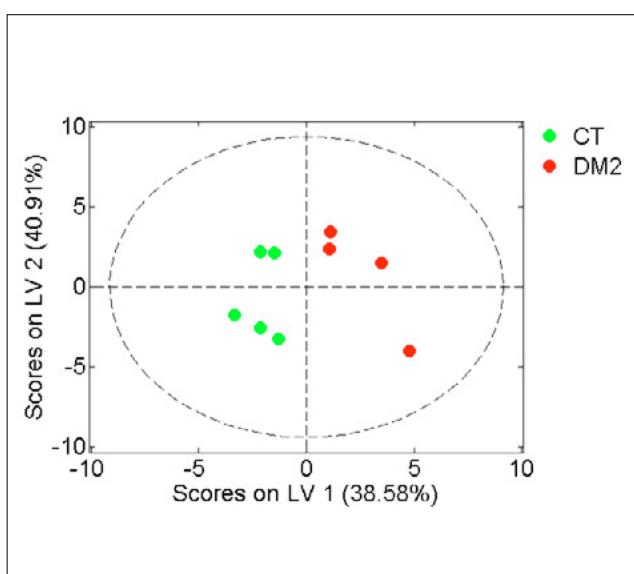
Comparative metabolomic analysis for the detection of biomarkers in diabetes

METADIAB: 2009-2011

Coordinator: Xavier Correig

Ciberdem groups: Correig X, Gomis R, Novials A ■

For more information see page 29.



Clustering of HDL fractions from normal and type 2 diabetic subjects using NMR-derived information.

# Proinsulin and tyrosine hydroxylase/dopamine effects in cardiac development

Centro de Investigaciones Biológicas, Consejo Superior de Investigaciones Científicas, Madrid  
[www.cib.csic.es](http://www.cib.csic.es)



**Principal Investigator** Flora de Pablo [fdepablo@cib.csic.es](mailto:fdepablo@cib.csic.es) **Associate researcher** Catalina Hernández **Postdoctoral fellow** Patricia Vázquez **Lab technician** Cayetana Murillo

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Research grants: 1

National projects: 1

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## Programmes

Programme 2. Mechanisms promoting the development of diabetes and its vascular complications. Associated disorders and co-morbidities. Strategies for prevention and treatment.

## Keywords

Proinsulin. Islet development. Insulin action. Cardiac complications.

## Main lines of research

-To explore whether higher than physiological embryonic expression of proinsulin has deleterious consequences during morphogenesis of the heart in a maternally independent model of development. The data show that

inappropriately high proinsulin (which may occur in obese and type 2 diabetic pregnancies) leads to abnormal cardiac-specific gene expression and major heart malformations.

-To characterize tyrosine hydroxylase (TH) expression pattern in mouse pancreas development, the analysis of TH function by studying pancreatic cell markers in TH-/ developing mice, and the effects of dopamine in embryonic pancreas explants. TH appears to be required to yield a normal number of beta cells in mice. Dopamine increases insulin expression in developing pancreas explants.

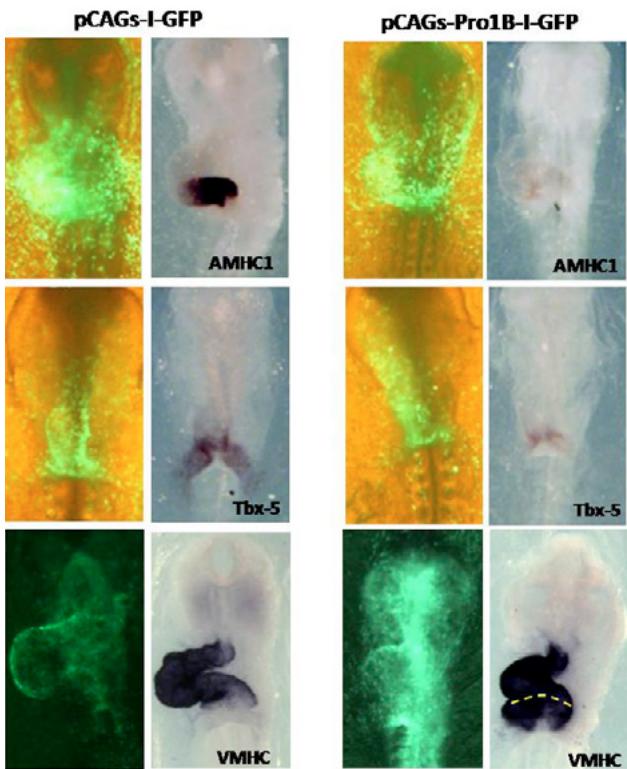
## Research grants

Regulación y función del locus TH/INS en el desarrollo embrionario y la diferenciación

BFU2010-15868: 2011-2013

Principal Investigator: Flora de Pablo

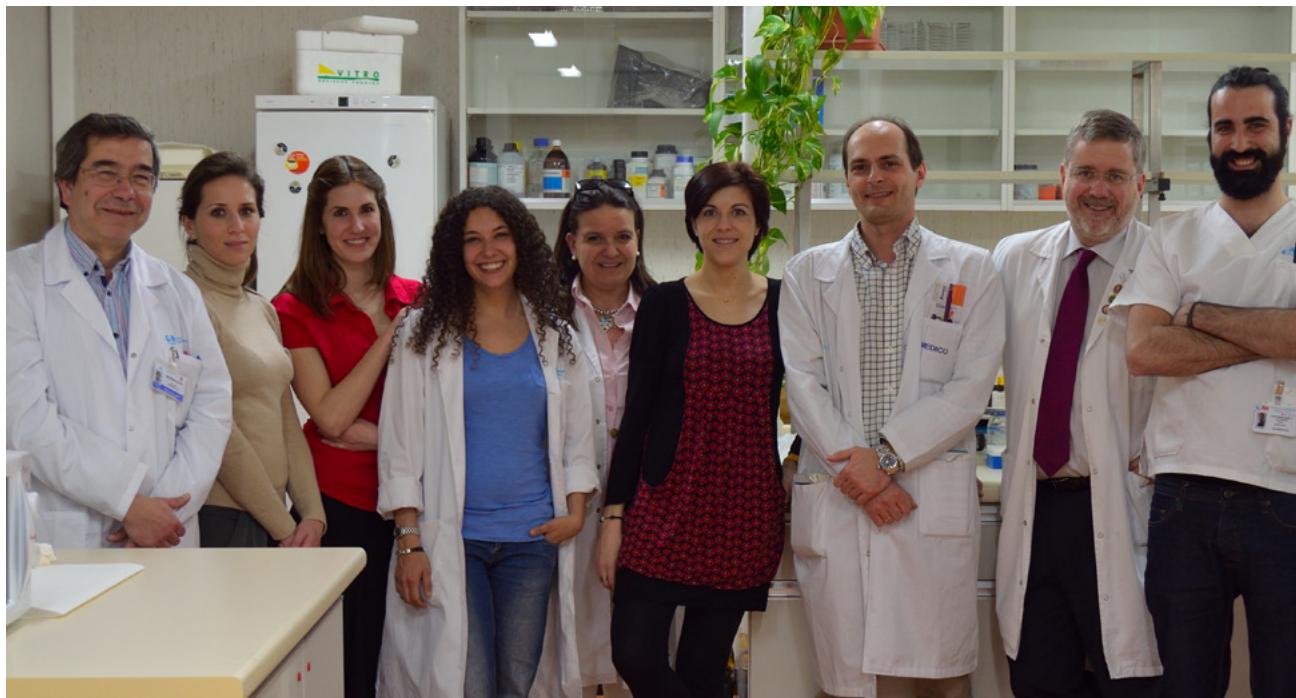
*National project. Programme 2 ■*



The effect of proinsulin overexpression in gene expression during cardiogenesis. *In situ* hybridization is shown for genes related to the atrial (AMHC1, Tbx5) and ventricular (VMHC) regions after electroporation of the bicistronic proinsulin-GFP expressing construct (pcAGs-I-Pro1B-GFP) into chick embryos in the precardiogenic region. The control is a GFP-only containing plasmid. The yellow line marks the normal area of expression of VMHC1. Excess of proinsulin decreased expression of the atrial AMHC1 and Tbx5 and increased expression of VMHC1. In parallel to dysregulated spatial gene expression, there was a high rate of cardiac malformations.

# Diabetes, Obesity and Human Reproduction

Universidad de Alcalá, Hospital Universitario Ramón y Cajal and Instituto Ramón y Cajal de Investigación Sanitaria IRYCIS,  
Madrid  
[www.hrc.es](http://www.hrc.es)



**Principal Investigator** Héctor F Escobar Morreale [hescobarm.hrc@salud.madrid.org](mailto:hescobarm.hrc@salud.madrid.org) **Associate researchers** Francisco Álvarez, Susana Borruel, María Rosa Insenser, Manuel Luque, María Ángeles Martínez, Rafael Montes, José Luis San Millán **PhD student** Macarena Alpañés **Lab manager** Elena Fernández

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Publications: 3

First decile: 2

Q1: 1

With other international groups: 1

Research grants: 2

National projects: 2

Scientific collaborations within Ciberdem: 1

Clinical trials: 1

Clinical practice guidelines: 1

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## Programmes

Programme 4. Use of biomedical approach systems to develop personalized therapies for diabetes.

## Keywords

Biomarkers and imaging. Insulin sensitivity and resistance. Polycystic ovary syndrome. Proteomics.

## Main lines of research

The influence of the balance between androgens and oestrogens on the development of abdominal adiposity and visceral adipose tissue dysfunction in humans as pathogenetic factors of insulin resistance and diabetes, including:

- a) an integrated approach to the influence of sex hormones on the amount and dysfunction of visceral and subcutaneous fat as studied by clinical research, molecular genetics, molecular biology, genomics, proteomics and metabolomics.
- b) the identification of pathogenetic markers of diabetes in severe obesity and predictors of diabetes remission after bariatric surgery.
- c) the role of disordered iron metabolism on the metabolic associations of polycystic ovary syndrome.

## Publications

Circulating inflammatory markers in polycystic ovary syndrome: a systematic review and metaanalysis  
Escobar-Morreale HF, Luque-Ramírez M, González F  
*Fertil Steril*, 95, 1048-1058 (2011)  
PMID 21168133. 1st decile. IF 3.958. With other international groups. Programme 4

Role of androgen-mediated enhancement of erythropoiesis in the increased body iron stores of patients with polycystic ovary syndrome  
Escobar-Morreale HF, Luque-Ramírez M  
*Fertil Steril*, 95, 1730-1735 (2011)  
PMID 21300335. 1st decile. IF 3.958. Programme 4

Role of decreased circulating hepcidin concentrations in the iron excess of women with the polycystic ovary syndrome  
Luque-Ramírez M, Álvarez-Blasco F, Alpañés M, Escobar-Morreale HF  
*J Clin Endocrinol Metab*, 96, 846-852 (2011)  
PMID 21209031. Q1. IF 6.495. Programme 4

## Research grants

Influencia de los andrógenos en el desarrollo de la adiposidad abdominal y de la disfunción metabólica del tejido adiposo visceral en humanos, como factores etiopatogénicos de la resistencia insulínica y la diabetes  
ISCIII, Fondo de Investigación Sanitaria, PI081147: 2009-2011

Principal Investigator: Héctor F Escobar Morreale  
*National project. Programme 4*

Protocolo de investigación sobre el perfil de riesgo cardiovascular asociado a mujeres con síndrome de ovario poliquístico o hiperandrogenismo ovulatorio, y evolución del mismo durante el tratamiento con metformina frente a un anticonceptivo oral mas un antiandrógeno (espiroenolactona)

Ministerio de Sanidad, EC10-096: 2011

Principal Investigator: Héctor F Escobar Morreale  
*National project. Programme 4*

## Scientific collaborations within Ciberdem

Determinants of insulin resistance and glucose tolerance disorders, including diabetes, in severe obesity and their changes after bariatric surgery-induced weight loss  
DIASOBS: 2009-2011

Coordinator: Héctor F Escobar Morreale

Ciberdem groups: Escobar-Morreale HF, Correig X, Montanya E, Simó R, Vendrell J

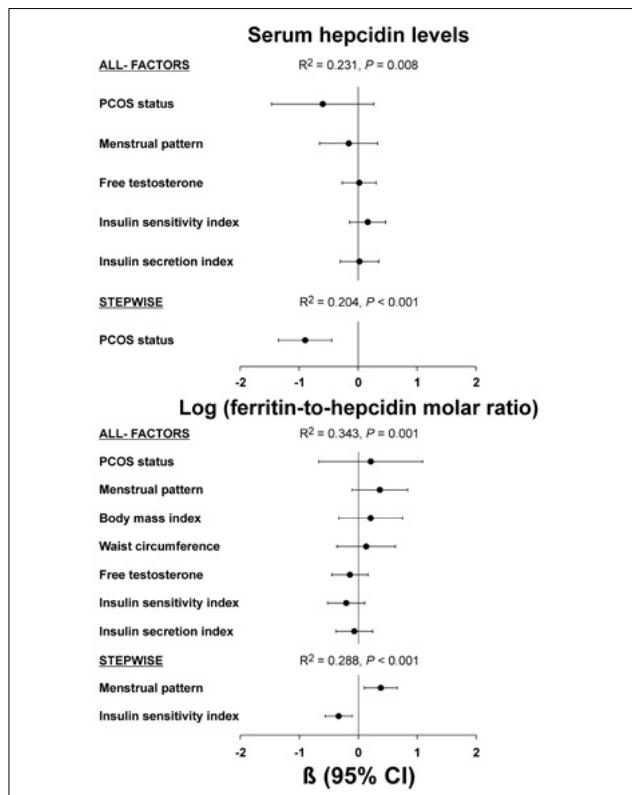
## Clinical trials

Protocolo de investigación sobre el perfil de riesgo cardiovascular asociado a mujeres con síndrome de

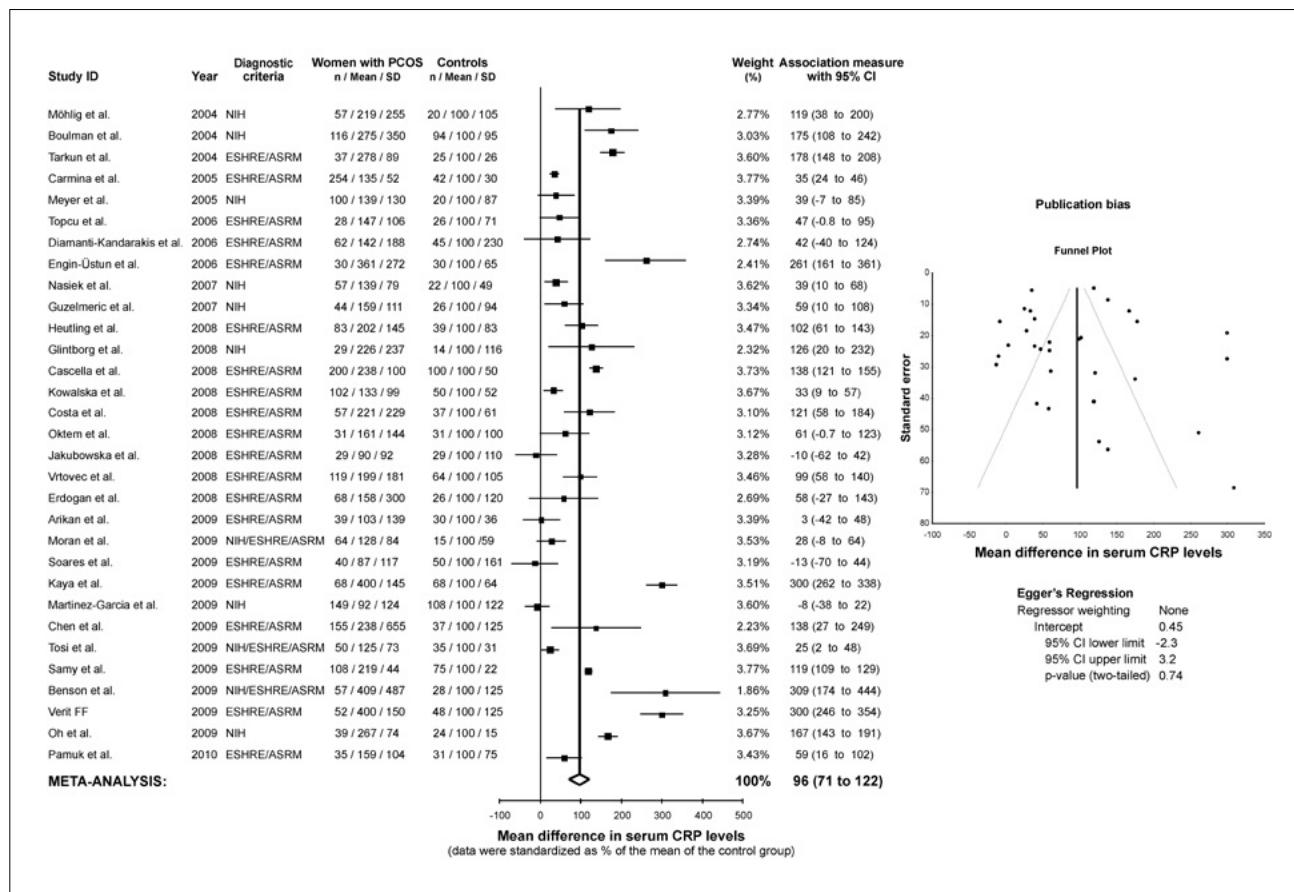
ovario poliquístico o hiperandrogenismo ovulatorio, y evolución del mismo durante el tratamiento con metformina frente a un anticonceptivo oral más un antiandrógeno (espiroenolactona)  
2008-004531-38: 2010-2011  
Coordinator: Héctor F Escobar Morreale  
*Programme 4*

## Clinical practice guidelines

Epidemiology, diagnosis and management of hirsutism: a consensus statement by the Androgen Excess and Polycystic Ovary Syndrome Society  
Escobar-Morreale HF, Carmina E, Dewailly D, Gabinieri A, Kelestimur F, Moghetti P, Pugeat M, Qiao J, Wijeyaratne CN, Witchel SF, Norman RJ  
*Hum Reprod Update*, 18, 146-170 (2012). Epub 2011 Nov 6  
*Programme 4* ■



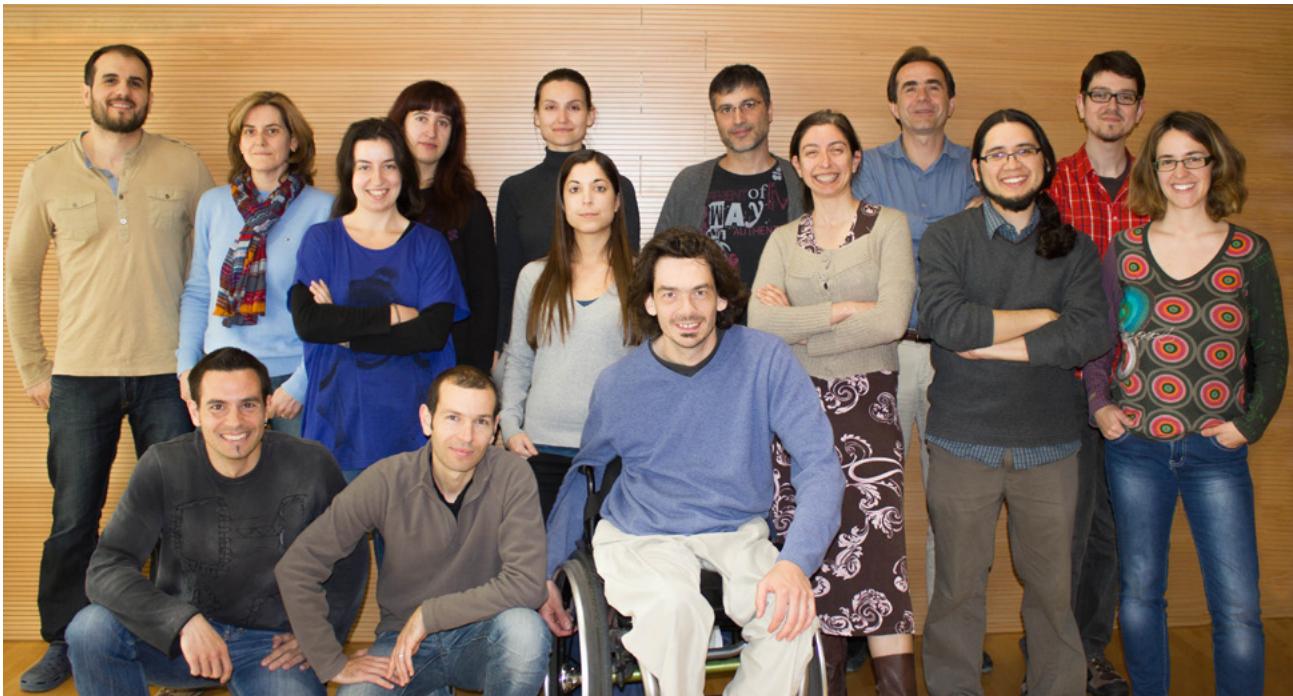
All factors and stepwise (probability for entry ≤ 0.05, probability for removal ≥ 0.10) multiple regression analysis of the circulating hepcidin concentrations and logarithm of the ferritin-to-hepcidin molar ratio, considering patients with PCOS and controls as a whole. The circles correspond to the standardized regression coefficients ( $\beta$ , or the change in terms of standard deviations in the dependent variable that results from a change of one standard deviation in an independent variable) and the error bars indicate the 95% confidence interval of  $\beta$ .  $R^2$  = coefficient of determination. Menstrual dysfunction was coded as regular cycles of normal length = 0, oligomenorrhea = 1, amenorrhoea = 2. PCOS = polycystic ovary syndrome.



Meta-analysis of serum C-reactive protein (CRP) levels in women with PCOS and controls. Evidence dissemination bias was assessed by funnel plot and Egger's regression. NIH, National Institute of Health, ESHRE/ASRM, European Society of Human Reproduction and Embryology / American Society of Reproductive Medicine.

# Genomic programming of beta cells

Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelona  
[www.betacellregulation.net](http://www.betacellregulation.net)



**Principal Investigator** Jorge Ferrer [jferrer@clinic.ub.es](mailto:jferrer@clinic.ub.es) **Postdoctoral fellows** Ildem Akerman, Lorenzo Pasquali, Santiago Rodríguez, Marta Batlle, Miguel Ángel Maestro **Research assistant** Natalia Castro **PhD students** Ignasi Moran, Myriam Solar, Joris van Arensbergen, Nikolina Nakic, Miguel A Correa **Lab manager** Carme Sanahuja **Lab technicians** Xavier Garcia, Vanesa Grau

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Publications: 3

First decile: 2

Q1: 1

With other international groups: 1

Research grants: 5

International projects: 1

European projects: 2

National projects: 2

Scientific collaborations within Ciberdem: 1

PhD theses: 1

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## Programmes

Programme 3. Impact of beta cell dysfunction and plasticity on the natural history of diabetes. Development of novel treatment strategies.

Programme 4. Use of biomedical approach systems to develop personalized therapies for diabetes.

## Keywords

Genetics type 2 diabetes. Insulin synthesis. Islet degeneration and damage. Islet development. Islet transplantation. Monogenic diabetes.

## Main lines of research

- Mouse genetic analysis of beta-cell regulation.
- Understanding the epigenome of pancreatic beta cells and its implications for the development, plasticity and growth of beta cells.
- The regeneration of pancreatic beta cells.

## Publications

Glucose as a mitogenic hormone

Ferrer J

Cell Metab, 13, 357-358 (2011)

[PMID 21459319](https://pubmed.ncbi.nlm.nih.gov/21459319/). 1st decile. IF 18.207.

Programme 3

Hepatic nuclear factor 1alpha (HNF1alpha) dysfunction down-regulates X-box-binding protein 1 (XBP1) and sensitizes beta-cells to endoplasmic reticulum stress  
Kirkpatrick CL, Wiederkehr A, Baquié M, Akhmedov D, Wang H, Gauthier BR, Akerman I, Ishihara H, Ferrer J, Wollheim CB  
*J Biol Chem*, 286, 32300-32312 (2011)  
PMID 21784843. Q1. IF 5.328. With other international groups. Programme 3

Removing the brakes on cell identity  
Akerman I, van Arensbergen J, Ferrer J  
*Dev Cell*, 20, 411-412 (2011)  
PMID 21497752. 1st decile. IF 13.946. Programme 3

#### Research grants

Linking non-coding RNAs to beta-cell programming efforts  
NIH, NIDDK / LINC BETA - 2U01 DK072473-06: 2011-2012  
Principal Investigator: Jorge Ferrer  
*International project. Programme 3*

Collaborative European Effort to Develop Diabetes Diagnosis  
University of Exeter, CE\_FP7\_HealthB07: 2008-2012  
Principal Investigator: Jorge Ferrer  
*European project. Programme 3*

Biology of Liver and Pancreatic Development and Disease  
University of Birmingham, CE\_FP7\_PEOPLE-ITN-08, Marie Curie Training Network: 2009-2013  
Principal Investigator: Jorge Ferrer  
*European project. Programme 4*

Regulación epigenética y plasticidad de las células beta pancreáticas  
Ministerio de Ciencia e Innovación, SAF2008-03116: 2009-2011  
Principal Investigator: Jorge Ferrer  
*National project. Programme 4*

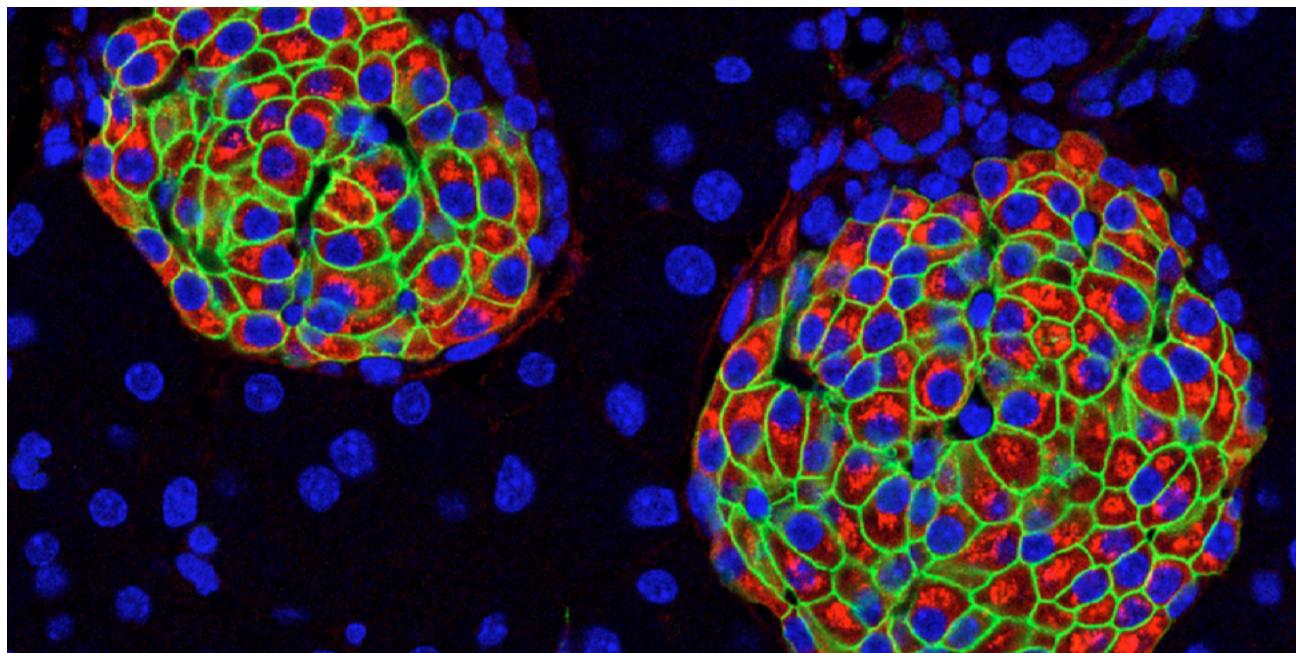
Epibetacell- Empleo de epigenomas celulares para optimizar la terapia celular a partir de células madre  
Ministerio de Ciencia e Innovación, PLE2009-0162: 2010-2012  
Principal Investigator: Jorge Ferrer  
*National project. Programme 3*

#### Scientific collaborations within Ciberdem

Clinical, genetic and functional characterization of monogenic diabetes: from the bench to the bedside  
MODIAB: 2009-2011  
Coordinator: Luis Castaño  
Ciberdem groups: Ferrer J, Castaño L, Blázquez E, Vallejo M

#### PhD theses

The role of Polycomb-mediated gene repression in Beta Cell identity  
Author: Joris van Arensbergen  
Thesis advisor: Jorge Ferrer  
University: Universitat de Barcelona  
Thesis defense date: April 28, 2011  
Programme 3 ■



Mouse pancreatic islets stained with antibodies against insulin (red), glut2 (green) and ToPro-3 (blue).

# Mechanisms of control of glucose and fatty acid metabolism in skeletal muscle cells and metabolic impairment in atrophy

Departament de Bioquímica i Biologia Molecular, Facultat de Biologia, Universitat de Barcelona  
[www.bq.ub.es](http://www.bq.ub.es)



Principal Investigator Anna Maria Gómez Foix [agomezfoix@ub.edu](mailto:agomezfoix@ub.edu) Associate researcher Cèlia García Research assistants Maria Guitart, Marta Montori PhD students Emma Mormeneo, Oscar Osorio Lab manager Anna Orozco

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Publications: 2

First decile: 1

Q1: 1

With other Ciberdem groups: 2

With other CIBERs: 1

Research grants: 3

National projects: 1

Autonomous Community projects: 2

Scientific collaborations within Ciberdem: 1

PhD theses: 1

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## Programmes

Programme 4. Use of biomedical approach systems to develop personalized therapies for diabetes.

## Keywords

Insulin sensitivity and resistance. Lipid metabolism. Carbohydrate metabolism.

## Main lines of research

-Mechanisms of control of skeletal muscle glycogen metabolism. Differential functionality of the protein phosphatase 1 (PP1) glycogen-associated regulatory subunits present in human skeletal muscle GM (PPP1R3A), PTG (PPP1R3C) and PPP1R6 (PPP1R3D).

-Metabolic control role of the fatty acid transport protein 1 (FATP1) in muscle and deleterious effect in high-fat-diet induced diabetes.

-Transcriptional and metabolic adaptations of noninnervated cultured primary human myotubes compared to human skeletal muscle.

## Publications

New emerging role of protein-tyrosine phosphatase 1B in the regulation of glycogen metabolism in basal and TNF- $\alpha$ -induced insulin-resistant conditions in an immortalised muscle cell line isolated from mice

Alonso-Chamorro M, Nieto-Vazquez I, Montori-Grau M, Gomez-Foix AM, Fernandez-Veledo S, Lorenzo M  
*Diabetologia*, 54, 1157-1168 (2011)  
[PMID 21311858](#). 1st decile. IF 6.973. With other Ciberdem groups: Benito M, Vendrell J. Programme 2

University: Universitat de Barcelona  
 Thesis defense date: July 1, 2011  
 Programme 4 ■

Plasma PTX3 protein levels inversely correlate with insulin secretion and obesity, whereas visceral adipose tissue PTX3 gene expression is increased in obesity  
 Osorio-Conles O, Guitart M, Chacón MR, Maymo-Masip E, Moreno-Navarrete JM, Montori-Grau M, Näf S, Fernandez-Real JM, Vendrell J, Gómez-Foix AM  
*Am J Physiol Endocrinol Metab*, 301, E1254-1261 (2011)  
[PMID 21900125](#). Q1. IF 4.686. With other Ciberdem groups: Vendrell J. With other CIBERs: Ciberobn. Programme 2

### Research grants

Estudio de los mecanismos de disfuncionalidad del proceso metabólico del glucógeno asociados a la atrofia en células de músculo esquelético humano  
 Ministerio de Ciencia e Innovación, SAF 2009-07559: 2010-2012  
 Principal Investigator: Anna Maria Gómez Foix  
*National project. Programme 4*

Acreditació de Grup de Recerca de Catalunya  
 Generalitat de Catalunya, 2009 SGR 10: 2009-2013  
 Principal Investigator: Anna Maria Gómez Foix  
*Autonomous Community project. Programme 4*

Desenvolupament d'un dispositiu d'electroporació a plaques estàndard multipouet  
 Centro de Innovación y Desarrollo Empresarial (CIDEM), Generalitat de Catalunya, VALTEC09-1-00061: 2009-2011  
 Principal Investigator: Anna Maria Gómez Foix  
 Coordinator: Ramon Bragós  
*Autonomous Community project. Programme 4*

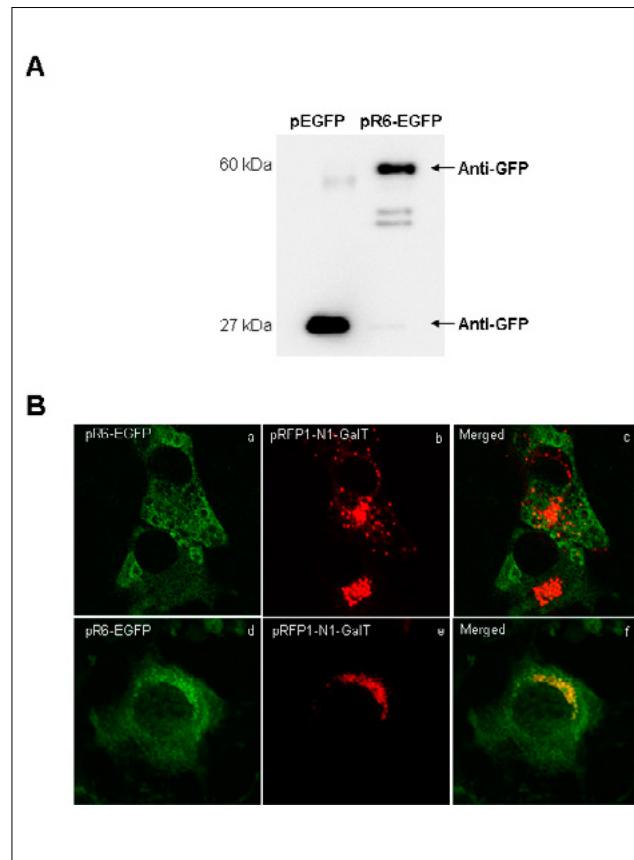
### Scientific collaborations within Ciberdem

Adult adipose tissue-derived progenitor cells: the influence of the clinical phenotype and adipose depot origin on their biological properties  
 STEMOB: 2009-2011  
 Coordinator: Joan J Vendrell

Ciberdem groups: Gómez-Foix AM , Vendrell J, Zorzano A, Balsinde J, Montanya E, Simó R, Vázquez-Carrera M

### PhD theses

Deficiencia de Glucógeno Fosforilasa Muscular humana en cultivos de músculo esquelético humano y en la enfermedad de McArdle. Efecto del Coactivador PGC-1alfa en los cultivos de músculo esquelético  
 Author: Emma Mormeneo Beltrán  
 Thesis advisor: Anna Maria Gómez Foix



Cytolocation of R6-EGFP: (A) 293 cells were transfected with 5 µg of plasmids encoding EGFP or R6-EGFP with the aid of Gene-Juice, at 48 h post-transfection a Western blotting analysis was performed on cell extracts (30 µg protein) and membranes were hybridized with an antibody against GFP. (B) (a to f) C2C12 myoblasts were cotransfected with pR6-EGFP and pRFP1-N1-GalT, at 48 h post-transfection, cells were incubated with 25 mM glucose (a to c) or without glucose (d to f) for 16 h and a colocation analysis of EGFP and RFP was performed. The image shows the fluorescent signal of EGFP (a, d) and RFP (b, e) and the colocation of the signal of EGFP and RFP (c, f).

# Diabetes and obesity: biopathology and cellular plasticity

Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelona  
[www.idibaps.org](http://www.idibaps.org)



**Principal Investigator** Ramon Gomis [rgomis@clinic.ub.es](mailto:rgomis@clinic.ub.es) **Associate researchers** Roser Casamitjana, Ignacio Conget, Enric Esmatjes, Liliam Flores, Rosa Gasa, Felicia Hanzu, Marga Giménez, Belén Nadal, Marcelina Parrizas, Josep Vidal, Emilio Ortega, Sara Cervantes, Marc Claret, María José Coves, Rita Malpique **Postdoctoral fellows** Rebeca Fernández, Sandra Rebuffat, Elena Gonzalez, Eduardo Fernández **PhD students** Joana Duarte, Miriam Ejarque, Katerina Papageorgiou, Fabián Pardo, Gemma Pujadas, Silvia Canivell, Marc Schneeberger, Marta Pradas, Hugo Alves **Lab technicians** Yaiza Esteban, Ainhoa García, Lídia Sánchez

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Publications: 10

First decile: 4

Q1: 2

Q2: 4

With other Ciberdem groups: 2

With other CIBERs: 1

With other international groups: 6

Research grants: 15

European projects: 2

National projects: 7

Autonomous Community projects: 2

Private funds: 4

Scientific collaborations within Ciberdem: 6

Clinical trials: 10

Clinical practice guidelines: 1

PhD theses: 1

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## Programmes

Programme 2. Mechanisms promoting the development of diabetes and its vascular complications. Associated disorders and co-morbidities. Strategies for prevention and treatment.

Programme 3. Impact of beta cell dysfunction and plasticity on the natural history of diabetes. Development of novel treatment strategies.

## Keywords

Clinical diabetes. Endothelium. Islet degeneration and damage. Islet development.

## Main lines of research

-The effects of pancreatic-mesenteric adipose tissue on beta-cell plasticity.

- Crosstalk between adipose tissue and endothelium in obesity and type 2 diabetes: the role of adipocytokines in the aetiology and development of the atherothrombotic complications in both diseases.
- The molecular determinants involved in pancreatic beta-cell apoptosis and regeneration: clinical applications.
- Transcriptional networks which control beta-cell population and function.
- Metabolic and molecular targets of the antidiabetic effect of sodium tungstate.
- The role of the hypothalamus in energy homeostasis control in obesity.
- Epigenetic regulation of adipogenesis.
- Genetic determinants involved in the risk of type 2 diabetes.

## Publications

Amylin effect in extrapancreatic tissues participating in glucose homeostasis, in normal, insulin-resistant and type 2 diabetic state

Moreno P, Acitores A, Gutiérrez-Rojas I, Nuche-Berenguer B, El Assar M, Rodriguez-Mañas L, Gomis R, Valverde I, Visa M, Malaisse WJ, Novials A, González N, Villanueva-Peña Carrillo ML

*Peptides*, 32, 2077-2085 (2011)

*PMID 21939703*. Q2. IF 2.654. With other Ciberdem groups: Novials A, Villanueva-Peña Carrillo ML. With other international groups. Programme 2

Development and functional characterization of insulin-releasing human pancreatic beta cell lines produced by electrofusion

McCluskey JT, Hamid M, Guo-Parke H, McClenaghan NH, Gomis R, Flatt PR

*J Biol Chem*, 286, 21982-21992 (2011)

*PMID 21515691*. Q1. IF 5.328. With other international groups. Programme 3

Efficacy and safety of initial combination therapy with linagliptin and pioglitazone in patients with inadequately controlled type 2 diabetes: a randomized, double-blind, placebo-controlled study

Gomis R, Espadero RM, Jones R, Woerle HJ, Dugi KA

*Diabetes Obes Metab*, 13, 653-661 (2011)

*PMID 21410628*. Q2. IF 3.415. With other international groups. Programme 2

Glucose and fructose as functional modulators of overall dog, but not boar sperm function

Fernández-Novell JM, Ballester J, Altirriba J, Ramíó-Lluch L, Barberà A, Gomis R, Guinovart JJ, Rodríguez-Gil JE

*Reprod Fertil Dev*, 23, 468-480 (2011)

*PMID 21426864*. 1st decile. IF 2.553. With other Ciberdem groups: Guinovart JJ. Programme 2

Incidence and prevalence of unrecognized myocardial infarction in people with diabetes: a substudy of the Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycemia in Diabetes (RECORD) study

MacDonald MR, Petrie MC, Home PD, Komajda M, Jones NP, Beck-Nielsen H, Gomis R, Hanefeld M, Pocock SJ, Curtis PS, McMurray JJ

*Diabetes Care*, 34, 1394-1396 (2011)

*PMID 21562320*. 1st decile. IF 7.141. With other international groups. Programme 2

Increased neuronal nitric oxide synthase dimerisation is involved in rat and human pancreatic beta cell hyperactivity in obesity

Mezghenna K, Pomiès P, Chalançon A, Castex F, Leroy J, Niclauss N, Nadal B, Cambier L, Cazevieille C, Petit P, Gomis R, Berney T, Gross R, Lajoix AD

*Diabetologia*, 54, 2856-2866 (2011)

*PMID 21847584*. 1st decile. IF 6.973. With other international groups. Programme 3

Repeated episodes of hypoglycemia as a potential aggravating factor for preclinical atherosclerosis in subjects with type 1 diabetes

Giménez M, Gilabert R, Monteagudo J, Alonso A, Casamitjana R, Paré C, Conget I

*Diabetes Care*, 34, 198-203 (2011)

*PMID 20929996*. 1st decile. IF 7.141. Programme 2

Sequence and epigenetic determinants in the regulation of the Math6 gene by Neurogenin3

Pujadas G, Felipe F, Ejarque M, Sanchez L, Cervantes S, Lynn FC, Gomis R, Gasa R

*Differentiation*, 82, 66-76 (2011)

*PMID 21676531*. Q2. IF 3.069. With other international groups. Programme 3

Sodium tungstate regulates food intake and body weight through activation of the hypothalamic leptin pathway

Amigó-Correig M, Barceló-Batllo S, Piquer S, Soty M, Pujadas G, Gasa R, Bortolozzi A, Carmona MC, Gomis R

*Diabetes Obes Metab*, 13, 235-242 (2011)

*PMID 21205112*. Q2. IF 3.415. With other CIBERs: Cibersam. Programme 2

Translational evidence of endothelial damage in obese individuals: inflammatory and prothrombotic responses

Hanzú FA, Palomo M, Kalko SG, Parrizas M, Garaulet M,

Escolar G, Gomis R, Diaz-Ricart M

*J Thromb Haemost*, 9, 1236-1245 (2011)

*PMID 21481180*. Q1. IF 5.439. Programme 2

## Research grants

FOOD FOR LIFE - Supporting Healthy Lifestyles in the Mediterranean Area

Marie Curie Actions, International Research Staff Exchange Scheme (FP7-PEOPLE-IRSES-2008), 230848: 2009-2012 Principal Investigator: Ramon Gomis <i>European project. Programme 2</i>	Principal Investigator: Enric Esmatjes <i>National project. Programme 2</i>
The role of adipose tissue in obesity: beta cell crosstalk (ADIBET) FP7 PEOPLE-2007-3-1-IAPP, 218131: 2008-2012 Principal Investigator: Ramon Gomis <i>European project. Programme 3</i>	Diabetis experimental, investigació cel·lular i molecular en models de diabetis experimental Agència de Gestió d'Ajuts Universitaris i de Recerca. Generalitat de Catalunya, 2009 SGR 1426: 2009-2013 Principal Investigator: Ramon Gomis <i>Autonomous Community project. With other Ciberdem groups: Novials A. Programme 3</i>
Molecular targets induced by tungstate in obesity Ministerio de Educación y Ciencia, SAF2006-07382: 2006-2011 Principal Investigator: Ramon Gomis <i>National project. Programme 2</i>	Estudio aleatorizado prospectivo sobre los efectos del tratamiento médico intensivo con o sin bypass gástrico en Y de Roux, sobre el grueso de la íntima media carotidea en enfermos con obesidad grado I Agència d'avaluació de Tecnologia i Recerca Mèdiques, Generalitat de Catalunya: 2009-2012 Principal Investigator: Josep Vidal <i>Autonomous Community project. Programme 2</i>
Transcriptional cascade induced by neurogenin3 in the pancreas: a study of the transcription factors math6 and ebf1 Ministerio de Ciencia e Innovación, BFU2008-02299/BMC: 2009-2011 Principal Investigator: Rosa Gasa <i>National project. Programme 3</i>	GLP-1 y resolución tras el bypass gástrico de la diabetes tipo 2 asociada a obesidad Fundación Mutua Madrileña: 2009-2011 Principal Investigator: Josep Vidal <i>Private funds. Programme 2</i>
The role of LSD1 histone demethylase in adipogenesis Ministerio de Ciencia e Innovación, BFU2009-09988: 2010-2012 Principal Investigator: Marcelina Parrizas <i>National project. Programme 2</i>	Role of hypothalamic mitochondrial fusion in appetite and body weight control: potential therapeutical target for the treatment of obesity RecerCaixa, 2010ACUP_00275: 2011-2013 Principal Investigator: Marc Claret <i>Private funds. Programme 2</i>
Role of miRNAs in hypothalamic populations of neurons upon energy and glucose homeostasis: potential targets for obesity and diabetes treatment ISCIII, CP09/00233: 2010-2012 Principal Investigator: Marc Claret <i>National project. Programme 2</i>	Papel de la fracción no adipocitaria del tejido adiposo visceral en el inicio y la propagación de la enfermedad aterotrombótica Sociedad Española de Diabetes: 2009-2011 Principal Investigator: Ramon Gomis <i>Private funds. Programme 2</i>
MicroRNAs hipotalámicos y regulación del metabolismo energético: posibles dianas terapéuticas para el tratamiento de la obesidad y la diabetes ISCIII, PI10/01074: 2011-2013 Principal Investigator: Marc Claret <i>National project. Programme 2</i>	Plasticity of beta cell mass and type 2 diabetes Fundación Marcelino Botín: 2010-2012 Principal Investigator: Ramon Gomis <i>Private funds. Programme 3</i>
Determinantes moleculares de la plasticidad de la célula beta en diabetes: efectos del tungstato sódico SAF2010-19527: 2011-2013 Principal Investigator: Ramon Gomis <i>National project. Programme 3</i>	<b>Scientific collaborations within Ciberdem</b> Comparative metabolomic analysis for the detection of biomarkers in diabetes METADIAB: 2009-2011 Coordinator: Xavier Correig <i>Ciberdem groups: Gomis R, Correig X, Novials A</i>
Efectos del by-pass gástrico sobre la presión arterial y la disfunción endotelial en personas con obesidad grave Ministerio de Sanidad y Consumo, PI070124: 2006-2011	Mechanisms of endothelial dysfunction in diabetes: the role of amylin and circulating endothelial cells ENDODIAB: 2009-2011

Coordinator: Anna Novials <i>Ciberdem groups: Gomis R, Novials A, Villanueva Peñacarrillo ML</i>	D1690C00006: 2008-2012 Coordinator: Ramon Gomis <i>Programme 2</i>
Glycogen-induced dysfunctions in the pancreas and retina and their involvement in the ethiogenesis of diabetes mellitus GIDIPRED: 2009-2011 Coordinator: Joan J Guinovart <i>Ciberdem groups: Gomis R, Guinovart JJ, Simó R</i>	Efecto de liraglutida en el peso corporal en sujetos no diabéticos obesos o con sobrepeso y comorbilidad. Ensayo clínico aleatorizado, doble-ciego, controlado con placebo, grupos paralelos, multicéntrico, multinacional, con estratificación de sujetos a 56 o 160 semanas de tratamiento basadas en el estatus prediabético en la aleatorización 2008-001049-24: 2011-2015 Coordinator: Ramon Gomis <i>Programme 2</i>
Di@bet.es Study: 1st epidemiological study of the prevalence of type 2 diabetes in Spain Coordinator: Federico Soriguer <i>Ciberdem groups: Gomis R, Soriguer F, Carmena R, Castaño L, Serrano-Ríos M, Vendrell J</i>	Ensayo clínico fase III, de 24 semanas de duración y 28 semanas de seguimiento, multicéntrico, aleatorizado, doble ciego, estratificado por edad, controlado con placebo para evaluar la eficacia y seguridad de dapagliflozina 10mg una vez al día, en pacientes DM2, con historia de enfermedad cardiovascular e hipertensión arterial y, que presenten mal control glucémico con su tratamiento habitual D1690C00018: 2012 Coordinator: Ramon Gomis <i>Programme 2</i>
Telemed-diabetes Study Coordinator: Enric Esmatjes <i>Ciberdem groups: Gomis R, Carmena R, Serrano-Ríos M, Soriguer F, Castaño L</i>	Estudio de fase III, multicéntrico, internacional, aleatorizado, de grupos paralelos, doble ciego, de seguridad cardiovascular de BI10773 (10mg y 25mg administrados por vía oral una vez al día) comparado con el tratamiento habitual en pacientes con diabetes mellitus de tipo 2 con un riesgo cardiovascular aumentado 2010-2012 Coordinator: Josep Vidal <i>Programme 2</i>
Ciberdem Biobank Coordinator: Anna Novials <i>Ciberdem Biobank nodes: Gomis R, Novials A, Vendrell J, Masana L, Castaño L, Serrano-Ríos M, Soriguer F, Carmena R, Blanco-Vaca F</i>	Estudio clínico para evaluar la eficacia y seguridad de un complemento nutricional como adyuvante en la mejora del perfil lipídico y el control de peso 2011-2012 Coordinator: Josep Vidal <i>Programme 2</i>
<b>Clinical trials</b> Multicenter trial, international, randomized and 2x2 factorial to assess the effects of Lantus (glargin insulin) compared to the standard treatment with omega 3 fatty acids compared to placebo, in the decrease of cardiovascular morbility and mortality in high risk patients with altered fasting glucose (AFG), decrease of glucose tolerance (TGD) or type 2 diabetes in initial steps HOE901/4032: 2004-2012 Coordinator: Ramon Gomis <i>Programme 2</i>	Protocolo de estudio para la validación del conjunto grupo mínimo de datos (Minimum Data Set, MDS) en España 2011-2012 Coordinator: Josep Vidal <i>Programme 2</i>
Estudio de fase III, aleatorizado, doble ciego, controlado con placebo y de grupos paralelos para evaluar la eficacia y seguridad de Linagliptina (5 mg) administrada por vía oral una vez al día al menos 52 semanas en pacientes con diabetes tipo 2 en combinación con insulina como tratamiento de base 2008-008296-33: 2009-2011 Coordinator: Ramon Gomis <i>Programme 2</i>	Glucose Control in Type 2 Diabetes Mellitus with insulin pump therapy. OpT2mise 2011-2012 Coordinator: Ignacio Conget <i>Programme 2</i>
Ensayo en fase 3 de 24 semanas, internacional aleatorizado de grupos paralelos, doble ciego y controlado con placebo con un periodo de extensión de 24 semanas para evaluar la eficacia y seguridad de la dapaglifocina añadida al tratamiento de los pacientes con dm 2 que tienen un control insuficiente de la glucemia con insulina	Sensing With Insulin Pump Therapy to Control HbA1c. SWITCH study

2008-2011

Coordinator: Ignacio Conget

Programme 2

### Clinical practice guidelines

Insulinas: Nuevas opciones para optimizar el tratamiento de la Diabetes Mellitus

Aguilera E, Gaztambide S, Agullo E, Gonzalo MA, Calvo F, Lara JI, Conget I, Puig M, Duran S, Rovira A, Tinahones FJ, Faure E, Vázquez F, Fernández-García JC

Diabetomecum, ed Permanyer, ISBN 9788499262529 (2011)

Programme 3

### PhD theses

Molecular determinants of adipose tissue crosstalks in obesity

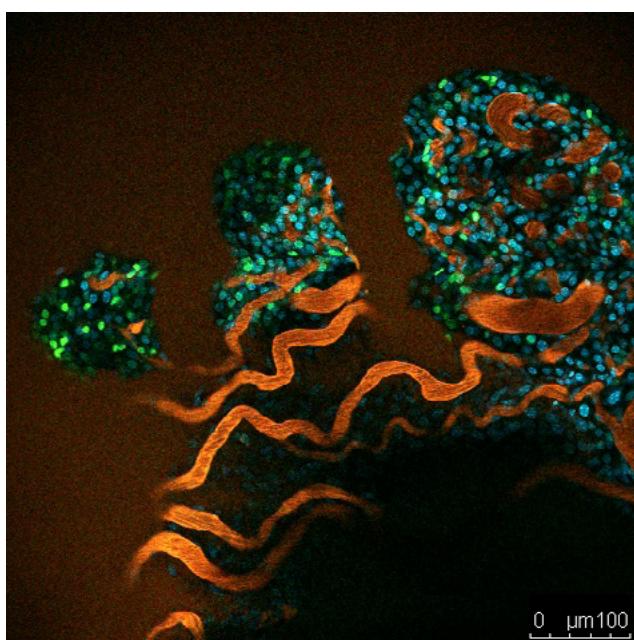
Author: Felicia Hanzu

Thesis advisor: Ramon Gomis

University: Universitat de Barcelona

Thesis defense date: January 17, 2011

European thesis. Programme 2 ■



Confocal image of pancreatic islet cells transplanted to the anterior chamber of the eye: vascularization (red), living islet cells (blue), dead islet cells (green).

# Metabolic engineering and diabetes therapy

Institut de Recerca Biomèdica, Barcelona  
[www.irbbbarcelona.org](http://www.irbbbarcelona.org)



**Principal Investigator** Joan J Guinovart [guinovart@irbbbarcelona.org](mailto:guinovart@irbbbarcelona.org) **Associate researchers** Joaquim Calbó, María del Mar García **Postdoctoral fellows** Adelaida Díaz, Jordi Duran, Carlos Rodríguez, Delia Zafra **Research assistant** Anna Adrover **PhD students** Óscar Blanco, Carles Martínez, Isabel Sáez, Jordi Vallès, Giorgia Testoni **Lab technicians** Emma Veza, Manuel Gris **Administrative staff** Carolina Sánchez

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Publications: 4

First decile: 3

Q1: 1

With other Ciberdem groups: 1

With other CIBERs: 1

With other international groups: 1

Research grants: 3

International projects: 1

National projects: 1

Autonomous Community projects: 1

Scientific collaborations within Ciberdem: 1

PhD theses: 3

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## Programmes

Programme 2. Mechanisms promoting the development of diabetes and its vascular complications. Associated disorders and co-morbidities. Strategies for prevention and treatment.

## Keywords

Carbohydrate metabolism. Insulin sensitivity and resistance. Metabolic syndrome. Oral pharmacological agents. Retinopathy.

## Main lines of research

- The control mechanisms of glucose storage in the liver and their alterations in diabetes mellitus. Characterization of novel compounds with anti-diabetic action.
- The role of glycogen metabolism in the glucose-sensing function of pancreatic beta-cell and liver.
- The consequences of altered glycogen deposition in various tissues in diabetes mellitus and in several neurodegenerative diseases.

## Publications

Neurodegeneration and functional impairments associated with glycogen synthase accumulation in a mouse model of

## Lafora disease

Valles-Ortega J, Duran J, Garcia-Rocha M, Bosch C, Saez I, Pujadas L, Serafin A, Cañas X, Soriano E, Delgado-García JM, Gruart A, Guinovart JJ  
*EMBO Mol Med*, 3, 667-681 (2011)  
*PMID 21882344. 1st decile. IF 8.833. With other CIBERs: Cibered. Programme 2*

Glucose and fructose as functional modulators of overall dog, but not boar sperm function

Fernández-Novell JM, Ballester J, Altirriba J, Ramió-Lluch L, Barberà A, Gomis R, Guinovart JJ, Rodríguez-Gil JE  
*Reprod Fertil Dev*, 23, 468-480 (2011)  
*PMID 21426864. 1st decile. IF 2.553. With other Ciberdem groups: Gomis R. Programme 2*

Processivity and subcellular localization of glycogen synthase depend on a non-catalytic high affinity glycogen-binding site

Díaz A, Martínez-Pons C, Fita I, Ferrer JC, Guinovart JJ  
*J Biol Chem*, 286, 18505-18514 (2011)  
*PMID 21464127. Q1. IF 5.328. Programme 2*

Restoration of hepatic glycogen deposition reduces hyperglycaemia, hyperphagia and gluconeogenic enzymes in a streptozotocin-induced model of diabetes in rats

Ros S, García-Rocha M, Calbó J, Guinovart JJ  
*Diabetologia*, 54, 2639-2648 (2011)  
*PMID 21811873. 1st decile. IF 6.973. With other international groups. Programme 2*

## Research grants

The dark side of a bright molecule: Determinants of glycogen-induced cell dysfunction  
Human Frontier Science Program, IO HFSP-J Guinovart: 2011-2014  
Principal Investigator: Joan J Guinovart  
*International project. Programme 2*

Estudio de un nuevo mecanismo de regulación del metabolismo del glucógeno. Análisis de las implicaciones patológicas de la acumulación anómala de polímeros de glucosa

Ministerio de Ciencia e Innovación, BFU2008-00769: 2009-2011  
Principal Investigator: Joan J Guinovart  
*National project. Programme 2*

Ayudas de apoyo a grupos de investigación  
Generalitat de Catalunya (AGAUR), SGR2009-1176: 2009-2013  
Principal Investigator: Joan J Guinovart  
*Autonomous Community project. Programme 2*

## Scientific collaborations within Ciberdem

Glycogen-induced dysfunctions in the pancreas and retina and their involvement in the ethiogenesis of diabetes mellitus

GIDIPRED: 2009-2011

Coordinator: Joan J Guinovart

Ciberdem groups: Guinovart JJ, Gomis R, Simó R

## PhD theses

Modulació transcripcional del metabolisme hepàtic per tungstat de sodi

Author: Laura Nocito Labad

Thesis advisor: Joan J Guinovart

University: Universitat de Barcelona

Thesis defense date: January 24, 2011

*Programme 2*

Estudio de la regulación de la glucógeno sintasa hepática por modificación postraduccional

Author: Oscar Blanco Presas

Thesis advisor: Joan J Guinovart

University: Universitat de Barcelona

Thesis defense date: April 28, 2011

*Programme 2*

Determinants de la unió a Glicogen i la translocació de la Glicogen Sintasa

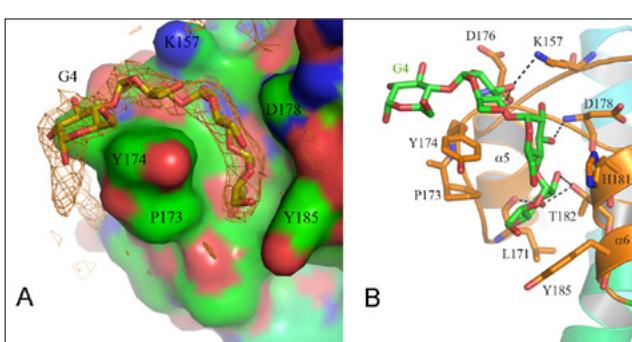
Author: Carles Martínez Pons

Thesis advisor: Joan J Guinovart

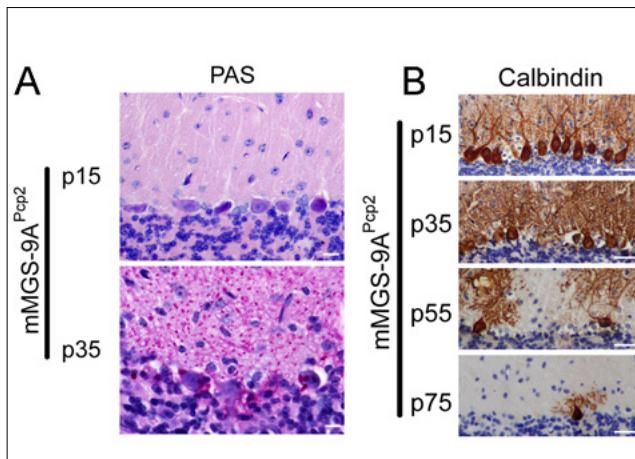
University: Universitat de Barcelona

Thesis defense date: December 1, 2011

*Programme 2 ■*



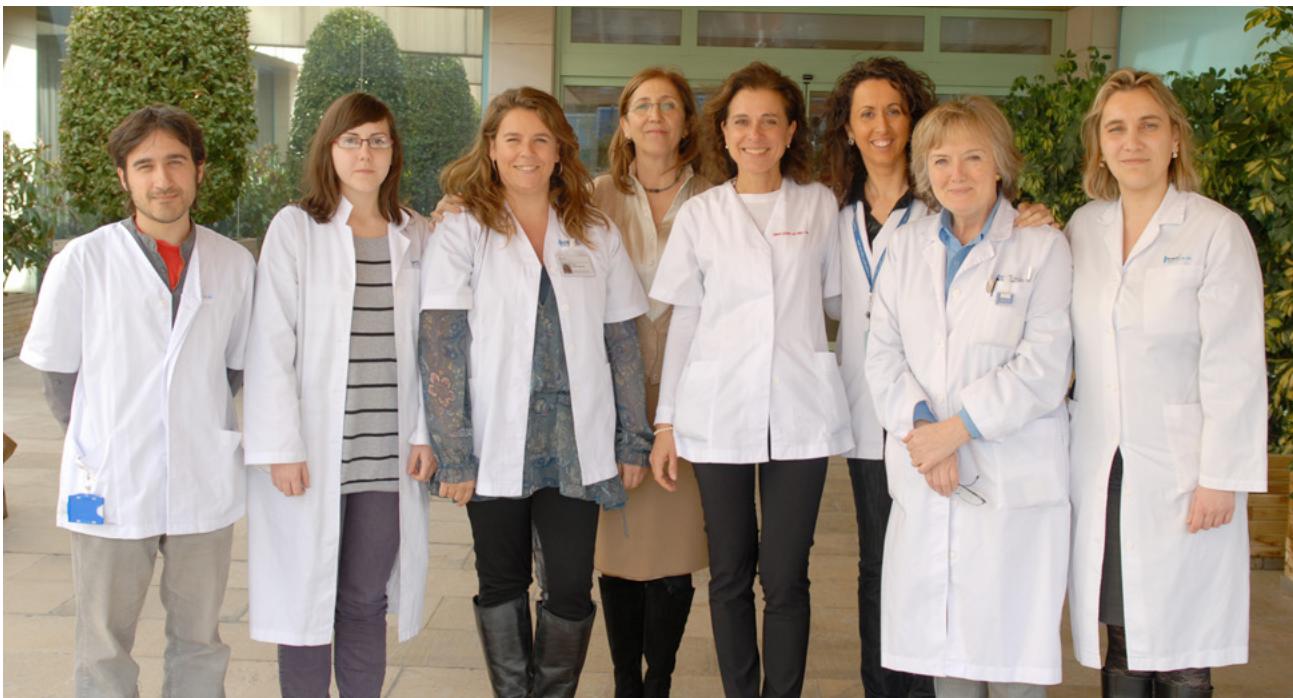
In the search for potential modulators of glycogen synthase, the crystal structure of monomeric PaGS has been obtained. This structure reveals the existence of a high affinity glycogen binding site, shown in the figure with surface (A) or ribbon (B) representations. Maltotetraose (shown as sticks) occupies the glycogen binding site by curling around the Y174 residue, and makes hydrogen bonds with K157, L171, D178 and T182.



We are studying the direct effects of glycogen accumulation in neurons as a potential model of diabetes-associated neurodegeneration. Therefore, we have generated transgenic mice expressing an active glycogen synthase mutant (mMGS-9A) specifically in cerebellar Purkinje neurons (Pcp2-driven). The figure shows glycogen accumulation and progressive loss of Purkinje neurons in these mice. A PAS (pink) and Hematoxilin (blue) staining of cerebellar sections of 15-day old (p15) and p35 mMGS-9APcp2 animals. B Cerebellar sections of p15-p75 mMGS-9APcp2 animals labelled to visualize Purkinje cells by Calbindin protein expression (brown). Sections were also labelled with Hematoxilin (blue). Scale bars 30  $\mu$ m.

# Prenatal growth restriction and subsequent risks for type 2 diabetes and cardiovascular disease

Hospital Sant Joan de Déu, Universitat de Barcelona  
[www.hsjdbcn.org](http://www.hsjdbcn.org)



**Principal Investigator** Lourdes Ibáñez [libanez@hsjbcn.org](mailto:libanez@hsjbcn.org) **Associate researchers** Paula Casano, María Victoria Marcos, Carme Valls **Postdoctoral fellows** Marta Díaz, David Sánchez Infantes **Research assistant** Mónica García Hurtado **PhD student** Giorgia Sebastiani

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Publications: 10

First decile: 4

Q1: 6

With other Ciberdem groups: 2

With other international groups: 8

Research grants: 13

International projects: 1

National projects: 7

Autonomous Community projects: 3

Private funds: 2

Clinical trials: 3

Clinical practice guidelines: 1

Awards: 2

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## Programmes

Programme 4. Use of biomedical approach systems to develop personalized therapies for diabetes.

## Keywords

Cytokines. Insulin sensitivity and resistance. Metabolic syndrome. Oral pharmacological agents. Paediatrics. Prediction/prevention of type 2 diabetes.

## Main lines of research

-The influence of early nutrition on growth patterns, body composition, endocrine-metabolic profile and future cardiovascular risks in small-for-gestational-age (SGA) newborns.

-The association of specific SNPs with catch-up growth characteristics, body composition and abdominal fat partitioning in SGA children.

-The association between placental expression of genes involved in glucose and lipid metabolism, inflammation and adipogenesis on longitudinal growth, glucose metabolism and risk factors for cardiovascular disease and type 2 diabetes in newborns born SGA, appropriate-for-

gestational-age (AGA) and large-for-gestational-age (LGA).  
 -The usefulness of insulin sensitizers as modifiers of pubertal onset and progression in SGA girls with excessive catch-up growth and advanced and rapidly progressive puberty.  
 -The effects of low-dose combinations of insulin sensitizers and antiandrogens on cardiovascular risk parameters, body fat and gene expression in adipose tissue in adolescents with ovarian hyperandrogenism, hyperinsulinism and cardiovascular risk factors.  
 -The influence of genetic polymorphisms on the clinical response to insulin sensitization.

## Publications

ASstream: an R package for annotating LC/MS metabolomic data  
 Alonso A, Julià A, Beltran A, Vinaixa M, Díaz M, Ibáñez L, Correig X, Marsal S  
*Bioinformatics*, 27, 1339-1340 (2011)  
[PMID 21414990](#). 1st decile. IF 4.877. With other Ciberdem groups: Correig X. Programme 4

Catch-up growth in girls born small for gestational age precedes childhood progression to high adiposity  
 Ibáñez L, Lopez-Bermejo A, Diaz M, de Zegher F  
*Fertil Steril*, 96, 220-223 (2011)  
[PMID 21549368](#). 1st decile. IF 3.958. With other international groups. Programme 4

Early metformin therapy (age 8-12 years) in girls with precocious pubarche to reduce hirsutism, androgen excess, and oligomenorrhea in adolescence  
 Ibáñez L, López-Bermejo A, Díaz M, Marcos MV, de Zegher F  
*J Clin Endocrinol Metab*, 96, E1262-1267 (2011)  
[PMID 21632811](#). Q1. IF 6.495. With other international groups. Programme 4

Early metformin therapy to delay menarche and augment height in girls with precocious pubarche  
 Ibáñez L, Lopez-Bermejo A, Diaz M, Marcos MV, de Zegher F  
*Fertil Steril*, 95, 727-730 (2011)  
[PMID 20883985](#). 1st decile. IF 3.958. With other international groups. Programme 4

Lower free thyroxin associates with a less favorable metabolic phenotype in healthy pregnant women  
 Bassols J, Prats-Puig A, Soriano-Rodríguez P, García-González MM, Reid J, Martínez-Pascual M, Mateos-Comerón F, de Zegher F, Ibáñez L, López-Bermejo A  
*J Clin Endocrinol Metab*, 96, 3717-3723 (2011)  
[PMID 21917863](#). Q1. IF 6.495. With other international groups. Programme 4

Metabolomics reveals reduction of metabolic oxidation in women with polycystic ovary syndrome after pioglitazone-flutamide-metformin polytherapy

Vinaixa M, Rodriguez MA, Samino S, Díaz M, Beltran A, Mallol R, Bladé C, Ibáñez L, Correig X, Yanes O  
*PLoS ONE*, 6, e29052 (2011)  
[PMID 22194988](#). Q1. IF 4.411. With other Ciberdem groups: Correig X. Programme 4

Pharmacokinetics of metformin in girls aged 9 years  
 Sánchez-Infantes D, Díaz M, López-Bermejo A, Marcos MV, de Zegher F, Ibáñez L  
*Clin Pharmacokinet*, 50, 735-738 (2011)  
[PMID 21973270](#). Q1. IF 4.513. With other international groups. Programme 4

Responsiveness to metformin in girls with androgen excess: collective influence of genetic polymorphisms  
 Díaz M, López-Bermejo A, Sánchez-Infantes D, Bassols J, de Zegher F, Ibáñez L  
*Fertil Steril*, 96, 208-213 (2011)  
[PMID 21575951](#). 1st decile. IF 3.958. With other international groups. Programme 4

Toward an early marker of metabolic dysfunction: omentin-1 in prepubertal children  
 Prats-Puig A, Bassols J, Bargalló E, Mas-Parareda M, Ribot R, Soriano-Rodríguez P, Berengüí À, Díaz M, de Zegher F, Ibáñez L, López-Bermejo A  
*Obesity*, 19, 1905-1907 (2011)  
[PMID 21720428](#). Q1. IF 3.531. With other international groups. Programme 4

Treatment of androgen excess in adolescent girls: ethinylestradiol-cyproteroneacetate versus low-dose pioglitazone-flutamide-metformin  
 Ibáñez L, Diaz M, Sebastiani G, Sánchez-Infantes D, Salvador C, Lopez-Bermejo A, de Zegher F  
*J Clin Endocrinol Metab*, 96, 3361-3366 (2011)  
[PMID 21865363](#). Q1. IF 6.495. With other international groups. Programme 4

## Research grants

Infant manifestations of adult obesity susceptibility genotypes  
 Research Unit, European Society for Paediatric Endocrinology, ESPE Research Unit Grant: 2010-2012  
 Principal Investigators: Lourdes Ibáñez, Ken Ong, Francis de Zegher, David Dunger, Barbara Heude, Marie-Aline Charles  
 Coordinator: Ken Ong  
*International project. Programme 4*

Intrauterine restriction and endocrine-metabolic abnormalities (proficient post-doc contracts in health research "Sara Borrell")  
 MICINN-ISCIII, CD10/00234: 2010-2014  
 Principal Investigator: David Sánchez Infantes  
*National project. Programme 4*

Intensificación de la actividad investigadora en el SNS

ISCIII, INT10/205: 2011-2012

Principal Investigator: Lourdes Ibáñez

*National project. Programme 4*

Efectos endocrino-metabólicos y sobre la adiposidad visceral de la administración de metformina a dosis bajas en niños prepuberales con bajo peso al nacer para la edad gestacional, recuperación postnatal espontánea de peso y talla, y marcadores de riesgo

ISCIII, EC08/00160: 2009-2012

Principal Investigator: Lourdes Ibáñez

*National project. Programme 4*

Influencia del tipo de alimentación en etapas tempranas de la vida sobre el riesgo cardiovascular futuro y el desarrollo psiconeurologico en recién nacidos con retraso de crecimiento intrauterino

ISCIII, PI08/0443: 2009-2011

Principal Investigator: Lourdes Ibáñez

*National project. Programme 4*

Etinil-estradiol+acetato de ciproterona versus pioglitazona+flutamida+metformina a dosis bajas en adolescentes con hiperandrogenismo ovárico e hiperinsulinismo: efectos sobre parámetros de inflamación crónica, diabetes tipo 2 y riesgo cardiovascular

ISCIII, PI09/90444: 2010-2011

Principal Investigator: Lourdes Ibáñez

*National project. Programme 4*

Ayuda para contratos de formación en investigación Río Hortega - Nuria Sanz

ISCIII, CM10/00094: 2011-2014

Principal Investigator: Lourdes Ibáñez

*National project. Programme 4*

Efectos sobre marcadores de riesgo cardiovascular de la adición de metformina al tratamiento con hormona de crecimiento en pacientes prepuberales con antecedentes de peso bajo al nacer para la edad gestacional y sin recuperación de talla postnatal

ISCIII, TRA-131: 2010-2012

Principal Investigator: Paula Casano

*National project. Programme 4*

Endocrine-metabolic profile and body composition in infants born large-for-gestational age

Hospital Sant Joan de Déu, AFR 09/00020: 2009-2011

*Principal Investigator: Lourdes Ibáñez*

Associate investigator: Miriam Pérez Cruz

*Autonomous Community project. Programme 4*

The influence of the erythrocyte fatty acid profile (as a surrogate of lipid intake in pregnant women during the third

trimester) on postnatal growth, and on the adipokine profile in newborns born both small and appropriate for gestational age

Hospital Sant Joan de Déu, AFR 10/00026: 2010-2012

Principal Investigator: Lourdes Ibáñez

Associate investigator: Nuria Sanz

*Autonomous Community project. Programme 4*

Repercussió de les alteracions prenatales i perinatales en el desenvolupament postnatal

Agència de Gestió d'Ajuts Universitaris i de Recerca, 2009SGR828: 2009-2013

Principal Investigator: Lourdes Ibáñez

*Autonomous Community project. Programme 4*

The effects of metformin on cardiovascular risk factors in prepubertal children born small for gestational age without postnatal catch-up growth, currently treated with growth hormone

Pfizer, PCP00046: 2009-2012

Principal Investigator: Lourdes Ibáñez

Associate investigators: Paula Casano, Marta Díaz, Carme Valls, María Victoria Marcos

*Private funds. Programme 4*

Efectos de la alimentación precoz sobre los depósitos de grasa visceral y el grosor de la íntima carotidea en lactantes y niños con bajo peso al nacer para la edad gestacional

Nutribén Alter Farmacia SA, PCP00045: 2009-2011

Principal Investigator: Lourdes Ibáñez

*Private funds. Programme 4*

### Clinical trials

Efectos sobre marcadores de riesgo cardiovascular de la adición de metformina al tratamiento con hormona de crecimiento en pacientes prepuberales con antecedentes de peso bajo al nacer para la edad gestacional y sin recuperación de talla postnatal

2009-016246-12: 2009-2012

Coordinator: Paula Casano

*Programme 4*

Etinil-estradiol+acetato de ciproterona versus pioglitazona+flutamida+metformina a dosis bajas en adolescentes con hiperandrogenismo ovárico e hiperinsulinismo: efectos sobre parámetros de inflamación crónica, diabetes tipo 2 y riesgo cardiovascular

2009-012226-37: 2010-2011

Coordinator: Lourdes Ibáñez

*Programme 4*

Efectos endocrino-metabólicos y sobre la adiposidad visceral de la administración de metformina a dosis bajas en niños prepuberales con bajo peso al nacer para la edad gestacional, recuperación postnatal espontánea de peso y

talla, y marcadores de riesgo

2009-009944-21: 2009-2012

Coordinator: Lourdes Ibáñez

Programme 4

### Clinical practice guidelines

Follow-up of the small-for-gestational-age child: clinical guidelines

López ID, Muñoz Ade A, Muñoz JB, Rodríguez PC, Gómez EG, Ollero MJ, Rodríguez JM, Dehlia AC, Estrada RC, Toda LI

An Pediatr (Barc), 76, 104.e1-7 (2012). Epub 2011 Oct 19

Programme 4

### Awards

Accésit de Investigación de la Sociedad Española de Endocrinología Pediátrica (2011)

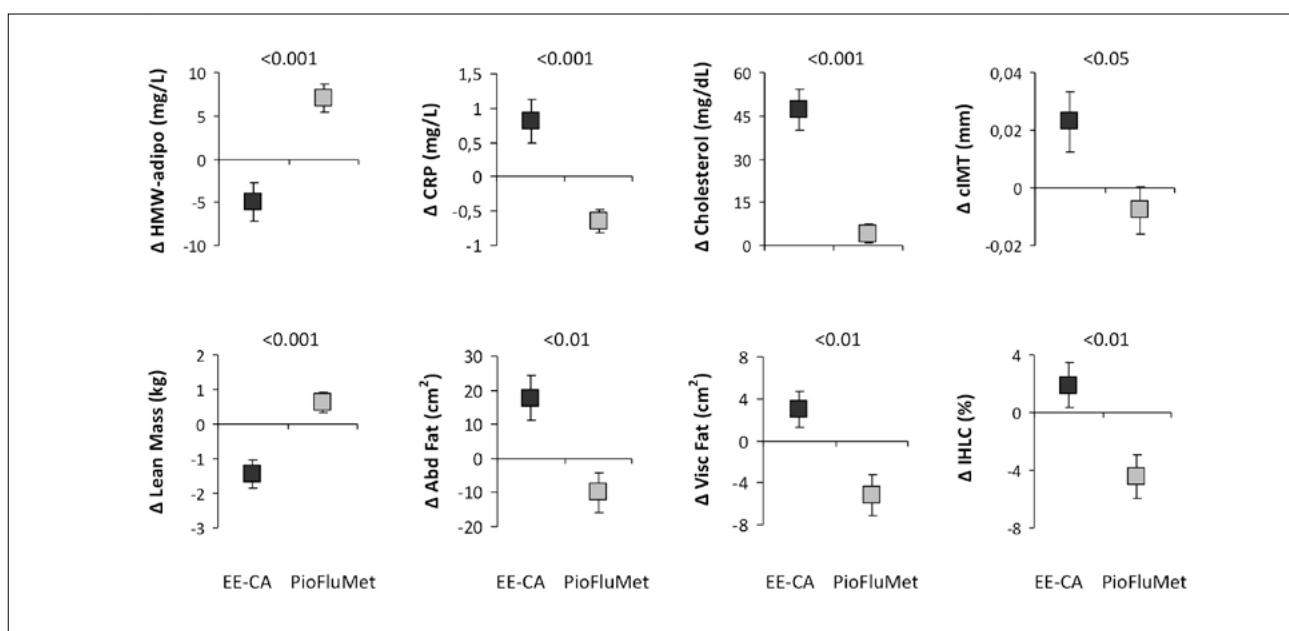
Awardee: Lourdes Ibáñez

Programme 4 ■

Premio al Mejor Póster, 37 Congreso Anual de la Sociedad Española de Endocrinología Pediátrica (2011)

Awardee: Lourdes Ibáñez

Programme 4 ■



Changes over 6 months in HMW-adiponectin (HMW-adipo), C-reactive protein (CRP), total cholesterol, carotid intima-media thickness (cIMT), lean mass, abdominal and visceral fat areas (Abd Fat and Visc Fat, by MRI) and intrahepatic lipid content (IHLC, by MRI) in adolescent girls with androgen excess treated with ethinylestradiol-cyproteroneacetate (EE-CA, N=17; dark grey) or low-dose pioglitazone-flutamide-metformin (PioFluMet, N=17; light grey). Results are shown as mean and SEM. J Clin Endocrinol Metab, 96, 3361-3366 (2011).

# Islet cell and stem cell physiology

Universidad Pablo de Olavide, Centro Andaluz de Biología Molecular y Medicina Regenerativa, Sevilla  
[www.cabimer.es](http://www.cabimer.es)



**Principal Investigator** Franz Martín [fmarber@upo.es](mailto:fmarber@upo.es) **Associate researchers** Francisco Bedoya, Genoveva Berná, Gladys Cahuana, Remedios Ramírez, Bernat Soria, Juan Tejedo, Anabel Rojas, Ángeles Ortega **PhD students** Manuel Carrasco, Rafael Tapia, Estefanía Caballano, Carmen Salguero, Irene Delgado, Enrique Jurado, Daniela Pezolla, Emilio López **Lab technicians** Raquel Araujo, Irene Díaz Contreras, Antonio Cárdenas, Ana Belén Hitos

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Publications: 2

First decile: 2

Research grants: 16

National projects: 8

Autonomous Community projects: 8

Scientific collaborations within Ciberdem: 1

Clinical trials: 4

PhD theses: 2

Patents: 1

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## Programmes

Programme 3. Impact of beta cell dysfunction and plasticity on the natural history of diabetes. Development of novel treatment strategies.

## Keywords

Beta-cell signal transduction. Islet degeneration and damage. Islet development.

## Main lines of research

- The study of interactive pathways implicated in 'stemness'.
- The role of NO in embryonic stem cell differentiation and survival.
- Transcriptional network operating during pancreas development.
- The differentiation of human embryonic stem cells (hESCs) to beta-cell like.
- The obtention of IPS and differentiation to beta-cell like.
- The role of endothelial factors in adult islet-cell proliferation.
- The regulation of beta-cell survival.
- Clinical trials for diabetes complications.

## Publications

Angiographic demonstration of neoangiogenesis after intra-arterial infusion of autologous bone marrow mononuclear cells in diabetic patients with critical limb ischemia Ruiz-Salmeron R, de la Cuesta-Diaz A, Constantino-Bermejo

M, Pérez-Camacho I, Marcos-Sánchez F, Hmadcha A, Soria B Cell Transplant, 20, 1629-1639 (2011)	Investigación y desarrollo de nuevas posibilidades de aplicaciones terapéuticas en el aceite de oliva
<u>PMID 22289660. 1st decile. IF 6.204. Programme 3</u>	MICINN, IPT-060000-2010-028: 2010-2013 Principal Investigator: Franz Martín <i>National project. Programme 3</i>
Exogenous nucleosides modulate expression and activity of transcription factors in Caco-2 cells Ortega Á, Gil Á, Sánchez-Pozo A J Nutr Biochem, 22, 595-604 (2011) <u>PMID 20970311. 1st decile. IF 4.538. Programme 3</u>	Guía para la sustantación de declaraciones en salud en alimentos: funciones inmune, cognitiva y síndrome metabólico MICINN, IPT-20111008: 2011-2014 Principal Investigator: Franz Martín <i>National project. Programme 3</i>
<b>Research grants</b> TERCEL Network ISCIII, RD06/0010/0025: 2010-2011 Principal Investigator: Bernat Soria Associate investigators: Franz Martín, Karim Hmdcha, Francisco Bedoya, Juan Tejedo <i>National project. Programme 3</i>	The role of endothelial factors in the obtention of insulin-secreting cells from adult pancreatic stem cells Consejería de Salud, Junta de Andalucía, PI00022/2008: 2009-2012 Principal Investigator: Franz Martín Associate investigators: Patricia Moreno, Elvira León, Verónica Rivero, Javier Navarro <i>Autonomous Community project. Programme 3</i>
The role of GATA4 transcription factor in endoderm and pancreas development ISCIII, PI108/0018: 2009-2011 Principal Investigator: Anabel Rojas <i>National project. Programme 3</i>	NO regulation of mouse and human beta-cell and pancreatic islet survival during the isolation process Consejería de Salud, Junta de Andalucía, PI0095/07: 2008-2011 Principal Investigator: Juan R Tejedo Associate investigators: Francisco J Bedoya, Gladys M Cahuana <i>Autonomous Community project. Programme 3</i>
Diabetes mellitus cell therapy: the role of intercellular signalling pathways and intracellular material transfer ISCIII, PI-10/00964: 2011-2013 Principal Investigator: Bernat Soria Associate investigators: Franz Martín, Karim Hmadcha, Miguel Martín, Lourdes Acosta, Ana Serna, Alfredo Santana, Rafael Ruiz, Antonio de la Cuesta, Inmaculada Pérez Camacho, Yolanda Aguilera, Mónica Navarro <i>National project. Programme 3</i>	Transcriptional control during endoderm pancreas development Consejería de Salud, Junta de Andalucía, PI0008/10: 2010-2012 Principal Investigator: Anabel Rojas Associate investigators: Raquel Araujo <i>Autonomous Community project. Programme 3</i>
Cell therapy for critical lower-limb ischemia in type 2 diabetes insulinized patients: a study of insulin demand MSPS/Dirección General de Terapias Avanzadas, TRA-120: 2010-2012 Principal Investigator: Bernat Soria Associate investigators: Karim Hmadcha, Rafael Ruiz, Antonio de la Cuesta, Inmaculada Pérez Camacho, Franz Martín <i>National project. Programme 3</i>	Monoclonal antibody characterization Fundación Progreso y Salud: 2010-2011 Principal Investigator: Franz Martín Associate investigators: Genoveva Berná, Gladys M Cahuana <i>Autonomous Community project. Programme 3</i>
Uso del óxido nítrico para generar líneas celulares a partir de células madre y progenitores de origen adulto MICINN, IPT-2011-1615-900000: 2011-2014 Principal Investigator: Bernat Soria, Juan Tejedo <i>National project. Programme 3</i>	Obtención de células productoras de insulina a partir de células pluripotenciales (Terapia celular de la diabetes mellitus) Consejería de Innovación, Ciencia y Empresa. Junta de Andalucía, CTS-6505: 2011-2013 Principal Investigator: Bernat Soria <i>Autonomous Community project. Programme 3</i>
Métodos para la verificación del cumplimiento de la dieta en caso de intolerancia alimentarias mediante la detección de marcadores serológicos MICINN, IPT-2011-0952-900000: 2011-2014 Principal Investigator: Franz Martín <i>National project. Programme 3</i>	Regulación del estado de autorenovación y pluripotencia de células troncales embrionarias por el Oxido Nítrico

Consejería de Salud, Junta de Andalucía, PI-0723:  
2011-2012  
Principal Investigator: Juan Tejedo  
*Autonomous Community project. Programme 3*

Optimización de la producción de endodermo definitivo  
Consejería de Salud, Junta de Andalucía, PI 0105/2010:  
2011-2013  
Principal Investigator: Francisco Bedoya  
*Autonomous Community project. Programme 3*

Elaboración de una novedosa bebida de naranja de baja graduación alcohólica y evaluación de su potencial efecto beneficioso para la salud  
Consejería de Innovación, Ciencia y Empresa. Junta de Andalucía, CTS-4026: 2010-2012  
Principal Investigator: Soledad Fernández Pachón  
*Autonomous Community project. Programme 3*

#### **Scientific collaborations within Ciberdem**

The production of monoclonal antibodies which selectively react with cell surface molecules on human pancreatic beta cells  
ANTIBECCELL: 2009-2011  
Coordinator: Juan Tejedo  
Ciberdem groups: Martín F, Montanya E, Nadal A

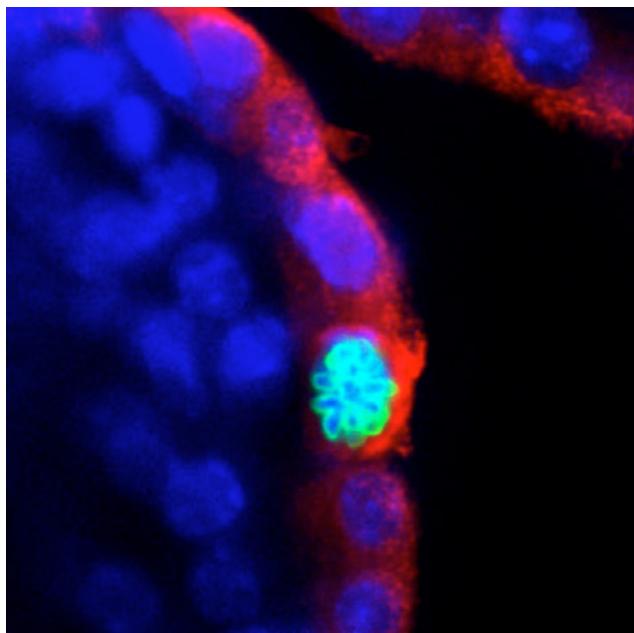
#### **Clinical trials**

Uso de las células troncales mesenquimales de tejido adiposo (CeTMAd) como terapias de regeneración celular en el síndrome de isquemia crónica crítica de miembros inferiores en pacientes diabéticos

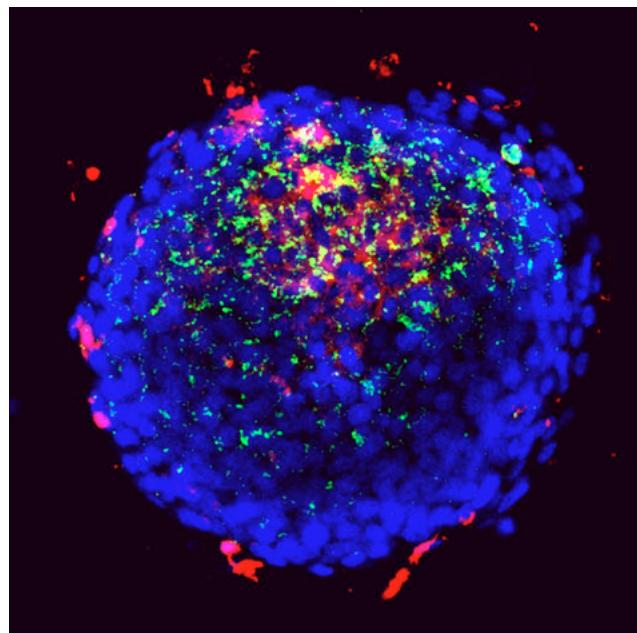
2008-001837-88: 2010-2012  
Coordinator: Antonio de la Cuesta  
*Programme 3*

Ensayo clínico fase I/II multicéntrico, abierto y aleatorizado para el estudio del uso de las células troncales mesenquimales de tejido adiposo (CeTMAd) como terapia de regeneración celular en el síndrome de isquemia crónica crítica de miembros inferiores en pacientes no diabéticos  
2009-013554-32: 2009-2012  
Coordinator: R Ruiz Salmeron  
*Programme 3*

Ensayo clínico fase I/II multicéntrico, abierto, aleatorizado y controlado para el estudio del uso de las células madre como terapia celular en isquemia crítica del miembro inferior en pacientes diabéticos tipo 2 insulinizados: estudio de las necesidades de insulina  
2010-019774-33: 2011-2012  
Coordinator: Bernat Soria  
*Programme 3*



Beta cell on the edge of an islet replicating itself. DAPI (in blue), insulin (in red) and Ki67 (in green).



Pancreatic islet expressing a glucokinase mutation entering into apoptosis. DAPI (in blue), TUNEL (in red) and EGFP (in green).

Ensayo clínico multicéntrico fase I/II aleatorizado y controlado con placebo, para evaluación de seguridad y factibilidad de la terapia con dos dosis distintas de células troncales mesenquimales autólogas de tejido adiposo (CeTMAd) en pacientes con esclerosis múltiple secundariamente progresiva, que no responden adecuadamente a los tratamientos registrados

2008-004015-35: 2008-2011

Coordinator: Óscar Fernández

*Programme 3*

#### **PhD theses**

Caracterización de marcadores de líneas de células troncales embrionarias humanas

Author: Gemma García Jurado

Thesis advisor: Juan Tejedo

University: Universidad Pablo de Olavide

Thesis defense date: May 13, 2011

*Programme 3*

Epigenética de los procesos de autorrenovación, pluripotencialidad y diferenciación de las células troncales

Author: Angélica Horrillo Ledesma

Thesis advisor: Bernat Soria

University: Universidad Pablo de Olavide

Thesis defense date: January 20, 2011

*Programme 3*

#### **Patents**

Empleo de anticuerpos anti-beta-lactoglobulina en el diagnóstico y seguimiento de la celiaquía

Patent application number: P201131979

Inventors: Franz Martín, Bernat Soria, María Ángeles Ortega

Fundación Progreso y Salud-Universidad Pablo de Olavide

*Programme 3 ■*

# Lipids and Arteriosclerosis Research Unit

Institut d'Investigació Sanitària Pere Virgili, Hospital Universitari Sant Joan de Reus  
[www.iispv.cat](http://www.iispv.cat)



**Principal Investigator** Lluís Masana [luis.masana@urv.cat](mailto:luis.masana@urv.cat) **Research directors** Josep Ribalta, Rosa Solà **Senior researchers** Anna Cabré, Joan Carles Vallvé **Associate researchers** Núria Plana, Raimon Ferré **Nutritionist** Jordi Merino **Postdoctoral fellows** Iolanda Lázaro, Gemma Aragonès, Montserrat Guardiola, Rosa Maria Valls, Valentini Konstantinidou, Sandra Guaita **PhD students** Úrsula Catalán, Marta González, Isabel Martorell, Anna Pedret, Paula Saavedra, Daiana Ibarretxe **Lab manager** Josefa Girona **Lab technicians** Mercedes Heras, Carme Buixadera, Sara Fernández, Roser Rosales **Administrative staff** Sílvia Solé

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Publications: 10

First decile: 1

Q1: 5

Q2: 4

With other Ciberdem groups: 1

With other CIBERS: 2

With other networks: 1

With other international groups: 2

Research grants: 5

National projects: 5

Scientific collaborations within Ciberdem: 1

Clinical trials: 6

Clinical practice guidelines: 2

PhD theses: 1

Spin-offs: 1

Awards: 1

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## Programmes

Programme 1. Molecular and physiological determinants of lifestyle in diabetes/obesity. Population studies for genetic-epigenetic association analysis in type 2 diabetes mellitus and related traits.

Programme 2. Mechanisms promoting the development of diabetes and its vascular complications. Associated disorders and co-morbidities. Strategies for prevention and treatment.

## Keywords

Insulin sensitivity and resistance. Metabolic syndrome. Biomarkers and imaging. Endothelium. Macrovascular disease. Nutrigenomics.

## Main lines of research

- Atherogenic dyslipidaemia in diabetes, obesity and metabolic syndrome.
- The characterization of plasma lipoprotein subclasses by NMR, metabolomics and lipidomics.
- Adipose tissue dysfunction as a major determinant of AD.
- Fatty Acid-Binding Proteins (FABPs) and insulin resistance in different tissues.
- Fatty acids and adipokine-induced endothelial dysfunction.
- AD and subclinical atherosclerosis.
- FFA, extracellular matrix and artery wall dysfunction in diabetes.
- The epigenetics of atherosclerosis.
- The impact of nutrition on metabolic and cardiovascular risk.
- Nutrigenomics.

## Publications

A primary-school-based study to reduce prevalence of childhood obesity in Catalunya (Spain)--EDAL-Educació en alimentació: study protocol for a randomised controlled trial  
Giralt M, Albaladejo R, Tarro L, Moriña D, Arija V, Solà R  
Trials, 12, 54 (2011)

PMID 21352597. Q2. IF 2.080. Programme 1

Bioavailability of phenols from a phenol-enriched olive oil  
Suárez M, Valls RM, Romero MP, Macià A, Fernández S, Giralt M, Solà R, Motilva MJ  
Br J Nutr, 106, 1691-1701 (2011)

PMID 21736768. Q2. IF 3.072. Programme 1

Clinical features of patients with hypertriglyceridemia referred to lipid units: registry of hypertriglyceridemia of the Spanish Arteriosclerosis Society  
Valdivielso P, Pintó X, Mateo-Gallego R, Masana L, Alvarez-Sala L, Jarauta E, Suárez M, García-Arias C, Plana N, Laguna F; Registro de HTG de la SEA  
Med Clin (Barc), 136, 231-238 (2011)

PMID 21239026. Q2. IF 1.413. Programme 1

Effect of a traditional Mediterranean diet on apolipoproteins B, A-I, and their ratio: a randomized, controlled trial  
Solà R, Fitó M, Estruch R, Salas-Salvadó J, Corella D, de La Torre R, Muñoz MA, López-Sabater Mdel C, Martínez-González MA, Arós F, Ruiz-Gutierrez V, Fiol M, Casals E, Wärnberg J, Buil-Cosiales P, Ros E, Konstantinidou V, Lapetra J, Serra-Majem L, Covas MI  
Atherosclerosis, 218, 174-180 (2011)

PMID 21640348. Q1. IF 4.086. With other CIBERs: Ciberesp, Ciberobn. With other international groups. Programme 1

Functional analysis of LDLR promoter and 5' UTR mutations in subjects with clinical diagnosis of familial hypercholesterolemia  
De Castro-Orós I, Pampín S, Bolado-Carrancio A, De Cubas

A, Palacios L, Plana N, Puzo J, Martorell E, Stef M, Masana L, Civeira F, Rodríguez-Rey JC, Pocoví M  
Hum Mutat, 32, 868-872 (2011)

PMID 21538688. Q1. IF 5.956. With other CIBERs: Ciberer. With other networks: Recava. Programme 2

High-density lipoprotein cholesterol and apolipoprotein A1 levels strongly influence the reactivity of small peripheral arteries  
Ferré R, Aragonès G, Plana N, Merino J, Heras M, Buixadera C, Masana L  
Atherosclerosis, 216, 115-119 (2011)

PMID 21367423. Q1. IF 4.086. Programme 2

Mannose binding lectin 2 haplotypes do not affect the progression of coronary atherosclerosis in men with proven coronary artery disease treated with pravastatin  
Alipour A, Cabezas MC, Elte JW, Vallvé JC, Ribalta J, Zwinderman AH, Defesche JC, Jukema JW  
Atherosclerosis, 215, 125-129 (2011)

PMID 21211797. Q1. IF 4.086. With other international groups. Programme 2

Nutritional biomarkers and foodomic methodologies for qualitative and quantitative analysis of bioactive ingredients in dietary intervention studies  
Puiggròs F, Solà R, Bladé C, Salvadó MJ, Arola L  
J Chromatogr A, 1218, 7399-7414 (2011)

PMID 21917262. 1st decile. IF 4.194. Programme 1

Surface fitting of 2D diffusion-edited <sup>1</sup>H NMR spectroscopy data for the characterisation of human plasma lipoproteins

Mallol R, Rodríguez MA, Heras M, Vinaixa M, Cañellas N, Brezmes J, Plana N, Masana L, Correig X  
Metabolomics, 7, 572-582 (2011)

DOI 10.1007/s11306-011-0273-8. Q2. IF 3.608. With other Ciberdem groups: Correig X. Programme 2

Toxicology evaluation of a procyanidin-rich extract from grape skins and seeds

Lluís L, Muñoz M, Nogués MR, Sánchez-Martos V, Romeu M, Giralt M, Valls J, Solà R  
Food Chem Toxicol, 49, 1450-1454 (2011)

PMID 21443917. Q1. IF 2.602. Programme 2

## Research grants

Dislipemia aterógena de la obesidad, síndrome metabólico y diabetes tipo 2: caracterización metabólica y mecanismos patogénicos

FIS, PI081409: 2009-2012

Principal Investigator: Lluís Masana

Associate investigator: Jesús Brezmes

National project. With other Ciberdem groups: Correig X. Programme 2

<p>Caracterización bioquímica, metabólica y genética de la hipertrigliceridemia asociada a alto riesgo cardiovascular FIS, PI081579: 2009-2012 Principal Investigator: Josep Ribalta Associate investigator: Nicolau Cañellas <i>National project. With other Ciberdem groups: Correig X.</i> <i>Programme 2</i></p>	<p>continuada en pacientes con hipercolesterolemia primaria y dislipidemia mixta 2010-021627-27: 2011-2013 Coordinator: Lluís Masana <i>Programme 2</i></p>
<p>Aceite de oliva virgen y función de las lipoproteínas de alta densidad (HDL), un modelo de preparación especializada de un alimento funcional Ministerio de Ciencia e Innovación, AGL2009-13517-C03-03: 2008-2012 Research Director: Rosa Solà <i>National project. Programme 1</i></p>	<p>Estudio multicéntrico y aleatorizado para evaluar la tolerabilidad y eficacia de AMG 145 en el colesterol LDL, en comparación con ezetimiba, en sujetos hipercolesterolémicos incapaces de tolerar una dosis eficaz de un inhibidor de la HMG-CoA reductasa (Estudio GAUS) 20090159-26: 2011-2012 Coordinator: Lluís Masana <i>Programme 2</i></p>
<p>Ensayo de intervención nutricional aleatorizado, doble ciego, controlado con placebo, para valorar la eficacia y la seguridad de yogur suplementado con mobilee™ comparado con yogur no suplementado, sobre la función articular, evolución ecográfica y calidad de vida de adultos con gonalgia de baja intensidad Ministerio de Ciencia e Innovación, CENIT: 2010-2011 Research Director: Rosa Solà <i>National project. Programme 1</i></p>	<p>Estudio multicéntrico, controlado con placebo, aleatorizado y a doble ciego para evaluar la tolerabilidad y eficacia de AMG 145 en el colesterol LDL en sujetos con hipercolesterolemia familiar heterocigotica (Estudio RUTHERFORD) 20090158-39: 2011-2012 Coordinator: Lluís Masana <i>Programme 2</i></p>
<p>Papel de los diferentes tipos de ácidos grasos y de la proteína de unión a ácidos grasos 4 (FABP4) en el remodelado de la pared arterial asociado a pacientes diabéticos ISCIII, PI10/02547: 2011-2013 Principal Investigator: Joan Carles Vallvé <i>National project. Programme 2</i></p>	<p>Ensayo en Fase III de largo plazo, randomizado, en grupos paralelos, doble ciego, controlado con placebo, para evaluar la seguridad y eficacia de 50µg y 100 µg/día de eprotirome en pacientes con hipercolesterolemia familiar heterocigótica que están bajo un tratamiento de referencia habitual adecuado 2011-001483-21: 2011-2012 Coordinator: Lluís Masana <i>Programme 2</i></p>
<p><b>Scientific collaborations within Ciberdem</b> Ciberdem Biobank Coordinator: Anna Novials <i>Ciberdem Biobank nodes: Masana L, Gomis R, Novials A, Vendrell J, Castaño L, Serrano-Ríos M, Soriguer F, Carmena R, Blanco-Vaca F</i></p>	<p>Efectos de compuestos bioactivos combinados (armolipid plus ®) sobre el perfil lipídico y los criterios clínicos de síndrome metabólico en pacientes con niveles de c-ldl serico elevados 01AP022020511: 2011-2012 Coordinator: Rosa Solà <i>Programme 2</i></p>
<p><b>Clinical trials</b> Cardiovascular Fixed Combination Pill ASR: Ensayo clínico farmacodinámico de la combinación a dosis fijas de ácido acetilsalicílico, simvastatina y ramipril (Cardiovascular Polypill); Colesterol LDL 2010-019-720-32: 2010-2011 Coordinator: Nuria Plana <i>Programme 2</i></p>	<p><b>Clinical practice guidelines</b> Triglyceride-rich lipoproteins and high-density lipoprotein cholesterol in patients at high risk of cardiovascular disease: evidence and guidance for management Chapman MJ, Ginsberg HN, Amarenco P, Andreotti F, Borén J, Catapano AL, Descamps OS, Fisher E, Kovanen PT, Kuivenhoven JA, Lesnik P, Masana L, Nordestgaard BG, Ray KK, Reiner Z, Taskinen MR, Tokgözoglu L, Tybjærg-Hansen A, Watts GF; European Atherosclerosis Society Consensus Panel Eur Heart J, 32, 1345-1361 (2011) <i>Programme 2</i></p>
<p>Estudio de 12 semanas internacional, multicéntrico, doble ciego, aleatorizado, con grupos paralelos, controlado con placebo para evaluar la eficacia y la seguridad de niacina de liberación prolongada (LP)/laropiprant sumado a terapia modificadora de lípidos</p>	

ESC/EAS Guidelines for the management of dyslipidaemias:  
the Task Force for the management of dyslipidaemias of the  
European Society of Cardiology (ESC) and the European  
Atherosclerosis Society (EAS)

European Association for Cardiovascular Prevention &  
Rehabilitation, Reiner Z, Catapano AL, De Backer G,  
Graham I, Taskinen MR, Wiklund O, Agewall S, Alegria  
E, Chapman MJ, Durrington P, Erdine S, Halcox J, Hobbs  
R, Kjekshus J, Filardi PP, Riccardi G, Storey RF, Wood D;  
ESC Committee for Practice Guidelines (CPG) 2008-2010  
and 2010-2012 Committees, Bax J, Vahanian A, Auricchio  
A, Baumgartner H, Ceconi C, Dean V, Deaton C, Fagard  
R, Filippatos G, Funck-Brentano C, Hasdai D, Hobbs R,  
Hoes A, Kearney P, Knuuti J, Kohl P, McDonagh T, Moulin C,  
Poldermans D, Popescu BA, Reiner Z, Sechtem U, Sirnes  
PA, Tendera M, Torbicki A, Vardas P, Widimsky P, Windecker  
S, Funck-Brentano C, Poldermans D, Berkenboom G, De  
Graaf J, Descamps O, Gotcheva N, Griffith K, Guida GF,  
Gulec S, Henkin Y, Huber K, Kesaniemi YA, Lekakis J,  
Manolis AJ, Marques-Vidal P, Masana L et al.

Eur Heart J, 32, 1769-1818 (2011)

*Programme 2*

#### PhD theses

Utilitat de la tonometria arterial perifèrica per a l'avaluació  
del risc cardiovascular

Author: Raimon Ferré Vallès

Thesis advisor: Lluís Masana

University: Universitat Rovira i Virgili

Thesis defense date: October 20, 2011

*Programme 2*

#### Spin-offs

Beyond Food SL

Description: Support to industry for the validation of  
functional food

Researchers: L Masana, R Solà, JC Vallvé, J Ribalta, J  
Girona, C Prats

Collaborating institution: Universitat Rovira i Virgili

Year of creation: 2007

*Programme 1*

#### Awards

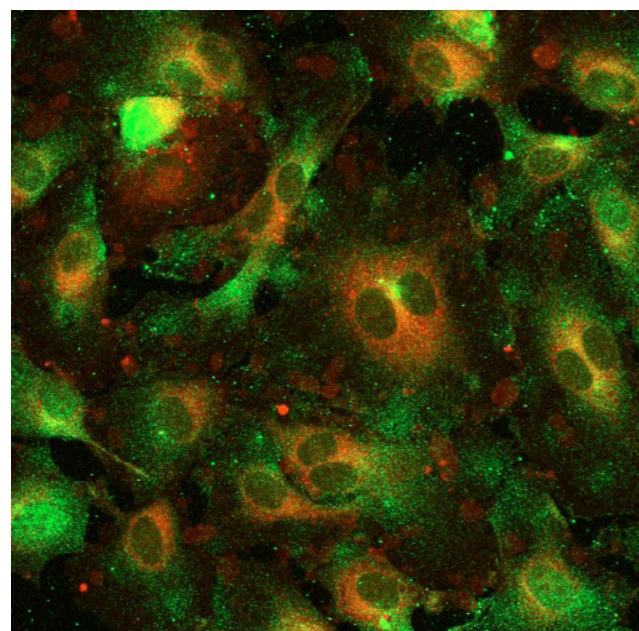
Premi extraordinari de doctorat del curs 2010-2011,  
Universitat Rovira i Virgili (2011)

Awardee: Iolanda Lázaro López

*Programme 2* ■



J774.A1 macrophages.



Colocalization of FABP4 in the membrane of vascular endothelial cells.

# Group of Research into Diabetes and Metabolism

Hospital Universitari de Bellvitge, Institut d'Investigació Biomèdica de Bellvitge, Universitat de Barcelona

[www.bellvitgehospital.cat](http://www.bellvitgehospital.cat)

[www.idibell.cat](http://www.idibell.cat)

[www.ub.edu](http://www.ub.edu)



**Principal Investigator** Eduard Montanya [montanya@ub.edu](mailto:montanya@ub.edu) **Associate researchers** José Manuel Gómez, Montserrat Nacher, Manuel Pérez, Juan Soler, Noelia Téllez, Nuria Vilarrasa **Research assistant** Elisabet Estil·les **PhD students** Jorge Caballero, Mar Pairó, Marina Vilaseca **Lab technician** Jessica Escoriza

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Publications: 4

First decile: 1

Q1: 3

With other CIBERs: 1

With other international groups: 1

Research grants: 4

European projects: 1

National projects: 1

Autonomous Community projects: 1

Private funds: 1

Scientific collaborations within Ciberdem: 3

PhD theses: 1

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## Programmes

Programme 3. Impact of beta cell dysfunction and plasticity on the natural history of diabetes. Development of novel treatment strategies.

Programme 4. Use of biomedical approach systems to develop personalized therapies for diabetes.

## Keywords

Islet degeneration and damage. Islet transplantation. Gastro-entero pancreatic factors.

## Main lines of research

The study of the cellular and molecular biology of pancreatic islet cells and the study of insulin resistance in obesity. The specific focus of the group is the mechanisms of destruction, protection and regeneration of pancreatic beta cells with a particular interest in the cell therapy of diabetes, and the metabolic and molecular regulation of insulin resistance by adipose tissue.

## Publications

Gastrin treatment stimulates  $\beta$ -cell regeneration and improves glucose tolerance in 95% pancreatectomized rats  
Téllez N, Joanny G, Escoriza J, Vilaseca M, Montanya E  
Endocrinology, 152, 2580-2588 (2011)  
[PMID 21558313](https://pubmed.ncbi.nlm.nih.gov/21558313/). Q1. IF 4.993. Programme 3

Glucose-dependent changes in SNARE protein levels in pancreatic  $\beta$ -cells  
Torrejón-Escribano B, Escoriza J, Montanya E, Blasi J  
Endocrinology, 152, 1290-1299 (2011)  
[PMID 21285315](#). Q1. IF 4.993. With other CIBERs: Ciberdem. Programme 3

Evaluation of bone mineral density loss in morbidly obese women after gastric bypass: 3-year follow-up  
Vilarrasa N, San José P, García I, Gómez-Vaquero C, Miras PM, de Gordejuela AG, Masdevall C, Pujol J, Soler J, Gómez JM  
Obes Surg, 21, 465-472 (2011)  
[PMID 21188546](#). Q1. IF 3.078. Programme 4

Heterozygous inactivation of the Na/Ca exchanger increases glucose-induced insulin release,  $\beta$ -cell proliferation, and mass  
Nguidjoe E, Sokolow S, Bigabwa S, Pachera N, D'Amico E, Allagnat F, Vanderwinden JM, Sener A, Manto M, Depreter M, Mast J, Joanny G, Montanya E, Rahier J, Cardozo AK, Eizirik DL, Schurmans S, Herchuelz A  
Diabetes, 60, 2076-2085 (2011)  
[PMID 21659499](#). 1st decile. IF 8.889. With other international groups. Programme 3

### Research grants

IMMEEDIA-Immunomodulatory Effects of Exercise in Type 1 Diabetes  
IRSES-247472: 2010-2014  
Coordinator: R Cobella  
Principal Investigator: Eduard Montanya  
European project. Programme 4

Diferenciación de células productoras de insulina a partir de células troncales del páncreas adulto. Aplicación en terapia celular de la diabetes  
ISCIII, PI10/00636: 2010-2013  
Principal Investigator: Eduard Montanya  
National project. Programme 3

Grup de Recerca en Diabetes i Metabolisme  
Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR), 2009SGR201: 2009-2013  
Coordinator: Eduard Montanya  
Autonomous Community project. Programme 4

Transcriptómica de la regeneración endocrina. Identificación de las vías implicadas en la diferenciación postnatal del páncreas endocrino  
Sociedad Española de Diabetes: 2011  
Principal Investigator: Noelia Téllez  
Private funds. Programme 4

### Scientific collaborations within Ciberdem

Adult adipose tissue-derived progenitor cells: the influence

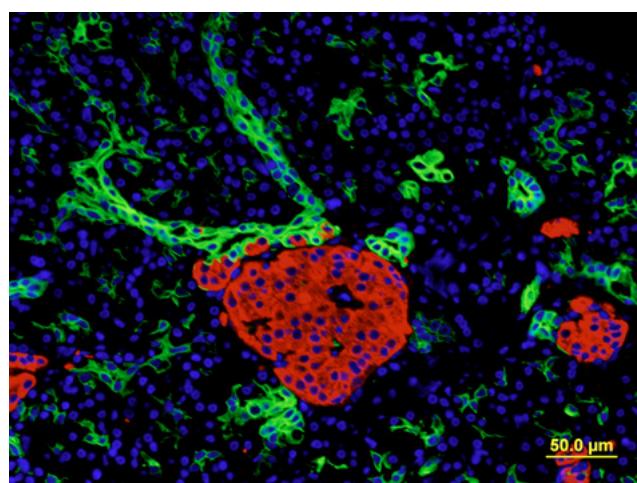
of the clinical phenotype and adipose depot origin on their biological properties  
STEMOB: 2009-2011  
Coordinator: Joan J Vendrell  
Ciberdem groups: Montanya E, Vendrell J, Zorzano A, Balsinde J, Gómez-Foix AM, Simó R, Vázquez-Carrera M

Determinants of insulin resistance and glucose tolerance disorders, including diabetes, in severe obesity and their changes after bariatric surgery-induced weight loss  
DIASOBS: 2009-2011  
Coordinator: Héctor F Escobar Morreale  
Ciberdem groups: Montanya E, Correig X, Escobar-Morreale HF, Simó R, Vendrell J

The production of monoclonal antibodies which selectively react with cell surface molecules on human pancreatic beta cells  
ANTIBECELL: 2009-2011  
Coordinator: Juan Tejedo  
Ciberdem groups: Montanya E, Martín F, Nadal A

### PhD theses

Efectos de la administración de un análogo del GLP-1 sobre las células endocrinas del páncreas  
Author: Géraldine Joanny Ordóñez  
Thesis advisor: Eduard Montanya  
University: Universitat de Barcelona  
Thesis defense date: November 25, 2011  
Programme 3 ■



Human pancreas section showing the abundance of ductal structures (CK 19 staining, green), and close contact with islets and insulin positive cells (insulin staining, red).

# Unit of Cell Physiology and Nutrition IB-UMH

Instituto de Bioingeniería, Universidad Miguel Hernández, Elx  
<http://diabetes.umh.es>



**Principal Investigator** Angel Nadal [nadal@umh.es](mailto:nadal@umh.es) **Associate researchers** Esther Fuentes, Elena García, Ivan Quesada, Cristina Ripoll, Ana Belén Ropero **Postdoctoral fellows** Paloma Alonso Magdalena, Elaine Vieira, Patricia Ñeco **PhD students** Ernesto Caballero, Marta García Arévalo, Alejandro González, Laura Marroquí, Alba Moratalla, Beatriz Merino **Lab technicians** María Luisa Navarro, Diego Sevilla, María Salomé

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Publications: 7

First decile: 2

Q1: 2

Q2: 3

With other Ciberdem groups: 1

With other CIBERs: 1

With other international groups: 2

Research grants: 4

European projects: 1

National projects: 2

Autonomous Community projects: 1

Scientific collaborations within Ciberdem: 1

Awards: 1

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## Programmes

Programme 3. Impact of beta cell dysfunction and plasticity on the natural history of diabetes. Development of novel treatment strategies.

## Keywords

Beta-cell signal transduction. Insulin secretion. Insulin sensitivity and resistance. Cytokines.

## Main lines of research

-We study the link between endocrine disruptors and type 2 diabetes. We investigate the actions of oestrogens and environmental oestrogenic pollutants in the function of pancreatic alpha and beta cells with an emphasis on the molecular mechanisms involved.

-Signal transduction pathways involved in the function and pathology of alpha and beta-cells. We study the activation of signalling pathways by leptin receptors. Additionally, we investigate the adaptations of islet-cells to obesity and malnutrition states.

-The role of ANP (atrial natriuretic peptide) receptors in beta-cell function and blood glucose homeostasis.

## Publications

A role for the putative cannabinoid receptor GPR55 in the islets of Langerhans  
 Romero-Zerbo SY, Rafacho A, Díaz-Arteaga A, Suárez J, Quesada I, Imbernon M, Ross RA, Dieguez C, Rodríguez de Fonseca F, Nogueiras R, Nadal A, Bermúdez-Silva FJ  
*J Endocrinol*, 211, 177-185 (2011)

PMID 21885477. Q2. IF 3.099. With other CIBERs: Ciberobn. With other international groups. Programme 3

Endocrine disruptors in the etiology of type 2 diabetes mellitus  
 Alonso-Magdalena P, Quesada I, Nadal A

*Nat Rev Endocrinol*, 7, 346-353 (2011)

PMID 21467970. 1st decile. IF 9.191. Programme 3

Involvement of ATP-sensitive potassium (K(ATP)) channels in the loss of beta-cell function induced by human islet amyloid polypeptide  
 Soty M, Visa M, Soriano S, Carmona Mdel C, Nadal Á, Novials A

*J Biol Chem*, 286, 40857-40866 (2011)

PMID 21984830. Q1. IF 5.328. With other Ciberdem groups: Novials A. Programme 3

Leptin downregulates expression of the gene encoding glucagon in alphaTC1-9 cells and mouse islets  
 Marroquí L, Vieira E, Gonzalez A, Nadal A, Quesada I  
*Diabetologia*, 54, 843-851 (2011)  
PMID 21234744. 1st decile. IF 6.973. Programme 3

Regulation of K(ATP) channel by 17 $\beta$ -estradiol in pancreatic  $\beta$ -cells

Soriano S, Ripoll C, Fuentes E, Gonzalez A, Alonso-Magdalena P, Ropero AB, Quesada I, Nadal A  
*Steroids*, 76, 856-860 (2011)

PMID 21470558. Q2. IF 3.106. Programme 3

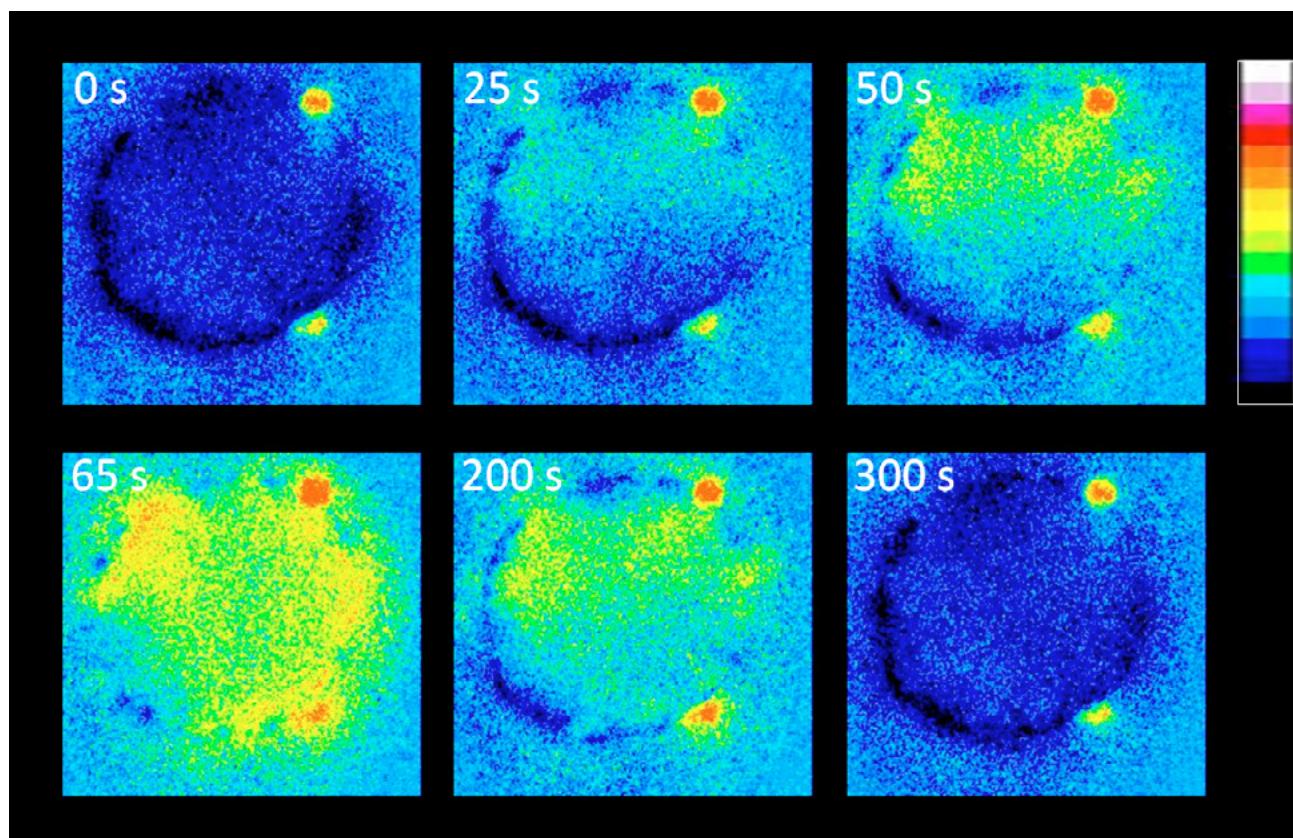
Role of estrogen receptors alpha, beta and GPER1/GPR30 in pancreatic beta-cells

Nadal A, Alonso-Magdalena P, Soriano S, Ripoll C, Fuentes E, Quesada I, Ropero AB  
*Front Biosci*, 16, 251-260 (2011)

PMID 21196169. Q2. IF 4.048. Programme 3

The F-actin cortical network is a major factor influencing the organization of the secretory machinery in chromaffin cells

Torregrosa-Hetland CJ, Villanueva J, Giner D, Lopez-Font I, Nadal A, Quesada I, Viniegra S, Expósito-Romero G, Gil A,



Intracellular calcium changes in an islet of Langerhans in response to elevated glucose levels.

Gonzalez-Velez V, Segura J, Gutiérrez LM  
J Cell Sci, 124, 727-734 (2011)  
*PMID 21303931. Q1. IF 6.290. With other international groups. Programme 3*

#### **Research grants**

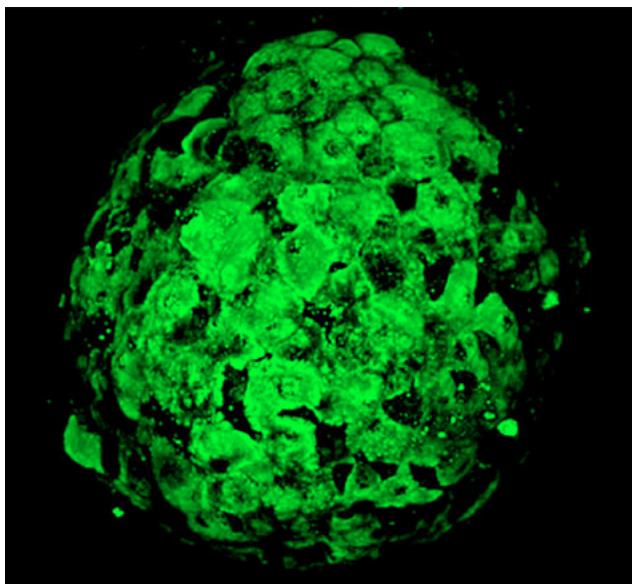
Circadian regulation in the control of insulin and glucagon release and its role in Type 2 diabetes  
European Commission (Programme PEOPLE), 234879: 2009-2011  
Principal Investigator: Ivan Quesada  
Associate investigator: Elaine Vieira  
*European project. Programme 3*

Efectos a corto y largo plazo de la activación de los receptores de estrógenos sobre el contenido, la secreción y la supervivencia de la célula-beta pancreática  
MICINN, BFU2008-01492: 2009-2011

Principal Investigator: Angel Nadal  
*National project. Programme 3*

Análisis de la función de la leptina y la resistencia a la leptina en células alfa y beta del islote de Langerhans  
MICINN, BFU2010-21773: 2011-2013  
Principal Investigator: Ivan Quesada  
*National project. Programme 3*

Caracterización del efecto insulinotrópico rápido de agonistas específicos del receptor de estrógenos B: implicaciones en el tratamiento de la diabetes  
Generalitat Valenciana, PROMETEO/2011/080: 2011  
Principal Investigator: Angel Nadal  
*Autonomous Community project. Programme 3*



3D reconstruction of an islet of Langerhans showing an immunocytochemistry for insulin.

#### **Scientific collaborations within Ciberdem**

The production of monoclonal antibodies which selectively react with cell surface molecules on human pancreatic beta cells  
ANTIBECCELL: 2009-2011  
Coordinator: Juan Tejedo  
*Ciberdem groups: Nadal A, Martín F, Montanya E*

#### **Awards**

First EYPS European Young Physiologists Symposium.  
Award at the Congress of FEPS (Federation of European Physiological Societies) and Turkish Society of Physiological Sciences (2011)  
Awardee: Paloma Alonso-Magdalena  
*Programme 3 ■*

# Metabolic and molecular disturbances in diabetes

Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelona  
[www.idibaps.org](http://www.idibaps.org)



**Principal Investigator** Anna Novials [anovials@clinic.ub.es](mailto:anovials@clinic.ub.es) **Associate researchers** Antonio Ceriello, Pablo García-Rovés, Carles Lerín, Joan Marc Servitja **Postdoctoral fellows** Maud Soty, Paola Casini **Research assistants** Serafín Murillo, Laura Brugnara **PhD students** Montse Visa, Lisa Cadavez, Alba Moreno **Lab technician** Carlos Castaño

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Publications: 8

First decile: 3

Q1: 2

Q2: 3

With other Ciberdem groups: 2

With other CIBERs: 1

With other international groups: 6

Research grants: 7

European projects: 1

National projects: 4

Autonomous Community projects: 1

Private funds: 1

Scientific collaborations within Ciberdem: 3

Clinical trials: 2

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## Programmes

Programme 1. Molecular and physiological determinants of lifestyle in diabetes/obesity. Population studies for genetic-

epigenetic association analysis in type 2 diabetes mellitus and related traits.

Programme 3. Impact of beta cell dysfunction and plasticity on the natural history of diabetes. Development of novel treatment strategies.

## Keywords

Islet amyloid polypeptide/amylin. Islet degeneration and damage. Exercise. Endothelium. Nutrition.

## Main lines of research

-Mechanisms of pancreatic islet dysfunction in type 2 diabetes mellitus, in particular, the process of cytotoxicity as induced by amyloidogenesis.

-Signalling and transcriptional networks in the pancreatic beta cell, mainly related to the modulation of the transcriptional programme under stress conditions.

- Impact of lifestyle on diabetes: metabolic and molecular responses to exercise and nutrition in diabetic patients and animal models.
- Impact of glucose oscillations on cardiovascular complications of diabetes: mechanisms of endothelial dysfunction.

## Publications

Amylin effect in extrapancreatic tissues participating in glucose homeostasis, in normal, insulin-resistant and type 2 diabetic state

Moreno P, Acitores A, Gutiérrez-Rojas I, Nuche-Berenguer B, El Assar M, Rodriguez-Mañas L, Gomis R, Valverde I, Visa M, Malaisse WJ, Novials A, González N, Villanueva-Peña Carrillo ML  
*Peptides*, 32, 2077-2085 (2011)  
PMID 21939703. Q2. IF 2.654. *With other Ciberdem groups: Gomis R, Villanueva-Peña Carrillo ML. With other international groups. Programme 2*

Hypothalamic mitochondrial dysfunction associated with anorexia in the anx/anx mouse

Lindfors C, Nilsson IA, Garcia-Roves PM, Zuberi AR, Karimi M, Donahue LR, Roopenian DC, Mulder J, Uhlén M, Ekström TJ, Davisson MT, Hökfelt TG, Schalling M, Johansen JE  
*Proc Natl Acad Sci U S A*, 108, 18108-18113 (2011)  
PMID 22025706. 1st decile. IF 9.771. *With other international groups. Programme 1*

Involvement of ATP-sensitive potassium (K(ATP)) channels in the loss of beta-cell function induced by human islet amyloid polypeptide

Soty M, Visa M, Soriano S, Carmona Mdel C, Nadal Á, Novials A  
*J Biol Chem*, 286, 40857-40866 (2011)  
PMID 21984830. Q1. IF 5.328. *With other Ciberdem groups: Nadal A. Programme 3*

Laforin, a dual specificity phosphatase involved in Lafora disease, regulates insulin response and whole-body energy balance in mice

Vernia S, Heredia M, Criado O, Rodriguez de Cordoba S, Garcia-Roves PM, Cansell C, Denis R, Luquet S, Foufelle F, Ferre P, Sanz P  
*Hum Mol Genet*, 20, 2571-2584 (2011)  
PMID 21493628. 1st decile. IF 8.058. *With other CIBERs: Ciberer. With other international groups. Programme 1*

Leukocyte telomere length is associated with complications of type 2 diabetes mellitus

Testa R, Olivieri F, Sirolla C, Spazzafumo L, Rippo MR, Marra M, Bonfigli AR, Ceriello A, Antonicelli R, Franceschi C, Castellucci C, Testa I, Procopio AD  
*Diabet Med*, 28, 1388-1394 (2011)  
PMID 21692845. Q2. IF 3.036. *With other international groups. Programme 1*

Meal-induced increases in C-reactive protein, interleukin-6 and tumour necrosis factor  $\alpha$  are attenuated by prandial + basal insulin in patients with Type 2 diabetes

Beisswenger PJ, Brown WV, Ceriello A, Le NA, Goldberg RB, Cooke JP, Robbins DC, Sarwat S, Yuan H, Jones CA, Tan MH; IOOI Study Investigators  
*Diabet Med*, 28, 1088-1095 (2011)  
PMID 21517955. Q2. IF 3.036. *With other international groups. Programme 1*

Mitochondrial DNA backgrounds might modulate diabetes complications rather than T2DM as a whole

Achilli A, Olivier A, Pala M, Hooshiar Kashani B, Carossa V, Perego UA, Gandini F, Santoro A, Battaglia V, Grugni V, Lancioni H, Sirolla C, Bonfigli AR, Cormio A, Boemi M, Testa I, Semino O, Ceriello A, Spazzafumo L, Gadaleta MN, Marra M, Testa R, Franceschi C, Torroni A  
*PLoS ONE*, 6, e21029 (2011)  
PMID 21695278. Q1. IF 4.411. *With other international groups. Programme 1*

Post hoc subgroup analysis of the HEART2D trial demonstrates lower cardiovascular risk in older patients targeting postprandial versus fasting/premeal glycemia  
Raz I, Ceriello A, Wilson PW, Battouï C, Su EW, Kerr L, Jones CA, Milicevic Z, Jacober SJ  
*Diabetes Care*, 34, 1511-1513 (2011)

PMID 21593301. 1st decile. IF 7.141. *With other international groups. Programme 1*

## Research grants

Molecular Mechanisms Underlying the Development of Insulin Resistance: Role of Betaine Supplementation  
Marie Curie Action Call, PCIG-GA-2011-293502: 2011-2014  
Principal Investigator: Carles Lerín  
*European project. Programme 1*

The role of the BACE enzyme (beta-site amyloid precursor protein cleaving enzyme) in pancreatic islet function  
Ministerio de Sanidad y Consumo, PI080088: 2009-2011

Principal Investigator: Anna Novials  
Associate investigators: Sílvia Casas, Paola Casini, Maud Soty  
*National project. Programme 3*

Design, characterization and follow-up of training designed to produce metabolic improvements in type 2 diabetic patients  
Ministerio de Ciencia e Innovación, DPS2008-06922: 2009-2011

Principal Investigator: Joan Aureli Cadefau  
Associate investigator: Anna Novials  
*National project. Programme 1*

Regulation and function of microRNAs in pancreatic islets  
MICINN, BFU2010-17639: 2010-2012

Principal Investigator: JM Servitja  
*National project. Programme 3*

Defective antioxidant response in endothelial cells exposed to oscillating glucose: the role of Nrf2  
MICINN, PI10/01256: 2011-2013  
Principal Investigator: Antonio Ceriello  
*National project. Programme 1*

Diabetis experimental, investigació cel·lular i molecular en models de diabetis experimental  
Agència de Gestió d'Ajuts Universitaris i de Recerca. Generalitat de Catalunya, 2009 SGR 1426: 2009-2013  
Principal Investigator: Ramon Gomis  
*Autonomous Community project. With other Ciberdem groups: Gomis R. Programme 3*

Epigenetic control of gene expression in pancreatic islets  
EFSD/Lilly Fellowship 2010: 2010-2012  
Principal Investigator: JM Servitja  
*Private funds. Programme 3*

#### Scientific collaborations within Ciberdem

Comparative metabolomic analysis for the detection of biomarkers in diabetes  
METADIAB: 2009-2011  
Coordinator: Xavier Correig  
*Ciberdem groups: Novials A, Correig X, Gomis R*

Mechanisms of endothelial dysfunction in diabetes: the role of amylin and circulating endothelial cells  
ENDODIAB: 2009-2011

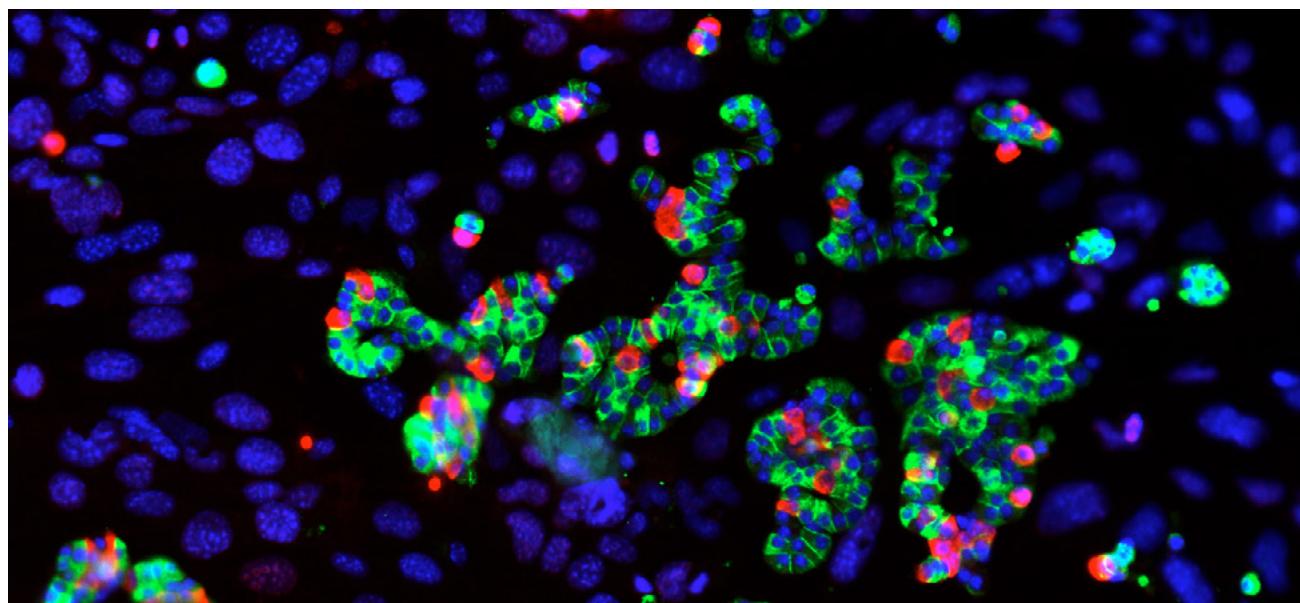
Coordinator: Anna Novials  
Ciberdem groups: Novials A, Gomis R, Villanueva-Peñacarrillo ML

Ciberdem Biobank  
Coordinator: Anna Novials  
Ciberdem Biobank nodes: Novials A, Gomis R, Vendrell J, Masana L, Castaño L, Serrano-Ríos M, Soriguer F, Carmena R, Blanco-Vaca F

#### Clinical trials

Multicenter trial, international, randomized and 2x2 factorial, to assess the effects of Lantus (glargin insulin) compared to the standard treatment with omega 3 fatty acids compared to placebo, in the decrease in cardiovascular morbidity and mortality in high risk patients with altered fasting glucose (AFG), decrease in glucose tolerance (TGD) or type 2 diabetes in initial steps  
HOE901/4032: 2004-2012  
Coordinator: Anna Novials  
*Programme 1*

A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Phase 3 Trial to Evaluate the Safety and Efficacy of Dapagliflozin in Subjects with Type 2 Diabetes with inadequately controlled hypertension on an Angiotensin-Converting Enzyme Inhibitor (ACEI) or Angiotensin Receptor Blocker (ARB)  
MB102-073: 2011-2012  
Coordinator: Anna Novials  
*Programme 1 ■*



Representative image showing the reorganization in cell clusters of disaggregated islet cells when co-cultured in the presence of an endothelial cell basement. The immunolabelling shows insulin (green) and glucagon (red) expression in the cell clusters.

# Diabetobe

Hospital Clínico San Carlos, Madrid  
[www.madrid.org](http://www.madrid.org)



**Principal Investigator** Manuel Serrano Ríos [mserrano.hcsc@salud.madrid.org](mailto:mserrano.hcsc@salud.madrid.org) **Associate researchers** María Teresa Martínez Larrad, Jesús Álvarez Fernández, Arturo Corbatón, Vicente Estrada, Cristina Fernández, Nuria Pescador **Research assistants** Covadonga Caso, Bernat Jiménez, Carina Zabena **Lab technicians** Ainara González **Administrative staff** María del Mar González

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Publications: 4

First decile: 3

Q2: 1

With other CIBERs: 1

With other international groups: 2

Research grants: 4

International projects: 3

Private funds: 1

Scientific collaborations within Ciberdem: 5

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## Programmes

Programme 1. Molecular and physiological determinants of lifestyle in diabetes/obesity. Population studies for genetic-epigenetic association analysis in type 2 diabetes mellitus and related traits.

## Keywords

Genetics type 2 diabetes. Metabolic syndrome. Prediction/

prevention of type 1 diabetes. Proteomics. Insulin sensitivity and resistance. Lipid metabolism.

## Main lines of research

- A genome wide study of the Spanish population. Search for loci for FG, FI, HbA1C and others.
- A genomic, lipidomic and proteomic study of subcutaneous/abdominal adipose tissue and its relationship to type 2 diabetes and obesity.
- Genes and inflammatory markers in children with obesity and/or metabolic syndrome.
- Analysis of genetic markers, circulating adipokines and insulin-resistance status in HIV naïve patients and those undergoing retroviral treatment.
- Analysis of genetic markers, circulating adipokines and insulin-resistance status in obesity and associated metabolic disorders.
- Nutritional primary prevention of type 1 diabetes in children (TRIGR).

## Publications

Genome-wide association identifies nine common variants associated with fasting proinsulin levels and provides new insights into the pathophysiology of type 2 diabetes

Strawbridge RJ, Dupuis J, Prokopenko I, Barker A, Ahlgren E, Rybin D, Petrie JR, Travers ME, Bouatia-Naji N, Dimas AS, Nica A, Wheeler E, Chen H, Voight BF, Taneera J, Kanoni S, Peden JF, Turrini F, Gustafsson S, Zabena C, Almgren P, Barker DJ, Barnes D, Dennison EM, Eriksson JG, Eriksson P, Eury E, Folkersen L, Fox CS, Frayling TM, Goel A, Gu HF, Horikoshi M, Isomaa B, Jackson AU, Jameson KA, Kajantie E, Kerr-Conte J, Kuulasmaa T, Kuusisto J, Loos RJ, Luan J, Makrilia K, Manning AK, Martínez-Larrad MT et al. Diabetes, 60, 2624-2634 (2011)

PMID 21873549. 1st decile. IF 8.889. With other international groups. Programme 1

HbA(1c) in adults without known diabetes from southern Europe. Impact of the new diagnostic criteria in clinical practice

Bernal-Lopez MR, Santamaría-Fernandez S, Lopez-Carmona D, Tinahones FJ, Mancera-Romero J, Peña-Jimenez D, Jansen-Chaparro S, Baca-Osorio AJ, Cuesta-Muñoz AL, Serrano-Rios M, Gomez-Huelgas R Diabet Med, 28, 1319-1322 (2011)

PMID 21966956. Q2. IF 3.036. Programme 1

Hypertriglyceridemic waist: an alternative to the metabolic syndrome? Results of the IMAP Study (multidisciplinary intervention in primary care)

Gomez-Huelgas R, Bernal-López MR, Villalobos A, Mancera-Romero J, Baca-Osorio AJ, Jansen S, Guijarro R, Salgado F, Tinahones FJ, Serrano-Rios M Int J Obes, 35, 292-299 (2011)

PMID 20548300. 1st decile. IF 5.125. With other CIBERs: Ciberobn. Programme 1

Physical activity attenuates the influence of FTO variants on obesity risk: a meta-analysis of 218,166 adults and 19,268 children

Kilpeläinen TO, Qi L, Brage S, Sharp SJ, Sonestedt E, Demerath E, Ahmad T, Mora S, Kaakinen M, Sandholt CH, Holzapfel C, Autenrieth CS, Hyppönen E, Cauchi S, He M, Kutalik Z, Kumari M, Stančáková A, Meidner K, Balkau B, Tan JT, Mangino M, Timpson NJ, Song Y, Zillikens MC, Jablonski KA, Garcia ME, Johansson S, Bragg-Gresham JL, Wu Y, van Vliet-Ostaptchouk JV, Onland-Moret NC, Zimmermann E, Rivera NV, Tanaka T, Stringham HM, Silbernagel G, Kanoni S, Feitosa MF, Snitker S, Ruiz JR, Metter J, Larrad MT et al. PLoS Med, 8, e1001116 (2011)

PMID 22069379. 1st decile. IF 15.617. With other international groups. Programme 1

## Research grants

Trial to reduce IDDM in children at genetic risk. TRIGR

National Institutes of Health, 5U01HD040364-08: 2007-2011

Principal Investigator: Castaño L

Coordinator: Akerblom H

Associate investigators: Martul P, Bilbao JR, Rica I

Con 2 o más grupos Ciberdem: Sí (con CASTAÑO L)

*International project. Programme 1*

Nutritional Primary Prevention of Type1 Diabetes in Children

NIH, QLK1-CT-2002-00372: 2002-2016

Principal Investigator: Manuel Serrano Ríos

*International project. Programme 1*

Meta-analyses of Glucose and Insulin-Related Traits Consortium

MAGIC, 2008-2013

Principal Investigator: Manuel Serrano Ríos

*International project. Programme 1*

Metabolic syndrome, genes, inflammation markers

Lilly SA: 2006-2011

Principal Investigator: Manuel Serrano Ríos

*Private funds. Programme 1*

## Scientific collaborations within Ciberdem

Cooperative population and database studies for genetic association analysis in T2DM and related traits

INGENFRED: 2009-2011

Coordinator: Felipe Javier Chaves

Ciberdem groups: Serrano-Ríos M, Blanco-Vaca F, Carmena R, Soriguer F

The impact of overnutrition, diabetes-obesity, and undernutrition on the regulation of energy homeostasis in the central nervous system. From animal models to humans

IODURE: 2009-2011

Coordinator: Manuel Serrano Ríos

Ciberdem groups: Serrano-Ríos M, Alvarez C, Blázquez E, Burks D, Vallejo M

Di@bet.es Study: 1st epidemiological study of the prevalence of type 2 diabetes in Spain

Coordinator: Federico Soriguer

Ciberdem groups: Serrano-Ríos M, Soriguer F, Carmena R, Castaño L, Gomis R, Vendrell J

Telemed-diabetes Study

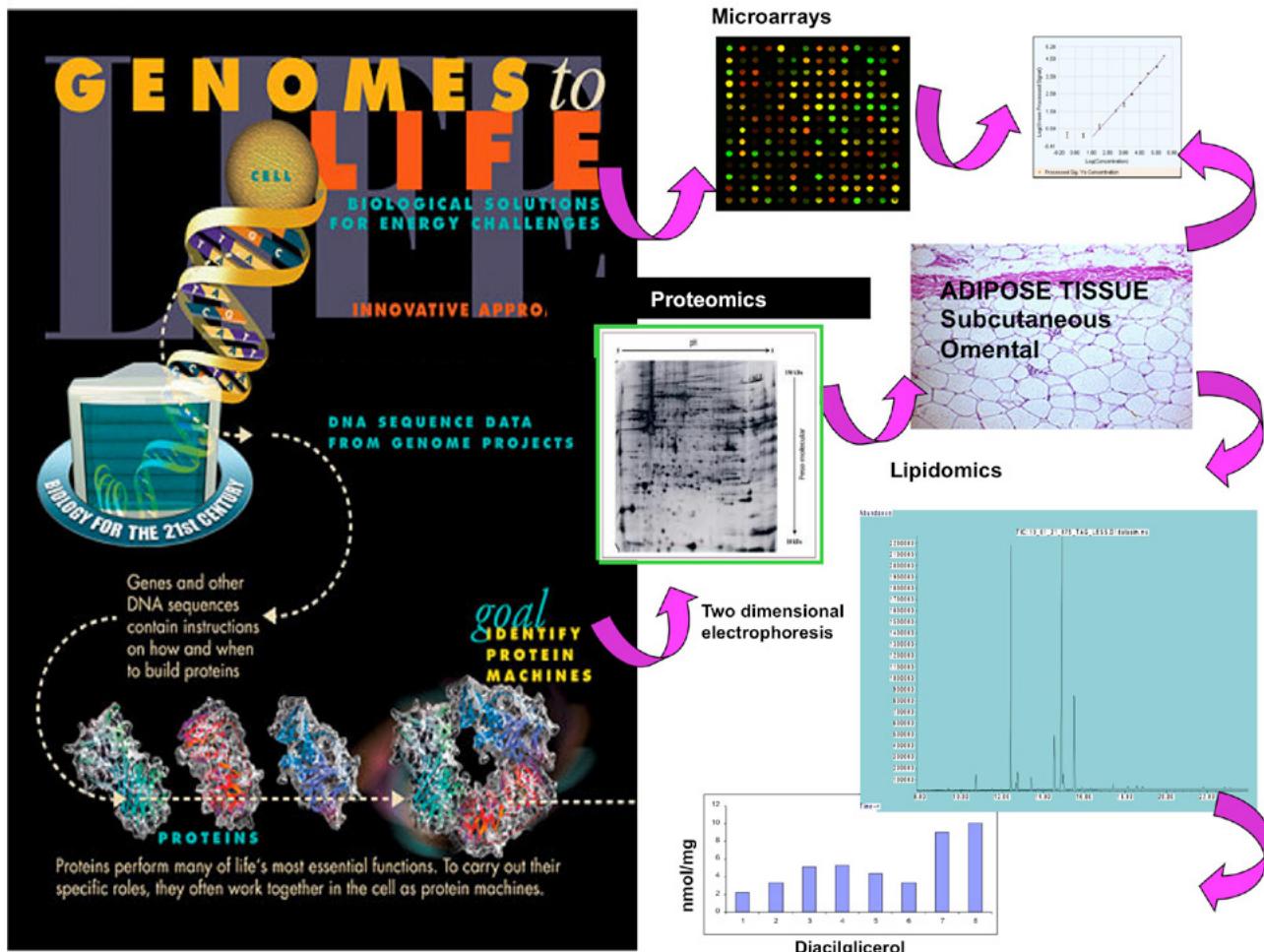
Coordinator: Enric Esmatges

Ciberdem groups: Serrano-Ríos M, Carmena R, Gomis R, Soriguer F, Castaño L

Ciberdem Biobank

Coordinator: Anna Novials

Ciberdem Biobank nodes: Serrano-Ríos M, Gomis R, Novials A, Vendrell J, Masana L, Castaño L, Soriguer F, Carmena R, Blanco-Vaca F ■



Genomes to life.

# Diabetes and Metabolism Research Group

Institut de Recerca Hospital Universitari Vall d'Hebron, Barcelona  
[www.vhir.org](http://www.vhir.org)



**Principal Investigator** Rafael Simó [rafael.simo@vhir.org](mailto:rafael.simo@vhir.org) **Associate researchers** Cristina Hernández, Albert Lecube, Jordi Mesa **Postdoctoral fellows** Marta García Ramírez, David Martínez Selva, Josep A Villena, Patricia Bogdanov **Research assistants** Anna Barbosa, Lidia Corraliza **PhD students** Marta Villarroel, Cristina Sáez **Lab technician** Lorena Ramos

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Publications: 9

First decile: 2

Q1: 3

Q2: 4

With other Ciberdem groups: 3

With other CIBERs: 1

With other networks: 2

With other international groups: 2

Research grants: 13

European projects: 1

National projects: 7

Autonomous Community projects: 1

Private funds: 4

Scientific collaborations within Ciberdem: 4

Clinical trials: 7

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## Programmes

Programme 2. Mechanisms promoting the development

of diabetes and its vascular complications. Associated disorders and co-morbidities. Strategies for prevention and treatment.

Programme 4. Use of biomedical approach systems to develop personalized therapies for diabetes.

## Keywords

Clinical diabetes. Retinopathy. Lipid metabolism. Metabolic syndrome.

## Main lines of research

-The physiopathology of diabetic retinopathy. A new approach using integrated biological systems.

-Insulin resistance and obesity: new pathogenic candidates and the study of co-morbidities.

-Endothelial dysfunction, dyslipidaemia and cardiovascular disease in type 2 diabetes.

-Non-invasive monitorization of blood glucose. The clinical development of a new system of glucose monitoring based on near-infrared technology.

## Publications

Differential effects of gemfibrozil and fenofibrate on reverse cholesterol transport from macrophages to feces in vivo

Rotllan N, Llaverías G, Julve J, Jauhainen M, Calpe-Berdiel L, Hernández C, Simó R, Blanco-Vaca F, Escolà-Gil JC

Biochim Biophys Acta, 1811, 104-110 (2011)

PMID 21126601. Q1. IF 5.084. With other Ciberdem groups: Blanco-Vaca F. With other international groups. Programme 2

Effect of atorvastatin on lipoprotein (a) and interleukin-10: a randomized placebo-controlled trial

Hernández C, Francisco G, Ciudin A, Chacón P, Montoro B, Llaverias G, Blanco-Vaca F, Simó R

Diabetes Metab, 37, 124-130 (2011)

PMID 21131223. Q2. IF 3.033. With other Ciberdem groups: Blanco-Vaca F. Programme 2

Erythropoietin protects retinal pigment epithelial cells against the increase of permeability induced by diabetic conditions: essential role of JAK2/ PI3K signaling

Garcia-Ramírez M, Hernández C, Ruiz-Meana M, Villaruelo M, Corraliza L, García-Dorado D, Simó R

Cell Signal, 23, 1596-1602 (2011)

PMID 21620963. Q2. IF 4.243. With other networks: Recava. Programme 2

Fenofibric acid prevents retinal pigment epithelium disruption induced by interleukin-1 $\beta$  by suppressing AMP-activated protein kinase (AMPK) activation

Villaruelo M, Garcia-Ramírez M, Corraliza L, Hernández C, Simó R

Diabetologia, 54, 1543-1553 (2011)

PMID 21369818. 1st decile. IF 6.973. Programme 2

Fenofibric acid reduces fibronectin and collagen type IV overexpression in human retinal pigment epithelial cells grown in conditions mimicking the diabetic milieu: functional implications in retinal permeability

Trudeau K, Roy S, Guo W, Hernández C, Villaruelo M, Simó R, Roy S

Invest Ophthalmol Vis Sci, 52, 6348-6354 (2011)

PMID 21715349. 1st decile. IF 3.466. With other international groups. Programme 2

Phagocytic activity is impaired in type 2 diabetes mellitus and increases after metabolic improvement

Lecube A, Pachón G, Petriz J, Hernández C, Simó R

PLoS ONE, 6, e23366 (2011)

PMID 21876749. Q1. IF 4.411. Programme 4

Prevalence and risk factors accounting for true silent myocardial ischemia: a pilot case-control study comparing type 2 diabetic with non-diabetic control subjects

Hernández C, Candell-Riera J, Ciudin A, Francisco G, Aguadé-Bruix S, Simó R

Cardiovasc Diabetol, 10, 9 (2011)

PMID 21255408. Q2. IF 2.720. With other networks: Recava. Programme 2

Study of the potential association of adipose tissue GLP-1 receptor with obesity and insulin resistance

Vendrell J, El Bekay R, Peral B, García-Fuentes E, Megia A, Macias-Gonzalez M, Fernández Real J, Jimenez-Gomez Y, Escoté X, Pachón G, Simó R, Selva DM, Malagón MM, Tinahones FJ

Endocrinology, 152, 4072-4079 (2011)

PMID 21862620. Q1. IF 4.993. With other Ciberdem groups: Vendrell J. With other CIBERs: Ciberobn. Programme 2

TNF- $\alpha$  system and lung function impairment in obesity

Lecube A, Sampol G, Muñoz X, Ferrer R, Hernández C, Simó R

Cytokine, 54, 121-124 (2011)

PMID 21296591. Q2. IF 3.537. With other CIBERs: Ciberes. Programme 2

## Research grants

Neurodegeneration as an early event in the pathogenesis of diabetic retinopathy. A study of the mechanisms involved and new therapeutic strategies

European Association for the Study of Diabetes Foundation, EFSD-Sanofi/Aventis Programme: 2011-2012

Principal Investigator: R Simó

Associate investigators: C Hernández, M García Ramírez, M Villaruelo, L Corraliza, L Ramos

*European project*. Programme 2

Neurodegeneración en la patogénesis de la retinopatía diabética incipiente. Estudio de los mecanismos implicados a través de un abordaje integrado de biología de sistemas

Ministerio de Ciencia e Innovación, SAF 2009-07408: 2010-2012

Principal Investigator: Rafael Simó

Associate investigator: Miguel Ángel Rodríguez

*National project*. With other Ciberdem groups: Correig X. Programme 2

Impacto del uso de insulina en el riesgo de cáncer en pacientes con diabetes mellitus tipo 2

Ministerio de Sanidad y Política Social, SAS/2377/2010: 2010-2012

Principal Investigator: R Simó

Associate investigator: IDIAP (Instituto de Investigación en Asistencia Primaria, Barcelona)

*National project*. Programme 2

Depósito de glucógeno en la retina y neurodegeneración: un nuevo mecanismo implicado en la patogénesis de la retinopatía diabética ISCIII, FIS, PI10/01219: 2010-2013 Principal Investigator: C Hernández Associate investigators: M García Ramírez, L Corraliza <i>National project. Programme 2</i>	Novo Nordisk SA: 2010-2012 Principal Investigator: R Simó Associate investigators: C Hernández, M García Ramírez, M Villarroel, L Corraliza, DM Selva <i>Private funds. Programme 2</i>
Role of PGC-1beta in white adipose tissue and its contribution to the development of obesity and type 2 diabetes Ministerio de Ciencia e Innovación, SAF2008-03644: 2009-2011 Principal Investigator: Josep A Villena <i>National project. Programme 2</i>	Desarrollo de variantes moleculares y análogos de somatostatina con potencial aplicación en retinopatía diabética y otras enfermedades oculares BCN Peptides, SA: 2008-2011 Principal Investigator: R Simó <i>Private funds. Programme 2</i>
Function of PGC-1® and PGC-1® coactivators in adipose tissue. Implications in obesity and insulin resistance Ministerio de Ciencia e Innovación, RYC-2006-002429: 2007-2012 Principal Investigator: Josep A Villena <i>National project. Programme 4</i>	Efecto del fenofibrato sobre la permeabilidad de la barrera retiniana externa en cultivos de células de epitelio pigmentario de retina Abbot, SA: 2009-2011 Principal Investigator: R Simó <i>Private funds. Programme 2</i>
Sex hormone-binding globulin (SHBG): Identificación de los mecanismos moleculares que regulan su expresión y papel en la distribución de la grasa corporal y en el desarrollo de la diabetes mellitus (DM) tipo2 ISCIII, Programa Miguel Servet, CP08/00058: 2009-2011 Principal Investigator: David M Selva <i>National project. Programme 4</i>	<b>Scientific collaborations within Ciberdem</b> Identification of neurodegenerative mechanisms that promote the development of diabetic retinopathy: the role of insulin signalling and apoptosis NEURONET-DIAB: 2009-2011 Coordinator: Deborah Burks <i>Ciberdem groups: Simó R, Burks D, Valverde AM</i>
Papel de la sex hormone-binding globulin (SHBG) y de los esteroides sexuales en la distribución de la grasa corporal y en la aparición de la diabetes mellitus tipo 2 ISCIII, FIS, PI09/0144: 2009-2011 Principal Investigator: David M Selva Associate investigator: L Ramos <i>National project. Programme 4</i>	Glycogen-induced dysfunctions in the pancreas and retina and their involvement in the ethiogenesis of diabetes mellitus GIDIPRED: 2009-2011 Coordinator: Joan J Guinovart <i>Ciberdem groups: Simó R, Gomis R, Guinovart JJ</i>
Suport a grups de recerca Generalitat de Catalunya, AGAUR, 2009SGR 739: 2009-2013 Principal Investigator: R Simó Associate investigators: C Hernández, M García Ramírez, M Villarroel, L Corraliza, A Lecube, J Mesa, DM Selva, L Ramos <i>Autonomous Community project. Programme 4</i>	Adult adipose tissue-derived progenitor cells: the influence of the clinical phenotype and adipose depot origin on their biological properties STEMOB: 2009-2011 Coordinator: Joan J Vendrell <i>Ciberdem groups: Simó R, Vendrell J, Zorzano A, Balsinde J, Gómez-Foix AM, Montanya E, Vázquez-Carrera M</i>
Implication of oestrogen-related receptors in the etiology of diabetic cardiomyopathy: role as potential targets for treatment of diabetic cardiomyopathy Fundació La Marató de TV3, 082610: 2009-2011 Principal Investigator: Josep A Villena <i>Private funds. Programme 2</i>	Determinants of insulin resistance and glucose tolerance disorders, including diabetes, in severe obesity and their changes after bariatric surgery-induced weight loss DIASOBS: 2009-2011 Coordinator: Héctor F Escobar Morreale <i>Ciberdem groups: Simó R, Correig X, Montanya E, Escobar-Morreale HF, Vendrell J</i>
Neuroprotection by enhancing GLP-1R signalling, a new therapeutic strategy in the early stages of diabetic retinopathy	<b>Clinical trials</b> Durable-Response Therapy Evaluation for Early- or New-Onset Type 1 Diabetes. TRX4_DM_007_EU_08

DEFEND-1: 2008-2011

Coordinator: Cristina Hernández

*Programme 2*

Durable-Response Therapy Evaluation for Early- or New-Onset Type 1 Diabetes. TRX4\_DM\_007\_EU\_08

DEFEND-2: 2010-2011

Coordinator: Cristina Hernández

*Programme 2*

Estudio de extensión de 26 semanas, multinacional, multicéntrico, abierto, de dos grupos paralelos y con ajuste de dosis para comparar la eficacia y seguridad de una combinación de un análogo soluble de insulina (SIAC) administrado una vez al día (OD) frente a insulina glargina (OD), ambas en combinación con metformina, en sujetos con Diabetes tipo 2

NN5401-3726: 2010-2011

Coordinator: Jorge Mesa

*Programme 2*

A open label extension to trials assessing the safety and efficacy of BI 10773 as monotherapy in type 2 diabetic patients. Original study ID 1245.24

EudraCT 2008-007938-21: 2010-2014

Coordinator: Jorge Mesa

*Programme 2*

Estudio multicéntrico aleatorizado, doble ciego y controlado con placebo para evaluar resultados cardiovasculares después del tratamiento con alogliptina en combinación con la asistencia habitual en sujetos con diabetes tipo2 y síndrome coronario agudo SYR-322\_302: 2009-2013

Coordinator: Jorge Mesa

*Programme 2*

Ensayo clínico Fase I, doble ciego, controlado con placebo, de seguridad del colirio BCN070660 en pacientes diabéticos tipo II

EudraCT 2011-000325-77: 2011-2012

Coordinator: Rafael Simó

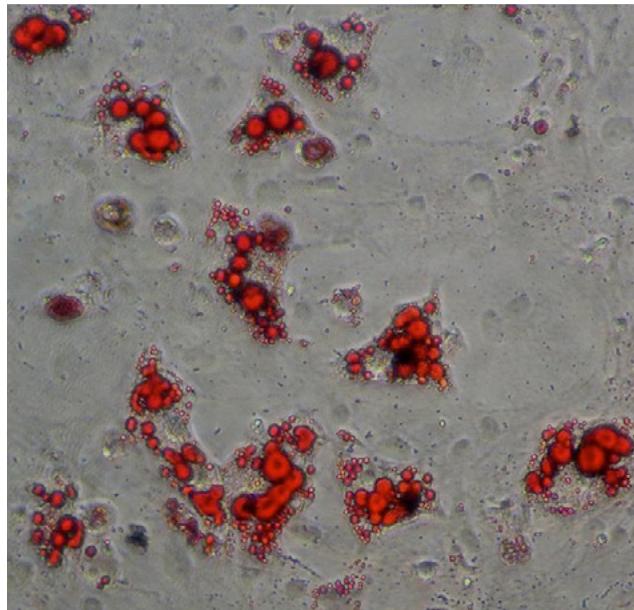
*Programme 2*

Ensayo para comparar la eficacia y seguridad de NN5401 frente a insulina glargina en sujetos con diabetes tipo 2 sin tratamiento previo con insulina

NN5401-3590: 2011-2012

Coordinator: Rafael Simó

*Programme 2* ■



Study of zinc-alpha2-glycoprotein effects on lipolysis of differentiated human adipocytes from visceral fat depot origin. Section stained with Oil Red O.

# Endocrinology and Nutrition Service

Hospital Regional Universitario Carlos Haya, Málaga  
[www.carloshaya.net](http://www.carloshaya.net)  
[www.imabis.org](http://www.imabis.org)



**Principal Investigator** Federico Soriguer [federico.soriguer.sspa@juntadeandalucia.es](mailto:federico.soriguer.sspa@juntadeandalucia.es) **Associate researchers** María Cruz Almaraz, Isabel Esteva de Antonio, Juan Miguel Gómez-Zumaquero, María Stella González, Gabriel Olveira, Gemma Rojo-Martínez, María Soledad Ruiz de Adana, Sergio Valdés, Inmaculada González Molero **Postdoctoral fellow** Eva García **Research assistants** Sara García, Francisca Linares, Gracia María Martín, Nuria Porras **Nursing assistant** M José Moreno **PhD students** Carolina Gutiérrez, Juan José Haro, Elehazara Rubio **Lab technician** María José Beltrán **Administrative staff** Patricia González

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Publications: 10

Q1: 6

Q2: 4

With other Ciberdem groups: 1

With other CIBERs: 8

Research grants: 13

European projects: 1

National projects: 8

Autonomous Community projects: 4

Scientific collaborations within Ciberdem: 4

Clinical trials: 6

PhD theses: 1

Awards: 2

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## Programmes

Programme 1. Molecular and physiological determinants of

lifestyle in diabetes/obesity. Population studies for genetic-epigenetic association analysis in type 2 diabetes mellitus and related traits.

## Keywords

Insulin therapy. Metabolic syndrome. Prediction/prevention of type 2 diabetes.

## Main lines of research

- The biomolecular epidemiology of diabetes, obesity and metabolic syndrome (Pizarra Study, Egabro Study, Di@bet.es Study, Di@bet.an Study).
- The study of insulin resistance in patients with extreme obesity undergoing bariatric surgery.
- Fatty acids, insulin resistance and adipocyte metabolism.
- New technologies applied to the treatment of type 1 diabetes.

## Publications

Children whose diet contained olive oil had a lower likelihood of increasing their body mass index Z-score over 1 year  
Haro-Mora JJ, García-Escobar E, Porras N, Alcázar D, Gatzambide J, Ruiz-Órpez A, García-Serrano S, Rubio-Martín E, García-Fuentes E, López-Siguero JP, Soriguer F, Rojo-Martínez G

Eur J Endocrinol, 165, 435-439 (2011)  
PMID 21715417. Q2. IF 3.482. With other CIBERs: Ciberobn. Programme 1

Dietary polyunsaturated fatty acids may increase plasma LDL-cholesterol and plasma cholesterol concentrations in carriers of an ABCG1 gene single nucleotide polymorphism: study in two Spanish populations

Abellán R, Mansego ML, Martínez-Hervás S, Morcillo S, Pineda-Alonso M, Carmena R, Real JT, Redon J, Rojo-Martínez G, Martín-Escudero JC, Chaves FJ

Atherosclerosis, 219, 900-906 (2011)  
PMID 21978921. Q1. IF 4.086. With other Ciberdem groups: Carmena R. With other CIBERs: Ciberobn. Programme 1

Effect of insulin analogues on 3t3-I1 adipogenesis and lipolysis

García-Escobar E, Rodríguez-Pacheco F, Haro-Mora JJ, Gomez-Zumaquero JM, Rubio-Martín E, Gutierrez-Repiso C, Soriguer F, Rojo-Martínez G

Eur J Clin Invest, 41, 979-986 (2011)  
PMID 21366560. Q1. IF 2.736. With other CIBERs: Ciberobn. Programme 1

ELOVL6 genetic variation is related to insulin sensitivity: a new candidate gene in energy metabolism

Morcillo S, Martín-Núñez GM, Rojo-Martínez G, Almaraz MC, García-Escobar E, Mansego ML, de Marco G, Chaves FJ, Soriguer F

PLoS ONE, 6, e21198 (2011)  
PMID 21701577. Q1. IF 4.411. With other Ciberdem groups: Carmena R. Programme 1

Glycosylated hemoglobin as a hyperuricemia risk marker in general population

García-Escobar E, Pérez-Valero V, Maseda D, Valdés S, Yahyaoui R, Hernando V, Vicioso MI, Ruiz de Adana MS, Espinosa Rodríguez M, Rojo-Martínez G, Soriguer F

Med Clin (Barc), 136, 465-470 (2011)  
PMID 21345460. Q2. IF 1.413. With other CIBERs: Ciberobn. Programme 1

Iodine concentration in cow's milk and its relation with urinary iodine concentrations in the population

Soriguer F, Gutierrez-Repiso C, Gonzalez-Romero S, Olveira G, Garriga MJ, Velasco I, Santiago P, de Escobar GM, Garcia-Fuentes E; Iodine Deficiency Disorders Group of Spanish Society of Endocrinology and Nutrition

Clin Nutr, 30, 44-48 (2011)

PMID 20675020. Q1. IF 3.410. With other CIBERs: Ciberobn. Programme 1

Iodine intakes of 100-300 µg/d do not modify thyroid function and have modest anti-inflammatory effects

Soriguer F, Gutiérrez-Repiso C, Rubio-Martín E, Linares F, Cardona I, López-Ojeda J, Pacheco M, González-Romero S, Garriga MJ, Velasco I, Santiago P, García-Fuentes E

Br J Nutr, 105, 1783-1790 (2011)  
PMID 21262066. Q2. IF 3.072. With other CIBERs: Ciberobn. Programme 1

Stearoyl-CoA desaturase-1 is associated with insulin resistance in morbidly obese subjects

García-Serrano S, Moreno-Santos I, Garrido-Sánchez L, Gutierrez-Repiso C, García-Almeida JM, García-Arnés J, Rivas-Marín J, Gallego-Perales JL, García-Escobar E, Rojo-Martinez G, Tinahones F, Soriguer F, Macias-Gonzalez M, García-Fuentes E

Mol Med, 17, 273-280 (2011)  
PMID 21060977. Q1. IF 5.908. With other CIBERs: Ciberobn. Programme 1

Thyroid hormone levels predict the change in body weight: a prospective study

Soriguer F, Valdes S, Morcillo S, Esteva I, Almaraz MC, de Adana MS, Tapia MJ, Dominguez M, Gutierrez-Repiso C, Rubio-Martín E, Garrido-Sánchez L, Perez V, Garriga MJ, Rojo-Martinez G, Garcia-Fuentes E

Eur J Clin Invest, 41, 1202-1209 (2011)  
PMID 21470220. Q1. IF 2.736. With other CIBERs: Ciberobn. Programme 1

Vitamin D deficiency in Spain: a population-based cohort study

González-Molero I, Morcillo S, Valdés S, Pérez-Valero V, Botas P, Delgado E, Hernández D, Olveira G, Rojo G, Gutierrez-Repiso C, Rubio-Martín E, Menéndez E, Soriguer F

Eur J Clin Nutr, 65, 321-328 (2011)  
PMID 21179052. Q2. IF 2.563. Programme 1

## Research grants

REPROBESITY: Search For New Therapeutic Agents Against Complicated Obesity By Reprofiling Existing Drugs European Union, Seventh Framework Programme, FP7-HEALTH-2007-B: 2009-2012

Principal Investigator: Fernando Rodríguez de Fonseca European project. Programme 1

Estudio de los polimorfismos de los genes Ar, Er beta y Cyp19, y de reordenaciones en los cromosomas X e Y, en dos poblaciones de personas con trastorno de identidad de género (TIG)

Ministerio de Ciencia e Innovación, Proyectos de

Investigación Fundamental no orientada: 2010-2012 Principal Investigator: Eduardo Pásaro Associate investigators: Rosa Fernández, Blanca Laffon, Antonio Guillamón, Isabel Esteva, Maricruz Almaraz, Raquel Yahyahoui, Juan Haro, Esther Gómez Gil <i>National project. Programme 1</i>	Consejería de Salud Junta de Andalucía, PI 0525/2009: 2010-2011 Principal Investigator: Gabriel Olveira Fuster <i>National project. Programme 1</i>
Epigenética y riesgo de diabetes mellitus tipo 2 ISCIII, PS09/0217: 2010-2012 Principal Investigator: Sonsoles Morcillo Espina Associate investigators: Juan Miguel Gómez Zumaquero, Elehazara Rubio Martín, Gracia María Martín Núñez, Gabriel Olveira, M Soledad Ruiz de Adana, Isabel Esteva de Antonio <i>National project. Programme 1</i>	Yodoprofilaxis durante el embarazo, repercusión sobre la función tiroidea de la gestante y el desarrollo intelectual de la prole Consejería de Salud Junta de Andalucía, PI0469/2009: 2010-2011 Principal Investigator: Piedad Santiago Fernández <i>National project. Programme 1</i>
Estudio del papel biológico de la SCD1 como posible mediador entre la obesidad e insulineresistencia en individuos obesos mórbidos desde una aproximación in vivo e in vitro ISCIII, PS09/01060: 2010-2012 Principal Investigator: Eduardo García Fuentes Associate investigators: Sara García Serrano, Carolina Gutiérrez Repiso, Gabriel Olveira, Eva García Escobar, José Luis Gallego Perales, Juan García Arnés <i>National project. Programme 1</i>	Nuevos retos sobre el papel de las hormonas tiroideas en la regulación del peso corporal. Efecto de SNPs en el gen del receptor alpha de las hormonas tiroideas en la respuesta a una intervención sobre estilos de vida mediante dieta mediterránea y ejercicio físico en individuos con prediabetes. Estudio Egabro/Pizarra Consejería de Salud Junta de Andalucía, PI-0327-2010: 2011-2012 Principal Investigator: Sergio Valdés Hernández Associate investigators: M Cruz Almaraz, Inmaculada González Molero, Isabel Cardona, Elehazara Rubio Martín <i>Autonomous Community project. Programme 1</i>
Adaptación psicosocial, calidad de vida, y demanda de asistencia sanitaria durante 10 años en personas diagnosticadas de trastorno de la identidad de género Ministerio de Igualdad, IMG 2009-PI040964: 2010-2011 Principal Investigator: Esther Gómez Gil Associate investigators: I Esteva, MC Almaraz, J Martínez, A Guillamón, M Salamero, T Godás <i>National project. Programme 1</i>	Implicación del Transporte de Ácidos Grasos y del Factor de Crecimiento del Endotelio Vascular B (Vegf-B) en el Desarrollo de Diabetes. Estudio de Prevención Primaria de la Diabetes Tipo 2 Consejería de Salud Junta de Andalucía, PI-0532-2010: 2011-2012 Principal Investigator: Gemma Rojo Martínez Associate investigators: María José Leña Carrillo, Fuensanta Lima Rubio, Nuria Porras Pérez, Gabriel Olveira Fuster, Araceli Chicano Gálvez, Juan Miguel Gómez Zumaquero <i>Autonomous Community project. Programme 1</i>
Prevención de la diabetes mellitus tipo 2. Estudio Egabro-Pizarra ISCIII, PI08/1592: 2009-2011 Principal Investigator: Gemma Rojo Martínez Associate investigators: Federico Soriguer, Sergio Valdés, Curra Linares, Juan Haro Mora, Raquel Yahyahoui, Francisco Rivas Ruiz, Pedro Benito López, María Sierra Corpas <i>National project. Programme 1</i>	Estudio de la función tiroidea e ingesta de yodo en el periodo final de la gestación en mujeres embarazadas sanas Consejería de Salud Junta de Andalucía, PI 0501/2009: 2010-2011 Principal Investigator: Inés Velasco López Associate investigators: Federico Soriguer, Ernesto González, José Alberto Herrera, María Gallego, Jessica Martín, M José Garriga <i>Autonomous Community project. Programme 1</i>
Estudio de la variabilidad genética de la delta-9-desaturasa en la población general y su asociación con la obesidad ISCIII, CP07/00187: 2008-2011 Principal Investigator: Juan Miguel Gómez Zumaquero <i>National project. Programme 1</i>	Prevención de la Diabetes mellitus tipo 2. Estudio Egabro-Pizarra Consejería de Innovación Junta de Andalucía, P09-CTS-5125: 2010-2012 Principal Investigator: Gemma Rojo Martínez <i>Autonomous Community project. Programme 1</i>
Evaluación del estrés oxidativo en Fibrosis quística y Bronquiectasias: Una aproximación nueva a partir de biomarcadores celulares y plasmáticos	

## Scientific collaborations within Ciberdem

Cooperative population and database studies for genetic association analysis in T2DM and related traits  
INGENFRED: 2009-2011  
Coordinator: Felipe Javier Chaves  
*Ciberdem groups: Soriguer F, Blanco-Vaca F, Carmena R, Serrano-Ríos M*

Di@bet.es Study: 1st epidemiological study of the prevalence of type 2 diabetes in Spain  
Coordinator: Federico Soriguer  
*Ciberdem groups: Soriguer F, Carmena R, Castaño L, Gomis R, Serrano-Ríos M, Vendrell J*

Telemed-diabetes Study  
Coordinator: Enric Esmatjes  
*Ciberdem groups: Soriguer F, Carmena R, Gomis R, Serrano-Ríos M, Castaño L*

Ciberdem Biobank  
Coordinator: Anna Novials  
*Ciberdem Biobank nodes: Soriguer F, Gomis R, Novials A, Vendrell J, Masana L, Castaño L, Serrano-Ríos M, Carmena R, Blanco-Vaca F*

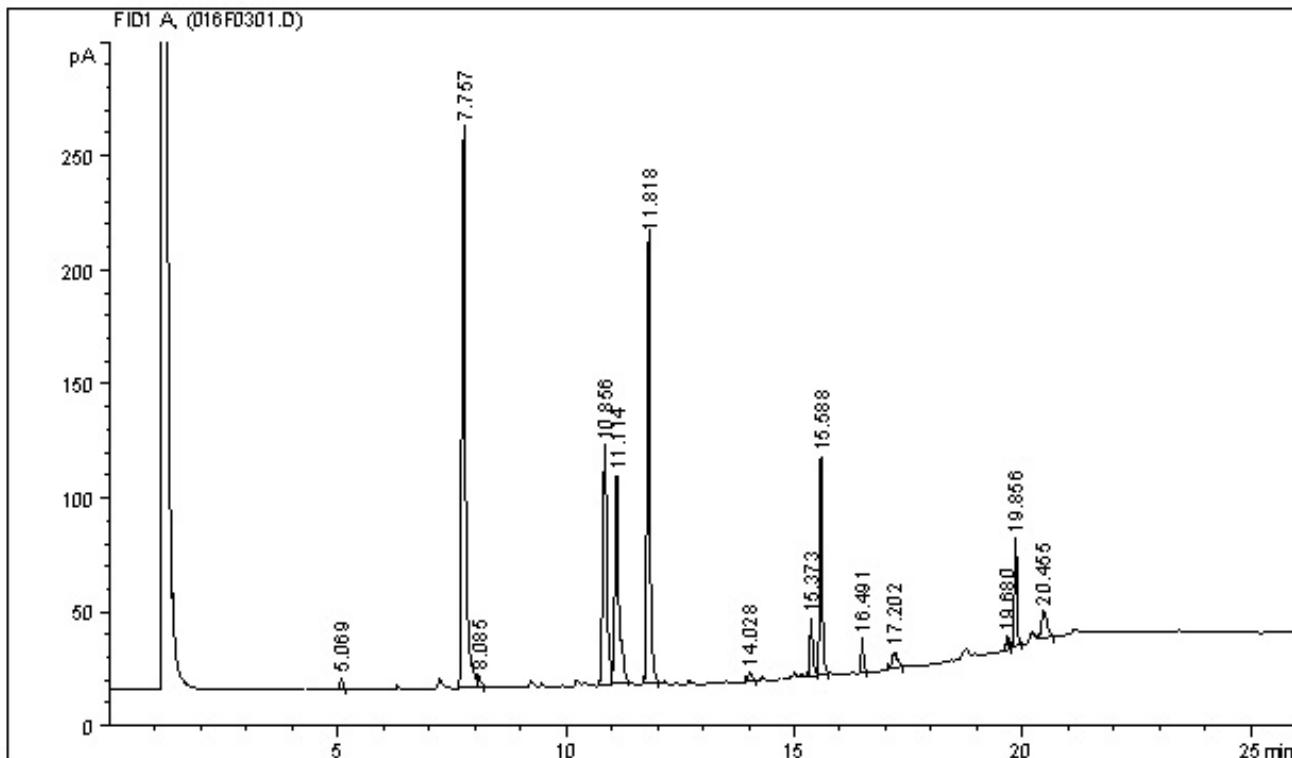
## Clinical trials

Ensayo clínico con un nuevo suplemento de nutrición enteral por vía oral en pacientes con insuficiencia renal crónica en predialisis  
1834-H-183: 2011-2013  
Coordinator: Gabriel Olveira  
*Programme 1*

Ensayo multicéntrico, abierto, aleatorizado, de dos grupos paralelos y con ajuste de dosis para comparar el cambio en el peso de pacientes con sobrepeso u obesos con diabetes tipo 2 tras 26 semanas de tratamiento con insulina detemir una vez al día frente a insulina NPH una vez al día, ambos con insulina aspart en las comidas

NN304-3614: 2009-2012  
Coordinator: Marta Domínguez  
*Programme 1*

Estudio en fase 4 para investigar los efectos de la intervención dietética sobre el cambio en el peso corporal y la relación entre el cambio en el peso corporal y el IMC basal en pacientes con DM tipo 2 mal controlada en tratamiento con antidiabéticos orales que están empezando el tratamiento con insulina Detemir en combinación con Metformina



FAMEs chromatogram.

NN304-3785: 2010-2011  
Coordinator: Montserrat Gonzalo  
*Programme 1*

Estudio fase 2 de búsqueda de dosis de Nepidermina (Factor de Crecimiento Epidérmico humano recombinante), administrada intralesionalmente para el tratamiento de pacientes con ulceras de pie diabético no isquémicas y no complicadas

PPh/EGF/01: 2011  
Coordinator: María Cruz Almaraz  
*Programme 1*

Estudio descriptivo ProAct  
RD000954: 2011-2013  
Coordinator: Soledad Ruiz de Adana  
*Programme 1*

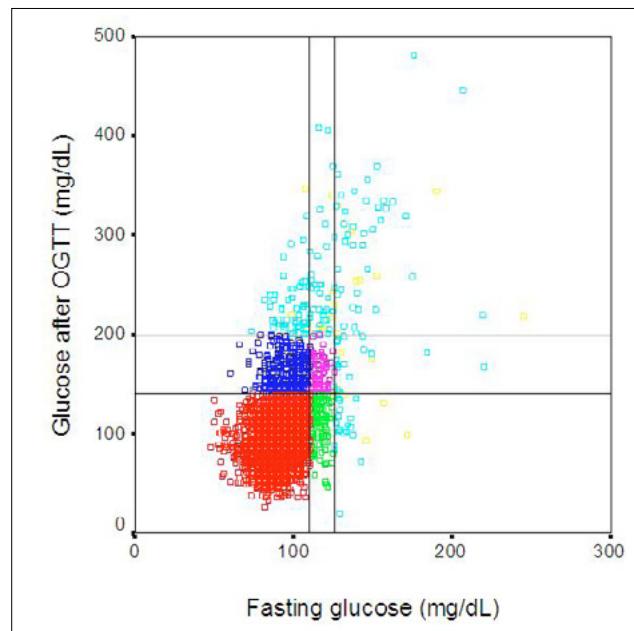
Utilización de la MCG retrospectiva para evaluar las nuevas propuestas insulínicas en el manejo de la hiperglucemía inducida por corticoides en el paciente hospitalizado

2011-2012  
Coordinator: Soledad Ruiz de Adana  
*Programme 1*

**PhD theses**  
Factores nutricionales y características del tejido adiposo relacionadas con elevada adiposidad durante la infancia  
Author: Juan J Haro Mora  
Thesis advisor: Gemma Rojo  
University: Universidad de Málaga  
Thesis defense date: December 1, 2011  
*Programme 1*

**Awards**  
II Ayudas SED a Proyectos de Investigación en Diabetes Clínica y Básica para Jóvenes Investigadores (2011)  
Awardee: Sonsoles Morcillo  
*Programme 1*

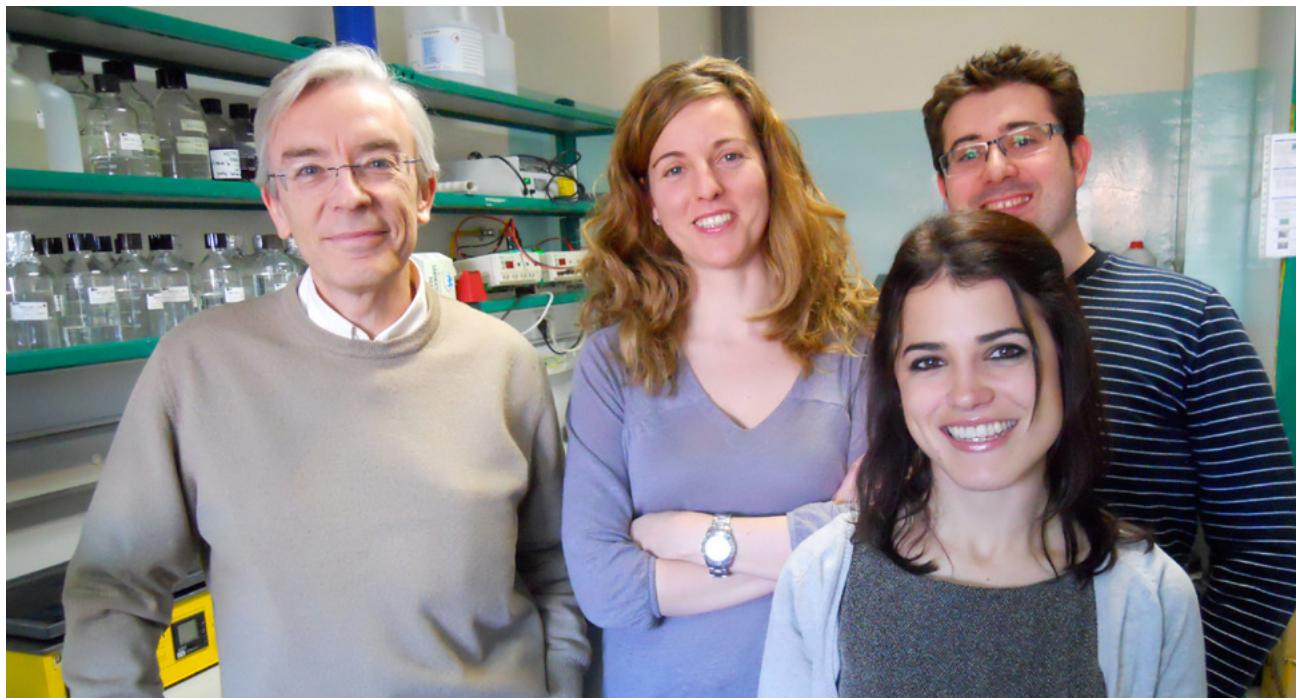
Premio Fundación SEEN a la trayectoria de un Grupo de Endocrinología y Nutrición (2011)  
Awardee: Federico Soriguer  
*Programme 1* ■



The Di@bet.es Study: fasting and post-OGTT serum glucose.

# Transcriptional mechanisms of pancreatic function

Instituto de Investigaciones Biomédicas Alberto Sols, Consejo Superior de Investigaciones Científicas, Universidad Autónoma de Madrid  
[www.iib.uam.es](http://www.iib.uam.es)



**Principal Investigator** Mario Vallejo [mvallejo@iib.uam.es](mailto:mvallejo@iib.uam.es) **Postdoctoral fellows** Mercedes Mirasierra, Antonio Fernández Pérez **PhD student** Laura Ruiz

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Publications: 1

First decile: 1

Research grants: 1

National projects: 1

Scientific collaborations within Ciberdem: 2

PhD theses: 1

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## Programmes

Programme 3. Impact of beta cell dysfunction and plasticity on the natural history of diabetes. Development of novel treatment strategies.

## Keywords

Insulin synthesis. Islet degeneration and damage. Islet development. Diabetic pregnancy.

## Main lines of research

-The characterization of phenotypic alterations of pancreatic

islets in the absence of Alx3.

-The requirement of Alx3 for the maintenance of glucose homeostasis and metabolic activity *in vivo*.

-The identification of transcriptional targets regulated by Alx3.

-Alx3 and diabetic pregnancy: the role of Alx3 in the regulation of the development of the neural tube and vulnerability to hyperglycaemic insult in its absence.

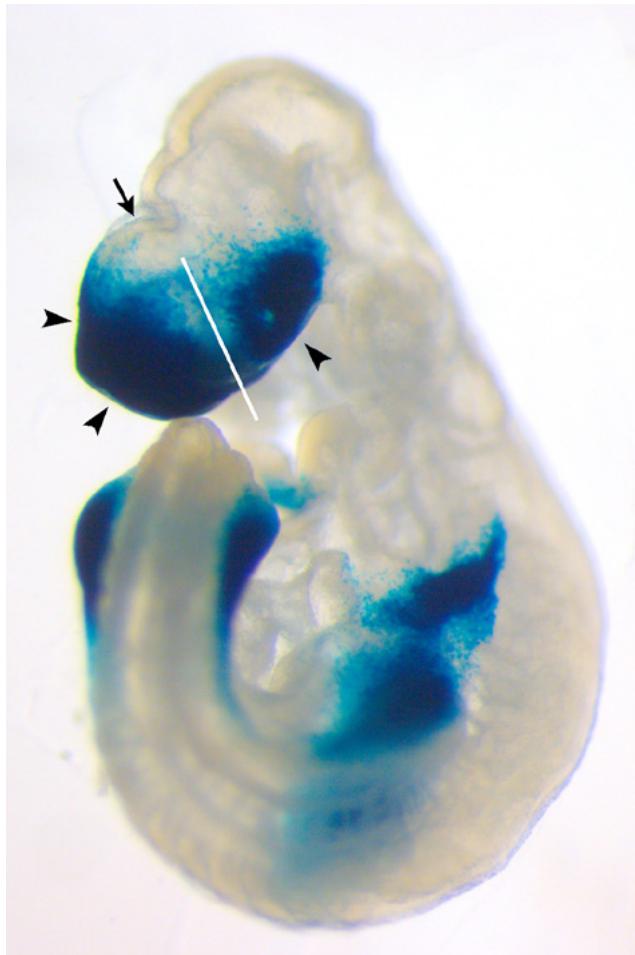
## Publications

Alx3-deficient mice exhibit decreased insulin in beta cells, altered glucose homeostasis and increased apoptosis in pancreatic islets

Mirasierra M, Fernández-Pérez A, Díaz-Prieto N, Vallejo M  
Diabetologia, 54, 403-414 (2011)  
[PMID 21104068. 1st decile. IF 6.973. Programme 3](https://pubmed.ncbi.nlm.nih.gov/21104068/)

## Research grants

A pleiotropic role for the homeoprotein Alx3 in the



Alx3 deficiency increases the risk of embryonic malformations during diabetic pregnancy. Shown is a heterozygote  $\text{Alx3}^{+/-}$  mouse embryo extracted from a diabetic mother at 10.5 days of gestation. The embryo has been stained with  $\beta$ -galactosidase to monitor the pattern of expression of Alx3. Expression of Alx3 in the craniofacial mesenchyme (arrowheads) has been altered by maternal hyperglycaemia, making it asymmetrical and displacing the midline (solid white line) to the left. Malformations in the telencephalic vesicles are also observed (arrow). Expression of Alx3 in the lateral mesoderm in this embryo is normal. Our studies show that Alx3 deficiency increases the risk of embryonic malformations during diabetic pregnancy by 20%.

maintenance of cell viability and survival

MICINN, BFU2008-01283: 2009-2011

Principal Investigator: Mario Vallejo

National project. Programme 3

#### Scientific collaborations within Ciberdem

Clinical, genetic and functional characterization of monogenic diabetes: from the bench to the bedside

MODIAB: 2009-2011

Coordinator: Luis Castaño

Ciberdem groups: Vallejo M, Castaño L, Ferrer J, Blázquez E

The impact of overnutrition, diabetes-obesity, and undernutrition on the regulation of energy homeostasis in the central nervous system. From animal models to humans

IODURE: 2009-2011

Coordinator: Manuel Serrano Ríos

Ciberdem groups: Vallejo M, Alvarez C, Blázquez E, Burks D, Serrano-Ríos M

#### PhD theses

Regulación de la expresión del gen homeodominio Alx3 y sus implicaciones en la generación de malformaciones congénitas asociadas a la embriopatía diabética

Author: Patricia García Sanz

Thesis advisor: Mario Vallejo

University: Universidad Autónoma de Madrid

Thesis defense date: March 1, 2011

Programme 3 ■

# Molecular mechanisms of insulin resistance and sensitivity in peripheral tissues

Instituto de Investigaciones Biomédicas Alberto Sols, Consejo Superior de Investigaciones Científicas, Madrid  
[www.iib.uam.es](http://www.iib.uam.es)



**Principal Investigator** Ángela Martínez Valverde [avalverde@iib.uam.es](mailto:avalverde@iib.uam.es) **Postdoctoral fellows** Águeda González, Jesús Revuelta, Beatriz Santamaría **PhD students** Virginia Pardo, Maysa Ahmed Abd El-Hamid

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Publications: 2

First decile: 2

With other CIBERs: 2

Research grants: 3

National projects: 1

Private funds: 2

Scientific collaborations within Ciberdem: 1

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## Programmes

Programme 2. Mechanisms promoting the development of diabetes and its vascular complications. Associated disorders and co-morbidities. Strategies for prevention and treatment.

## Keywords

Cytokines. Insulin action. Insulin sensitivity and resistance. Retinopathy. Nephropathy.

## Main lines of research

- The beneficial effects of PTP1B inhibition by genetic and pharmacological approaches in systemic IRS-2-deficient mice in the enhancement of IRS-1-mediated insulin signalling in the liver.
- The effects of PTP1B deficiency on age-induced inflammation, senescence and peripheral insulin resistance.
- The effects of insulin sensitization by PTP1B deficiency on hepatic regeneration in mice fed on chow or a high-fat diet: molecular mechanisms involved.
- The study of the critical nodes of the insulin-signalling cascade in human biopsies from patients with non-alcoholic hepatic steatosis (NAFLD), steatohepatitis (NASH) and hepatitis virus C infection (HCV).
- Autophagy as a potential mediator of the progression of non-alcoholic hepatic liver disease.
- The role of PTP1B in IGF-I-mediated signalling in the retina:

possible benefits of PTP1B inhibition in the impairment of survival of photoreceptor cells by IRS2 deficiency.

-Stress and survival signalling pathways in diabetic retinopathy.

## Publications

Hepatic insulin resistance is associated with increased apoptosis and fibrogenesis in nonalcoholic steatohepatitis and chronic hepatitis C

García-Monzón C, Lo Iacono O, Mayoral R, González-Rodríguez A, Miquilena-Colina ME, Lozano-Rodríguez T, García-Pozo L, Vargas-Castrillón J, Casado M, Boscá L, Valverde AM, Martín-Sanz P

J Hepatol, 54, 142-152 (2011)

PMID 20888662. 1st decile. IF 9.334. With other CIBERs:

Ciberehd. Programme 2

Protein Tyrosine Phosphatase 1B (PTP1B) deficiency accelerates hepatic regeneration in mice

Revuelta-Cervantes J, Mayoral R, Miranda S, González-Rodríguez A, Fernández M, Martín-Sanz P, Valverde AM  
Am J Pathol, 178, 1591-1604 (2011)

PMID 21406170. 1st decile. IF 5.224. With other CIBERs:

Ciberehd. Programme 2

## Research grants

Estudio de la sensibilidad hepática a la insulina por la inhibición de la proteína tirosina fosfatasa 1B

Ministerio de Ciencia e Innovación, SAF2009-08114: 2010-2012

Principal Investigator: Ángela Martínez Valverde

Associate investigators: Águeda González, Jesús Revuelta, Beatriz Santamaría, Maysa Mobasher, Virginia Pardo

National project. Programme 2

The role of PTP1B in hepatocyte apoptosis

Hoffmann-La Roche: 2009-2012

Principal Investigator: Ángela Martínez Valverde

Associate investigators: Águeda González, Maysa Mobasher, Cristina Rondinone

Private funds. Programme 2

Effect of GLP-1 on the gut-to-liver axis in the hepatoprotection against non-alcoholic fatty liver disease

EFSD/ Amylin Programme 2011: 2011-2013

Principal Investigator: Ángela Martínez Valverde

Private funds. Programme 2

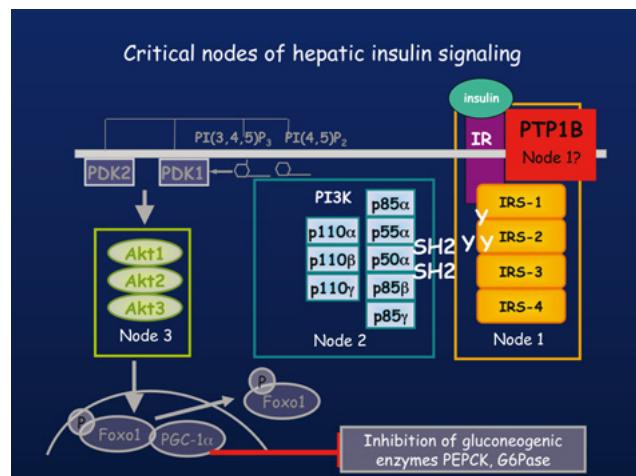
## Scientific collaborations within Ciberdem

The identification of neurodegenerative mechanisms that promote the development of diabetic retinopathy: the role of insulin signalling and apoptosis

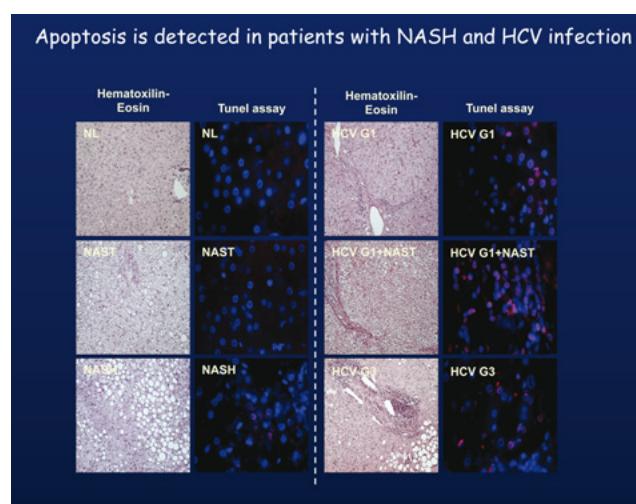
NEURONET-DIAB: 2009-2011

Coordinator: Deborah Burks

Ciberdem groups: Valverde AM, Burks D, Simó R ■



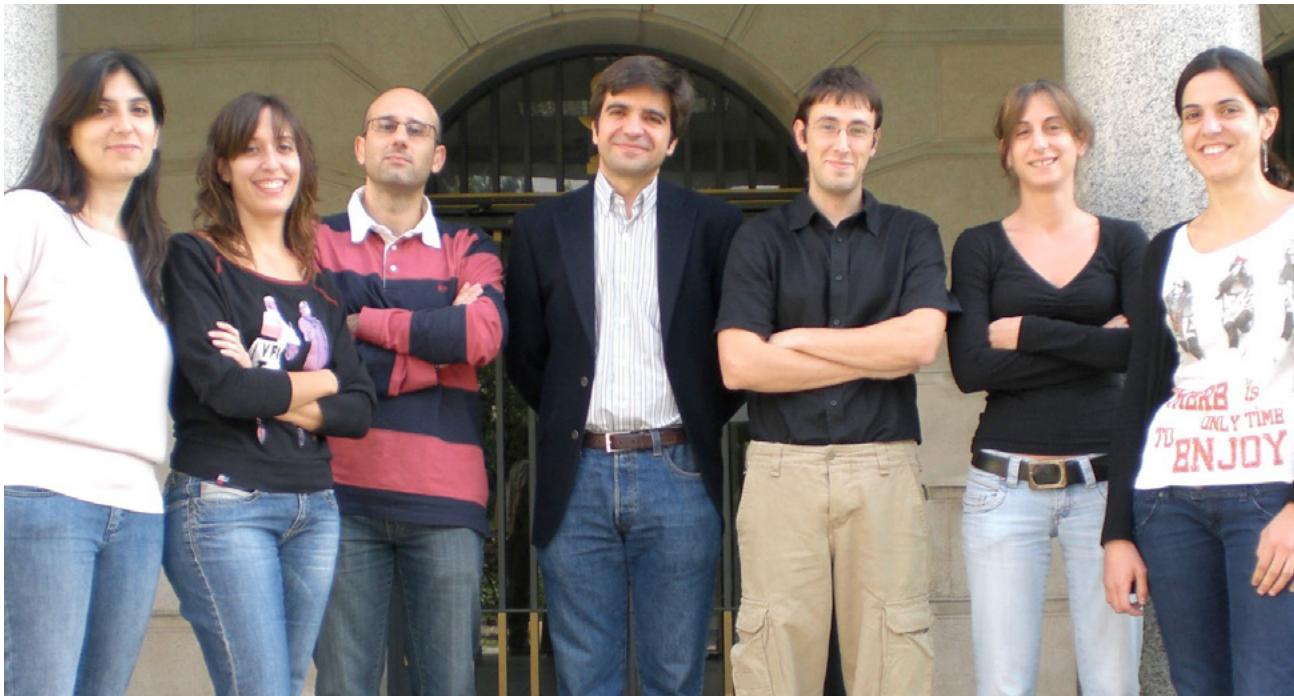
Critical nodes of hepatic insulin signaling.



Increased hepatocyte apoptosis and collagen gene expression in NASH and HCV patients.

# Pharmacological targets in inflammation and metabolic diseases

Unitat de Farmacologia, Facultat de Farmàcia, Universitat de Barcelona  
[www.ub.edu](http://www.ub.edu)



Principal Investigator Manuel Vázquez Carrera [mvazquezcarrera@ub.edu](mailto:mvazquezcarrera@ub.edu) Postdoctoral fellow Xavier Palomer PhD students Lucía Serrano Marco, Emma Barroso, Laia Salvadó, Eva Capdevila Lab technician David Álvarez Guardia

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Publications: 5

First decile: 2

Q1: 3

With other Ciberdem groups: 1

With other international groups: 3

Research grants: 1

National projects: 1

Scientific collaborations within Ciberdem: 1

PhD theses: 3

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## Programmes

Programme 4. Use of biomedical approach systems to develop personalized therapies for diabetes.

## Keywords

Insulin sensitivity and resistance. Lipid metabolism. Cardiac complications. PPAR.

## Main lines of research

A study of the molecular mechanisms involved in the link between inflammation and insulin resistance:

- a) evaluating the molecular mechanisms by which PPAR agonists prevent inflammation and insulin resistance,
- b) studying how monounsaturated fatty acids prevent saturated fatty-acid-induced insulin resistance,
- c) evaluating the mechanisms through which PPAR agonists may prevent the development of metabolic syndrome, dyslipidaemia and cardiac hypertrophy.

## Publications

Activation of peroxisome proliferator-activated receptor- $\beta/\delta$  (PPAR- $\beta/\delta$ ) ameliorates insulin signaling and reduces SOCS3 levels by inhibiting STAT3 in interleukin-6-stimulated adipocytes

Serrano-Marco L, Rodríguez-Calvo R, El Kochairi I, Palomer X, Michalik L, Wahli W, Vázquez-Carrera M

Diabetes, 60, 1990-1999 (2011)

PMID 21617181. 1st decile. IF 8.889. With other international groups. Programme 4

Liver AMP/ATP ratio and fructokinase expression are related to gender differences in AMPK activity and glucose intolerance in rats ingesting liquid fructose

Vilà L, Roglans N, Perna V, Sánchez RM, Vázquez-Carrera M, Alegret M, Laguna JC

J Nutr Biochem, 22, 741-751 (2011)

PMID 21115336. 1st decile. IF 4.538. Programme 4

PPAR $\beta/\delta$  activation blocks lipid-induced inflammatory pathways in mouse heart and human cardiac cells

Alvarez-Guardia D, Palomer X, Coll T, Serrano L, Rodríguez-Calvo R, Davidson MM, Merlos M, El Kochairi I, Michalik L, Wahli W, Vázquez-Carrera M

Biochim Biophys Acta, 1811, 59-67 (2011)

PMID 21070867. Q1. IF 5.084. With other international groups. Programme 4

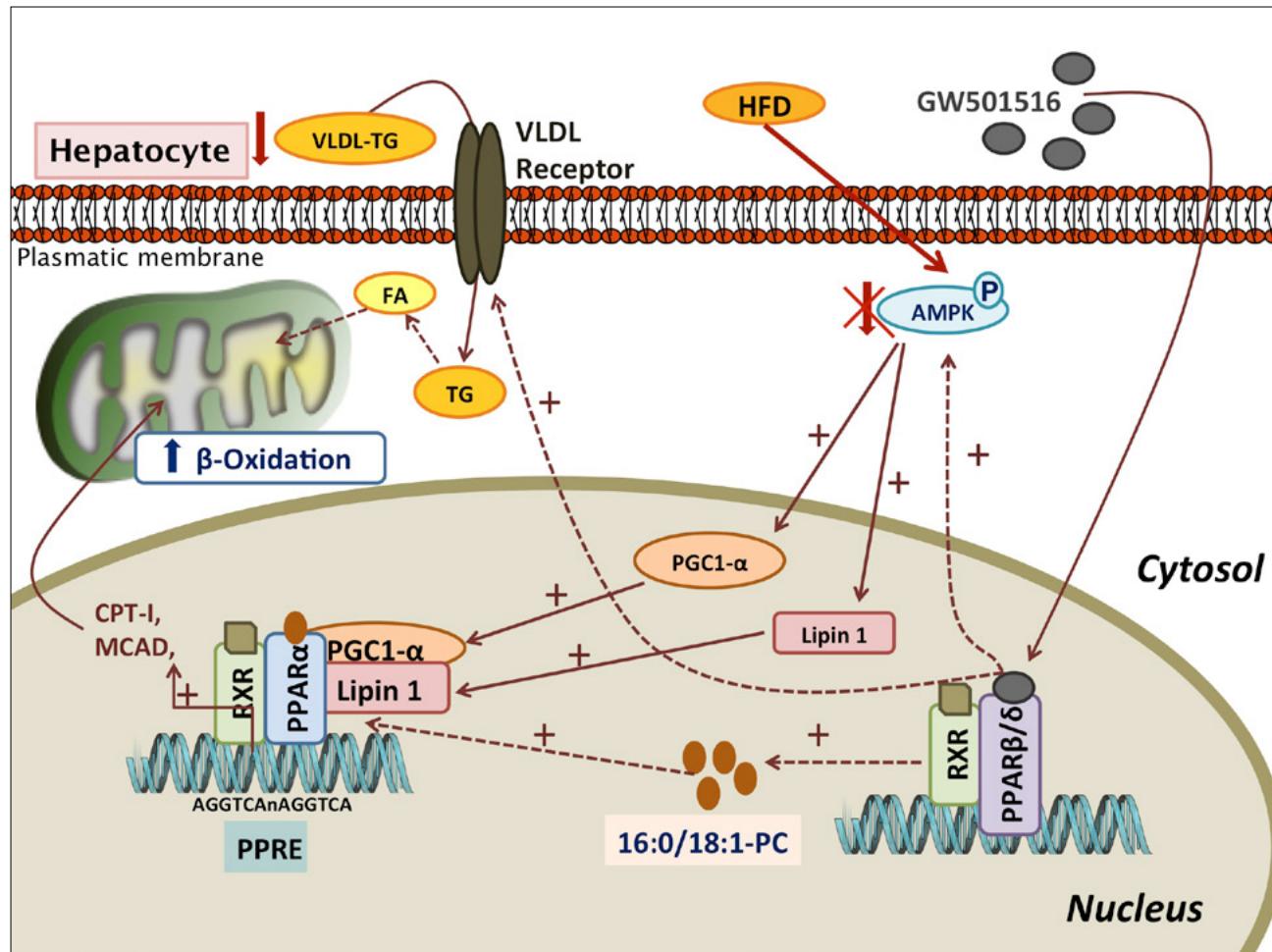
The interplay between NF-kappaB and E2F1 coordinately regulates inflammation and metabolism in human cardiac cells  
Palomer X, Alvarez-Guardia D, Davidson MM, Chan TO, Feldman AM, Vázquez-Carrera M

PLoS ONE, 6, e19724 (2011)  
PMID 21625432. Q1. IF 4.411. With other international groups. Programme 4

The PPAR $\beta/\delta$  activator GW501516 prevents the down-regulation of AMPK caused by a high-fat diet in liver and amplifies the PGC-1 $\alpha$ -Lipin 1-PPAR $\alpha$  pathway leading to increased fatty acid oxidation

Barroso E, Rodríguez-Calvo R, Serrano-Marco L, Astudillo AM, Balsinde J, Palomer X, Vázquez-Carrera M  
Endocrinology, 152, 1848-1859 (2011)

PMID 21363937. Q1. IF 4.993. With other Ciberdem groups: Balsinde J. Programme 4



A schematic representation of the potential effects of the PPAR $\delta$  agonist GW501516 (dashed lines) on liver metabolism.

### **Research grants**

Vías moleculares que conectan la inflamación con la resistencia a la insulina y la hipertrofia cardíaca. Estudio de los efectos de los ligandos de PPAR-beta/delta, el ácido oleico y las estatinas en modelos celulares y animales de resistencia a la insulina, síndrome metabólico e hipertrofia cardíaca

MICINN, SAF2009-06939: 2009-2011

Principal Investigator: Manuel Vázquez Carrera

*National project. Programme 4*

### **Scientific collaborations within Ciberdem**

Adult adipose tissue-derived progenitor cells: the influence of the clinical phenotype and adipose depot origin on their biological properties

STEMOB: 2009-2011

Coordinator: Joan J Vendrell

Ciberdem groups: Vázquez-Carrera M, Vendrell J, Zorzano A, Balsinde J, Gómez-Foix AM, Montanya E, Simó R

### **PhD theses**

Efecto de la activación de PPARbeta/delta sobre la oxidación de ácidos grasos y el proceso inflamatorio

Author: Emma Barroso Fernández

Thesis advisor: Manuel Vázquez Carrera

University: Universitat de Barcelona

Thesis defense date: January 31, 2011

*Programme 4*

Estudio de los mecanismos moleculares implicados en la asociación entre inflamación y alteraciones metabólicas en células cardíacas

Author: David Álvarez Guardia

Thesis advisor: Manuel Vázquez Carrera

University: Universitat de Barcelona

Thesis defense date: June 14, 2011

*Programme 4*

PPARbeta/delta, inflamación y resistencia a la insulina en adipositos

Author: Lucía Serrano Marco

Thesis advisor: Manuel Vázquez Carrera

University: Universitat de Barcelona

Thesis defense date: October 11, 2011

*Programme 4 ■*

# Diabetes and Metabolic Associated Diseases Research Group

Hospital Universitari de Tarragona Joan XXIII, Institut d'Investigació Sanitària Pere Virgili  
[www.iispv.cat](http://www.iispv.cat)



**Principal Investigator** Joan J Vendrell [jvo@comt.es](mailto:jvo@comt.es) **Associate researchers** Luís Gallart, Cristina Gutiérrez, Ana Megía, Matilde Rodríguez, Inmaculada Simón **Predoctoral fellow** Rosa Elena Yáñez **Postdoctoral fellows** Xavier Escoté, Lourdes Garrido, Mercedes Miranda, Olga Gisela Pachón, Sonia Fernández, María Esther Solano, Silvia Daniela Naf **Lab technicians** Miriam Campos, Francesc Xavier Duran, Elsa Maymó, Kelly Roche **Administrative staff** María de la Coba, Anna Estivill

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Publications: 9

First decile: 3

Q1: 5

Q2: 1

With other Ciberdem groups: 4

With other CIBERs: 5

With other international groups: 2

Research grants: 6

National projects: 4

Autonomous Community projects: 1

Private funds: 1

Scientific collaborations within Ciberdem: 4

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## Programmes

Programme 2. Mechanisms promoting the development of diabetes and its vascular complications. Associated disorders and co-morbidities. Strategies for prevention and treatment.

Programme 4. Use of biomedical approach systems to develop personalized therapies for diabetes.

## Keywords

Insulin sensitivity and resistance. Metabolic syndrome. Prediction/prevention of type 2 diabetes.

## Main lines of research

- Inflammatory mechanisms in type 2 diabetes and insulin resistance (chronic activation of the immune system).
- Genetic susceptibility markers in diabetes (genetic and environmental interaction in diabetes).
- Adipose cell biology – regulatory mechanisms of different adipose tissue cell types. Mesenchymal stem-cell biology (genes involved in adipose cell differentiation – paracrine/endocrine analysis of adipose tissue inflammatory mechanisms in obesity and diabetes).
- Gestational diabetes mellitus.

## Publications

A study of fatty acid binding protein 4 in HIV-1 infection and in combination antiretroviral therapy-related metabolic disturbances and lipodystrophy

Escoté X, Megia A, López-Dupla M, Miranda M, Veloso S, Alba V, Domingo P, Pardo P, Viladés C, Peraire J, Giralt M, Richart C, Vendrell J, Vidal F; HIV-1 Lipodystrophy Study Group

HIV Med, 12, 428-437 (2011)

PMID 21251185. Q2. IF 3.575. With other CIBERs: Ciberobn. Programme 2

CD14 modulates inflammation-driven insulin resistance

Fernández-Real JM, Pérez del Pulgar S, Luche E, Moreno-Navarrete JM, Waget A, Serino M, Sorianello E, Sánchez-Pla A, Pontaqué FC, Vendrell J, Chacón MR, Ricart W, Burcelin R, Zorzano A

Diabetes, 60, 2179-2186 (2011)

PMID 21700881. 1st decile. IF 8.889. With other Ciberdem groups: Zorzano A. With other CIBERs: Ciberobn. With other international groups. Programme 2

Lipodystrophy and insulin resistance in combination antiretroviral treated HIV-1-infected patients: implication of resistin

Escoté X, Miranda M, Veloso S, Domingo P, Alonso-Villaverde C, Peraire J, Viladés C, Alba V, Olona M, Castro A, López-Dupla M, Sirvent JJ, Vicente V, Vendrell J, Richart C, Vidal F; HIV-1 Lipodystrophy Study Group

J Acquir Immune Defic Syndr, 57, 16-23 (2011)

PMID 21317795. Q1. IF 4.262. Programme 2

Maternal and cord blood adiponectin multimeric forms in gestational diabetes mellitus: a prospective analysis

Ballesteros M, Simón I, Vendrell J, Ceperuelo-Mallafré V, Miralles RM, Albaiges G, Tinahones F, Megia A

Diabetes Care, 34, 2418-2423 (2011)

PMID 21911780. 1st decile. IF 7.141. With other CIBERs: Ciberobn. Programme 2

New emerging role of protein-tyrosine phosphatase 1B in the regulation of glycogen metabolism in basal and TNF- $\alpha$ -induced insulin-resistant conditions in an immortalised muscle cell line isolated from mice

Alonso-Chamorro M, Nieto-Vazquez I, Montori-Grau M, Gomez-Foix AM, Fernandez-Veledo S, Lorenzo M

Diabetologia, 54, 1157-1168 (2011)

PMID 21311858. 1st decile. IF 6.973. With other Ciberdem groups: Benito M, Gómez-Foix AM. Programme 2

Plasma PTX3 protein levels inversely correlate with insulin secretion and obesity, whereas visceral adipose tissue PTX3 gene expression is increased in obesity

Osorio-Conles O, Guitart M, Chacón MR, Maymo-Masip E, Moreno-Navarrete JM, Montori-Grau M, Naf S, Fernandez-Real JM, Vendrell J, Gómez-Foix AM

Am J Physiol Endocrinol Metab, 301, E1254-1261 (2011)  
PMID 21900125. Q1. IF 4.686. With other Ciberdem groups: Gómez-Foix AM. With other CIBERs: Ciberobn. Programme 2

Stromal stem cells from adipose tissue and bone marrow of age-matched female donors display distinct immunophenotypic profiles

Pachón-Peña G, Yu G, Tucker A, Wu X, Vendrell J, Bunnell BA, Gimble JM

J Cell Physiol, 226, 843-851 (2011)

PMID 20857424. Q1. IF 3.986. With other international groups. Programme 2

Study of the potential association of adipose tissue GLP-1 receptor with obesity and insulin resistance

Vendrell J, El Bekay R, Peral B, García-Fuentes E, Megia A, Macias-Gonzalez M, Fernández Real J, Jimenez-Gomez Y, Escoté X, Pachón G, Simó R, Selva DM, Malagón MM, Tinahones FJ

Endocrinology, 152, 4072-4079 (2011)

PMID 21862620. Q1. IF 4.993. With other Ciberdem groups: Simó R. With other CIBERs: Ciberobn. Programme 2

The stress-activated protein kinase Hog1 develops a critical role after resting state

Escoté X, Miranda M, Rodríguez-Porrata B, Mas A, Cordero R, Posas F, Vendrell J

Mol Microbiol, 80, 423-435 (2011)

PMID 21371138. Q1. IF 4.819. Programme 2

## Research grants

Estudio de la regulación del gen LPIN1 en pacientes con obesidad y diabetes mellitus tipo 2. Análisis in vitro en adipocitos humanos de su respuesta a diferentes estímulos lipolíticos

ISCIII, FIS, 08/1195: 2009-2011

Principal Investigator: Joan Vendrell Ortega

National project. Programme 2

Estudio del efecto de la citocina TWEAK en la insulino resistencia del adipocito. Relación de la fracción soluble y de su expresión génica con marcadores inflamatorios en pacientes obesos con diabetes tipo 2 y con diferente grado de insulino resistencia

ISCIII, FIS, 08/0733: 2009-2011

Principal Investigator: Matilde Rodríguez Chacón

Associate investigators: M Victoria Ceperuelo, Ana Megía

National project. Programme 2

Papel de las isoformas circulantes de adiponectina en la diabetes gestacional. Relación con el metabolismo hidrocarbonado y el desarrollo antropométrico fetal

ISCIII, FIS, 09/2152: 2010-2012

Principal Investigator: Inmaculada Simón Muela

Associate investigator: Ana Megía  
National project. Programme 2

Papel de las Fosfatifato Fosfatases (PAP, Lipin) en la regulación de funciones celulares por medio del control de la biosíntesis de fosfolípidos y su relación con la obesidad  
ISCIII, PI 10/00967: 2011-2013

Principal Investigator: Mercedes Miranda  
National project. Programme 2

Grup de recerca en diabetis i co-morbiditats associades.  
DiReCor

Generalitat de Catalunya, AGAUR, 2009 SGR 01257:  
2009-2013

Principal Investigator: Joan Vendrell Ortega

Associate investigators: Miriam Campos, Victoria Ceperuelo, Xavier Escoté, Luis Gallart, Cristina Gutiérrez, Elsa Maymó, Ana Megía, Mercedes Miranda, Matilde Rodríguez, Inmaculada Simón

Autonomous Community project. Programme 4

El papel de la citoquina TWEAK en la diabetes gestacional y su relación con otras adiponectinas y la sensibilidad a la insulina

Novo Nordisk: 2009-2011

Principal Investigator: Joan Vendrell Ortega

Associate investigators: Xavier Escoté, Ana Megía, Inmaculada Simón

Private funds. Programme 2

### Scientific collaborations within Ciberdem

Adult adipose tissue-derived progenitor cells: the influence of the clinical phenotype and adipose depot origin on their biological properties

STEMOB: 2009-2011

Coordinator: Joan J Vendrell

Ciberdem groups: Vendrell J, Zorzano A, Balsinde J, Gómez-Foix AM, Montanya E, Simó R, Vázquez-Carrera M

Determinants of insulin resistance and glucose tolerance disorders, including diabetes, in severe obesity and their changes after bariatric surgery-induced weight loss

DIASOBS: 2009-2011

Coordinator: Héctor F Escobar Morreale

Ciberdem groups: Vendrell J, Correig X, Montanya E, Escobar-Morreale HF, Simó R

Di@bet.es Study: 1st epidemiological study of the prevalence of type 2 diabetes in Spain

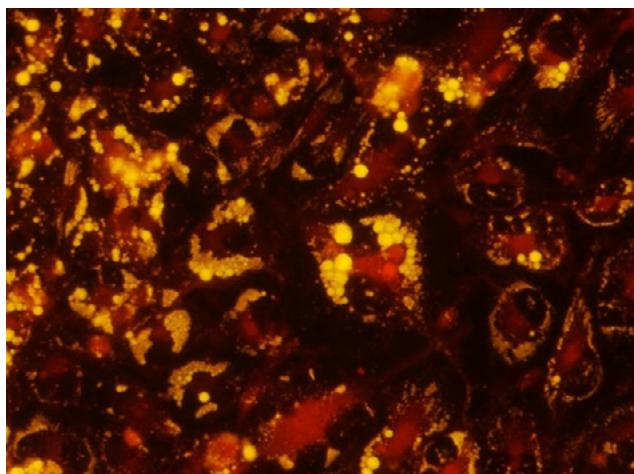
Coordinator: Federico Soriguer

Ciberdem groups: Vendrell J, Soriguer F, Carmena R, Castaño L, Gomis R, Serrano-Ríos M

Ciberdem Biobank

Coordinator: Anna Novials

Ciberdem Biobank nodes: Vendrell J, Gomis R, Novials A, Masana L, Castaño L, Serrano-Ríos M, Soriguer F, Carmena R, Blanco-Vaca F ■



Differentiated human visceral adipocytes.

# Molecular characteristics, and action of incretins, the physiopathology of glucose, lipids and bone metabolism

Fundación Jiménez Díaz, Madrid

[www.fjd.es](http://www.fjd.es)



**Principal Investigator** María Luisa Villanueva Peñacarrillo [mlvillanueva@fjd.es](mailto:mlvillanueva@fjd.es) **Associate researchers** Nieves González, Isabel Valverde, Alicia Acitores **PhD students** Irene Gutiérrez, Irene Ramos

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Publications: 1

Q2: 1

With other CiberDEM groups: 1

With other international groups: 1

Research grants: 2

National projects: 2

Scientific collaborations within CiberDEM: 1

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## Programmes

Programme 2. Mechanisms promoting the development of diabetes and its vascular complications. Associated disorders and co-morbidities. Strategies for prevention and treatment.

## Keywords

Glucose transport. Incretins. Insulin sensitivity and resistance. Lipid metabolism. Islet amyloid polypeptide/amylin.

## Main lines of research

-The effects and mechanisms in the action of GLP-1 action (glucagon-like-peptide 1) –an incretin with antidiabetic properties– and also that of GLP-1-homologue peptides, on glucose, lipids and bone metabolism.

-The mechanism of insulin secretion.

-The genetic characteristics, pharmacology and function of the human BRS-3 receptor, a possible target for the treatment of diabetes and obesity.

-The effect of amylin on glucose and bone metabolism.

## Publications

Amylin effect in extrapancreatic tissues participating in glucose homeostasis, in normal, insulin-resistant and type 2 diabetic state

Moreno P, Acitores A, Gutiérrez-Rojas I, Nuche-Berenguer B, El Assar M, Rodriguez-Mañas L, Gomis R, Valverde I, Visa M, Malaisse WJ, Novials A, González N, Villanueva-Peña Carrillo ML

Peptides, 32, 2077-2085 (2011)  
PMID 21939703. Q2. IF 2.654. With other Ciberdem groups:  
Gomis R, Novials A. With other international groups.  
Programme 2

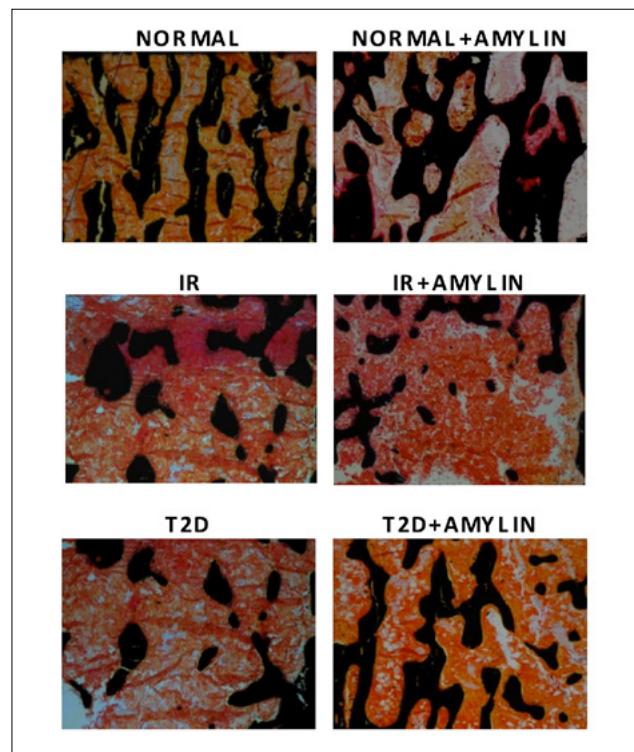
#### Research grants

The genetic characteristics, pharmacology and function of the human BRS-3 receptor, a possible target for the treatment of diabetes and obesity  
ISCIII, FIS CP08/00158: 2009-2011  
Principal Investigator: Nieves González Gómez  
National project. Programme 2

A molecular characterization of GLP-1 receptor in extrapancreatic tissues  
ISCIII, PS09/01185: 2010-2012  
Principal Investigator: Nieves González Gómez  
Associate investigators: ML Villanueva Peñacarrillo, Irene Ramos Álvarez, Irene Gutiérrez Rojas  
National project. Programme 2

#### Scientific collaborations within Ciberdem

Mechanisms of endothelial dysfunction in diabetes: the role of amylin and circulating endothelial cells  
ENDODIAB: 2009-2011  
Coordinator: Anna Novials  
Ciberdem groups: Villanueva-Peña Carrillo ML, Gomis R, Novials A ■



Representative light microscopy images showing the femur trabecular structure from normal (N), insulin resistant (IR) and type 2 diabetic (T2D) rats, untreated or treated with amylin, by using Von Kossa's staining.

# Heterogenic and polygenic diseases. Genexartis

Institut de Recerca Biomèdica, Barcelona  
[www.irbbarcelona.org](http://www.irbbarcelona.org)



**Principal Investigator** Antonio Zorzano [antonio.zorzano@irbbarcelona.org](mailto:antonio.zorzano@irbbarcelona.org) **Associate researchers** Marta Camps, Anna Gumà, Manuela Sánchez Feutrie, Xavier Testar **Postdoctoral fellows** Maria Àngels Díaz, Saska Ivanova, Iliana López, Deborah Naon, Montserrat Romero, David Sebastián, Eleonore Sorianello **Research assistant** Juan Carlos Monasterio **PhD students** Víctor Francis, María Isabel Hernández, Vicente Martínez, Caroline Mauvezin, Sónia Pereira, David Sala, Ana Sancho **Lab manager** Olga Bausà **Technologist** Jessica Segalés

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Publications: 3

First decile: 2

Q1: 1

With other Ciberdem groups: 1

With other CIBERS: 3

With other international groups: 2

Research grants: 6

European projects: 3

National projects: 2

Autonomous Community projects: 1

Scientific collaborations within Ciberdem: 1

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## Programmes

Programme 4. Use of biomedical approach systems to develop personalized therapies for diabetes.

## Keywords

Insulin action. Insulin sensitivity and resistance. Carbohydrate metabolism. Lipid metabolism. Oral pharmacological agents. Mitochondrial metabolism. Autophagy.

## Main lines of research

Molecular mechanisms involved in the development of insulin resistance and the identification of novel targets for diabetes therapy:

- a) analysis of the role of mitochondrial dynamics proteins in metabolic homeostasis, in the control of insulin signalling, and in the response to cell stress,
- b) a study of the role of DOR protein in insulin-resistant states,
- c) analysis of the metabolism role of neuregulins.

## Publications

CD14 modulates inflammation-driven insulin resistance  
Fernández-Real JM, Pérez del Pulgar S, Luche E, Moreno-Navarrete JM, Waget A, Serino M, Sorianello E, Sánchez-Pla A, Pontaqué FC, Vendrell J, Chacón MR, Ricart W, Burcelin R, Zorzano A  
*Diabetes*, 60, 2179-2186 (2011)  
PMID 21700881. 1st decile. IF 8.889. With other Ciberdem groups: Vendrell J. With other CIBERs: Ciberobn. With other international groups. Programme 2

Molecular basis of substrate-induced permeation by an amino acid antiporter  
Kowalczyk L, Ratera M, Paladino A, Bartoccioni P, Errasti-Murugarren E, Valencia E, Portella G, Bial S, Zorzano A, Fita I, Orozco M, Carpéné X, Vázquez-Ibar JL, Palacín M  
*Proc Natl Acad Sci U S A*, 108, 3935-3940 (2011)  
PMID 21368142. 1st decile. IF 9.771. With other CIBERs: Ciberer. Programme 4

Role of diabetes- and obesity-related protein in the regulation of osteoblast differentiation  
Linares GR, Xing W, Burghardt H, Baumgartner B, Chen ST, Ricart W, Fernández-Real JM, Zorzano A, Mohan S  
*Am J Physiol Endocrinol Metab*, 301, E40-48 (2011)  
PMID 21467300. Q1. IF 4.686. With other CIBERs: Ciberobn. With other international groups. Programme 4

## Research grants

Transnational cooperation for technological innovation in the development of molecules for the treatment of obesity and diabetes  
SUDOE (European Community Initiative INTERREG IV for Southwestern Europe), SOE1/P1/E178: 2009-2012  
Principal Investigator: A Zorzano  
*European project. Programme 4*

Integration of the system models of mitochondrial function and insulin signalling and its application in the study of complex diseases  
European Union, Seventh Framework Programme (FP7), HEALTH-F4-2008-223450: 2008-2011  
Principal Investigator: A Zorzano  
*European project. Programme 4*

Adipose tissue: a key target for prevention of the metabolic syndrome  
European Science Foundation, COST Action BM0602: 2007-2011  
Principal Investigator: Antonio Zorzano  
Coordinator: Jürgen Eckel  
*European project. Programme 4*

Genetic determinants of the metabolic alterations in obesity and/or type 2 diabetes and their participation in insulin resistance

Ministerio de Ciencia e Innovación, SAF2008-03803: 2009-2013

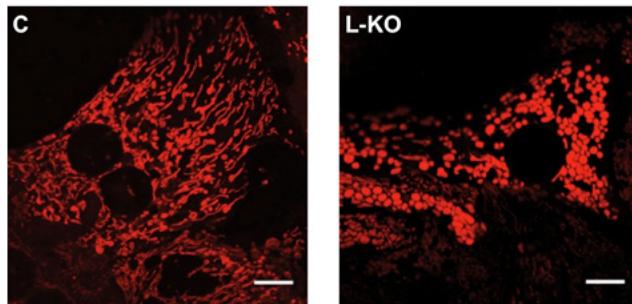
Principal Investigator: Antonio Zorzano  
*National project. Programme 4*

Caracterización de los efectos de las neuregulinas en modelos de resistencia a la insulina  
Ministerio de Ciencia e Innovación, SAF2008-01723: 2009-2013  
Principal Investigator: Antonio Zorzano  
Coordinator: Anna Gumà  
*National project. Programme 4*

Molecular basis of metabolic disorders  
Departament d'Innovació, Universitats i Empresa, Generalitat de Catalunya, 2009SGR915: 2009-2013  
Principal Investigator: Antonio Zorzano  
*Autonomous Community project. Programme 4*

## Scientific collaborations within Ciberdem

Adult adipose-tissue-derived progenitor cells: the influence of the clinical phenotype and adipose depot origin on their biological properties  
STEMOB: 2009-2011  
Coordinator: Joan J Vendrell  
Ciberdem groups: Zorzano A, Vendrell J, Balsinde J, Gómez-Foix AM, Montaña E, Simó R, Vázquez-Carrera M ■



The mitochondrial morphology of isolated hepatocytes from control (C) and Mfn2 knockout mice (L-KO). Altered mitochondrial morphology is observed in L-KO mice.

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\*Source: DIAMAP, Road Map for Diabetes Research in Europe.

# Publications index\*

A primary-school-based study to reduce prevalence of childhood obesity in Catalunya (Spain)--EDAL-Educació en alimentació: study protocol for a randomised controlled trial

Giralt M, Albaladejo R, Tarro L, Moriña D, Arija V, Solà R

Trials, 12, 54 (2011)

A role for the putative cannabinoid receptor GPR55 in the islets of Langerhans

Romero-Zerbo SY, Rafacho A, Díaz-Arteaga A, Suárez J, Quesada I, Imbernon M, Ross RA, Dieguez C, Rodríguez de Fonseca F, Nogueiras R, Nadal A, Bermúdez-Silva FJ

J Endocrinol, 211, 177-185 (2011)

A study of fatty acid binding protein 4 in HIV-1 infection and in combination antiretroviral therapy-related metabolic disturbances and lipodystrophy

Escoté X, Megia A, López-Dupla M, Miranda M, Veloso S, Alba V, Domingo P, Pardo P, Viladés C, Peraire J, Giralt M, Richart C, Vendrell J, Vidal F; HIV-1 Lipodystrophy Study Group

HIV Med, 12, 428-437 (2011)

Activation of peroxisome proliferator-activated receptor- $\beta$ /- $\delta$  (PPAR- $\beta$ /- $\delta$ ) ameliorates insulin signaling and reduces SOCS3 levels by inhibiting STAT3 in interleukin-6-stimulated adipocytes

Serrano-Marco L, Rodríguez-Calvo R, El Kochairi I, Palomer X, Michalik L, Wahli W, Vázquez-Carrera M

Diabetes, 60, 1990-1999 (2011)

Altered arachidonate distribution in macrophages from caveolin-1 null mice leading to reduced eicosanoid synthesis

Astudillo AM, Pérez-Chacón G, Meana C, Balgoma D, Pol A, Del Pozo MA, Balboa MA, Balsinde J

J Biol Chem, 286, 35299-35307 (2011)

Alx3-deficient mice exhibit decreased insulin in beta cells, altered glucose homeostasis and increased apoptosis in pancreatic islets

Mirasierra M, Fernández-Pérez A, Díaz-Prieto N, Vallejo M

Diabetologia, 54, 403-414 (2011)

Amylin effect in extrapancreatic tissues participating in glucose homeostasis, in normal, insulin-resistant and type 2 diabetic state

Moreno P, Acitores A, Gutiérrez-Rojas I, Nuche-Berenguer B, El Assar M, Rodriguez-Mañas L, Gomis R, Valverde I, Visa M, Malaisse WJ, Novials A, González N, Villanueva-Peña Carrillo ML

Peptides, 32, 2077-2085 (2011)

Angiographic demonstration of neoangiogenesis after intra-arterial infusion of autologous bone marrow mononuclear cells in diabetic patients with critical limb ischemia

Ruiz-Salmeron R, de la Cuesta-Díaz A, Constantino-Bermejo M, Pérez-Camacho I, Marcos-Sánchez F, Hmadcha A, Soria B  
Cell Transplant, 20, 1629-1639 (2011)

\*Only those published in 2011, with Ciberdem listed among the affiliations, which are related to Ciberdem's field of research and are located in the first or second quartile of their subject category are included.

AStream: an R package for annotating LC/MS metabolomic data  
Alonso A, Julià A, Beltran A, Vinaixa M, Díaz M, Ibañez L, Correig X, Marsal S  
Bioinformatics, 27, 1339-1340 (2011)

ATP-binding cassette G5/G8 deficiency causes hypertriglyceridemia by affecting multiple metabolic pathways  
Méndez-González J, Julve J, Rotllan N, Llaverias G, Blanco-Vaca F, Escolà-Gil JC  
Biochim Biophys Acta, 1811, 1186-1193 (2011)

Bioavailability of phenols from a phenol-enriched olive oil  
Suárez M, Valls RM, Romero MP, Macià A, Fernández S, Giralt M, Solà R, Motilva MJ  
Br J Nutr, 106, 1691-1701 (2011)

Catch-up growth in girls born small for gestational age precedes childhood progression to high adiposity  
Ibáñez L, Lopez-Bermejo A, Diaz M, de Zegher F  
Fertil Steril, 96, 220-223 (2011)

Caveolin-1 deficiency causes cholesterol-dependent mitochondrial dysfunction and apoptotic susceptibility  
Bosch M, Marí M, Herms A, Fernández A, Fajardo A, Kassan A, Giralt A, Colell A, Balgoma D, Barbero E, González-Moreno E, Matias N, Tebar F, Balsinde J, Camps M, Enrich C, Gross SP, García-Ruiz C, Pérez-Navarro E, Fernández-Checa JC, Pol A  
Curr Biol, 21, 681-686 (2011)

CD14 modulates inflammation-driven insulin resistance  
Fernández-Real JM, Pérez del Pulgar S, Luche E, Moreno-Navarrete JM, Waget A, Serino M, Sorianello E, Sánchez-Pla A, Pontaqué FC, Vendrell J, Chacón MR, Ricart W, Burcelin R, Zorzano A  
Diabetes, 60, 2179-2186 (2011)

Children whose diet contained olive oil had a lower likelihood of increasing their body mass index Z-score over 1 year  
Haro-Mora JJ, García-Escobar E, Porras N, Alcázar D, Gatzambide J, Ruiz-Órppez A, García-Serrano S, Rubio-Martín E, García-Fuentes E, López-Siguero JP, Soriguer F, Rojo-Martínez G  
Eur J Endocrinol, 165, 435-439 (2011)

Circulating inflammatory markers in polycystic ovary syndrome: a systematic review and metaanalysis  
Escobar-Morreale HF, Luque-Ramírez M, González F  
Fertil Steril, 95, 1048-1058 (2011)

Clinical features of patients with hypertriglyceridemia referred to lipid units: registry of hypertriglyceridemia of the Spanish Arteriosclerosis Society  
Valdivielso P, Pintó X, Mateo-Gallego R, Masana L, Alvarez-Sala L, Jarauta E, Suárez M, García-Arias C, Plana N, Laguna F; Registro de HTG de la SEA  
Med Clin (Barc), 136, 231-238 (2011)

Development and functional characterization of insulin-releasing human pancreatic beta cell lines produced by electrofusion  
McCluskey JT, Hamid M, Guo-Parke H, McClenaghan NH, Gomis R, Flatt PR  
J Biol Chem, 286, 21982-21992 (2011)

Dietary polyunsaturated fatty acids may increase plasma LDL-cholesterol and plasma cholesterol concentrations in carriers of an ABCG1 gene single nucleotide polymorphism: study in two Spanish populations  
Abellán R, Mansego ML, Martínez-Hervás S, Morcillo S, Pineda-Alonso M, Carmena R, Real JT, Redon J, Rojo-Martínez G, Martín-Escudero JC, Chaves FJ  
Atherosclerosis, 219, 900-906 (2011)

Different impacts of cardiovascular risk factors on oxidative stress  
Mansego ML, Redon J, Martínez-Hervás S, Real JT, Martínez F, Blesa S, Gonzalez-Albert V, Saez GT, Carmena R, Chaves FJ  
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Differential effects of gemfibrozil and fenofibrate on reverse cholesterol transport from macrophages to feces in vivo  
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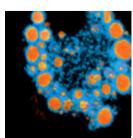
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Confocal microscopy analysis of human macrophages shows that lipin-1 $\alpha$  (blue) localizes to the periphery of lipid droplets where triglycerides accumulate (orange). Lack of functioning of lipin-1 $\alpha$  results in insulin resistance.



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It is not easy for researchers to carry out their tasks in times of economic crisis, but no more difficult than it is for the rest of the population, who have to adapt to a period not of growth, but of recession. At all times in history, there have been difficult moments for scientific investigation, although this has never prevented talented researchers from bringing new knowledge to humanity. We are pleased to be able to say that, as this annual report shows, we have made significant advances which are of great importance to our health system, such as the Di@bet.es Study, which provides us with accurate information on the prevalence of diabetes in the Spanish population, and the results obtained by researchers using the Metabolomics Platform. We single these out because they are collective achievements, a general effort on the part of all our researchers. **Ramon Gomis, Ciberdem Scientific Director**

