ANNUAL REPORT 2014

ciberdem

Centro de Investigación Biomédica en Red

Diabetes y Enfermedades Metabólicas Asociadas

Index

1. ORGANIZATION

INTRODUCTION

The Centro de Investigación Biomédica en Red (CIBER) is a consortium depending on Instituto de Salud Carlos III (Ministry of Economy and Competitiveness). CIBERDEM, CIBER de Diabetes y Enfermedades Metabólicas Asociadas (Diabetes and Associated Metabolic disorders) is formed by 30 research groups located in different hospitals, universities and research centres throughout Spain.

CIBERDEM's primary objective is to promote research on diabetes and associated metabolic disorders by identifying the genes making one more inclined to suffer said diseases and disorders and the environmental factors contributing to their development, to clarify the molecular mechanisms involved in the impairment of insulin secretion and signaling; to determine the molecular and cellular mechanisms of pancreatic beta cell formation and destruction; to study strategies for replacing said cell mass; and to conduct research on the signals linking obesity and diabetes. Research on the complications of diabetes and associated metabolic disorders is also of special interest.

To meet its objectives, CIBERDEM seeks to generate an attractive framework for the incorporation of basic and clinical research staff, as well as the development of biomedical platforms suitable for conducting research of excellence in diabetes and associated metabolic disorders. In turn, CIBERDEM promotes translational research, favoring the transfer of acquired diabetes knowledge to other disciplines, and vice versa.

CIBERDEM's mission is to lead the research effort of excellence in diabetes and associated metabolic disorders, and to speed up the translation of scientific results to clinical practice.

CIBERDEM conducted research activities relating to the following fields:

- **Type 1 Diabetes Mellitus. Autoimmunity.**
- **Type 2 Diabetes Mellitus. Insulin signaling and resistance.**
- **Genetics of Diabetes Mellitus.**
- **Diabetes Mellitus. Microvascular complications.**
- **Dyslipidemia, inflammation and endothelial dysfunction.**
- **Pancreatic islet dysfunction, destruction and regeneration.**
- **Diabetes and Obesity. Biological interferences between tissues.**
- **Diabetes and associated metabolic disorders. Glucotoxicity and lipotoxicity.**
- **Metabolic syndrome. Physiopathology and epidemiology.**

Research in CIBERDEM comprises four scientific programmes

P1

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

P2

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

P3

Impact of beta cell dysfunction and plasticity on diabetes. Development of new treatment strategies.

P4

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

CIBERDEM's strategic lines of research are grouped into four categories:

- **Transversal research projects**
- **Technological platforms,** such as CIBERDEM Biobank and Metabolomics Platform.
- **Research support activities,** among which the "special actions", aid packages so that CIBERDEM groups can have access to cutting-edge technological services stand out.
- **Training plan,** such as organizing courses for CIBERDEM research community (pre-doctoral, etc.).

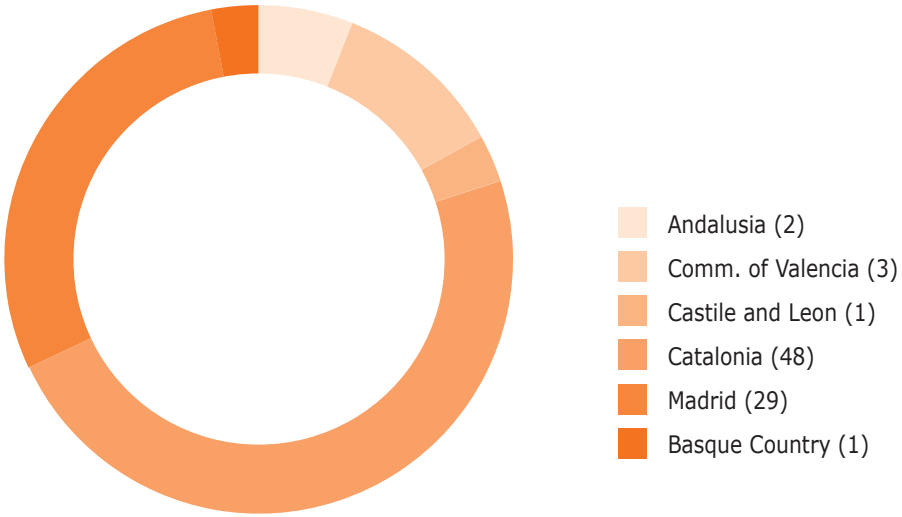
CIBERDEM's nature, purposes and operation are described in its By-laws published in the Boletín Oficial del Estado (BOE) (Official State Journal) no. 42, February 18, 2011.

RESEARCH GROUPS AND CONSORTIUM INSTITUTIONS

Group	Lead Researcher	ISCII IP	Institution	Region
1	Álvarez Escolá, Carmen	CB07/08/0013	Universidad Complutense de Madrid	Madrid
2	Balsinde Rodríguez, Jesús	CB07/08/0004	Agencia Estatal Consejo Superior De Investigaciones Científicas	Castilla y León
3	Benito de las Heras, Manuel R.	CB07/08/0001	Universidad Complutense de Madrid	Madrid
4	Blanco Vaca, Francisco	CB07/08/0016	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Cataluña
5	Blázquez Fernández, Enrique	CB07/08/0010	Universidad Complutense de Madrid	Madrid
6	Bosch Tubert, Fàtima	CB07/08/0037	Universidad Autónoma de Barcelona	Cataluña
7	Burks, Deborah	CB07/08/0043	Fundación Centro de Investigación Príncipe Felipe	C. Valenciana
8	Carmena Rodríguez, Rafael	CB07/08/0018	Fundación para la Investigación del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)	C. Valenciana
10	Castaño González, Luis	CB07/08/0025	Asociación Instituto de Investigación Sanitaria de Biocruces	País Vasco
11	Correig Blanchart, Francesc X.	CB07/08/0014	Fundación Instituto de Investigación Sanitaria Pere Virgili	Cataluña
32	Egido de los Ríos, Jesús	CB07/08/2007	Instituto de Investigación Sanitaria - Fundación Jiménez Díaz	Madrid
13	Escobar Morreale, Héctor F.	CB07/08/0005	Servicio Madrileño de Salud	Madrid
14	Ferrer Marrades, Jorge	CB07/08/0021	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Cataluña
15	Gómez Foix, Anna Maria	CB07/08/0011	Universidad de Barcelona	Cataluña
16	Gomis de Barbarà, Ramon	CB07/08/0009	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Cataluña
17	Guinovart Cirera, Joan Josep	CB07/08/0045	Fundación privada Instituto de Recerca Biomédica (IRB-Barcelona)	Cataluña
19	Ibáñez Toda, Lourdes	CB07/08/0044	Fundación para la Investigación y Docencia Sant Joan de Deu	Cataluña
21	Martín Bermudo, Francisco	CB07/08/0006	Universidad Pablo de Olavide	Andalucía
22	Martínez Valverde, Ángela María	CB07/08/0033	Agencia Estatal Consejo Superior De Investigaciones Científicas	Madrid

Group	Lead Researcher	ISCII IP	Institution	Region
23	Masana Marín, Luis	CB07/08/0028	Fundación Instituto de Investigación Sanitaria Pere Virgili	Cataluña
24	Montanya Mias, Eduard	CB07/08/0022	Fundación IDIBELL	Cataluña
25	Nadal Navajas, Ángel	CB07/08/0002	Universidad Miguel Hernández	C. Valenciana
12	Novials Sardà, Anna Maria	CB07/08/2005	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Cataluña
9	Rojo Martínez, Gemma	CB07/08/0019	Fundación Pública Andaluza para la Investigación de Málaga en Biomedicina y Salud (FIMABIS)	Andalucía
26	Serrano Ríos, Manuel	CB07/08/0030	Servicio Madrileño de Salud	Madrid
27	Simó Canonge, Rafael	CB07/08/0024	Fundación Hospital Universitario Vall D´hebron - Institut De Recerca (VHIR)	Cataluña
28	Vallejo Fernández de la Reguera, Mario	CB07/08/0029	Agencia Estatal Consejo Superior De Investigaciones Científicas	Madrid
29	Vázquez Carrera, Manuel	CB07/08/0003	Universidad de Barcelona	Cataluña
30	Vendrell Ortega, Joan Josep	CB07/08/0012	Fundación Instituto de Investigación Sanitaria Pere Virgili	Cataluña
31	Zorzano Olarte, Antonio	CB07/08/0017	Fundación privada Instituto de Recerca Biomédica (IRB-Barcelona)	Cataluña

Territorial distribution of the research groups



CIBERDEM's organizational structure is based on the strategic objectives and the By-laws governing the Consortium. CIBERDEM's management and administration is made up of the following bodies:

Board of Trustees

The Board of Trustees is formed by three representatives from Instituto de Salud Carlos III and one representative from each of the Consortium Institutions. The Board of Trustees is chaired by the Director of Instituto de Salud Carlos III, the General Manager of the consortium acting as Secretary of the Board.

Permanent Commission

The Permanent Commission is formed by the President of the Board of Trustees, or the appointed person, the Scientific Director of the Consortium, the General Manager of said Consortium – acting as the Secretary - and four members representative of the Consortium Institutions.

Scientific Director

In 2014, the Scientific Director was Dr. Luis Castaño. He was appointed as acting Scientific Director by the CIBERDEM Permanent Commission and the appointment was ratified by the Board of Trustees on 18 December 2012.

Members of the CIBERDEM Scientific Management

- **Scientific Director:** Luis Castaño
- **Scientific Sub-Director:** Anna Novials

Steering Committee

In 2014, the members of the Steering Committee were:

Luis Castaño, Scientific Director and President of the Steering Committee

Anna Novials, Scientific Sub-Director and Programme 3 Coordinator

Rafael Carmena, Programme 1 Coordinator

Manuel Benito, Programme 2 Coordinator

Antonio Zorzano, Programme 4 Coordinator

Fatima Bosh, Teaching Programme Coordinator

Manuel Sánchez, CIBER General Manager

External Scientific Advisory Committee

The External Scientific Advisory Committee is formed by prominent individuals in the health sciences field whose professional and scientific careers are in alignment with Consortium objectives. This Committee is a scientific advisory body that performs annual evaluation of CIBERDEM's activity and research groups. It consists of a President appointed by the President of the Board of Trustees, and 4 members appointed by the Board of Trustees.

CIBERDEM's External Scientific Advisory Committee Members:

- **President:** Jose M. Ordovas, Universidad de Tufts, Boston (USA)
- **Members:** F.Xavier Pi-Sunyer, Universidad de Columbia, New York (USA), Decio Eizirik, Universidad Libre, Bruselas (Bélgica), Antonio Vidal-Puig, Universidad de Cambridge, Cambridge (UK), Antonio Vidal-Puig, Universidad de Cambridge, Cambridge (UK), Ele Ferrannini, Universidad de Pisa, Pisa (Italia)

Presidente: **Jose M. Ordovas**, Tufts University, Boston (USA)

Director, Nutrition and Genomics Laboratory, Human Nutrition Research Center on Aging (HNR-CA) at Tufts University, Boston (Massachusetts) and Professor in Nutrition and Genetics, School of Medicine and Nutrition, Tufts University.

Mr. Jose M. Ordovas is a pioneer in research on the importance of diet and eating habits in relation to the genome. His work in the genetic field of cardiovascular diseases led to his appointment as the Head of Genetic Studies of the well-known Framingham Study. His articles have been published in the most prestigious journals with the greatest international impact on biomedical research, such as The New England Journal of Medicine, Science, JAMA, The Lancet, etc. His career in this field has earned him many awards, such as the Nutrition Science Award (2007) from the American Society for Nutrition, or the USDA Secretary's Honor Award (2006), the most important distinction awarded by the US Department of Agriculture (USDA), among others. In 2004, the Sociedad Española de Arteriosclerosis named him an Honorary Member.

Member: **F. Xavier Pi-Sunyer**, Columbia University, New York (USA)

Professor of Medicine at Columbia University (New York). Chief of Endocrinology, Diabetes and Nutrition Department of St. Luke's-Roosevelt Hospital Center and Director of the New York Obesity Research Center. He chaired the Committee of the National Heart, Lung and Blood Institute, defining and designing new governmental guidelines for the prevention and treatment of obesity. He also served as the President of the American Diabetes Association (ADA), the American Society for Clinical Nutrition and the North American Association for the Study of Obesity, and as a member of various diabetes and obesity advisory committees. He has written over 300 international articles and a number of book chapters. He served as the Editor of the International Journal of Obesity from 1994-2005 and as the Editor-in-Chief of Obesity Research from 1995-2000.

Member: **Decio Eizirik**, Université Libre, Brussels (Belgium)

Director, Experimental Medicine Laboratory, Université Libre, Brussels (ULB), Belgium. He has published over 220 articles in international journals and received many awards including, most importantly, the Juvenile Diabetes Research Foundation Award (JDRF), the Diabetes Care Research Award and the EASD/Eli Lilly Award. He is the coordinator of the Beta Cell Gene Expression Bank and of several competitive European projects in the field of diabetes. He served as the Honorary Scientific Secretary of the European Association for the Study of Diabetes (EASD) (2004-2007) and the Assistant Editor of the Diabetologia journal (1998-2004). He is currently the member of the Scientific Committee for the National Programme of Diabetes Research in France. His research interests focus on molecular mechanisms regulating beta cell apoptosis and the search for new approaches to prevent progressive cell mass loss in diabetes.

Member: **Antonio Vidal-Puig**, University of Cambridge, Cambridge (UK)

M.D, PhD in Endocrinology. He completed his post-doctoral internship at Harvard and then lived out his research career there until 1999 when he moved to the University of Cambridge. He is now the Associate Professor of Metabolic Medicine and Honorary Consultant in Metabolic Medicine at the University of Cambridge. He is also the Assistant Director of the MRC-CORD Research Centre for Obesity and Related Diseases of the University of Cambridge and Director of Wellcome Trust's Mouse Programme. His areas of scientific interest include adipocyte biology, mitochondrial biology, lipotoxicity and genetically modified animal models.

Member: **Ele Ferrannini**, Università degli Studi di Pisa, Pisa (Italia)

Professor of Internal Medicine, Università degli Studi di Pisa, Chief of the Metabolic Medicine Unit of the CNR (National Research Council), Instituto de Fisiología Clínica de Pisa, and Professor of Clinical Medicine, Diabetes Department, University de Texas, USA. He has published over 400 original articles in the field of diabetes, metabolic medicine and hypertension. He is a member of various scientific associations. His participation in the Executive Council of the European Association for the Study of Diabetes (EASD) as the President (2004-2008) and his role as the Editor-in-Chief of Diabetologia (1994-1998), the official journal of the EASD, must be given special mention. He now serves as the President of the European Group for the Study of Insulin Resistance.

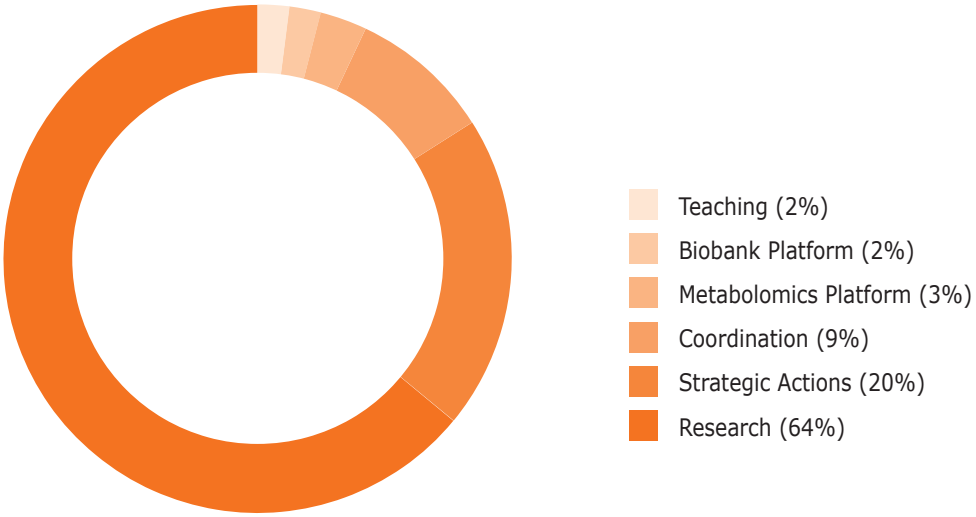
Lines of research: insulin resistance and atherosclerosis, impact of oxidative stress and blood pressure on endothelial function, autoimmunity in adult-onset diabetes, physiopathology of insulin secretion, impact of hyperinsulinemia on the nervous system, pathogenesis of insulin resistance and hyperinsulinism in obesity, effect on weight loss; coronary atherosclerosis in diabetes, atherosclerosis in diabetes.

CIBERDEM BUDGET

2014 BUDGET DRAFT

Concept	Total
Research	2.102.719,95
Strategic Actions	663.654,57
Coordination	300.000,00
Metabolomics Platform	105.000,00
Biobank Platform	70.732,50
Teaching	55.925,60
TOTAL	**3.298.032,62**

Budget Distribution by concept



CIBERDEM STAFF

Number of employees during the year to December 31 distinguishing by category and gender.

	MEN			Total MEN
	Indefinite	Work & service	Postdoctoral	
CIBERDEM	15	4	1	20
PhD	9	2	1	12
Degree Holder	1	1		2
Diploma Holder	1			1
Technician	4	1		5
Grand total	15	4	1	20

	WOMEN			Total WOMEN
	Indefinite	Work & service	Postdoctoral	
CIBERDEM	48	16		64
PhD	22	9		31
Degree Holder	15	4		19
Diploma Holder	2	1		3
Technician	9	2		11
Grand total	48	16		64

	Indefinite	Work & service	Postdoctoral	Total general
CIBERDEM	63	20	1	84
Doctor	31	11	1	43
Degree Holder	16	5		21
Diploma Holder	3	1		4
Technician	13	3		16
Grand total	**63**	**20**	**1**	**84**

2. SCIENTIFIC PROGRAMMES

PROGRAMME 1

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

Objectives:

- Strategies for establishing nutritional guidelines in lifestyle studies and in diabetes/obesity prevention.
- The impact of overnutrition, diabetes-obesity and malnutrition in energy homeostasis regulation in the central nervous system.
- 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 insulin resistance syndrome and its long-term complications in Mediterranean immigrant populations.
- Characterization of low HDL syndrome in type 2 diabetes.

Coordinator: **Dr. Rafael Carmena**

Associated groups: **8**

Lead Researcher	Institution	Region
Álvarez Escolá, Carmen	Universidad Complutense de Madrid	Madrid
Blázquez Fernández, Enrique	Universidad Complutense de Madrid	Madrid
Carmena Rodríguez, Rafael	Fund. Hospital Clínico Universitario de Valencia	C. Valenciana
Casimiro-Soriguer Escofet, Federico José	Fundación Instituto Mediterráneo para el Avance de la Biotecnología Sanitaria	Andalucía
Correig Blanchar, Francesc Xavier	Fund. Inst. d'Investigació Sanitària Pere Virgili	Cataluña
Novials Sardà, Anna Mª	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Cataluña
Masana Marín, Luis	Fund. Inst. d'Investigació Sanitaria Pere Virgili	Cataluña
Serrano Ríos, Manuel	Servicio Madrileño de Salud	Madrid

PROGRAMME 2

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

Objectives:

- Identification of neurodegenerative mechanisms which promote the development of diabetic retinopathy: the role of insulin signaling and apoptosis.
- Glycogen-induced dysfunctions in the pancreas and retina and the involvement thereof in the etiopathogenesis 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.

Coordinator: **Dr. Manuel Benito**

Associated groups: **9**

Lead researcher	Institution	Region
Benito de las Heras, Manuel Román	Universidad Complutense de Madrid	Madrid
Blanco Vaca, Francisco	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Cataluña
Gomis de Bárbara, Ramón	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Cataluña
Guinovart Cirera, Joan Josep	Fundació Privada Institut de Recerca Biomèdica (IRB)	Cataluña
Martinez Valverde, Ángela María	Consejo Superior de Investigaciones Científicas	Madrid
Masana Marin, Luis	Fund. Institut d'Investigació Sanitaria Pere Virgili	Cataluña
Simo Canonge, Rafael	Fund. Instituto de Investigación Vall D'hebron	Cataluña
Vendrell Ortega, Joan J.	Fund. Institut d'Investigació Sanitaria Pere Virgili	Cataluña
Egido De los Ríos, Jesús	Instituto de Investigación Sanitario Fundación Jiménez Díaz	Madrid

PROGRAMNE 3

Impact of beta cell dysfunction and plasticity on diabetes. Development of new treatment strategies.

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 detecting diabetes biomarkers.

Coordinator: **Dra. Anna Novials**
Associated groups: **10**

Lead researcher	Institution	Region
Bosh Tubert, Fátima	Universidad Autónoma de Barcelona	Cataluña
Burks, Deborah	Fund. Centro de Investigación Príncipe Felipe	C. Valenciana
Castaño González, Luis	Fundación Vasca de Innovación e Investigación Sanitarias	País Vasco
Novials Sardà, Anna Mª	Instituto de Invest. Biomédicas August Pi i Sunyer	Cataluña
Ferrer Marrades, Jorge	Instituto de Invest. Biomédicas August Pi i Sunyer	Cataluña
Gomis de Barbarà, Ramón	Instituto de Invest. Biomédicas August Pi i Sunyer	Cataluña
Martín Bermudo, Francisco	Universidad Pablo de Olavide	Andalucía
Montanya Mias, Eduard	Fundación IDIBELL	Cataluña
Nadal Navajas, Ángel	Universidad Miguel Hernández	C. Valenciana
Vallejo Fernández de la Reguera, Mario	Consejo Superior de Investigaciones Científicas	Madrid

PROGRAMME 4

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

Objectives:

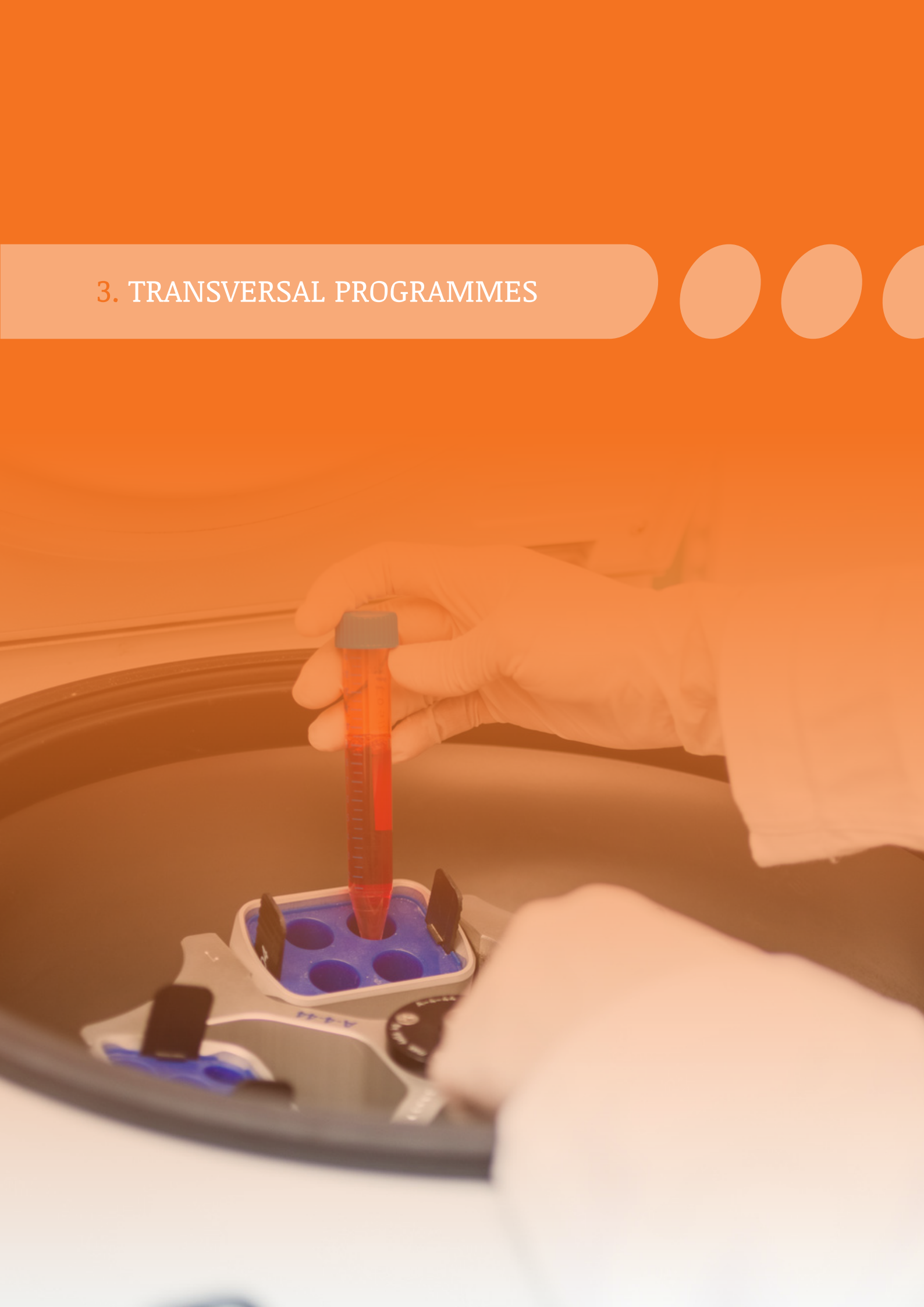
- Determinants of insulin resistance and glucose tolerance disorders (including diabetes) in severely obese individuals and their changes after bariatric surgery-induced weight loss.
- Adipose tissue-derived adult progenitor cells: the influence of clinical phenotype and fat depot origin on their biological properties.

Coordinator: **Dr. Antonio Zorzano**

Associated groups: **10**

Lead researcher	Institution	Region
Balsinde Rodriguez, Jesús	Consejo Superior de Investigaciones Científicas	Castilla y León
Escobar Morreale, Héctor Francisco	Servicio Madrileño de Salud	Madrid
Ferrer Marrades, Jorge	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Cataluña
Gómez Foix, Ana María	Universitat de Barcelona	Cataluña
Ibáñez Toda, Lourdes	Fundación para la Investigación y Docencia Sant Joan de Déu	Cataluña
Montanya Mias, Eduard	Fundación IDIBELL	Cataluña
Simó Canonge, Rafael	Fund. Instituto de Investigación Vall D'hebron	Cataluña
Vázquez Carrera, Manuel	Universitat de Barcelona	Cataluña
Vendrell Ortega, Joan J.	Fund. Institut d'Investigació Sanitària Pere Virgili	Cataluña
Zorzano Olarte, Antonio	Fundació Privada Institut de Recerca Biomèdica (IRB)	Cataluña

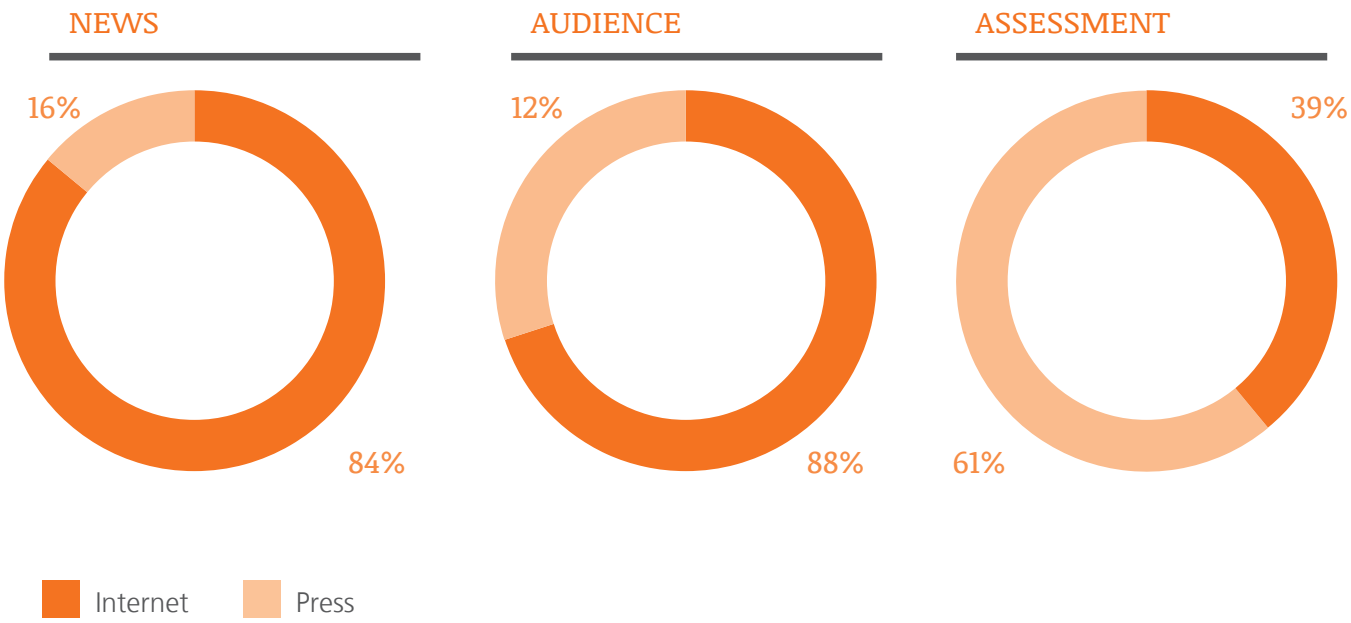
3. TRANSVERSAL PROGRAMMES



Communication results for this period:

CIBERDEM APPEARANCES IN THE MEDIA:

	News	Audience	Economic assessment*
INTERNET	133	8137600	128.281 €
PRESS	21	3462000	81.542 €
total	**154**	**11599600**	**209.823 €**



* Consists of the monetary value of each appearance in the media. Calculated according to the amount of space taken up by the news in the media according to advertising fee.

MOST OUTSTANDING APPEARANCES IN THE MEDIA:

Date	Headline / Subject addressed	Researcher mentioned	Nº of hits
10/06/2014	Los azúcares ocultos, los más perjudiciales para las personas con diabetes	Serafín Murillo	21
13/11/2014	Observan por primera vez una conexión entre hígado y apetito	Joan Guinovart	19
02/01/2014	El Instituto de Investigación Biomédica de Málaga participa en un estudio de investigación sobre la leche de cabra	Gemma Rojo	10
12/01/2014	Identifican mutaciones genéticas del páncreas asociadas a diabetes melitus 2	Lorenzo Pasquali	8
13/11/2014	Día de la Diabetes	Estudio Di@bet.es	8
27/06/2014	La terapia combinada precoz, clave en el control de la hiperglucemia	Luis Castaño	7
18/08/2014	El Gobierno reparte 9 millones entre un centenar de investigaciones de la región	Jesús Balsinde	7
11/11/2014	Buscan mecanismos comunes entre diabetes y enfermedades neurodegenerativas		5
09/04/2014	Identificada una posible diana para combatir la pérdida de masa muscular	Antonio Zorzano	4
03/11/2014	El biólogo-gastrónomo Jorge Cuéllar elaborará 8 tapas inspiradas en 8 proyectos de investigación del CIBER		4

Press clipping comprising all appearances in the press monthly can be consulted on the CIBER intranet.

SOCIAL MEDIA:

CIBERDEM has maintained its presence in Twitter (https://twitter.com/ciberdem) as seen in the following table:

	January 2014	December 2014
Updates	725	870
Followers	533	782
Klout (level of influence, values between 1 and 100)	42	42

CIBER NEWSLETTER:

Likewise, the CIBER news bulletin which includes content relating to CIBERDEM and the rest of the subject areas was started mid 2014. The bulletin is sent bimonthly through the *Mailchimp* platform to a total of 4,240 subscribers. Three CIBER bulletins were issued and distributed in 2014. **http://www.ciberisciii.es/comunicacion/boletines**

PARTICIPATION IN DISSEMINATION EVENTS

Semana de la Ciencia. Actividad: TapaConCiencia.

CIBERDEM participated in the "TapaConCiencia" dissemination activity during the Semana de la Ciencia of Madrid with 250 participants. Eight research projects corresponding to CIBER subject areas were disclosed in the activity. These research projects inspired Chef Jorge Cuellar to design 8 elaborate "tapas".

Researcher Mariona Balfegó represented CIBERDEM in this activity in which she explained her research in the Pilchardus Project "Is a sardine-rich diet beneficial for people with diabetes?" Her intervention was accompanied by a "tapa" consisting of sardines marinated in citric juice with pear ali-oli prepared by the chef.

The action raised great interest among the general public as well as among some mainstream media, scientific and gastronomic specialists who interviewed the researchers participating in the activity.

ACTUALIDAD

Auténtica divulgación científica

Un biólogo y ocho investigadores biomédicos se subieron al escenario de la mágica sala de columnas del Círculo de Bellas de Madrid el pasado 5 de noviembre. Su objetivo era muy ambicioso. Mientras los investigadores trataban de transmitir a un entregado público y en apenas 10 minutos en qué se basaban sus estudios, el biólogo explicaba y cocinaba en directo unas tapas con ingredientes vinculados a esas investigaciones. Cada dos ponencias, un equipo de cátering distribuía las citadas tapas entre las casi 300 personas que asistieron al evento. Detrás de esta valiente fórmula, TapaConCiencia, en donde no podían suceder más cosas a la vez, está el Centro de Investigación Biomédica en Red (CIBER) del Instituto de Salud Carlos III.

Jorge Cuéllar, investigador en biología y concursante del programa televisivo Masterchef que se hizo famoso por cocinar "chaperoninas", fue el encargado de dar forma a las ocho tapas inspiradas en los ocho proyectos de investigación que se presentaron en este evento, enmarcado en la Semana de la Ciencia que se celebró en Madrid a comienzos de noviembre.

Cuéllar y su equipo -Cristóbal, Miguel Ángel y Celia, algunos de sus compañeros del programa Masterchef- elaboraron las tapas al mismo tiempo que los científicos presentaban proyectos punteros de las ocho áreas temáticas del CIBER: salud mental, diabetes, nanomedicina, salud pública, enfermedades raras, respiratorias, hepáticas, obesidad y nutrición.

"Para favorecer la salud mental nada mejor que una tapa nutritiva y rica en ácidos grasos poli-insaturados (omega 3), magnesio, calcio, hierro y vitaminas tipo D o B12", comentaba Jorge mientras elaboraba un delicioso tartar de atún marinado con salsa coreana con base de aguacate, huevas de arenque y sésamo en donde todos esos componentes estaban presentes.

Los beneficios del aceite de oliva en forma de gazpachuelo

José López Miranda (CIBER de Fisiopatología de la Obesidad y la Nutrición, e IMIBIC) expuso los múltiples beneficios del consumo de aceite de oliva virgen enmarcado en un patrón de dieta mediterránea.

Propuesta gastronómica: Gazpachuelo virgen extra con moluscos, marisco y brotes marinos.

Sardinas marinadas para la diabetes

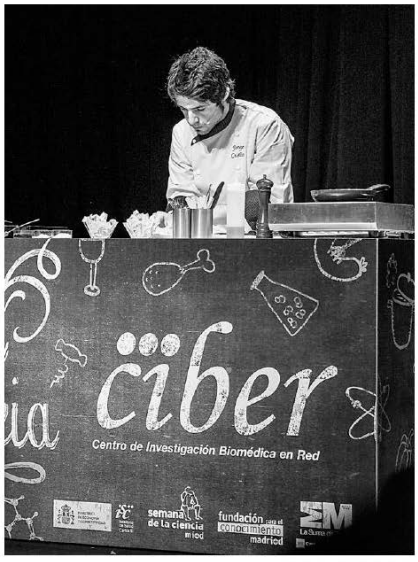
Mariona Balfegó (CIBER de Diabetes y Enfermedades Metabólicas Asociadas, e IDIBAPS) divulgó el Proyecto Pilchardus, que sugiere que una dieta rica en sardinas es beneficiosa para las personas con diabetes. Una parte fundamental de Pilchardus ha sido el desarrollo gastronómico de productos a base de sardinas, que fueran apetecibles y suavizaran su sabor fuerte.

Propuesta gastronómica: Sardinas marinadas en jugo de cítricos con alioli de pera.

La representación del exoma con hélices de plátano frito

Víctor Martínez González (CIBER de Enfermedades Raras y Hospital La Paz) presentó el CIBERER Exome Server, una base de datos con las variantes genéticas no patológicas más comunes en la población española, que será de gran utilidad en la investigación.

Propuesta gastronómica: Hélices de plátano frito rellenas de lubina y queso fresco.



Jorge Cuéllar preparó las propuestas

2013 ANNUAL REPORT

The CIBERDEM annual report was prepared in 2014. The reports are available on the web page in interactive format (Flipbook) and in pdf, both in English and Spanish.

http://ciberdem.org/memoria.php

http://www.ciberisciii.es/comunicacion/memorias-anuales;

CIBERDEM WEBSITE NEWS UPDATE

The CIBERDEM website was periodically updated to reflect the activity, publications and news of the centre **http://www.ciberdem.org**. Likewise, the most noteworthy news and events were included in the web page **www.ciberisciii.es** along with outstanding news and events from other CIBER subject areas.

4. PLATFORMS

CIBERDEM Biobank

http://www.ciberdem.org/biobanco.php

The objective of the CIBERDEM Biobank is to make well characterised and standardised biological samples of main metabolic disorders with a high added value available to the scientific community to promote, facilitate and develop biomedical research according to the laws in force.

The CIBERDEM Biobank consists of CIBERDEM groups in the following centres:

- Hospital Clínic de Barcelona: Dr. Ramon Gomis y Dra. Anna Novials
- Hospital Joan XXIII: Dr. Joan Vendrell
- Hospital Sant Joan de Reus: Dr. Masana
- Hospital Josep Trueta: Dr. Fernández-Real
- Hospital de Cruces: Dr. Luís Castaño
- Hospital Clínico de Madrid: Dr. Serrano-Ríos
- Hospital Clínico de Valencia: Dr. Carmena
- Hospital Carlos Haya de Málaga: Dr. C. Soriguer
- Hospital de la Santa Creu i Sant Pau: Dr. Blanco-Vaca

Donor information is stored in the BCGene computer platform. This application complies with the requirements of Organic Law on Personal Data Protection 15/1999 and will be accessible from all participating nodes to facilitate data entry by clinical teams.

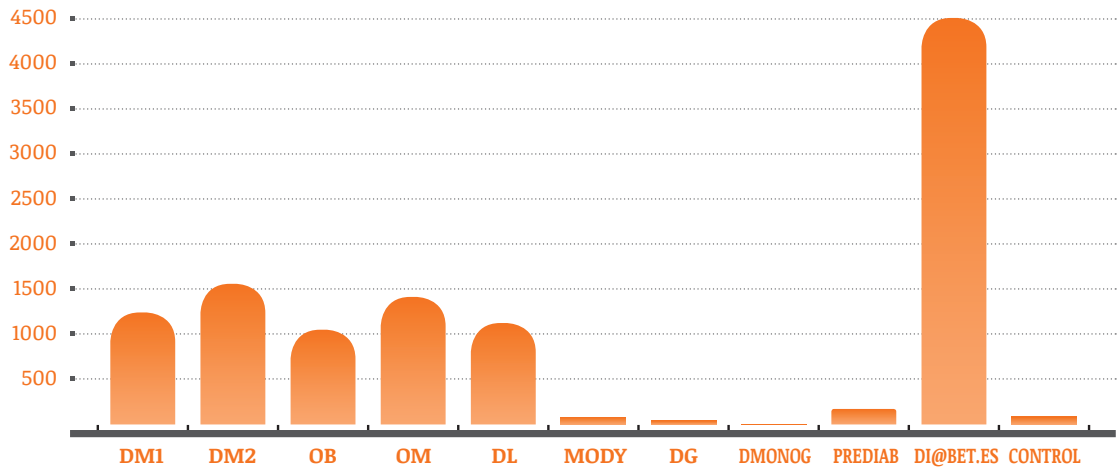
In 2014, collaboration with the Red de Grupos de Estudios de la Diabetes en Atención Primaria (GEDAPS) was continued for collecting samples associated with the PREDAPS study relating to prediabetic patient follow-up, the general objective being to determine the risk of diabetes and the risk of vascular complications in prediabetic patients and identify the factors associated with these risks. It is a prospective study in which the follow-up of a cohort of prediabetic subjects and another cohort of subjects without glucose metabolism alterations is to be performed for 10 years. Male and female patients visiting primary healthcare centres who are over 29 years old and less than 75 years old and sign the informed consent have started to be recruited for that purpose.

Collection of blood samples from patients recruited for the Project was started through collaboration with CIBERDEM in the last fiscal year in order to build a biorepository of serum, plasma and buffycoat samples representative of the population affected by prediabetes. In 2014, samples were again collected from patients included in the study which, due to the availability of clinical follow-up among donors, provides a high added value to the collection, as donor samples in different phases of the disease can be analysed.

Additionally in 2014, basic collection of the biobank has been continued, incorporating new samples of the main metabolic diseases.

The following tables show the summary of the samples stored in the Biobank facilities.

DONORS INCLUDED



In summary, a total of 522 samples were processed in 2014, generating a total of more than 4400 stored aliquots. Likewise, a total of 1008 stored aliquots were assigned in the mentioned period for scientifically and ethically approved research projects for CIBERDEM researchers.

Metabolomics Platforms

http://www.ciberdem.org/metabolomica.php

The Metabolomics Platform is a technological service platform created by the Universitat Rovira i Virgili (hereinafter URV) and the CIBERDEM by means of a collaboration agreement.

The main objective of the Metabolomics Platform is to work as an integrated laboratory, i.e., as a consultation point directly involved in metabolomics-related experiments proposed by the research groups. Our collaborations start with defining the objectives, dimension and characteristics of both the sample set and experiment designs. After that, the data is processed by our team and we are involved in the interpretation of results, delivering robust, relevant and useful clinical conclusions for the different research groups.

The equipment currently available in the field of NMR and LC/GC-MS allows large-scale measurements of body fluids (for example, serum or urine, as well as tissues or biopsies from humans and/or animal models).

The use of advanced statistics, chemometrics, multivariate algorithms allows transforming a large dataset into metabolic profiles, and ultimately into clinical information. Our goal is to introduce metabolomics as a complementary research tool both for clinical diagnostics and for clarifying unknown mechanisms associated with a specific disease.

The Metabolomics Platform particularly focuses on the needs of CIBERDEM and URV research groups. However, its services and potential scientific collaborations are available to other CIBER groups and biomedical research groups both in Spain and abroad.

Currently the Platform has full access to the following analytical platforms:

- Nuclear Magnetic Resonance (NMR)
- 600 MHz Bruker Avance III + cryoprobe + ScanJet.
- 500 MHz Bruker Avance III + HR-MAS probe.

Mass Spectrometry (MS):

- 1 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

Global Results:

Concept	2012	2013	2014
Number of collaborations with CIBERDEM groups	11	11	6
Published articles	10	6	7

Publications 2014

Gómez, J.; Brezmes, J.; Mallol, R.; Rodríguez, M.A.; Vinaixa, M.; Salek, R.M.;Correig, X.; Cañellas, N. Dolphin: a tool for automatic targeted metabolite profiling using 1D and 2D 1H-NMR data. Analytical and Bioanalytical Chemistry, 406 (30), pp. 7967-7976, 2014.

Saez, I.; Duran, J.; Sinadinos, C.; Beltran, A.; Yanes, O.; Tevy, MF; Martínez-Pons, C.; Milán, M.; Guinovart, JJ. Neurons have an active glycogen metabolism that contributes to tolerance to hypoxia. J Cereb Blood Flow Metab, 2014, Feb 26. doi: 10.1038/jcbfm.2014.33.

Brugnara, L.; Vinaixa, M.; Murillo, S.; Samino, S.; Rodriguez, M.A.; Beltran, A.; Lerin, C.; Davison, G.; Correig, X.; Novials, A. Metabolomics approach for analyzing the effects of exercise in subjects with type 1 diabetes mellitus (Note). Diabetes Technology & Therapeutics, 16-1, p. S95-S96, 2014.

Alonso, A.; Rodríguez, M.A.; Vinaixa, M.; Tortosa, R.; Correig, X.; Julià, A.; Marsal, S. Focus: A robust workflow for one-dimensional NMR spectral analysis. Analytical Chemistry, 86-2, p.1160-1169, 2014.

Hanzu, F. A.; Vinaixa, M.; Papageorgiou, A.; Parrizas, M.; Correig, X.; Delgado, S.; Carmona, F.; Samino, S.; Vidal, J.; Gomis, R. Obesity rather than regional fat depots marks the metabolomic pattern of adipose tissue: An untargeted metabolomic approach. Obesity, 22 (3), P. 698-704, 2014.

Malpique, R.; Figueiredo, H.; Esteban, Y.; Rebuffat, S.; Hanzu, F.; Vinaixa, M.; Yanes, O.; Correig, X.; Barceló-Batllori, S.; Gasa, R.; Kalko, S.G.; Gomis, R. . Integrative analysis reveals novel pathways mediating the interaction between adipose tissue and pancreatic islets in obesity in rats. Diabetologia, 57-6, p. 1219-1231, 2014.

Book chapters:

Beltran, A.; Samino, S.; Yanes, O. Sample Preparation Methods for LC-MS-Based Global Aqueous Metabolite Profiling. Daniel Raftery (ed.), 2014, Mass Spectrometry in Metabolomics: Methods and Protocols, Methods in Molecular Biology, vol. 1198. DOI 10.1007/978-1-4939-1258-2_5, © Springer Science+Business Media New York 2014.

5. PROJECTS

Estudio di@bet.es

CIBERDEM PROJECT

http://www.ciberdem.org/estudio_diabetes.php

CIBERDEM GROUPS: Dr. Gemma Rojo, Dr. Rafael Carmena, Dr. Joan Vendrell, Dr. Luis Castaño, Dr. Manuel Serrano Ríos and Dr. Ramon Gomis.

The di@bet.es study is a project organised and managed by CIBERDEM as one of its strategic activities. The field study and the phenotype library, serotype library and DNA library collection was developed in 2008-2011, more than 30 researches throughout Spain had contributed to its development.

It is the first study conducted in Spain with the aim of studying the epidemiology of type 2 diabetes in the entire national territory and has furthermore allowed knowing the prevalence of others risk factors associated with diabetes such as obesity, arterial hypertension, hyperlipidemias or metabolic syndrome. It has also allowed systematic collection of precise clinical, nutritional, sociological and sanitary habit information, in addition to a serotype library and DNA library deposited in the CIBERDEM Biobank and is available to the scientific community.

The first manuscript with the results of the main objectives was published in January 2012 (Diabetologia (2012) 55:88-93). Currently, 17 articles have been published based on the transverse study data in the listed journals and at least 6 others are in different editorial states. Derivative projects funded by AES 2011 are starting to yield results.

The di@bet.es study is a collaborative project in which many groups have provided their experience to study the variety of risk factors related to diabetes, making the results available to all other groups to facilitate the study and integration.

The study on the incidence of diabetes in Spain that will be carried out through a coordinated project funded by ISCIII (AES 2014) was designed in 2014:

- **Sub-Project 1 PI14/00710, PI: Gemma Rojo Martínez:** Incidence of type 2 diabetes in the di@bet.es study: the role of fatty acids and VEGFB-regulated transport system in the development of metabolic disorders.
- **Sub-Project 2 PI14/01104, PI: Luis Castaño González:** Incidence of type 2 diabetes in Spain (Northern Spain: Basque Country and Navarre). Prevalence of monogenic diabetes in Spain, characteristics and clinical diagnosis.
- **Sub-Project 3 PI14/00970, PI:** Elías Delgado Álvarez: Determination of epigenetic markers associated with the development of type 2 diabetes mellitus in the Spanish population
- **Sub-Project 4 PI14/00874, PI: Felipe Javier Chaves Martínez (Carmena Group):** Identification of sequence variations and methylation-hydroxymethylation in the exome associated with the development of type 2 diabetes.
- **Sub-Project 5 PI14/00465, PI:** Matilde Rodríguez Chacón (Vendrell Group): Identification and characterisation of sTWEAK-regulated microRNas in the adipocyte and the role thereof in insulin resistance-associated inflammatory response. Analysis of its usefulness as biomarkers in the Pizarra and di@bet.es studies.

The di@bet.es study also intervenes in the integrated Project **PIE14/00031** whose CIBER coordinator is JM Mato: Understanding obesity (Ob), metabolic syndrome (MetS), type 2 diabetes (T2DM) and fatty liver disease (FL): a multidisciplinary approach. Three CIBERDEM groups participating in this project **(G Rojo, R Carmena and R Gomís**).

Publications 2014

Amor AJ, Masana L, Soriguer F, Goday A, Calle-Pascual A, Gaztambide S, Rojo-Martínez G, Valdés S, Gomis R, Ortega E; on behalf of Di@bet.es study group.

Estimating Cardiovascular Risk in Spain by the European Guidelines on Cardiovascular Disease Prevention in Clinical Practice. Rev Esp Cardiol (Engl Ed). 2014 Nov 18. pii: S1885-5857(14)00360-0. doi: 10.1016/j.rec.2014.05.023. [Epub ahead of print] PubMed PMID: 25444376.

Valdés S, Maldonado-Araque C, García-Torres F, Goday A, Bosch-Comas A, Bordiú 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 M, Menéndez E, Mora-Peces I, Ortega E, Pascual-Manich G, Serrano-Rios M, Urrutia I, Vázquez JA, Vendrell J, Soriguer F, Rojo-Martínez G.

Ambient temperature and prevalence of obesity in the Spanish population: The Di@bet.es study. Obesity (Silver Spring). 2014 Nov;22(11):2328-32. doi: 10.1002/oby.20866. Epub 2014 Aug 13. PubMed PMID: 25124468.

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

Variable patterns of obesity and cardiometabolic phenotypes and their association with lifestyle factors in the Di@bet.es study. Nutr Metab Cardiovasc Dis. 2014 Sep;24(9):947-55. doi: 10.1016/j.numecd.2014.04.019. Epub 2014 Jun 9. PubMed PMID: 24984822.

Rojo-Martínez G, Maymó-Masip E, Rodríguez MM, Solano E, Goday A, Soriguer F, Valdés S, Chaves FJ, Delgado E, Colomo N, Hernández P, Vendrell J, Chacón MR.

Serum sCD163 levels are associated with type 2 diabetes mellitus and are influenced by coffee and wine consumption: results of the Di@bet.es study. PLoS One. 2014 Jun 30;9(6):e101250. doi: 10.1371/journal.pone.0101250. eCollection 2014. PubMed PMID: 24978196; PubMed Central PMCID: PMC4076325.

Valdés S, García-Torres F, Maldonado-Araque C, Goday A, Calle-Pascual A, Soriguer F, Castaño L, Catalá M, Gomis R, Rojo-Martínez G; Di@bet.es study group.

Prevalence of obesity, diabetes and other cardiovascular risk factors in Andalusia (southern Spain). Comparison with national prevalence data. The Di@bet.es study. Rev Esp Cardiol (Engl Ed). 2014 Jun;67(6):442-8. doi: 10.1016/j.rec.2013.09.029. Epub 2014 Feb 26. PubMed PMID: 24863592.

Soriguer F, Colomo N, Valdés S, Goday A, Rubio-Martín E, Esteva I, Castaño L, Ruiz de Adana MS, Morcillo S, Calle A, García-Fuentes E, Catalá M, Gutiérrez-Repiso C, Delgado E, Gomis R, Ortega E, Rojo-Martínez G. Modifications of the homeostasis model assessment of insulin resistance index with age. Acta Diabetol. 2014 Dec;51(6):917-25. doi: 10.1007/s00592-013-0523-5. Epub 2014 Apr 1. PubMed PMID: 24687694.

Martinez-Hervas S, Carmena R, Ascaso JF, Real JT, Masana L, Catalá M, Vendrell J, Vázquez JA, Valdés S, Urrutia I, Soriguer F, Serrano-Rios M, Rojo-Martínez G, Pascual-Manich G, Ortega E, Mora-Peces I, Menéndez E, Martínez-Larrad MT, López-Alba A, Gomis R, Goday A, Girbés J, Gaztambide S, Franch J, Delgado E, Castell C, Castaño L, Casamitjana R, Calle-Pascual A, Bordiú E. Prevalence of plasma lipid abnormalities and its association with glucose metabolism in Spain: the di@bet.es study. Clin Investig Arterioscler. 2014 May-Jun;26(3):107-14. doi: 10.1016/j.arteri.2013.12.001. Epub 2014 Jan 23. PubMed PMID: 24461346.

Pilchardus Study

PROJECT CIBERDEM

Status: Development

PILCHARDUS is a clinical research project that aims to test the hypothesis that a sardine-rich diet can improve metabolic control in patients with type 2 diabetes mellitus.

CIBERDEM is the driving force behind this multicenter study with the participation of Hospital Clínic de Barcelona as the coordinator and Hospital de la Vall d'Hebrón de Barcelona and Hospital Carlos Haya de Málaga as associated centres.

GROUPS INVOLVED: R. Gomis (coordinator), R. Simó, F. Soriguer, A. Novials and X. Correig (Metabolomics Platform).

The objectives of the study are to evaluate the effects of a sardine-rich diet on blood glucose control, inflammation markers, blood pressure, lipid metabolism and intestinal microbiota in patients with recently diagnosed type 2 diabetes or patients not undergoing pharmacological treatment.

Sixty-two patients will be included in the study. They will be randomly divided into two groups: the intervention group (sardine diet) and the control group (normal diet). The diet consists of replacing part of the daily protein intake with 100 g of sardines, 5 times a week for 6 months. Canned sardines or sardines processed in other ways are supplied. The Galician fish-canning company, Cerqueira, collaborated by providing all the canned sardines required for the study free of charge, and the food research centre, Fundación Alícia, led by Chef Ferran Adrià, designed sardine-based products to provide patients with a wide gastronomic variety of sardine-based meals and to prevent monotonous diets.

Medigene Study

EUROPEAN PROJECT

Status: Development

Website: http://www.medigene-fp7.eu/

The MEDIGENE Study is a study on the genetic and environmental factors influencing insulin resistance syndrome in Mediterranean immigrant populations. It is a 4-year collaborative project between CIBERDEM and other European institutions. It is subsidized by the European Commission under its FP7-Health-2011-two-stage framework programme with project number 279171 and coordinated by Dr. Florin Grigorescu of the Universitè Montpellier I, France.

The project began in the year 2012 and will be concluded at the end of 2015. The total budget for the 4-year project is 371,644.00€ distributed as follows:

	EU (75%)	CIBERDEM (25%)	PROJECT TOTAL
STAFF	78.386,25 €	26.128,75 €	104.515,00 €
DIRECT COSTS	95.821,87 €	31.940,62 €	127.762,50 €
INDIRECT COSTS	104.524,87 €	34.841,62 €	139.366,50 €
TOTAL	278.733,00 €	92.911,00 €	371.644,00 €

Cost distribution

The principal investigator of the project in CIBERDEM is Dr. Ramon Gomis, and his group is involved in several work packages and has several deliverables throughout its participation. There will be a very significant contribution in the project by the CIBERDEM Biobank and by other groups of the consortium such as the group of Dr. Luis Castaño.

In 2014, work has begun on WP5 "Epidemiological studies in immigrant population in host countries and obtaining new DNA samples" and work continued to be done on WP2 "Ancient DNA Studies in Tarragona" of the project.

The work on WP5 consisted of contacting different healthcare centres to identify the different immigrant communities from Morocco, Tunisia and Romania which can participate in the study. A team formed by a dietician (Mariona Balfegó) and an endocrinologist (Gloria Aranda) was sent for carrying out medical visit and nutritional survey so that they can then extract blood samples and thus obtain the DNA which has been processed by CIBERDEM researchers (Hugo Alves and Laura Brugnara). In 2014, about 140 samples were obtained and the study is expected to be continued in 2015.

The work of CIBERDEM on WP2 had continued to a lesser extent in 2014 and consisted of determining the genetics of ancient Roman populations in Tarragona and comparing it to modern populations of Catalonia and Italy as evidence of historical migrations and determining the prevalence of allelic variants. Various archaeological remains, primarily teeth, have been identified in collaboration with the Institut Català d'Arqueologia Clàssica (ICAC) of Tarragona, for obtaining ancient DNA samples. The extraction and amplification of DNA from dental samples have concluded in 2014.

DIATRAIN Project

The DIAbetes Trans-national Research Advancement for INvestigators (DIATRAIN) is an institutional mobility programme promoted by CIBERDEM since 2011

It is included under the FP7-People Co-funding of Regional, National and International Programme (FP7-People-2010-COFUND) of the European Commission. The objective of DIATRAIN is to provide outstanding experienced researchers with unique career development opportunities.

The DIATRAIN consists of two mobility programmes, the external Outgoing Mobility Programme (COMP) and the internal Incoming Mobility Programme (CIMP). Both programmes offer postdoctoral fellowships aimed at promoting the mobility of experienced researchers from and to CIBERDEM consortium research institutions.

International researchers will be able to approach any of the available research CIBERDEM groups through the CIMP mobility programme, while the COMP mobility programme will be used by CIBERDEM staff members to develop their research careers abroad.

The following has been granted throughout the DIATRAIN programme:

- 2-year CIMP aid was granted for the following researchers:
  Anthony Beucher (Group – Jorge Ferrer)
  Itzorzte Santin (Group – Luis Castaño)
  Alicia García (Group – Ramon Gomis)
  Miriam Ojeda (Group – Héctor Escobar)
- 12-month COMP aid was granted for the following researchers:
  Águeda González (IMS Cambridge)
  Sandra Rebufat (CPID Montpellier)
  Rebeca Fernández (Oxford)
  Marta Montori (IGMM Montpellier)
  Luke Noon (Mount Sinai NY)
  Clara Meana (Columbia University)
  Elena González (University of Pennsylvania)
  Francesc Xavier Duran (Università di Padova)

Website: http://diatrain.ciberdem.org

Joint Programming Initiative – HDHL

CIBERDEM participates in the Joint Programming Initiative Healthy Diet Healthy Life (HDHL) of the European Commission. The objective of this JPI is to bring together different researchers from different European countries to share their vision and create a common strategy concerning social challenges in the field of nutrition, food and health, which would be very difficult for these countries to deal with alone.

CIBERDEM participates in the JPI through two actions: DEDIPAC (Determinants of Diet and Physical Activity) and ENPADASI (European Nutritional Phenotype Assessment and Data Sharing Initiative). Several CIBERDEM groups collaborate in the European consortiums on healthy diet and health.

http://www.healthydietforhealthylife.eu

6. RESEARCH GROUPS

Endocrinology and metabolism

Programme: P1

Lead Researcher: Álvarez Escolá, Carmen

Group members

STAFF MEMBERS: Fernández Millán, Elisa

ASSOCIATED MEMBERS: Escrivá Pons, Fernando | Lizarraga Mollinedo, Esther | Martín Arribas, Mª Ángeles

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:

- The effect of nutrients on the growth, death and function of pancreatic alfa and beta cells: involvement of different growth factors.
- 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.
- Involvement of autophagy in the ineffective macromolecule turnover in IUGR individuals, which favors insulin resistance development.
- Changes in insulin/glucagon plasma levels and liver sensitivity associated with early undernutrition which could alter the available substrates for the growing brain.
- Impact of early undernutrition on the insulin and leptin hypothalamic responses and the hypothalamic expression of orexigenic and anorexigenic factors (NPY, POMC).
- The effect of early undernutrition followed by an overcaloric diet on the obesity risk and the white adipose tissue metabolism.
- Study of the ectopic lipid deposits in the skeletal muscle and liver consequence of nutritional rehabilitation.

Most relevant scientific articles

- Fernández-Millán E., Ramos S., Álvarez C., Bravo L., Goya L., Martín M.T. Microbial phenolic metabolites improve glucose-stimulated insulin secretion and protect pancreatic beta cells against tert-butyl hydroperoxide-induced toxicity via ERKs and PKC pathways. Food and Chemical Toxicology. 2014;66:245-253.
- Martín M.A., Fernández-Millán E., Ramos S., Bravo L., Goya L. Cocoa flavonoid epicatechin protects pancreatic beta cell viability and function against oxidative stress. Molecular Nutrition and Food Research. 2014;58(3):447-456.
- De Toro-Martín J., Fernández-Millán E., Lizarraga-Mollinedo E., López-Oliva E., Serradas P., Escrivá F. et al. Predominant role of GIP in the development of a metabolic syndrome-like phenotype in female wistar rats submitted to forced catch-up growth. Endocrinology. 2014;155(10):3769-3780.
- Mobasher M.A., De Toro-Martín J., González-Rodríguez A., Ramos S., Letzig L.G., James L.P. et al. Essential role of protein-tyrosine phosphatase 1B in the modulation of insulin signaling by acetaminophen in hepatocytes. Journal of Biological Chemistry. 2014;289(42):29406-29419.

Highlights

FUNDING

- Molecular and cellular mechanisms involved in T2DM and obesity pathogenesis in rats submitted to maternal undernutrition and refed a high fat diet after weaning. MINECO. Ref.BFU 2011-25420. IP: Carmen Álvarez Escolá. (2012-2015).
- Study of the mechanisms of insulin resistanceimplication in obesity, diabetes and metabolic syndrome. (MOIR). CAM. Ref.P2010/BMD-2423 Programs I+D Biomedicina/2010. Coordinator Manuel Ros Pérez. URJC. Group Enmeper: IP: Fernando Escrivá Pons.(2012-2015)

CONGRESS

- De Toro-Martín J, Fernández-Millán E, Lizárraga-Mollinedo E, Escrivá F, Álvarez C. Alpha-cell functionality shows gender-specific adaptations face to a nutritional insult in Wistar rats. Oral Presentation. 50th EASD Annual Meeting. Vienna 15 – 19 September 2014. Diabetologia 57, S65.
- Fernández-Millán E, de Toro-Martín J, Lizárraga-Mollinedo E, Escrivá F, Álvarez C. Defective autophagy results in reduced glycogen breakdown in the liver of IUGR newborn Wistar rats. Consequences for glucose homeostasis. Oral Presentation. 50th EASD Annual Meeting. Vienna 15 – 19 September 2014. Diabetologia. 57, S107.
- Lizárraga-Mollinedo E, de Toro-Martín J, Fernández-Millán E, García-San Frutos M, Fernández Agulló T, Ros M, Álvarez C, Escrivá F. Early undernutrition worsens the metabolic effects of high-lipid diets. Poster presentation. 50th EASD Annual Meeting. Vienna 15 – 19 September 2014. Diabetologia. 57, S299.

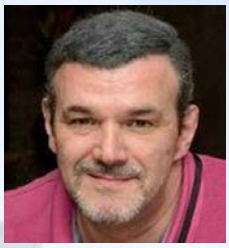
THESIS

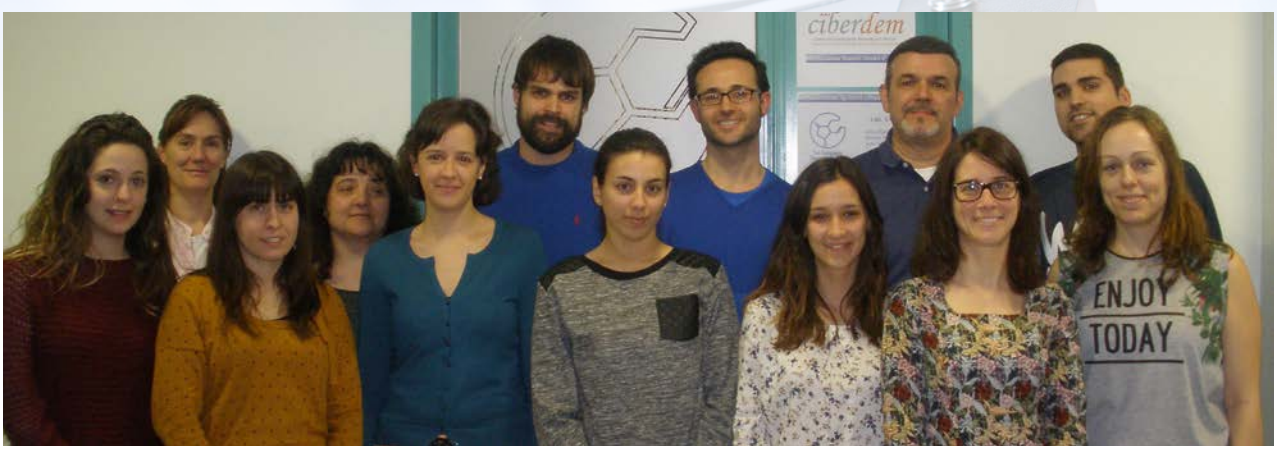
- Author:Esther Lizárraga Mollinedo. Director:Fernando Escrivá Pons. · Title: Effects of early undernutrition on the hepatic and cortical insulin sensitivity of suckling rats and metabolic consequences of nutritional rehabilitation in the adult age. · Sobresaliente cum Laude · University Complutense of Madrid · Date: 27/06/2014
- European Doctoral Thesis: Author:Juan de Toro Martín · Directors: Carmen Álvarez Escolá y Elisa Fernández Millán · Title: Nutritional programming of the metabolic síndrome in a model of early undernutrition and later refeeding with a high-fat diet in Wistar rats · Sobresaliente cum Laude. · University Complutense of Madrid · Date: 15/12/2014

Institution: Universidad Complutense de Madrid
Contact: Facultad de Farmacia. Ciudad Universitaria, S/N. 28040 Madrid.
Phone: (+34) 91 394 18 57 · E.mail: calvarez@farm.ucm.es · Website: http://www.ucm.es/biomol2

The Eicosanoid Research Division

Programme: P4





Lead Researcher: Balsinde Rodríguez, Jesús

Group members

STAFF MEMBERS: Meana González, Clara | Rubio Aranda, Julio Miguel.

ASSOCIATED MEMBERS: Astudillo del Valle, Alma | Balboa, Mª Ángeles | Duque de Cela, Montserrat | Gil de Gómez Sesma, Luis | Guijas Mate, Carlos | Lorden Losada, Gema | Montero Domínguez, Olimpio | Peña Moreno, Mª Lucía

Main lines of research

Lipids are key to signaling events in cells. Hence, they are the ultimate controllers and regulators of our bodily processes. Further, imbalances in lipids are the hallmark of a large number of illnesses. If we are going to cure these diseases, we must know what the lipids are and what they do. Within this context our current research lines can be defined as follows:

- Cellular regulation of phospholipase A2s and lipins as key regulators of the production of arachidonate-derived eicosanoids, substances which can have pro- or and anti-inflammatory activity. There are multiple phospholipase A2s and lipins in the cells and our goal is to delineate the role that each of these forms plays in the production of eicosanoids in obesity, diabetes and cardiovascular disease.
- Biosynthesis and degradation of lipid droplets during cellular activation. Lipid droplets are the cytoplasmic organelles where monocytes/macrophages store fat, yet they also serve many other interesting roles, e.g. they may function as docking platforms for a number of enzymes involved in lipid signaling or as an intracellular site for the synthesis of lipid mediators.
- Application of mass spectrometry-based lipidomic strategies for the identification and quantification of cellular lipidomes. A major goal in this regard is to determine the origin and identity of the individual phospholipid molecular species that are produced under different conditions, as a key step to address their biological roles in cells.
- Role of omega-3 fatty acid derivatives as deactivators of monocyte/macrophage activation via their antagonistic effects on inflammasome activation or other mechanisms of pathophysiological relevance.

.

Most relevant scientific articles

- Gil-De-Gómez L., Astudillo A.M., Guijas C., Magrioti V., Kokotos G., Balboa M.A. et al. Cytosolic group IVA and calcium-independent group VIA phospholipase A2s act on distinct phospholipid pools in zymosan-stimulated mouse peritoneal macrophages. Journal of Immunology. 2014;192(2):752-762.
- Castano D., Larequi E., Belza I., Astudillo A.M., Martínez-Anso E., Balsinde J. et al. Cardiotrophin-1 eliminates hepatic steatosis in obese mice by mechanisms involving AMPK activation. Journal of Hepatology. 2014;60(5):1017-1025.
- Fucho R., Martínez L., Baulies A., Torres S., Tarrats N., Fernández A. et al. ASMase regulates autophagy and lysosomal membrane permeabilization and its inhibition prevents early stage non-alcoholic steatohepatitis. Journal of Hepatology. 2014.
- Meana C., Pena L., Lorden G., Esquinas E., Guijas C., Valdearcos M. et al. Lipin-1 integrates lipid synthesis with proinflammatory responses during TLR activation in macrophages. Journal of Immunology. 2014;193(9):4614-4622.
- Guijas C., Rodríguez J.P., Rubio J.M., Balboa M.A., Balsinde J. Phospholipase A2 regulation of lipid droplet formation. Biochimica et Biophysica Acta - Molecular and Cell Biology of Lipids. 2014;1841(12):1661-1671.

Highlights

ACTIVE RESEARCH GRANTS IN 2014

• "Lipid Pathways Regulating the Inflammasome: Role of Omega-3 Fatty Acids and Lipin-2". Ministry of Economy and Competitiveness (SAF2013-48201-R). • "Mechanisms Governing Arachidonic Acid Availability in Human Macrophages". Regional Government of Castile & Leon, Education Department (CSI007U13). • "Lipin-1 Involvement in Intestinal Inflammation". Regional Government of Castile & Leon, Health Department (BIO/VA/03-14).

MOST RELEVANT RESULTS

• Demonstration that different phospholipase A2s expressed in the same cell act on different substrates. This may lead to different pro - and anti-inflammatory signals. We have detected subtle variations of specificity that might be useful for the design of selective inhibitors with possible therapeutic potential. • Demonstration that lipin-1 is involved in pro-inflammatory macrophage activation through its regulatory effects on lipid metabolism.

TRAINING

• Doctoral thesis: "Role of Cytosolic of Group IVA phospholipase A2 in adipocyte differentiation and in the development of obesity induced by a rich-fat diet"; Doctoral candiate, Lucía Peña Moreno. University of Valladolid.

OTHER ACTIVITIES

• One of our CIBERDEM contracted scientists, Dr. Clara Meana, spent 10 months in the laboratory of Prof. Ira Goldstein (New York University) with a fellowship from the COMP-DIATRAIN program.

The group IP, Prof. J. Balsinde, was distinguished by the Argentine Society for Biochemistry and Molecular Biology (SAIB) with the Alberto Sols Award Lecture, delivered during the 50 Congress SAIB in Rosario, Argentina. He also served as "Fakultetsopponent" for the PhD Thesis Evaluation Committee of the Norwegian University of Science and Technology (Trondheim, Norway). Finally, he continues to serve in the Editorial Boards of Journal of Lipid Research and Biochimica et Biophysica Acta - Molecular and Cell Biology of Lipids.

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Diabetes and Cardiovascular

Programme: P2

Lead Researcher: Benito de las Heras, Manuel R.

Group members

STAFF MEMBERS: Fernández López, Silvia | García Gómez, Gema | González Trujillos, Elena

ASSOCIATED MEMBERS: Bartolomé Herráinz, Alberto | Escribano Illanes, Óscar | Gómez Hernández, Almudena | Guillén Viejo, Carlos | Pedromo Loaiza, Liliana | Viana Huete, Vanesa

Main lines of research

- **Compensatory mechanisms to hepatic insulin resistance: Progression to type 2 diabetes.**

  The role of the liver-pancreas endocrine axis in triggering beta-cell hyperplasia.

  The role of autophagy, mitophagy and ER stress in the regulation of beta-cell pancreatic mass and beta-cell failure.

- **Adipose organ inflammatory disease and the cardiovascular damage.**

  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.

- **Brown fat function/dysfunction and adipose organ inflammatory disease.**

  New mouse models to study energy imbalance and body weight regulation: Brown adipose tissue-specific knockout of IGFIR and IGFIR/IR DKO.

  New mouse models of browning: Brown adipose tissue-specific knockout of p85 alpha/PI 3 kinase.

- **Molecular mechanisms of insulin resistance:**

  The role of IR isoforms in cardiomyocytes, endothelial and aortic vascular smooth muscle cells.

Most relevant scientific articles

- Gómez-Hernández A., Perdomo L., de las Heras N., Beneit N., Escribano T., Otero Y.F. et al. Antagonistic effect of TNF-alpha and insulin on uncoupling protein 2 (UCP-2) expression and vascular damage. Cardiovascular Diabetology. 2014;13(1).
- García-Guerra L., Vila-Bedmar R., Carrasco-Rando M., Cruces-Sande M., Martín M., Ruiz-Gómez A. et al. Skeletal muscle myogenesis is regulated by G protein-coupled receptor kinase 2. Journal of Molecular Cell Biology. 2014;6(4):299-311.
- Bartolomé A., Guillén C. Role of the mammalian target of rapamycin (mTOR) complexes in pancreatic β-cell mass regulation. Vitamins and Hormones. 2014;95:425-469.
- Bartolomé A., Kimura-Koyanagi M., Asahara S.-I., Guillen C., Inoue H., Teruyama K. et al. Pancreatic b-Cell failure mediated by mTORC1 hyperactivity and autophagic impairment. Diabetes. 2014;63(9):2996-3008.

Highlights

The reconstitution of iLIRKO with IRA isoform by means of adenoviral transfection, but not with isoform IRB, reverts hepatic insulin resistance, glucose intolerance and plasma hyperinsulinemia. More importantly, pancreatic beta cell hyperplasia is being retracted. In pancreatic beta cells, we have demonstrated that the Nicotanimide induces acetylation of TSC2, mTORC1 signaling pathway and cell proliferation, autophagy being downregulated. Resveratrol deacetylates TSC2, this effect being mediated by Sirt-1, inhibits mTORC1 and cell proliferation and upregulated autophagy. Thus, acetylation/deacetylation status of TSC2 mediated by Sirt-1 constitutes a novel molecular mechanism that regulates autophagy and apoptosis. Regarding the association between vascular insulin resistance and damage, we have demonstrated the protective role of oleic acid, but not palmitate, on the insulin resistance, activation of the proinflammatory pathway NF-Kb and cell proliferation in aortic SMVCs induced by TNF-alpha. Regarding the role of the energy balance on the adipose organ inflammatory disease, we have generated and developed a new IGFIR brown adipose tissue specific knockout, BATIGFIRKO. KO mice lose 25 % of UCP1 expression at 12 months. However, interscapular brown adipose tissue develops normally as compared with their controls, which might be explained by the overexpression of the insulin and BMP-7 protein machinery observed in the KO mice. More importantly, brown adipose tissue thermogenic function as estimated by cold acclimation was partially impaired. The expression of UCPs in insulin target tissues shows a differential profile. Thus, whereas the expression of UCP2 was increased in the liver or UCP-3 in the heart, the expression of UCP3 in the skeletal muscle was diminished. In the same way, the insulin signaling in vivo was also differentially affected. Thus, insulin signaling remained unchanged in inguinal and epididymal adipose tissue, and also in the heart and skeletal muscle. However, the insulin signaling in the liver was severely impaired associated to lipid accumulation in the liver in the KO mice. Overall, KO mice showed a manifest insulin resistance versus controls.

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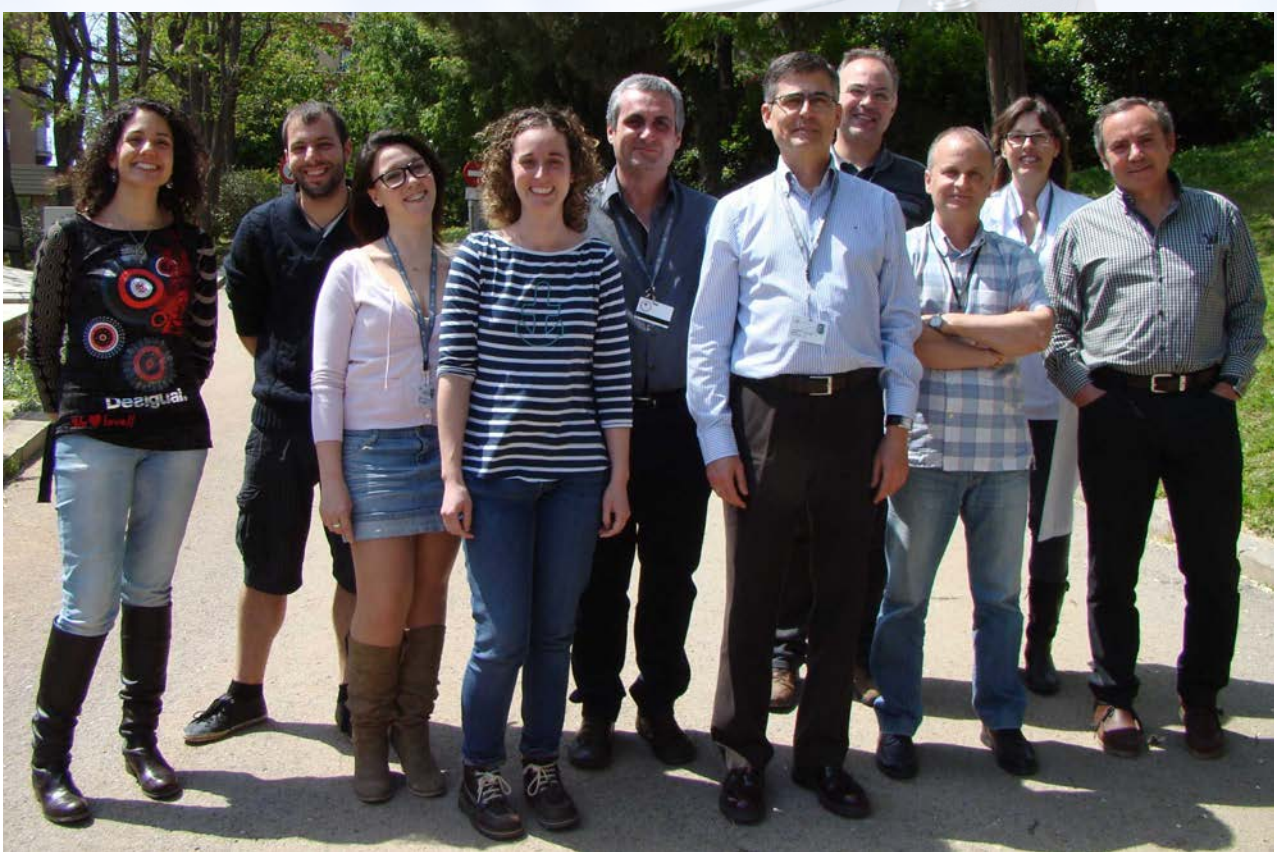
Metabolic disease and cardiovascular risk

Programme: P2



Lead Researcher: Blanco Vaca, Francisco

Group members

STAFF MEMBERS: Cedó Giné, Lidia | Santos Palacios, David

ASSOCIATED MEMBERS: Escolé Gil, Juan Carlos | Julve Gil, Josep | Laura Errico, Teresa | Martín, Jesús | Pérez Pérez, Antonio | Quesada Vázquez, Helena | Roig Martínez, Rosa | Rotllan Vila, Noemí

Main lines of research

- Hypertriglyceridemia and low HDL (Atherogenic dyslipidemia): modulation by diet and drugs and role in 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).

Most relevant scientific articles

- Julve J., Pardina E., Pérez-Cuéllar M., Ferrer R., Rossell J., Baena-Fustegueras J.A. et al. Bariatric surgery in morbidly obese patients improves the atherogenic qualitative properties of the plasma lipoproteins. Atherosclerosis. 2014;234(1):200-205.
- Martín-Campos J.M., Julve J., Roig R., Martínez S., Errico T.L., Martínez-Couselo S. et al. Molecular analysis of chylomicronemia in a clinical laboratory setting: Diagnosis of 13 cases of lipoprotein lipase deficiency. Clinica Chimica Acta. 2014;429:61-68.
- Amezaga N., Sanjurjo L., Julve J., Aran G., Pérez-Cabezas B., Bastos-Amador P. et al. Human scavenger protein AIM increases foam cell formation and CD36-mediated oxLDL uptake. Journal of Leukocyte Biology. 2014;95(3):509-520.
- Escolá-Gil J.C., Cedó L., Blanco-Vaca F. High-density lipoprotein cholesterol targeting for novel drug discovery: Where have we gone wrong? Expert Opinion on Drug Discovery. 2014;9(2):119-124.
- Vinagre I., Sánchez-Quesada J.L., Sánchez-Hernández J., Santos D., Ordónez-Llanos J., De Leiva A. et al. Inflammatory biomarkers in type 2 diabetic patients: Effect of glycemic control and impact of ldl subfraction phenotype. Cardiovascular Diabetology. 2014;13(1).

Highlights

Ten scientific papers were published by the group in 2014.

In January of 2014, Josep Julve left its postdoctoral position in CIBERDEM to become a Miguel Servet researcher, funded by Instituto de Salud Carlos III. This position was filled by Dr. Lídia Cedó.

Dr. Antonio Pérez was the supervisor of the thesis "Biomarkers of inflammation in type 2 diabetes. Effect of glucemic control and LDL phenotype" presented by Irene Vinagre in the Autonomous University of Barcelona. Dr Antonio Pérez participated in the clinical guide "Position of the Interdisciplinary Comitee on Cardiovascular Prevention and the Society of Cardiology in the dyslipidemia treatment. Divergences among the American and the European Guides" that was published in several Spanish journals.

Dr Francisco Blanco obtained new project funding from the Instituto de Salud Carlos III for the period 2015-2017. Karen Méndez Lara, a predoctoral fellow funded by the Generalitat of Catalonia, joined the group under the supervision of the PI of the group.

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Brain Glucose Sensor, Satiety Control, Insulin Resistance and Type 2 Diabetes

Programme: P1

Lead Researcher: Blázquez Fernández, Enrique

Group members

STAFF MEMBERS: Hurtado Carneiro, Verónica

ASSOCIATED MEMBERS: Álvarez Garcia, Elvira | Navas Hernández, María de los Ángeles | Roncero Rincón, Isabel | Ruiz Albusac, Juan Miguel | Sanz Miguel, Carmen | Velázquez Sánchez, Esther

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 and apoptosis 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.

Most relevant scientific articles

- Hurtado-Carneiro V., Roncero I., Egger S.S., Wenger R.H., Blázquez E., Sanz C. et al. PAS Kinase Is a Nutrient and Energy Sensor in Hypothalamic Areas Required for the Normal Function of AMPK and mTOR/S6K1. Molecular Neurobiology. 2014;50(2):314-326.

Highlights

During 2014 the following activities were carried out:

- Veronica Hurtado presented the Doctoral Thesis entitled: "Metabolic sensors in the brain. Intercommunication with the regulatory peptides of food intake". Directors: E. Alvarez and M. C. Sanz.
- Yannick Le Baud performed the Master Thesis Work in Human Nutrition and Applied Dietetics entitled: "Study of the molecular mechanisms involved in the effect of glucose on proliferation of cultured rat astrocytes. Effect of insulin and GLP-2. ". Tutors: J.M. Ruiz-Albusac and E. Velázquez.
- Pilar Dongil and Ana Pérez performed the Master Thesis Works in Research in Biomedical Sciences entitled: "Role of PASK in oxidative metabolism and mitochondrial function. Characterisation of regulators of mitochondrial biogenesis in control and deficient PASK MEFs" and "Effects of PASK on the proliferation and apoptosis processes, and on the control of the cell cycle in control and deficient MEFs PASK", respectively. Tutors: E. Alvarez and M. C. Sanz.

Likewise, we have initiated the study of interactions between diseases such as type 2 diabetes (T2DM) and Alzheimer's (AD), considered as the two major epidemics of the XXI century. By analyzing the resistance to insulin action, we want to know if this resistance is present in both disease entities and if such resistance is manifested centrally, peripherally or in both forms. In samples from different areas of healthy human brain used as control, from AD, AD + T2DM and T2DM of different ages, we study the insulin signal transduction pathway which is initiated by the phosphorylation of its own receptor, and rendering particular attention in the identification of phosphorylated residues of tyrosine and serine/threonine of the IRS-1 and of other mediators. Finally, in mice with overexpression of tau protein is studying the central and peripheral resistance to insulin.

This work was supported by a grant from the Mutua Madrileña Foundation.

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Transgenic Animal Models and Gene Therapy Approaches for Diabetes

Programme: P3

Lead Researcher: Bosch Tubert, Fàtima

Group members

STAFF MEMBERS: Casellas Comallonga, Alba

ASSOCIATED MEMBERS: Barrero Victorio, Jennifer | Carretero Romay, Ana | Elias Puigdomenech, Ivet | Ferre Masferrer, María del Tura | Franckhauser, Sylvie | García Martínez, Miguel | Haurigot, Virginia | Jiménez Cenzano, Verónica | Mallol Domínguez, Cristina | Melgarejo Bermúdez, Verònica | Molas Laplana, María | Moya Martínez, Marta | Muñoz Forero, Sergio Antonio | Nacher García, Víctor | Navarro Beltrán, Marcos | Otaegui Goya, Pedro José | Pujol Altarriba, Anna | Riu Pastor, Efrén | Roca Lecha, Carles | Ruberte Paris, Jesús | Villacampa Alcubierre, Pilar | Zaguirre Sánchez, Mireia

Main lines of research

- Study of causes and pathophysiological mechanisms of diabetes and obesity.
  - Study of the role of pancreatic ß cell alterations in the development of diabetes.
  - Identification of novel genes in adipose tissue involved in the development of diabetes and obesity.
  - Identification of novel mechanisms involved in browning of white adipose tissue.
- Development of new gene therapy approaches for diabetes.
  - Gene therapy approaches for the treatment of type 1 diabetes centered on genetic engineering of skeletal muscle to produce insulin and/or increase glucose uptake.
  - Gene therapy approaches for type 2 diabetes and obesity centered on genetic engineering of skeletal muscle and/or the liver.
  - Study of in vivo pancreas regeneration in diabetic animals:
    Regeneration of endocrine pancreas by IGF-1
    Betasel: in vivo selection of genes to improve beta cell mass
  - Development of new approaches for type 2 diabetes and obesity centered on genetic engineering of adipose tissue.

Most relevant scientific articles

- Morro M., Teichenne J., Jiménez V., Kratzer R., Marletta S., Maggioni L. et al. Pancreatic transduction by helper-dependent adenoviral vectors via intraductal delivery. Human Gene Therapy. 2014;25(9):824-836.
- Churlaud G., Jiménez V., Ruberte J., Amadoudji Zin M., Fourcade G., Gottrand G. et al. Sustained stimulation and expansion of Tregs by IL2 control autoimmunity without impairing immune responses to infection, vaccination and cancer. Clinical Immunology. 2014;151(2):114-126.
- Bogdanov P., Corraliza L., Villena J.A., Carvalho A.R., García-Arumi J., Ramos D. et al. The db/db mouse: A useful model for the study of diabetic retinal neurodegeneration. PLoS ONE. 2014;9(5).
- Mendes-Jorge L., Ramos D., Valenca A., López-Luppo M., Pires V.M.R., Catita J. et al. L-ferritin binding to Scara5: A new iron traffic pathway potentially implicated in retinopathy. PLoS ONE. 2014;9(9).

Highlights

In 2014 we have been participating in the project "Unravelling of novel factors capable of inducing browning of WAT in vivo" financed by the European Foundation for the Study of Diabetes (2013-2015). In addition, our group is participating in the EU, Programme "Capacities", "European infrastructure for phenotyping and archiving of model mammalian genomes (Infrafrontier-I3) (2013-2016)" with the aim to implement research infrastructure that provides capacities and open access for the systemic phenotyping, archiving and distribution of mouse models to the biomedical research community. In 2014, 2 new projects in which we are involved have been launched. One is the EU COST action "Development of a European network for preclinical testing of interventions in mouse models of age and age-related diseases (MouseAGE)". This COST Action, starting in 2014 and ending in 2018, aims to form a highly interactive and flexible European network, which will create a critical mass of scientists across disciplines, clinicians and industrial partners to reach consensus on ways to test preclinical interventions in aging mice. The other project is dedicated to "AAV-mediated gene therapy for the treatment of MPSIIID (Sanfilippo D)" financed by the Association Française contre les Myopathies (2014-2016).

In addition, our group has been involved in 6 new patents (1-Adenoassociated virus vectors for the treatment of lysosomal storage disorders. 2- Adeno-associated viral vectors useful in therapy, 3- Gene therapy compositions for use in the prevention and/or treatment of non-alcoholic fatty liver disease, 4- Vectors virals per al tractament de la diabetis: AAV8-IGF1, 5-Telomerase reverse transcriptase-based therapies, 6-Telomerase reverse transcriptase-based therapies for treatment of conditions associated with myocardial infarction).

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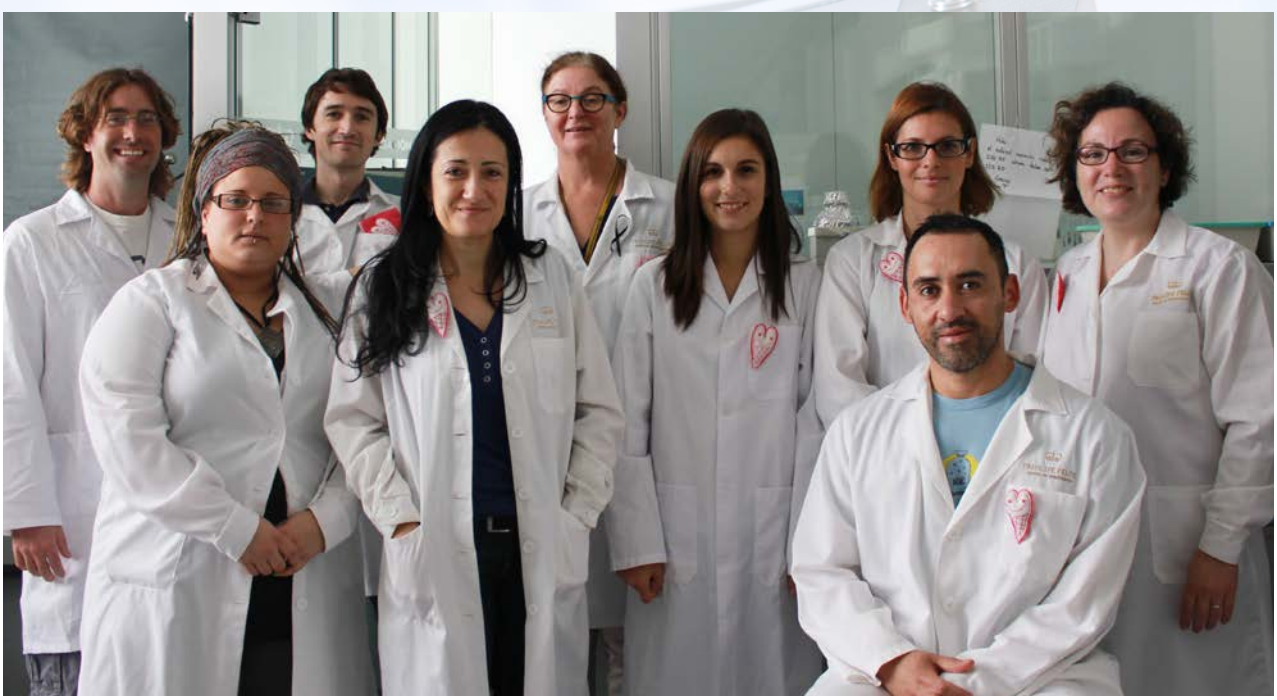
Laboratory of Molecular Endocrinology

Programme: P3



Lead Researcher: Burks, Deborah

Group members

STAFF MEMBERS: Acosta Umanzor, Carlos René | Noon, Luke

ASSOCIATED MEMBERS: González Navarro, Herminia | Leal Tassias, Aranzazu | Moreno Gimeno, Inmaculada | Sánchez Pérez, Ana María | Sanz González, Silvia María

Main lines of research

The incidence of diabetes and obesity is increasing at alarming rates throughout the world, creating a significant social and economic burden in industrialised countries. Defective expression or function of insulin signalling pathway components, such as the IRS (insulin receptor substrate) proteins, causes insulin resistance, which occurs with normal ageing but is also a hallmark of disease states such as diabetes. The overall aim of our research is to understand precisely how impaired insulin signalling contributes to metabolic diseases. Our research therefore focuses on several major themes:

- 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.

Most relevant scientific articles

- Oliveira J.M., Rebuffat S.A., Gasa R., Burks D.J., García A., Kalko S.G. et al. Tungstate promotes β-cell survival in Irs2-/- mice. American Journal of Physiology - Endocrinology and Metabolism. 2014;306(1).
- Martínez-Hervás S., Vinue A., Nunez L., Andrés-Blasco I., Piqueras L., Tomás Real J. et al. Insulin resistance aggravates atherosclerosis by reducing vascular smoothmuscle cell survival and increasing CX3CL1/CX3CR1 axis. Cardiovascular Research. 2014;103(2):324-336.

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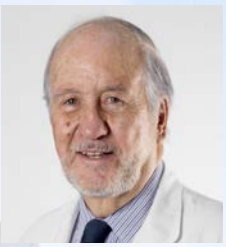
Dyslipidaemia, Inflammation and Endothelial Dysfunction

Programme: P1



Lead Researcher: Carmena Rodríguez, Rafael

Group members

STAFF MEMBERS: Benito Casado, Esther | García García, Ana Bárbara | Peiro Signes, Marta

ASSOCIATED MEMBERS: Ascaso Gimilio, Juan Francisco | Blesa Luján, Sebastián | Català Bauset, Miguel | Chaves Martínez, Felipe Javier | Martínez Hervás, Sergio | Real Collado, José Tomás

Main lines of research

- Study of genetic variations present in the exome related to development of type 2 diabetes and its consecuences.
- Study of insulin resistance and diabetes.
- Detection of genetic alterations (mutations or polymorphisms) involved in the development of complex diseases with high cardiovascular risk focused on genes related to the mitochondrial respiratory chain, oxidative stress, lipid metabolism and diabetes.
- Diagnosis, preventionand treatment of diabetic foot.
- Study of autosomal dominant hypercholesterolemias and familial combined hyperlipidemia.
- Effect of postprandial lipidemia on cardiovascular system, mainly on lipid profile, inflammatory markers and oxidative stress and the response of circulanting cells to stress caused by hyperlipidemia.
- Genetic factors involved in the regulation of Body Mass Index (BMI), waist circumference and obesity develpment.

Most relevant scientific articles

- Silvestre-Roig C., Fernández P., Mansego M.L., Van Tiel C.M., Viana R., Anselmi C.V. et al. Genetic variants in CCNB1 associated with differential gene transcription and risk of coronary in-stent restenosis. Circulation: Cardiovascular Genetics. 2014;7(1):59-70.
- Esmatjes E., Jansa M., Roca D., Pérez-Ferre N., Del Valle L., Martínez-Hervás S. et al. The efficiency of telemedicine to optimize metabolic control in patients with type 1 diabetes mellitus: Telemed study. Diabetes Technology and Therapeutics. 2014;16(7):435-441.
- Martínez-Hervás S., Vinue A., Nunez L., Andres-Blasco I., Piqueras L., Tomás Real J. et al. Insulin resistance aggravates atherosclerosis by reducing vascular smoothmuscle cell survival and increasing CX3CL1/CX3CR1 axis. Cardiovascular Research. 2014;103(2):324-336.
- Cortes R., Martínez-Hervás S., Ivorra C., De Marco G., González-Albert V., Rojo-Martínez G. et al. Enhanced reduction in oxidative stress and altered glutathione and thioredoxin system response to unsaturated fatty acid load in familial hypercholesterolemia. Clinical Biochemistry. 2014;47(18):291-297.
- Valdes S., Maldonado-Araque C., García-Torres F., Goday A., Bosch-Comas A., Bordiu E. et al. Ambient temperature and prevalence of obesity in the spanish population: The di@bet.es study. Obesity. 2014;22(11):2328-2332.

Highlights

The effects of insulin resistance (IR) on unstable atheromatous plaques were studied in a mouse model of IR-Metabolic Syndrome (MS) and in human subjects with and without IR-MS. The expression of main inflammatory mediators implicated in plaque vulnerability was measured. Results: IR promotes plaque vulnerability due to augmented inflammatory pathway expression.

We studied, in 14 patients with Familial Hypercholesterolemia (FH) and 20 controls, the response to an unsaturated oral fat load test (OFLT) analyzing the mRNA levels of genes involved in antioxidant systems. Results: An OFLT with predominantly unsaturated fat has a different effect on postprandial antioxidant enzymes mRNA levels in controls than in FH patients. Increased antioxidant enzymes mRNA does not reduce postprandial oxidative stress in FH. This could influence dietary patterns in FH.

The associations between ambient temperature and obesity in the Spanish population using an ecological focus was examined with data from the Di@bet.es study. The prevalence rates of obesity in different geographical areas, divided according to mean annual temperature quartiles, were 26.9% in quartile 1 (10.4-14.5°C) and 33.6% in quartile 4 (17.8-21.3°C) (P?=?0.003).

Diagnostic tools to assess restenosis risk after stent deployment are important in diabetic patients. The CCNB1 gene regulates cell proliferation, a key component of in-stent restenosis. Results: 3 SNP's in CCNB1 were associated with increased restenosis risk in 1000 patients (36.4% diabetics) undergoing coronary stent placement. These findings could provide diagnostic tools in risk stratification for restenosis.

Impact of an Internet-based telematic system on the management of patients with type 1 diabetes, >18 years old and with a HbA1c >8%. Intervention group (two visits and five telematic appointments) vs. control group (seven visits). Five different variables were studied. Results: interactive telematic appointments in subjects with type 1 diabetes and inadequate metabolic control is an efficient strategy, providing results comparable to those of face-to-face appointments.

Institution: Fundación para la Investigación del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)

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Hospital Universitario de Cruces
Endocrinology and Diabetes Research Group

Programme: P3

Lead Researcher: Castaño González, Luis

Group members

STAFF MEMBERS: Martínez Salazar, Rosa María | Santín Gómez, Izortze | Urrutia Echebarría, Inés María

ASSOCIATED MEMBERS: Aguayo Calcena, Anibal | Aniel Quiroga- Rodríguez, María Ángeles | Belar Beitia, Oihana | Bilbao Catalá, José Ramón | Castellanos Rubio, Ainara | Cortazar Galarza, Alicia | Gaztambide Saenz, Sonia | Gutiérrez Ziardegi, Galder | Ortiz Espejo, María | Pérez de Nanclares, Gustavo | Ramírez Domínguez, Miriam | Rica Etxebarria, Itxaso | Rivero, Sorkunde | Santamaría Sandi, Francisco Javier | Vázquez San Miguel, Federico | Vela, Amaia | Velayos Gainza, Teresa

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 enviromental factors and 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 (array-CGH approach), whole exome sequencing and next generation sequencing panels of candidate genes.
- 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.

Most relevant scientific articles

- Hirschler V., Maccallini G., Molinari C., Inés U., Castano L.A., Sánchez M. et al. Association between vitamin D and Apo B concentrations in Argentinean Indian children. Clinica Chimica Acta. 2014;429:147-151.
- Bonnefond A., Philippe J., Durand E., Muller J., Saeed S., Arslan M. et al. Highly sensitive diagnosis of 43 monogenic forms of diabetes or obesity through one-step pcrbased enrichment in combination with next-generation sequencing. Diabetes Care. 2014;37(2):460-467.
- Martín-Nunez G.M., Cabrera-Mulero R., Rubio-Martín E., Rojo-Martínez G., Olveira G., Valdés S. et al. Methylation levels of the SCD1 gene promoter and LINE-1 repeat region are associated with weight change: An intervention study. Molecular Nutrition and Food Research. 2014;58(7):1528-1536.
- Valdés S., Maldonado-Araque C., García-Torres F., Goday A., Bosch-Comas A., Bordiu E. et al. Ambient temperature and prevalence of obesity in the spanish population: The di@bet.es study. Obesity. 2014;22(11):2328-2332.
- Martín-Nunez G.M., Rubio-Martín E., Cabrera-Mulero R., Rojo-Martínez G., Olveira G., Valdés S. et al. Type 2 diabetes mellitus in relation to global LINE-1 DNA methylation in peripheral blood: A cohort study. Epigenetics. 2014;9(10):1322-1328.

Highlights

- Participation in international projects on diabetes prevention, either nutritional (TRIGR project-NIH 5U01HD040364-08) or about immunomodulation using antigens (Diamyd Project).
- Collaboration with the International Group of Pediatric Diabetes (Hvidore Group).
- Participation in the European MEDIGENE Project (FP7-279171-1) about characterization of diabetes in Mediterranean populations.
- Development of projects related to molecular characterization of monogenic diabetes (Basque Department of Education GV IT795-13 and Basque Health Department GV 2010111185).
- Completion of the study about "Epidemiology of Diabetes in the Basque Country" (Basque Health Department GV2010111058). Beginning of the "Incidence of diabetes and prevalence of monogenic diabetes in the Di@betes study" project (PI14/01104).

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Metabolomics Platform

Programme: P1

Lead Researcher: Correig Blanchart, Francesc X.

Group members

STAFF MEMBERS: Samino Gene, Sara | Yanes Torrado, Óscar

ASSOCIATED MEMBERS: Amigó Grau, Nuria | Beltrán Carbo, Antoni | Brezmes Llecha, Jesús Jorge | Domingo Almenara, Xavier | Gómez Álvarez, Josep | Llobet Valero, Eduard | Mallol Parera, Roger | Radu Ionescu, Radu | Rodríguez Gómez, Miguel Ángel | Vilalta Montlleo, Didac | Vinaixa Crevillent, María

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 and body fluid profiling with NIMS (Nanostructure Initiator Mass Spectrometry).
- Thirdhand smoke (THS) exposition assesment with metabolomics

Most relevant scientific articles

- Malpique R., Figueiredo H., Esteban Y., Rebuffat S.A., Hanzu F.A., Vinaixa M. et al. Integrative analysis reveals novel pathways mediating the interaction between adipose tissue and pancreatic islets in obesity in rats. Diabetologia. 2014;57(6):1219-1231.
- Hanzu F.A., Vinaixa M., Papageorgiou A., Parrizas M., Correig X., Delgado S. et al. Obesity rather than regional fat depots marks the metabolomic pattern of adipose tissue: An untargeted metabolomic approach. Obesity. 2014;22(3):698-704.
- Sáez I., Duran J., Sinadinos C., Beltrán A., Yanes O., Tevy M.F. et al. Neurons have an active glycogen metabolism that contributes to tolerance to hypoxia. Journal of Cerebral Blood Flow and Metabolism. 2014;34(6):945-955.
- Brugnara L., Vinaixa M., Murillo S., Samino S., Rodríguez M.A., Beltran A. et al. Metabolomics approach for analyzing the effects of exercise in subjects with type 1 diabetes mellitus. Diabetes Technology and Therapeutics. 2014;16(SUPPL. 1).
- Alonso A., Rodríguez M.A., Vinaixa M., Tortosa R., Correig X., Julia A. et al. Focus: A robust workflow for one-dimensional NMR spectral analysis. Analytical Chemistry. 2014;86(2):1160-1169.

Highlights

COLLABORATIONS

• Six collaborations with groups from CIBERDEM: Dr. Egido; Dra. Rojo Dr. Guinovart, Dr. Simó, Dr. Masana, Dra. Ibáñez; and 11 with other nacional groups: Dra. Colomina (URV); Dr. Guimerà (URV); Dr. Buschbeck (IMPPC); Dr. Gomis (IRB); Dr. Stracker (IRB); Dr. Garcia-Roves (IDIBAPS); Dr. Lerin (Fundació Sant Joan de Déu); Dr. Quintela (CNIO); Dra. Marsal (Vall d'Hebron); Dr. Borràs (St Joan de Reus); Dra.Bulló (CIBER-OBN). Seven collaborations with international groups: Dr. Martins-Green (University of California); Dr. Heck (The Netherlands Proteomics Center and Utrecht University); Dr. Shabaz Mohammed (University of Oxford); Dr. Kessler (University of Oxford); Dr. Harris (University of Oxford); Dr. Neumann (Leibniz Institute of Plant Biochemistry); Dr. Salek (EBI-EMBL).

RELEVANT PROJECTS

• SAF2011-30578: Identification of metabolic pathways in neurodegeneration of retina induced by hyperglycemia and ischemia through an approximation of metabolomics and proteomics • TEC2012-31074: Development of nanostructured surfaces and metabolic image processing algorithms for NIMS: application to the study of pancreatic islets in diabetic rats

RELEVANT RESULTS ACHIEVED

• Clinical validation of an advanced method of lipoproteins • Identification of biomarkers of subclinical atherosclerosis in PCOS patients • Development of algorithms for fluxomics experiments based on LC-MS • Creation and validation of a new algorithm for the identification of unknown metabolites by GC-MS • Deposition of nanoparticles for obtaining metabolic images by NP-LDI-MSI

EUROPEAN PATENTS

• PCT/EP2014/075873. Method for the characterization of lipoproteins. Mallol Parera, Roger; Amigó Grau, Núria; Correig Blanchar, Xavier; Masana Marín, Lluís; Rodríguez Martínez, Miguel Ángel; Heras Ibáñez, Mercedes; Plana Gil, Núria. • PCT/EP2014/075874. Methods for determining the lipid distribution between the core and the shell of a lipoprotein particle. Amigó Grau, Núria; Mallol Parera, Roger; Correig Blanchar, Xavier; Masana Marín, Lluís; Rodríguez Martínez, Miguel Ángel; Heras Ibáñez, Mercedes; Plana Gil, Núria

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Division of Nephrology and Hypertension

Programme: P2

Lead Researcher: Egido De los Ríos, Jesús

Group members

STAFF MEMBERS: Civantos Martín, Esther

ASSOCIATED MEMBERS: Arnés Pérez, Luis | González Gomez, Nieves | Martín Crespo, Estrella | Mas Fontao, Sebastián | Ramos Álvarez, Irene | Rovira Loscos, Adela | Valverde Alonso, Isabel

Main lines of research

- Vascular complications of diabetes (nephropathy and atherosclerosis)
- Inflammation and intracellular signals
- New therapeutic approaches to diabetic kidney disease
- Biomarkers
- Renal lipotoxicity in the diabetic patient

Most relevant scientific articles

- Rodrigues-Díez R., Aroeira L.S., Orejudo M., Bajo M.-A., Heffernan J.J., Rodrigues-Díez R.R. et al. IL-17A is a novel player in dialysis-induced peritoneal damage. Kidney International. 2014;86(2):303-315.
- Fernández-Fernández B., Ortiz A., Gómez-Guerrero C., Egido J. Therapeutic approaches to diabetic nephropathy - beyond the RAS. Nature Reviews Nephrology. 2014;10(6):325-346.
- Moreno J.A., Moreno S., Rubio-Navarro A., Gómez-Guerrero C., Ortiz A., Egido J. Role of chemokines in proteinuric kidney disorders. Expert Reviews in Molecular Medicine. 2014;16.
- Martínez-Pinna R., Lindholt J.S., Madrigal-Matute J., Blanco-Colio L.M., Esteban-Salan M., Torres-Fonseca M.M. et al. From tissue iron retention to low systemic haemoglobin levels, new pathophysiological biomarkers of human abdominal aortic aneurysm. Thrombosis and Haemostasis. 2014;112(1):87-95.
- Alique M., Civantos E., Sánchez-López E., Lavoz C., Rayego-Mateos S., Rodrigues-Díez R. et al. Integrin-linked kinase plays a key role in the regulation of angiotensin II-induced renal inflammation. Clinical Science. 2014;127(1):19-31.

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Diabetes, Obesity and Human Reproduction

Programme: P4

Lead Researcher: Escobar Morreale, Héctor F.

Group members

STAFF MEMBERS: Fernández Durán, Elena | Insenser Nieto, María Rosa | Martínez García, Mª Ángeles | Ojeda Ojeda, Miriam

ASSOCIATED MEMBERS: Álvarez Blasco, Francisco | Luque Ramírez, Manuel | Roldán Martín, María Belén | San Millán López, José Luis | Sanchón Rodríguez, Raúl

Main lines of research

- 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:
- 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, transcriptomics, proteomics and metabolomics.
- The identification of pathogenetic markers of diabetes in severe obesity and predictors of diabetes remission after bariatric surgery.
- The role of disordered iron metabolism on the metabolic associations of polycystic ovary syndrome.
- The effects of sex hormones on the metabolic and inflammatory responses to the oral administration of different macronutrients.

Most relevant scientific articles

- Dewailly D., Luján M.E., Carmina E., Cedars M.I., Laven J., Norman R.J. et al. Definition and significance of polycystic ovarian morphology: A task force report from the androgen excess and polycystic ovary syndrome society. Human Reproduction Update. 2014;20(3):334-352.
- Luque-Ramírez M., Martí D., Fernández-Durán E., Alpanes M., Álvarez-Blasco F., Escobar-Morreale H.F. Office blood pressure, ambulatory blood pressure monitoring, and echocardiographic abnormalities in women with polycystic ovary syndrome: Role of obesity and androgen excess. Hypertension. 2014; 63(3):624-629.
- Escobar-Morreale HF, Álvarez-Blasco F, Botella-Carretero JI, Luque-Ramírez M. The striking similarities in the metabolic associations of female androgen excess and male androgen deficiency. Human reproduction (Oxford, England). 2014; 29(10):2083-91.
- Alpanes M., Luque-Ramírez M., Martínez-García M.A., Fernández-Durán E., Álvarez-Blasco F., Escobar-Morreale H.F. Influence of adrenal hyperandrogenism on the clinical and metabolic phenotype of women with polycystic ovary syndrome. Fertility and Sterility. 2014
- Luque-Ramírez M., Escobar-Morreale H.F. Polycystic Ovary Syndrome as a Paradigm for Prehypertension, Prediabetes, and Preobesity. Current Hypertension Reports. 2014; 16(12):1-10.

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Genomic programming of beta cells

Programme: P3 y P4

Lead Researcher: Ferrer Marrades, Jorge

Group members

STAFF MEMBERS: García Hurtado, Javier | Grau Martinez, Vanessa | Maestro Garriga, Miguel Ángel | Sanahuja, Carme

ASSOCIATED MEMBERS: Akerman , Ildem | Armengol-, Mar | Castro Moran, Natalia | Cebola, Inés | Correa Tapia, Miguel Á. | Moran Castany, Ignasi | Mularoni, Loris | Nakic, Nikolina | Pasquali, Lorenzo | Rovira Clusellas, Meritxell

Main lines of research

- Dissection of the genetic mechanisms underlying the pathogenesis of human diabetes.
- Understanding the epigenome of pancreatic beta cells and its implications for the development, plasticity and growth of beta cells
- Mouse genetic analysis of beta-cell gene regulation.
- The regeneration of pancreatic beta cells

Most relevant scientific articles

- Pasquali L., Gaulton K.J., Rodríguez-Segui S.A., Mularoni L., Miguel-Escalada I., Akerman I. et al. Pancreatic islet enhancer clusters enriched in type 2 diabetes risk-associated variants. Nature Genetics. 2014;46(2):136-143.
- Shaw-Smith C., De Franco E., Allen H.L., Batlle M., Flanagan S.E., Borowiec M. et al. GATA4 mutations are a cause of neonatal and childhood-onset diabetes. Diabetes. 2014;63(8):2888-2894.
- Rodrigo-Torres D., Affo S., Coll M., Morales-Ibánez O., Millán C., Blaya D. et al. The biliary epithelium gives rise to liver progenitor cells. Hepatology. 2014.
- Thorens B., Tarussio D., Maestro M.A., Rovira M., Heikkila E., Ferrer J. Ins1Cre knock-in mice for beta cell-specific gene recombination. Diabetologia. 2014.
- Weedon M.N., Cebola I., Patch A.-M., Flanagan S.E., De Franco E., Caswell R. et al. Recessive mutations in a distal PTF1A enhancer cause isolated pancreatic agenesis. Nature Genetics. 2014;46(1):61-64.

Highlights

During 2014 the team has achieved several scientific goals, including the generation of epigenomic reference maps in embryonic and adult pancreatic islets, the discovery of novel Mendelian and polygenics variants that disrupt pancreatic enhancers and thereby contribute to diabetes mellitus, and the identification of long non-coding RNAs that control pancreatic beta cell regulatory networks. We have characterized a conditional mouse mutation of a chromatin regulator that is a potential molecular target to reprogram pancreatic beta cells from pancreatic exocrine cells. We are furthermore completing a study that will determine how allelic variation influences genome activity in pancreatic islets.

In addition to ongoing EU and national grants, the team has gained a new grant from Novonordisk Foundation that will support the generation of a new KO mouse model and a postdoctoral fellowship salary for 3 years. We have also obtained an EU Marie Curie Training Network that has just started. The team has recruited a new postdoctoral trainee who gained her own Marie Curie award. One of the postdoctoral trainees of the lab, Dr Lorenzo Pasquali, has obtained a Ramon y Cajal award and has been offered a Prinicipal Investigator position in Fundacio Joan Carreras/IMPPC.

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Mechanisms of Control of Glucose and Fatty Acid Metabolism in Skeletal Muscle Cells and Metabolic Impairment in Atrophy

Programme: P4

Lead Researcher: Gómez Foix, Anna Maria

Group members

STAFF MEMBERS: Montori Grau, Marta

ASSOCIATED MEMBERS: García Martínez, Celia | Orozco, Anna | Osorio Conles, Óscar

Main lines of research

- Mechanisms of control of skeletal muscle glycogen metabolism: differential functionality of the protein phosphatase 1 glycogen-associated regulatory subunits and function of GNIP1 (glycogenin Interacting Protein 1) / TRIM7.
- Participation and identity of signaling molecules derived from palmitate metabolism in the impairment of muscle cell insulin response and induction of an inflammatory signal. Metabolic control by the fatty acid transport protein 1 (FATP1) in the context of high-fat diet induced diabetes.
- Role of secretable proteins predominant in adipose tissue and muscle, such as PTX3, CCDC80 or collagen VI, in the modulation of insulin signaling and glucose metabolism in adipocytes and muscle cells.
- Development of an electroporator device directly applicable to adherent cells cultured on standard multiwell plates to facilitate molecular transfer.

Most relevant scientific articles

- Salvado L., Barroso E., Gómez-Foix A.M., Palomer X., Michalik L., Wahli W. et al. PPARβ/δ prevents endoplasmic reticulum stress-associated inflammation and insulin resistance in skeletal muscle cells through an AMPK-dependent mechanism. Diabetologia. 2014.
- Guitart M., Osorio-Conles O., Pentinat T., Cebria J., García-Villoria J., Sala D. et al. Fatty Acid Transport Protein 1 (FATP1) localizes in mitochondria in mouse skeletal muscle and regulates lipid and ketone body disposal. PLoS ONE. 2014;9(5).
- Fernández-Novell J.M., Ramio-Lluch L., Orozco A., Gómez-Foix A.M., Guinovart J.J., Rodriguez-Gil J.E. Glucose and fructose have sugar-specific effects in both liver and skeletal muscle in vivo: A role for liver fructokinase. PLoS ONE. 2014;9(10).
- García-SánchezT., Guitart M., Rosell-Ferrer J., Gómez-Foix A.M., Bragos R. A new spiral microelectrode assembly for electroporation and impedance measurements of adherent cell monolayers. Biomedical Microdevices. 2014;16(4):575-590.
- Sánchez T.G., Guitart M., Rosell-Ferrer J., Gómez-Foix A.M., Bragos R. Gene transfer to adherent cells by in situ electroporation with a spiral microelectrode assembly. IFMBE Proceedings. 2014;41:900-903.

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Diabetes and obesity: biopathology and cellular plasticity

Programme: P2 y P3

Lead Researcher: Gomis de Barbarà, Ramon

Group members

STAFF MEMBERS: Blanco Carrasco, Jesús | Esteban Romero, María Yaiza | Fernández Ruiz, Rebeca | García Alamán, Ainhoa | García Gómez-Valades, Alicia | González Ruano, Elena | Katte, Kimberly | Viaplana Masclans, Judith | Vieira, Cristina Elaine

ASSOCIATED MEMBERS: Canivell Fusté, Silvia | Casamitjana Abella, Roser | Cervantes Roldán, Sara | Claret Carles, Marc | Conget Donlo, Ignacio | Esmatjes Mompo, Enrique | Flores Meneses, Lilliam | Gasa Arnaldich, Rosa María | Giménez Álvarez, Margarita | Hanzu, Felicia Alexandra | Martins de Sousa Maia Malpique, Rita María | Mora Porta, Mireia | Nadal Martín, Belén | Nicod, Nathalie | Papageorgiou, Aikaterini | Pradas Juni, Marta | Schneeberger Pane, Marc | Vidal Cortada, Josep

Main lines of research

- The effects of pancreatic-mesenteric adipose tissue on beta-cell plasticity
- Crosstalk between adipose tissue and endothelium in metabolic diseases: 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
- Pancreatic islet transplantation: role of PTP1B
- The role of the hypothalamus in energy homeostasis control in obesity
- Genetic determinants involved in the risk of type 2 diabetes

Most relevant scientific articles

- Malpique R., Figueiredo H., Esteban Y., Rebuffat S.A., Hanzu F.A., Vinaixa M. et al. Integrative analysis reveals novel pathways mediating the interaction between adipose tissue and pancreatic islets in obesity in rats. Diabetologia. 2014;57(6):1219-1231.
- Jiménez A., Mari A., Casamitjana R., Lacy A., Ferrannini E., Vidal J. GLP-1 and glucose tolerance after sleeve gastrectomy in morbidly obese subjects with type 2 diabetes. Diabetes. 2014;63(10):3372-3377.
- Hanzu F.A., Vinaixa M., Papageorgiou A., Parrizas M., Correig X., Delgado S. et al. Obesity rather than regional fat depots marks the metabolomic pattern of adipose tissue: An untargeted metabolomic approach. Obesity. 2014;22(3):698-704.
- Oliveira J.M., Rebuffat S.A., Gasa R., Burks D.J., García A., Kalko S.G. et al. Tungstate promotes β-cell survival in Irs2-/- mice. American Journal of Physiology - Endocrinology and Metabolism. 2014;306(1).
- Schneeberger M., Gomis R., Claret M. Hypothalamic and brainstem neuronal circuits controlling homeostatic energy balance. Journal of Endocrinology. 2014;220(2).

Highlights

The most important highlights during 2014 include the following: First, the journal Diabetologia featured our article entitled "Integrative analysis reveals novel pathways mediating the interaction between adipose tissue and pancreatic islets in obesity" on the cover on the June issue. Also, the European Foundation for the Study of Diabetes (EFSD) nominated Dr. Rosa Gasa, member of our group, to coordinate the Diabetes Research Education Programme in Europe. This nomination is important, as it recognizes our group as an international point of reference in research to the extent that one of its members can lead the coordination of an international educational program of prestige, such as the one organized by the EFSD. On another note, group leader Ramon Gomis was named as one of the four coordinators of the Academia Europaea for Southern Europe. In terms of international projects, as deputy coordinators of the MEDIGENE project in which CIBERDEM participates, we have developed various strategies for conducting GWAS analyses in populations of the different participating countries (France, Italy, Spain, Greece, Morocco, Tunisia, Algeria and Egypt). Furthermore, we have prepared the biobank with samples of genomic and mitochondrial DNA taken from molars originating from the Roman population of the Tarragona Necropolis, with the corresponding amplification and sequencing. Finally, we wish to make special mention of the José Antonio Hedo Junior Basic Research Prize, which was awarded in 2014 by the Foundation of the Spanish Diabetes Society (SED) to group member Dr. Elaine Vieira.

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Metabolic Engineering and Diabetes Therapy

Programme: P2

Lead Researcher: Guinovart Cirera, Joan Josep

Group members

STAFF MEMBERS: Duran Castells, Jordi | López-Soldado Fernández, Iliana | Veza Estévez, Emma

ASSOCIATED MEMBERS: Adrover Palau, Anna | García Rocha, María del Mar | Mir Coll, Juan Ignacio | Slebe Concha, Juan Felipe | Testoni, Giorgia | Zapata , Claire- Alix

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.

Most relevant scientific articles

- Duran J., Gruart A., García-Rocha M., Delgado-García J.M., Guinovart J.J. Glycogen accumulation underlies neurodegeneration and autophagy impairment in lafora disease. Human Molecular Genetics. 2014;23(12):3147-3156.
- Sáez I., Duran J., Sinadinos C., Beltran A., Yanes O., Tevy M.F. et al. Neurons have an active glycogen metabolism that contributes to tolerance to hypoxia. Journal of Cerebral Blood Flow and Metabolism. 2014;34(6):945-955.
- Sinadinos C., Valles-Ortega J., Boulan L., Solsona E., Tevy M.F., Marquez M. et al. Neuronal glycogen synthesis contributes to physiological aging. Aging Cell. 2014.
- Oliveira J.M., Rebuffat S.A., Gasa R., Burks D.J., Garcia A., Kalko S.G. et al. Tungstate promotes β-cell survival in Irs2-/- mice. American Journal of Physiology - Endocrinology and Metabolism. 2014;306(1).
- Hernandez C., García-Ramírez M., García-Rocha M., Sáez-López C., Valverde A.M., Guinovart J.J. et al. Glycogen storage in the human retinal pigment epithelium: A comparative study of diabetic and non-diabetic donors. Acta Diabetologica. 2014;51(4):543-552.

Highlights

During 2014, we showed that glycogen accumulation has beneficial or harmful effects, depending on the tissue.

Thus, we confirmed that the increase in liver glycogen reduces obesity and appetite in mice after the administration of a high-fat diet. This finding could open up a new approach for the treatment of the obesity associated with diabetes. We also demonstrated that—in contrast to what it was known until now—neurons have an active glycogen metabolism and that this protects them under stress conditions such as hypoxia.

Furthermore, our studies indicate that Lafora disease is caused by the accumulation of aberrant glycogen in neurons, as animals unable to synthesize the polysaccharide do not develop the disease. We believe that glycogen accumulation in neurons may play a role in the conditions associated with diabetes, diabetic retinopathy, and diabetic neuropathy. In this regard, in collaboration with Dr. Rafael Simó, we demonstrated that the retinal pigment epithelium can store large amounts of glycogen—a capacity that was previously unknown. In another collaborative study between CIBERDEM and Dr. Ramon Gomis, we progressed in the study of tungstate as a protective compound for beta cells.

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Consequences of Prenatal and Perinatal Disorders on Postnatal Development. Disorders of Fetal Origin

Programme: P4

Lead Researcher: Ibáñez Toda, Lourdes

Group members

STAFF MEMBERS: Díaz Silva, Marta | Quílez Moya, Jovita

ASSOCIATED MEMBERS: Blasco Ruano, Israel | Casano Sancho, Paula | Infantes Sánchez, David | López Bermejo, Abel | Marcos Salas, María Victoria | Sebastiani, Giorgia

Main lines of research

- Childhood diabetes
- Physiological and pathological states in newborns and their effects on evolution
- Congenital malformations and their surgical management
- Foetal medicine: foetal well-being markers
- Intrauterine growth retardation and related disorders

Most relevant scientific articles

- De Zegher F., Pérez-Cruz M., Diaz M., Gómez-Roig M.D., López-Bermejo A., Ibánez L. Less myostatin and more lean mass in large-born infants from nondiabetic mothers. Journal of Clinical Endocrinology and Metabolism. 2014;99(11):E2367-E371.
- Díaz M., Aragonés G., Sánchez-Infantes D., Bassols J., Pérez-Cruz M., De Zegher F. et al. Mitochondrial DNA in placenta: Associations with fetal growth and superoxide dismutase activity. Hormone Research in Paediatrics. 2014;82(5):303-309.
- Díaz M, Bassols J, López-Bermejo A, de Zegher F, Ibáñez L. Metformin treatment to reduce central adiposity after prenatal growth restraint: a placebo-controlled pilot study in prepubertal children.Pediatric diabetes. 2014.
- Ibánez L., Ong K.K., López-Bermejo A., Dunger D.B., De Zegher F. Hyperinsulinaemic androgen excess in adolescent girls. Nature Reviews Endocrinology. 2014;10(8):499-508.
- Sanz N., Diaz M., López-Bermejo A., Sierra C., Fernandez A., De Zegher F. et al. Newborns with lower levels of circulating polyunsaturated fatty acids (PUFA) are abdominally more adipose. Pediatric Obesity. 2014;9(3).

Highlights

RESEARCH GROUP

Over 2014, the group has further developed the two main research lines: 1)ovarian androgen excess; 2)low birth weight and subsequent postnatal endocrine-metabolic and body composition abnormalities.

These are among the priority research lines of the Hospital Sant Joan de Déu, being part of a bigger line entitled: Adult Diseases of Fetal Origin, coordinated by Dr. Lourdes Ibáñez since 2008 (University of Barcelona; www.hsjdbcn.org).

The results of the recent progress have been presented in invited lectures at international forums, including at the ICE/ENDOCRINE SOCIETY meeting in Chicago (USA).

COLLABORATIONS

- Since 1998, the research group has developed joint research projects (and derived manuscripts) with the University of Leuven, Belgium (Prof. F. de Zegher), the University of Cambridge, UK (Prof. D.B. Dunger, Dr. K. Ong) and the University of Girona (Dr. A. López-Bermejo).
- The results of the project entitled: Infant manifestations of adult obesity susceptibility genotypes [collaborative study with Cambridge, INSERM (Paris) & Leuven], supported by a research grant from the European Society for Paediatric Endocrinology (ESPE) have been published in JAMA Pediatr 2014; 168:1122-30.
- Dr. Lourdes Ibáñez has been entitled as ESPE representative in a Clinical Consensus Manuscript on The Diagnosis of Polycystic Ovarian Syndrome during Adolescence (ESPE, AE-PCOS, APEG, APPES, ASPAE, JSPE, JSOG, NASPAG, PES, SLEP). The manuscript has been accepted for publication in Horm Res Paediatr (December, 2014).

AWARDS

- Dr. Lourdes Ibáñez has received the prestigious Premi Nacional de Recerca 2014 (Generalitat i Fundació Catalana per a la Recerca i la Innovació).

OTHER (DR. LOURDES IBÁÑEZ)

- Coordination & Direction of the Master in Paediatric & Adolescent Endocrinology (Universitat de Barcelona).
- Chair: Pediatric & Adolescent Gynecology Working Group, ESPE (www.eurospe.org) & SGA Working Group, SEEP (www.seep.es/privado/ctpubli6.asp).

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Islet Cell and Stem Cell Physiology

Programme: P3

Lead Researcher: Martín Bermudo, Francisco

Group members

STAFF MEMBERS: Araujo Legido, Raquel | Cárdenas García, Antonio Manuel | Díaz Contreras, Irene | Hitos Prados, Ana Belén

ASSOCIATED MEMBERS: Bedoya Bergua, Francisco Javier | Berna Amorós, Genoveva | Cahuana Macedo, Gladys Margot | Carrasco Fernández, Manuel | Ortega de la Torre, María de los Ángeles | Rojas González, Ana Isabel | Soria Escoms, Bernat | Tejedo Huaman, Juan Rigoberto

Main lines of research

- Role of GATA4 and GATA6 transcription factors to beta cell function and to acinar cell regeneration in cerulein-induced pancreatitis.
- Differentiation towards definitive endoderm (DE) and generation of beta cell-like from embryonic stem cells.
- Use of adult stem cells for pancreatic regeneration.
- Pancreatic acinar differentiation from embryonic stem cells.
- Survival of pancreatic beta cells and the role of nitric oxide.
- Role of nutrients in pathophysiology of Diabetes Mellitus.
- Uses of stem cells in cell therapy treatment of Diabetes Mellitus vascular complications.

Most relevant scientific articles

- Gálvez-Martin P., Hmadcha A., Soria B., Calpena-Campmany A.C., Clares-Naveros B. Study of the stability of packaging and storage conditions of human mesenchymal stem cell for intra-arterial clinical application in patient with critical limb ischemia. European Journal of Pharmaceutics and Biopharmaceutics. 2014;86(3):459-468.
- Gálvez P., Clares B., Bermejo M., Hmadcha A., Soria B. Standard requirement of a microbiological quality control program for the manufacture of human mesenchymal stem cells for clinical use. Stem Cells and Development. 2014;23(10):1074-1083.
- Delgado I., Carrasco M., Cano E., Carmona R., García-Carbonero R., Marin-Gomez L.M. et al. GATA4 loss in the septum transversum mesenchyme promotes liver fibrosis in mice. Hepatology. 2014;59(6):2358-2370.
- Cano D.A., Soria B., Martín F., Rojas A. Transcriptional control of mammalian pancreas organogenesis. Cellular and Molecular Life Sciences. 2014;71(13):2383-2402.
- Oliveras-López M.-J., Berna G., Jurado-Ruiz E., López-García de la Serrana H., Martín F. Consumption of extra-virgin olive oil rich in phenolic compounds has beneficial antioxidant effects in healthy human adults. Journal of Functional Foods. 2014;10:475-484.

Highlights

- Identification of GATA4 transcription factor as a liver fibrosis marker in biopsies from patients with SM. It has been studied the potential therapeutic target of GATA4 due to its ability to inactive stellate liver cells and allow the reversion of liver fibrosis.
- Characterization of human islet proteoma profile when culture in serum absence. In this situation human islets has a reticulum endoplasmic stress response. This will allow the design of tissue culture media able to improve human islet viability for islet transplantation.
- Development of two rodent models useful to study DM2 pathophysiology and to look for targets against DM2: i) knockout mice for presinilin. This model doesn´t develop SM, DM2 and NAFDL when fed with high caloric diets rich in saturated fats and sugars and ii) humanised mice with SM, DM2 and NAFDL. They are LDLR-Leiden -/- mice fed with diets with the same caloric profile, fats and saturated fats than spanish population.
- Improvement of maturation protocols to obtain beta cell surrogates from hESC and hIPS.
- Development of a tissue culture chemistry xenofree define medium to culture mesenchymal stem cells, from bone marrow and adipose tissue. The medium improve cell proliferation maintaining a stable cell genotype and fenotype and cell differentiation potential.
- Production of cells able to be used on cell therapy clinical assays under GMP conditions. Development of a certified quality system, under current legislation, to produce these cells. The cells have been used in cell therapy clinical assays to treat DM complications

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Molecular Mechanisms of Insulin Resistance, Insulin Sensitivity, Islet Development and Diabetic Complications

Programme: P2

Lead Researcher: Martínez Valverde, Ángela M.

Group members

STAFF MEMBERS: Arroba Espinosa, Ana Isabel | González Rodríguez, Águeda | Murillo Gómez, Cayetana | Pardo Marques, Virginia

ASSOCIATED MEMBERS: Ahmed, Maysha | De Pablo Dávila, Flora | Hernández Sánchez, Catalina | Santamaría Pérez, Beatriz

Main lines of research

- Autophagy as a potential mediator of the progression of the non-alcoholic hepatic liver disease (NAFLD) in humans.
- Effect of fatty acids and lipid species in the cross-talk between inflammatory and insulin signalling in hepatocytes.
- Drug-mediated insulin resistance in peripheral tissues: effects of chronic pharmacologycal treatments on insulin signalling and glucose homeostasis
- Role of protein tyrosyne phosphatase 1B (PTP1B) in IGF-I and proinsulin-mediated signalling in the retina: possible benefits of PTP1B inhibition in the impairment of survival of photoreceptor cells.
- Analysis of the balance between stress and survival signalling pathways in diabetic retinopathy in humans.
- Study of the polarization of microglia in diabetic retinopathy.
- Characterization of diabetic nephropathy in IRS2-deficient mice: role of the critical nodes of the insulin signalling in podocytes.
- Physiological role of proinsulin and the consequences of inappropriately high levels during cardiogenesis.
- Role of atypical catecholaminergic cells in developing mouse pancreas.
- Involvement of Tyrosine Hydroxilase in the metabolic adaptations to diet and temperature stressors.

Most relevant scientific articles

- González-Rodríguez A., Reibert B., Amann T., Constien R., Rondinone C.M., Valverde A.M. In vivo siRNA delivery of Keap1 modulates death and survival signaling pathways and attenuates concanavalin-A-induced acute liver injury in mice. DMM Disease Models and Mechanisms. 2014;7(9):1093-1100.
- Mobasher M.A., De Toro-Martín J., González-Rodríguez A., Ramos S., Letzig L.G., James L.P. et al. Essential role of protein-tyrosine phosphatase 1B in the modulation of insulin signaling by acetaminophen in hepatocytes. Journal of Biological Chemistry. 2014; 289(42):29406-29419.
- Vázquez P., Robles A.M., de Pablo F., Hernández-Sánchez C. Non-neural tyrosine hydroxylase, via modulation of endocrine pancreatic precursors, is required for normal development of beta cells in the mouse pancreas. Diabetologia. 2014;57(11):2339-2347.
- González-Rodríguez A., Mayoral R., Agra N., Valdecantos M.P., Pardo V., Miquilena-Colina M.E. et al. Impaired autophagic flux is associated with increased endoplasmic reticulum stress during the development of NAFLD. Cell Death and Disease. 2014;5(4).
- Francés De, Motiño O, Agrá N, González-Rodríguez A, Fernández-Álvarez A, Cucarella C et al. Hepatic cyclooxygenase-2 expression protects against diet-induced steatosis, obesity and insulin resistance.Diabetes. 2014.

Highlights

- Endoplasmic reticulum stress and autophagy as potential mediators for the progression of the non-alcoholic fatty liver disease (NAFLD) in humans.
- Pivotal role of the protein tyrosine phosphatase 1B (PTP1B) in the modulation of the responses to pro- and anti-inflammatory challenges in macrophages: implications in the hepatic inflammation during the progression of NAFLD.
- Drug-mediated insulin resistance in peripheral tissues: effects of chronic pharmacological treatments (paracetamol and immunossupressants) on insulin signalling and glucose homeostasis.
- Essential role of Keap1/Nrf2 signalling pathway in the modulation of the balance between death and survival signalling pathways in the liver.
- Hepatic cyclooxygenase-2 expression protects against diet-induced steatosis, obesity and insulin resistance by the modulation of the insulin signaling cascade.
- Role of PTP1B in IGF-I and proinsulin-mediated signalling in the retina: possible benefits of PTP1B inhibition in the impairment of survival of photoreceptor cells.
- Study of the polarization of microglia: implications in the progression of diabetic retinopathy.
- Characterization of diabetic nephropathy in IRS2-deficient mice: role of the critical nodes of the insulin signalling in podocytes.
- Role of atypical catecholaminergic cells in developing mouse pancreas.
- Involvement of tyrosine hydroxilase (TH) in the metabolic adaptations to diet and temperature stressors

FUNDING:

- Inhibition of Protein Tyrosine Phosphatase 1B in the treatment of type 2 diabetes: effects in diabetic complications and cell proliferation (SAF2012-33283).
- Study of the mechanisms of insulin resistance: implications in obesity, diabetes and metabolic syndrome. S2010/BMD-2423: MOIR-CM (Comunidad de Madrid).
- Neurodegeneration as an early event in the Pathogenesis of Diabetic Retinopathy: A multicentric, prospective, phase II-III, double blind randomized controlled trial to assess the efficacy of neuroprotective drugs administered topically to prevent or arrest Diabetic Retinopathy (EUROCONDOR) FP7-HEALTH-2011-two-stage HEALTH.2011.2.4.3.1 (2012-2016).

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Lipids and Arteriosclerosis Research Unit

Programme: P1 y P2

Lead Researcher: Masana Marín, Luis

Group members

STAFF MEMBERS: Cabre Llobet, Anna | Merino Ribas, Jordi | Rodríguez Calvo, Ricardo | Rosales Ribas, Roser

ASSOCIATED MEMBERS: Bosquet Agudo, Alba | Fernández Castillejo, Sandra | Ferré Vallès, Raimon | Girona Tell, Josefa | Guaita Esteruelas, Sandra | Guardiola Guionnet, Monserrat | Heras Ibáñez, Mercedes | Plana Gil, Núria | Ribalta Vives, Josep | Saavedra García, Paula | Solà Alberich, Rosa | Vallvé Torrente, Joan Carles

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.

Most relevant scientific articles

- Sattar N.A., Ginsberg H., Ray K., Chapman M.J., Arca M., Averna M. et al. The use of statins in people at risk of developing diabetes mellitus: Evidence and guidance for clinical practice. Atherosclerosis Supplements. 2014;15(1):1-15.
- Merino J., Sala-Vila A., Kones R., Ferre R., Plana N., Girona J. et al. Increasing long-chain n-3PUFA consumption improves small peripheral artery function in patients at intermediate-high cardiovascular risk. Journal of Nutritional Biochemistry. 2014;25(6):642-646.
- Guardiola M., Oliva I., Guillaumet A., Martín-Trujillo T., Rosales R., Vallve J.C. et al. Tissue-specific DNA methylation profiles regulate liver-specific expression of the APOA1/C3/A4/A5 cluster and can be manipulated with demethylating agents on intestinal cells. Atherosclerosis. 2014;237(2):528-535.
- Gylling H., Plat J., Turley S., Ginsberg H.N., Ellegard L., Jessup W. et al. Plant sterols and plant stanols in the management of dyslipidaemia and prevention of cardiovascular disease. Atherosclerosis. 2014;232(2):346-360.
- Megias-Rangil I., Merino J., Ferre R., Plana N., Heras M., Cabre A. et al. Subclinical atherosclerosis determinants in morbid obesity. Nutrition, Metabolism and Cardiovascular Diseases. 2014.

Institution: Agencia Estatal Consejo Superior de Investigaciones Científicas
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Group of research into Diabetes and metabolism

Programme: P3 y P4

Lead Researcher: Montanya Mias, Eduard

Group members

STAFF MEMBERS: Estil·Les Altamiras, Elisabet | Téllez Besoli, Noelia

ASSOCIATED MEMBERS: Caballero Corchuelo, Jorge | Gómez Sáez, José Manuel | Moreno Amador, José Luis | Nacher García, Montserrat | Pairo Delgado, María del Mar | Pérez Maraver, Manuel | San José Terrón, Patricia | Soler Ramón, Juan | Vilarrasa García, Nuria

Main lines of research

The group has two main lines of research focused on diabetes and obesity. The research on the molecular and cellular biology of pancreatic islets has an essential component of pre-clinical research with a particular emphasis on its translation to the treatment of diabetes. The specific focus of research line on pancreatic islets are the mechanisms of destruction and regeneration of pancreatic beta cells with a particular interest in the cell therapy of diabetes and regenerative medicine. This research includes also some aspects more directly related to beta cell function and chronic complications in diabetic patients. The group has also a strong interest in the link between obesity and diabetes, and has focused its efforts in the study of the metabolic and molecular regulation of insulin resistance by adipose tissue, the impact of bariatric surgery glucose metabolism and the metabolic and non-metabolic complications of obesity.

Most relevant scientific articles

- Montanya E. Insulin resistance compensation: not just a matter of β-cells? Diabetes. 2014;63(3):832-834.
- Ceperuelo-Mallafre V., Durán X., Pachón G., Roche K., Garrido-Sánchez L., Vilarrasa N. et al. Disruption of GIP/GIPR axis in human adipose tissue is linked to obesity and insulin resistance. Journal of Clinical Endocrinology and Metabolism. 2014;99(5).
- Pizarro-Delgado J., Fasciani I., Temperan A., Romero M., González-Nieto D., Alonso-Magdalena P. et al. Inhibition of connexin 36 hemichannels by glucose contributes to the stimulation of insulin secretion. American Journal of Physiology - Endocrinology and Metabolism. 2014;306(12).
- Téllez N., Montanya E. Gastrin induces ductal cell dedifferentiation and β-cell neogenesis after 90% pancreatectomy. Journal of Endocrinology. 2014;223(1):67-78.
- Salord N., Gasa M., Mayos M., Fortuna-Gutiérrez A.M., Montserrat J.M., Sánchez-de-la-Torre M. et al. Impact of OSA on biological markers in morbid obesity and metabolic syndrome. Journal of Clinical Sleep Medicine. 2014;10(3):263-270.

Highlights

The group has seen renewed the consideration of Consolidated Research Group (SGR) for the 2014-16 period, in the 2014 call "Support to research groups in Catalonia" of the Agència de Gestió d'Ajuts Universitaris (AGAUR). The global socre of the group in this call was high enough to obtain also financial support in the highly competitive area of Medical Sciences and Health. The group has been awarded financial support for a second research project in the 2014 program Research Projects in Health, and therefore the two main lines of research of the group maintain competitive financial support from the Instituto de Salud Carlos III. The group has participated in two proposals of the Horizon 2020 research program of the EU, and one of them had advanced to second stage or evaluation at the end of year 2014. In addition to publications, the group members have acitvelly participated in national and international scientific meetings with abstract presentations, invited lectures and as abstracts reviewers. They have also participate as reviewers of research projects for public and private national and international institutions. Several members of the group take part in the direction board of national and international scientific associations in the area of diabetes and obesity. In the teaching area, a doctoral thesis and two master degrees have been completed. In terms of clinical guidelines and social impact, the President of the Diabetes Advisory Council of the Autonomous Catalan Government is a member of the research group and several members of the group contributed to the organization for the Diabetes World Day.

Institution: Fundación IDIBELL

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Unit of Cell Physiology and Nutrition IB-UMH

Programme: P3

Lead Researcher: Nadal Navajas, Ángel

Group members

STAFF MEMBERS: Castellano Muñoz, Manuel | Navarro García, Mª Luisa

ASSOCIATED MEMBERS: Alonso-Magdalena, Paloma | Arévalo Provencio, Marta | Fuentes Marhuenda, Esther | Irles Vidal, Esperanza | Lluesma Gómez, Mónica | Merino Antolín, Beatriz | Quesada Moll, Iván | Ripoll Orts, Cristina | Villar Pazos, Sabrina

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.

Most relevant scientific articles

- García-Arévalo M., Alonso-Magdalena P., Santos J.R.D., Quesada I., Carneiro E.M., Nadal A. Exposure to bisphenol-A during pregnancy partially mimics the effects of a high-fat diet altering glucose homeostasis and gene expression in adult male mice. PLoS ONE. 2014;9(6).
- Saavedra-Avila N.A., Sengupta U., Sanchez B., Sala E., Haba L., Stratmann T. et al. Cyclin D3 promotes pancreatic β-cell fitness and viability in a cell cycle-independent manner and is targeted in autoimmune diabetes. Proceedings of the National Academy of Sciences of the United States of America. 2014;111(33).
- Vieira E., Burris T.P., Quesada I. Clock genes, pancreatic function, and diabetes. Trends in Molecular Medicine. 2014;20(12):685-693.
- Rafacho A., Goncalves-Neto L.M., Santos-Silva J.C., Alonso-Magdalena P., Merino B., Taboga S.R. et al. Pancreatic alpha-cell dysfunction contributes to the disruption of glucose homeostasis and compensatory insulin hypersecretion in glucocorticoid-treated rats. PLoS ONE. 2014;9(4).
- Marroqui L., Alonso-Magdalena P., Merino B., Fuentes E., Nadal A., Quesada I. Nutrient regulation of glucagon secretion: Involvement in metabolism and diabetes. Nutrition Research Reviews. 2014;27(1):48-62.

Highlights

During 2014 we have described the mechanisms behind the adaptation of pancreatic alpha cells to glucocorticoid (GC) treatment. We found that GC induced hyperglucagonemia because it alters both alpha-cell function and mass. A second research line, has demonstrated the role that exposure to the endocrine disruptor Bisphenol-A during pregnancy has in offspring glucose metabolism. We demonstrated that male offspring exposed to Bisphenol-A in utero presented altered glucose tolerance and insulin secretion, aggravated after high fat diet treatment. Those mice presented an altered expression of key genes involved in fatty acid oxidation and lypogenesis in white adipose tissue and the liver.

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Metabolic and Molecular Disturbances in Diabetes

Programme: P1 y P3

Lead Researcher: Novials Sardà, Anna Maria

Group members

STAFF MEMBERS: Alcarraz Vizán, Gema | Brugnara, Laura | Castaño Pérez, Carlos | Murillo García, Serafín

ASSOCIATED MEMBERS: Cadavez Trigo, Lisa | Ceriello, Antonio | García Rovés González, Pablo Miguel | Montane Mogas, Joel | Moreno Asso, Alba | Parrizas Jiménez, Marcelina | Servitja Duque, Joan Marc | Visa Majoral, Montse

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.

Most relevant scientific articles

- Ceriello A., Novials A., Canivell S., La Sala L., Pujadas G., Esposito K. et al. Simultaneous GLP-1 and insulin administration acutely enhances their vasodilatory, antiinflammatory, and antioxidant action in type 2 diabetes. Diabetes Care. 2014;37(7):1938-1943.
- Cadavez L., Montane J., Alcarraz-Vizan G., Visa M., Vidal-Fabrega L., Servitja J.-M. et al. Chaperones ameliorate beta cell dysfunction associated with human islet amyloid polypeptide overexpression. PLoS ONE. 2014;9(7).
- La Sala L., Pujadas G., De Nigris V., Canivell S., Novials A., Genovese S. et al. Oscillating glucose and constant high glucose induce endoglin expression in endothelial cells: the role of oxidative stress. Acta Diabetologica. 2014.
- Tom R.Z., Garcia-Roves P.M., Sjogren R.J.O., Jiang L.Q., Holmstrom M.H., Deshmukh A.S. et al. Effects of AMPK activation on insulin sensitivity and metabolism in leptin-deficient ob/ob mice. Diabetes. 2014;63(5):1560-1571.
- Ceriello A., Novials A., Ortega E., Pujadas G., La Sala L., Testa R. et al. Hyperglycemia following recovery from hypoglycemia worsens endothelial damage and thrombosis activation in type 1 diabetes and in healthy controls. Nutrition, Metabolism and Cardiovascular Diseases. 2014;24(2):116-123.

Highlights

Among the overall results of our scientific productivity during 2014, we highlight publications in high-impact journals in our field, both in basic and clinical research, with special mention of our findings on: the effect of GLP-1 on endothelial function in patients with diabetes; the protective effect of chaperones on the response of the pancreatic beta-cell to endoplasmic reticulum stress under conditions of glucolipotoxicity; and the effect of AMPK activation on insulin sensitivity in obese leptin-deficient ob/ob mice.

Over the past year our group has received grants from different funding sources: Health Research Fund (FIS) grant from the Instituto de Salud Carlos III; Research Group Support (SGR) grant from the Government of Catalonia; a prestigious international grant from the European Foundation for the Study of Diabetes (EFSD) for investigating microRNAs involved in the pathogenesis of diabetes. The previous year, our group entered a 3-year collaborative agreement with Grífols company to study the potential of one of its pharmaceutical products for treating diabetes, as well as an agreement with Novartis for studying microRNAs as prediabetes biomarkers.

Two doctoral theses were defended in 2014, the results of which have been published in the same year and also the current one.

In collaboration with the Spanish Diabetes Society (SED), our group organized a theoretical/practical course on translation diabetes research, aimed at resident endocrinologists.

Finally, in terms of social outreach activities, the clinician group members have presented several educational sessions open to the public on the importance of lifestyle in achieving good diabetes control.

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Endocrinology and Nutrition Service

Programme: P1

Lead Researcher: Rojo Martínez, Gemma

Group members

STAFF MEMBERS: García Escobar, Eva | García Serrano, Sara | Linares Parrado, Francisca

ASSOCIATED MEMBERS: Almaraz Almaraz, María Cruz | Bermúdez Silva, Francisco Javier | Colomo Rodríguez, Natalia | De Antonio Esteva, Isabel | Gómez Zumaquero, Juan Miguel | González Molero, Immaculada | González Romero, María Stella | Lago Sampedro, Ana María | Martín Nuñez, Gracia María | Monastero, Roberto | Olveira Fuster, Gabriel | Rodríguez Pacheco, Francisca | Rubio Martin, Elehazara | Ruiz de Adana Navas, Soledad | Ruz Maldonado, Inmaculada | Valdés Hernández, Sergio

Main lines of research

- The biomolecular epidemiology of diabetes, obesity and metabolic syndrome (Pizarra Study, Egabro Study, di@bet .es Study).
- The study of insulin resistance in patients with extreme obesity undergoing bariatric surgery.
- Fatty acids, insulin resistance and adipocyte metabolism.
- Artificial nutrition and hiperglycaemia.
- New technologies applied to the treatment of type 1 diabetes.
- To study biomarkers in animal models and in vitro to elucidate the mechanisms of disease.

Most relevant scientific articles

- Martín-Nunez G.M., Cabrera-Mulero R., Rubio-Martín E., Rojo-Martínez G., Olveira G., Valdés S. et al. Methylation levels of the SCD1 gene promoter and LINE-1 repeat region are associated with weight change: An intervention study. Molecular Nutrition and Food Research. 2014;58(7):1528-1536.
- Rojo-Martínez G., Maymo-Masip E., Mar Rodriguez M., Solano E., Goday A., Soriguer F. et al. Serum sCD163 levels are associated with type 2 diabetes mellitus and are influenced by coffee and wine consumption: Results of the di@bet.es study. PLoS ONE. 2014;9(6).
- Valdés S., Maldonado-Araque C., Garcia-Torres F., Goday A., Bosch-Comas A., Bordiu E. et al. Ambient temperature and prevalence of obesity in the spanish population: The di@bet.es study. Obesity. 2014;22(11):2328-2332.
- Martín-Nunez G.M., Rubio-Martin E., Cabrera-Mulero R., Rojo-Martínez G., Olveira G., Valdés S. et al. Type 2 diabetes mellitus in relation to global LINE-1 DNA methylation in peripheral blood: A cohort study. Epigenetics. 2014;9(10):1322-1328.
- Gutiérrez-Repiso C., Soriguer F., Rojo-Martínez G., García-Fuentes E., Valdés S., Goday A. et al. Variable patterns of obesity and cardiometabolic phenotypes and their association with lifestyle factors in the Di@bet.es study. Nutrition, Metabolism and Cardiovascular Diseases. 2014.

Highlights

We are a research group with epidemiological, clinical and experimental projects, whose ultimate purpose is the study of the nature-nurture relationships in explaining the high prevalence of metabolic diseases such as diabetes. Our methodology is based on an ongoing dialogue between clinical, experimental and epidemiological observations. The group operates from a holistic understanding of human biology, and investigates the natural history of the disease conducting trials and evaluation studies of clinical practice to monitor risk factors, prevent diabetes and the onset of secondary pathology or improve the quality of life of patients.

Doctoral thesis:

- "Prevalence of hyperglycemia and diabetes in non-critically ill patients with total parenteral nutrition" (M. José Guerrero Tapia directed by G Olveira).
- "Evaluation of carbohydrate metabolism and diabetes risk in patients hospitalized for ischemic heart disease." (Natalia Rodríguez Colomo directed by F Soriguer and G Rojo Martínez).
- "Biomechanics of diabetic foot disease: experimental study of patients with type 1 diabetes mellitus with and without peripheral neuropathy" (Miguel Á Pérez Verdun, directed by S González Romero.).

To highlight: the group's participation in the call of AES with two large collaborative projects selected for funding:

- "Incidence of type 2 diabetes in the di@bet.es study: role of fatty acid transport system regulated by VEGFB in the development of metabolic diseases (PI 14/00710, Rojo Martinez G IP) coordinated with 4 others subprojects, which together have been awarded more than 500000€ to study various biomarkers of risk for diabetes (di@bet.es study).
- Understanding obesity (Ob), metabolic syndrome (MetS), type 2 diabetes (T2DM) and fatty liver disease (FL): a multidisciplinary approach" (PIE14/00031), excellence integrated project coordinated with other 11 CIBER groups with a budget of 660000€.

The group currently participates in the DEDIPAC and ENPADASI actions of JPI "A Healthy Diet for a Healthy Life".

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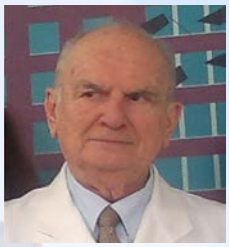
DIABETOBE

Programme: P1



Lead Researcher: Serrano Ríos, Manuel

Group members

STAFF MEMBERS: Pescador Sánchez, Nuria

ASSOCIATED MEMBERS: Bernat Jiménez, Antonia | Caso Pita, Covadonga | Corbatón Anchuelo, Arturo | Fernández Pérez, Cristina | Fernández Represa, Jesús Álvarez | Martínez Larrad, María Teresa | Zabena Carina, Alejandra

Main lines of research

- A genowide 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 obesity and associated metabolic disorders. Non coding microRNA. Target and Adipogenesis.
- The Segovia Study: a) The molecular and physiological determinants of lifestyle in diabetes/obesity studies. b) Analysis of genetic-epigenetic association in obesity/type 2 diabetes mellitus. c) Circulating MicroRNA levels in obesity, Type 2 DM and related conditions.

Most relevant scientific articles

- Martínez-Larrad M.T., Anchuelo A.C.N., Prado N.Y.D., Rueda J.M.I., Gabriel R., Serrano-Ríos M. Profile of individuals who are metabolically healthy obese using different definition criteria. A population-based analysis in the spanish population. PLoS ONE. 2014;9(9).
- Gutiérrez-Repiso C., Soriguer F., Rojo-Martinez G., García-Fuentes E., Valdes S., Goday A. et al. Variable patterns of obesity and cardiometabolic phenotypes and their association with lifestyle factors in the Di@bet.es study. Nutrition, Metabolism and Cardiovascular Diseases. 2014.
- Boada M., Antunez C., Ramírez-Lorca R., Destefano A.L., González-Pérez A., Gayan J. et al. ATP5H/KCTD2 locus is associated with Alzheimer's disease risk. Molecular Psychiatry. 2014;19(6):682-687.
- Gómez-Huelgas R., Pérez-Jiménez F., Serrano-Ríos M., González-Santos P., Román P., Camafort M. et al. Clinical decisions in patients with diabetes and other cardiovascular risk factors. A statement of the Spanish Society of Internal Medicine. Revista Clinica Espanola. 2014;214(4):209-215.
- Ruiz A., Heilmann S., Becker T., Hernández I., Wagner H., Thelen M. et al. Follow-up of loci from the International Genomics of Alzheimer's Disease Project identifies TRIP4 as a novel susceptibility gene. Translational Psychiatry. 2014;4.

Highlights

The main lines of research conducted during 2014 are:

- 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 obesity and associated metabolic disorders.
- The Segovia Study. The molecular and physiological determinants of lifestyle in diabetes/obesity studies. Analysis of genetic-epigenetic association in obesity type 2 diabetes mellitus. An epidemiological study. MicroRNA obesity and type 2 DM and related conditions.

These works were funded by:

- MOIR S2010/BMD-2423, Comunidad Autónoma de Madrid.
- Educational Grants from Eli Lilly Lab, Spain.

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Diabetes and Metabolism Research Group

Programme: P2 y P4

Lead Researcher: Simó Canonge, Rafael

Group members

STAFF MEMBERS: Bogdanov, Patricia Mónica | Corraliza Márquez, Lidia | García Ramírez, Marta | Ramos Pérez, Lorena

ASSOCIATED MEMBERS: Ciudín, Andreea | Enquix Elena, Natalia | Hernández Pascual, Cristina | Lecube Torello, Albert | Martínez Selva, David | Mesa Manteca, Jorge | Sáez López, Cristina | Sola Adell, Cristina | Villena Delgado, Josep Antoni

Main lines of research

- Physiopathology of diabetic retinopathy
  The main aim of this line of research is to identify new targets for the treatment of diabetic retinopathy (DR). In this regard it should be noted that we are coordinating the first clinical trial aimed at testing the effectiveness and safety of neuroprotective agents for the treatment of DR (EudraCT -2012-001200-38). This project has been funded by EC (EUROCONDOR-HEALTH-2011- FP7-278040). In addition, is also noteworthy that we are partners of the project "Early Prevention of Diabetes Complications in people with hyperglycaemia in Europe" (e-PREDICE. FP7-279074) in which we are the responsible for measuring the biomarkers of DR.
- Insulin resistance and obesity: new pathogenic candidates and the study of co-morbidities.
  The main objective is to investigate the pathogenic mechanisms of obesity and its co-morbidities and to find out new therapeutic targets. As a result of our recent findings we are giving priority to the role of sex hormone binding globulin (SHBG) and mitochondrial dysfunction in the pathogenesis of obesity, insulin-resistance and type 2 diabetes.

- Endothelial dysfunction, dyslipideamia and cardiovascular disease in type 2 diabetes.
  We are exploring non-classic cardiovascular risk factors. In this setting is worth mentioning our key participation in the project "Preventing cardiovascular ischemic events and arresting their consequences in type 2 diabetic population: a multidisciplinary clinical and experimental approach", which has been funded by the *Ministerio de Economía y Competitividad*.
- Diabetes as a metabolic accelerator of Alzheimer's disease.
  In this regard it should be noted that we are developing the project "Retinal Neurodegeneration in Type 2 diabetes as biomarker for Alzheimer´s disease" funded by European Foundation for the Study of Diabetes (EFSD).

Most relevant scientific articles

- Sacks F.M., Hermans M.P., Fioretto P., Valensi P., Davis T., Horton E. et al. Association between plasma triglycerides and high-density lipoprotein cholesterol and microvascular kidney disease and retinopathy in type 2 diabetes mellitus: A global case-control study in 13 countries. Circulation. 2014;129(9):999-1008.
- Simo R., Hernández C. Neurodegeneration in the diabetic eye: New insights and therapeutic perspectives. Trends in Endocrinology and Metabolism. 2014;25(1):23-33.
- Simo R., Sundstrom J.M., Antonetti D.A. Ocular anti-VEGF therapy for diabetic retinopathy: The role of VEGF in the pathogenesis of diabetic retinopathy. Diabetes Care. 2014;37(4):893-899.
- Saez-López C., Soriguer F., Hernández C., Rojo-Martínez G., Rubio-Martín E., Simo R. et al. Oleic acid increases hepatic sex hormone binding globulin production in men. Molecular Nutrition and Food Research. 2014;58(4):760-767.
- Simo R., Sáez-López C., Lecube A., Hernández C., Fort J.M., Selva D.M. Adiponectin upregulates SHBG production: Molecular mechanisms and potential implications. Endocrinology. 2014;155(8):2820-2830.

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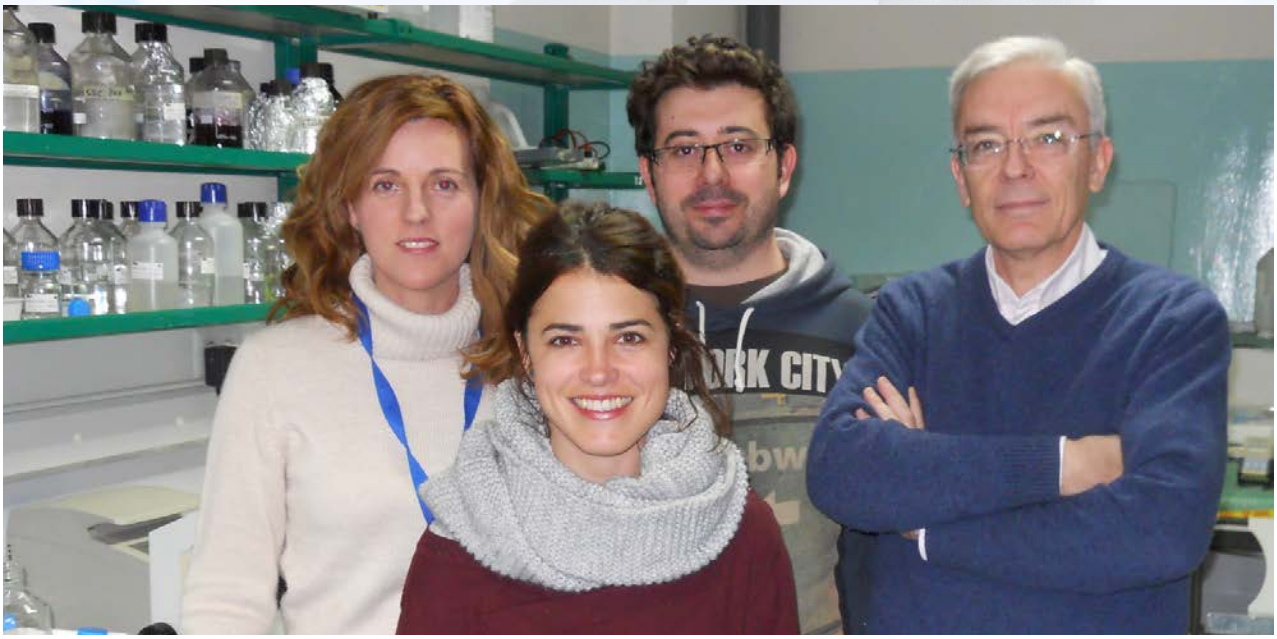
Transcriptional mechanisms of pancreatic function

Programme: P3



Lead Researcher: Vallejo Fdez. de la Reguera, Mario

Group members

STAFF MEMBERS: Fernández Pérez, Antonio | Mirasierra Cuevas, Mercedes

ASSOCIATED MEMBERS: Ruiz Cañas, Laura

Main lines of research

- The characterization of phenotypic alterations of pancreatic islets in the absence of the homeoprotein 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.

Most relevant scientific articles

- Fernández-Pérez A., Vallejo M. Pdx1 and USF transcription factors co-ordinately regulate Alx3 gene expression in pancreatic β-cells. Biochemical Journal. 2014;463:287-296.

Highlights

During 2014 we have discovered a mechanism by which Alx3 regulates glucagon gene expression in response to changes in glucose concentration. When glucose levels are high pancreatic glucagon secretion is inhibited, and our data indicate that its synthesis also decreases by an inhibitory mechanism that operates at the transcriptional level. Glucose induces the expression of Alx3 in pancreatic alpha cells, which promotes its interaction with the transcription factor Pax6, preventing the binding of Pax6 to one of the regulatory elements of the glucagon promoter. This mechanism may have implications in the pathogenesis of diabetes mellitus, as this disease may evolve with abnormally high levels of glucagon (Mirasierra M, Vallejo M:. Glucose-dependent inhibition of glucagon gene expression regulated by selective interactions between Alx3 and Pax6. Submitted).

Regarding studies on metabolic regulation, we found that Alx3 is expressed in the arcuate nucleus of the hypothalamus, and is involved in the regulation of food intake and energy metabolism. Some of these studies have been performed in collaboration with the group led by Dr. Sebastian Cerdán (Instituto de Investigaciones Biomédicas Alberto Sols, CSIC), which allowed the evaluation of glucose detection in the hypothalamus using functional magnetic resonance imaging (Lizarbe B, Fernández-Pérez A, Caz V, López-Larrubia P, Vallejo M, Cerdan S: Glucose sensing in the fasted mouse hypothalamus as detected by functional MRI methods An integrative approach. Submitted).

Finally, our group oversees the management of the Indirect Calorimetry and Energy Metabolism Unit (UCIME), which provides the use of a Phenomaster system (TSE Systems) as a technology platform provided by Ciberdem for evaluating energy metabolism in rodents.

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Pharmacological targets in inflammation and metabolic diseases

Programme: P4

Lead Researcher: Vázquez Carrera, Manuel

Group members

STAFF MEMBERS: Barroso Fernández, Emma de Juan | Palomer Tarrida, Francisco Javier

ASSOCIATED MEMBERS: Botteri, Gaia | Salvadó Serra, Laia

Main lines of research

Our main research topic is the study of the molecular mechanisms involved in the link between inflammation and insulin resistance. Specifically, we are interested in:

- Evaluating the molecular mechanisms by which PPAR agonists prevent inflammation and insulin resistance.
- Studying the molecular mechanisms responsible for metabolic alterations in diabetic cardiomyopathy.
- Studying how oleic acid prevents saturated fatty acid-induced insulin resistance.
- Assessing the links between insulin resistance and Alzheimer's disease.

Most relevant scientific articles

- Salvadó L., Barroso E., Gómez-Foix A.M., Palomer X., Michalik L., Wahli W. et al. PPARβ/δ prevents endoplasmic reticulum stress-associated inflammation and insulin resistance in skeletal muscle cells through an AMPK-dependent mechanism. Diabetologia. 2014.
- Palomer X., Capdevila-Busquets E., Botteri G., Salvadó L., Barroso E., Davidson M.M. et al. PPARβ/δattenuates palmitate-induced endoplasmic reticulum stress and induces autophagic markers in human cardiac cells. International Journal of Cardiology. 2014;174(1):110-118.
- Pedros I., Petrov D., Allgaier M., Sureda F., Barroso E., Beas-Zarate C. et al. Early alterations in energy metabolism in the hippocampus of APPswe/PS1dE9 mouse model of Alzheimer's disease. Biochimica et Biophysica Acta - Molecular Basis of Disease. 2014;1842(9):1556-1566.
- Torres M., Palomer X., Montserrat J.M., Vázquez-Carrera M., Farre R. Effect of ovariectomy on inflammation induced by intermittent hypoxia in a mouse model of sleep apnea. Respiratory Physiology and Neurobiology. 2014;202:71-74.
- Palomer X., Capdevila-Busquets E., Garreta G., Davidson M.M., Vázquez-Carrera M. PPARα attenuates palmitate-induced endoplasmic reticulum stress in human cardiac cells by enhancing AMPK activity. Clinica e Investigacion en Arteriosclerosis. 2014;26(6):255-267.

Highlights

PROJECTS

- Title: Hyperinsulinemia and inflammation as negative regulators of insulin sensitivity: exploring the effects of PPARβ/δ activators and oleic acid in in vitro and in vivo models of insulin resistance. Reference: SAF2012-30708. Financing entity: Ministerio de Economía y Competitividad. Principal researcher: Manuel Vázquez Carrera.
- Title: Synthesis and pharmacological evaluation of new molecules with antidiabetic properties (SAFNAD). Reference: UBAR012688. Financing entity: Generalitat de Catalunya (ACC10) and CIDQO 2012. Principal researcher: Santiago Vázquez Cruz.

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Complex Metabolic diseases and Mitochondria

Programme: P2 y P4

Lead Researcher: Vendrell Ortega, Joan Josep

Group members

STAFF MEMBERS: Durán Sanmartí, Francesc Xavier | Maymo Masip, Elsa | Miranda Guardiola, Mercedes

ASSOCIATED MEMBERS: Cerperuelo Mallafre, María Victoria | Ejarque Carbo, Miriam | Escoté Miró, Xavier | Fernández Veledo, Sonia | Gallart Millán, Lluís | Gutiérrez Fornés, Cristina | Llaurado Cabot, Gemma | Megía Colet, Anna | Näf Cortés, Silvia | Pachón Peña, Olga Gisela | Roche, Kelly | Rodríguez Chacón, Matilde | Serena Perello, Carolina | Simón Muela, Inmaculada | Solano Fraile, Esther | Yáñez García, Rosa Elena

Main lines of research

- Adipose Tissue Plasticity: Molecular basis of insulin resistance; Adipocyte apoptosis and proliferation during obesity; Adipose tissue-derived mesenchymal stem cells from obesity states; Browning capacity of white adipose tissue.
- Role of lipid metabolism in the functionality of adipose tissue during obesity. Study of the lipin protein family.
- Role of inflammation in obesity and insulin resistance.
- Metabolic disorders associated with Gestational Diabetes.
- Biomarkers of atherosclerotic risk in pathologies associated with a high cardiovascular morbidity and mortality.

Most relevant scientific articles

- García-Guerra L., Vila-Bedmar R., Carrasco-Rando M., Cruces-Sande M., Martín M., Ruiz-Gómez A. et al. Skeletal muscle myogenesis is regulated by G protein-coupled receptor kinase 2. Journal of Molecular Cell Biology. 2014;6(4):299-311.
- Ceperuelo-Mallafre V., Duran X., Pachón G., Roche K., Garrido-Sánchez L., Vilarrasa N. et al. Disruption of GIP/GIPR axis in human adipose tissue is linked to obesity and insulin resistance. Journal of Clinical Endocrinology and Metabolism. 2014;99(5).
- Vilades C., Escote X., López-Dupla M., Martínez E., Domingo P., Asensi V. et al. Involvement of the LPS-LPB-CD14-MD2-TLR4 inflammation pathway in HIV-1/HAART-associated lipodystrophy syndrome (HALS). Journal of Antimicrobial Chemotherapy. 2014;69(6):1653-1659.
- Lucas E., Jurado-Pueyo M., Fortuno M.A., Fernández-Veledo S., Vila-Bedmar R., Jiménez-Borreguero L.J. et al. Downregulation of G protein-coupled receptor kinase 2 levels enhances cardiac insulin sensitivity and switches on cardioprotective gene expression patterns. Biochimica et Biophysica Acta - Molecular Basis of Disease. 2014;1842(12):2448-2456.
- Garrido-Sánchez L., Roca-Rodríguez M.D.M., Fernández-Veledo S., Vendrell J., Yubero-Serrano E.M., Ocana-Wilhelmi L. et al. CCNG2 and CDK4 is associated with insulin resistance in adipose tissue. Surgery for Obesity and Related Diseases. 2014;10(4):691-696.

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Heterogenic And Polygenic Diseases

Programme: P4

Lead Researcher: Zorzano Olarte, Antonio

Group members

STAFF MEMBERS: Muñoz Neculman, Juan Pablo | Romero De Pablos, Montserrat | Saska, Ivanova | Sebastián Muñoz, David

ASSOCIATED MEMBERS: Camprubí, Marta Camps | Castrillón Rodríguez, Ignacio | Díaz Ramos, Maria Àngels | Enciso Salas, Hilda Yuliana | Guma García, Ana María | Hernández Álvarez, María Isabel | Martínez Cristóbal, Paula | Rodríguez Nuevo, Aida | Sabaté Pérez, Alba | Sánchez Feutrie, Manuela | Testar Ymbert, Xavier

Main lines of research

Molecular mechanisms involved in the development of insulin resistance and type 2 diabetes and identification of novel targets for diabetes therapy:

- Analysis of the role of mitochondrial dynamics proteins in metabolic homeostasis, in the control of insulin signalling, and in the response to cell stress,
- Role of interplay between autophagy, mitochondrial function and energy metabolism,
- Analysis of the metabolic role of neuregulins.

Most relevant scientific articles

- Martín O.J., Lai L., Soundarapandian M.M., Leone T.C., Zorzano A., Keller M.P. et al. A role for peroxisome proliferator-activated receptor γ coactivator-1 in the control of mitochondrial dynamics during post-natal cardiac growth. Circulation Research. 2014;114(4):626-636.
- Sala D., Ivanova S., Plana N., Ribas V., Durán J., Bach D. et al. Autophagy-regulating TP53INP2 mediates muscle wasting and is repressed in diabetes. Journal of Clinical Investigation. 2014;124(5):1914-1927.
- Pennanen C., Parra V., López-Crisosto C., Morales P.E., del Campo A., Gutiérrez T. et al. Mitochondrial fission is required for cardiomyocyte hypertrophy mediated by a Ca2+-calcineurin signaling pathway. Journal of Cell Science. 2014;127(12):2659-2671.
- Martorell-Riera A., Segarra-Mondejar M., Munoz J.P., Ginet V., Olloquequi J., Pérez-Clausell J. et al. Mfn2 downregulation in excitotoxicity causes mitochondrial dysfunction and delayed neuronal death. EMBO Journal. 2014;33(20):2388-2407.
- Rosell A., Meury M., Álvarez-Marimón E., Costa M., Perez-Cano L., Zorzano A. et al. Structural bases for the interaction and stabilization of the human amino acid transporter LAT2 with its ancillary protein 4F2hc. Proceedings of the National Academy of Sciences of the United States of America. 2014;111(8):2966-2971.

Highlights

- PATENT: Inventors: Carles Cantó Àlvarez, Sameer Kulkarni, Antonio Zorzano. Title: Methods and uses of mitofusins. Application number: 14192012.4-1408

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Centro de Investigación Biomédica en Red
Diabetes y Enfermedades Metabólicas Asociadas

MINISTERIO DE ECONOMIA Y COMPETITIVIDAD

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