

2014



research science innovation commitment





### Introduction

The Report for 2014 of the Sant Joan de Déu Barcelona Research Foundation covers the work carried out by a group of professionals who have endeavoured to generate new knowledge. It should be pointed out that the results which are presented here would not have been possible without the contributions of many different professionals, including physicians, basic researchers, technicians, advanced degree holders in a wide range of fields, and nursing personnel and administrative staff, among others.

The Foundation's work is set within the frame of the activity of the Hospitaller Order of St. John of God, an organisation which, with its spirit of hospitality and its universal character, seeks to shelter, attend to and help all people, especially those who are most vulnerable or who have problems of social integration or health.

The mission of the Foundation is to contribute to the improvement of people's health and welfare, promoting, supporting and coordinating research and innovation at the centres maintained by the Order of St. John of God in accordance with its values, striving to achieve efficiency and to carry out our tasks through networked operation while bearing in mind our ethical commitment and our scientific and social orientation at all times.

Specifically, the Foundation's research is organised around eight consolidated research groups, on which further information is provided in this report, and three emerging groups under training, which are also listed in this document. Our research, which is conducted in various fields of knowledge, is primarily focused on maternal and children's health and on mental health, although we also have groups which are doing research in other areas, for example on socially vulnerable populations.

Over the course of 2014, 207 research projects have been carried out. Of this total, 162 were competitive projects, with 145 of them receiving competitive financing from Spanish entities and 17 from international entities, while the other 45 projects obtained non-competitive financing. Likewise, 95 clinical trials and 72 observational studies were conducted. The biobanks of our two hospitals (Sant Joan de Déu Barcelona Healthcare Park and Hospital Sant Joan de Déu) continued to form part of the Biobanks RETICS (Thematic Network for Cooperative Health Research) of the Carlos III Health Institute. We wish to make special mention of our research groups' firm will to foster networking, as is made evident by their presence in cooperative research structures promoted by the Carlos III Health Institute. Indeed, in 2014 we formed part of the Centre for Biomedical Network Research on Rare Diseases (CIBERER), the Centre for Biomedical Network Research on Diabetes (CIBERDEM) and the Centre for Biomedical Network Research on Mental Health (CIBERSAM). We have also participated in the thematic networks on primary healthcare (RedIAPP), on maternal and children's health and development (SAMiD), and on innovation in medical and healthcare technologies (iTEMAS). Moreover, we are strengthening our international collaborations in addition to promoting collaborations at national level: for example, we are present in the European Innovation Partnership on Active and Healthy Ageing (EIP-AHA), we take part in the European COST network in the area of Social Sciences and Humanities, and we lead another COST network in the field of Forensic Psychiatry. In the European context, we participate in several initiatives, including a total of 12 projects of the 7th Framework Programme and of the SANCO Public Health Programme, both of which are promoted by the European Commission. It should also be pointed out that one Marie Curie Reintegration Grant project has been started in addition to the 11 FIS projects awarded by the Carlos III Health Institute, which include one Río Hortega grant, one Sara Borrell contract, and two intensification programmes.

While the Foundation keeps focusing on the transfer of knowledge, innovation has continued to be an area of special importance and interest. In 2014, 299 articles have been published with a total impact factor of 1,157 points. Likewise, in addition to the patents which have already been obtained, we have been actively seeking patent protection for two new inventions.

All this has entailed a significant increase in the funds devoted to research. Specifically, this year the Foundation's budget has totalled a sum of about 6.5 million euros.

We do not wish to conclude these words without expressing our gratitude to all the people who have made this wide-ranging activity possible. Firstly, we wish to thank those who have suffered illnesses and their families for helping us to achieve a better understanding of health problems and for cooperating on our Projects We are also especially thankful for the help we have received from the donors and volunteers of the Foundation who, with their effort and contributions, provide us with resources that are essential to further research. Their support gives an added value to our work since it goes to show that our efforts have a bearing and an impact on society.



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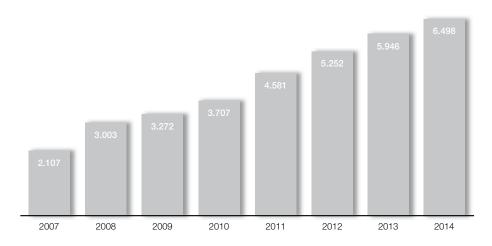
## Services and infrastructures

The Sant Joan de Déu Research Foundation makes available to its researchers a set of fundamental services and infrastructures for the performance of their Projects

In order to facilitate high-level research, the Foundation offers its professionals technical, scientific and support services as well as the most suitable infrastructures required to carry out their work:

- Methodological and statistical support.
- Neurological tissue bank, paediatric biological tissues bank and tumour bank.
- Library.
- Animal housing facility.
- Molecular diagnosis laboratory.
- · Sequencing unit.

# Financial resources management



(thousands of euros)



## Consolidated research groups

# **Developmental cancer**

The group is dedicated to clinical, translational and basic research on developmental tumours. The main goals are: 1) to develop all the molecular and cellular biology techniques necessary for the diagnosis, prognosis and monitoring of developmental tumour patients, and 2) to conduct research addressed to improving the diagnostic, prognostic and treatment processes of such patients.

#### Research team

Coordinator	Dr. Jaume Mora
Laboratory lead researchers	Guillermo Chantada, Mª Inmaculada Hernández, Mireia Camós, Carmen de Torres, Cinzia Lavarino, Ángel M. Carcaboso
Clinical lead researchers	Ruben Berrueco, Albert Català, Ofelia Cruz, Veronica Celis, Andreu Parareda, Susana Rives, Héctor Salvador, Montserrat Torrebadell, Andrés Morales
Post-doctoral researchers	Carlos Rodríguez, Silvia Mateo, Marta García, Sara Sánchez, Sonia Paco
Pre-doctoral researchers	Soledad Gómez, Roberta Malatesta, Nerea Vega, Carles Monterrubio, Nagoré Gené, Guillem Pascual, Elisabeth Figuerola, Anna Alonso, María Trabazo, Montse Meseguer, Sara Jaume
Laboratory and tumour bank technicians	Eva Rodríguez, Isadora Lemos, Noelia Salvador, Mónica Vilà, Camino Estella

### Research lines

### Preclinical pharmacology and drug release in solid tumours

Dr. Ángel Montero-Carcaboso

Search for new pharmacological treatments in solid tumours (neuroblastoma, diffuse intrinsic pontine glioma/DIPG, Ewing's sarcoma, retinoblastoma). Study of the penetration of chemotherapeutic agents in preclinical models of solid tumours. Development of preclinical disease models (neuroblastoma, DIPG, rhabdomyosarcoma, Ewing's sarcoma, retinoblastoma) from biobank samples. Development of new systems of chemotherapy release in solid tumours.

### Translational research on neuroblastoma

Dr. Jaume Mora

Study of the origin of neuroblastoma and phenotypic and genotypic characterisation of the various cell populations forming the neuroblastoma. Research on the existence of tumour stem cells or progenitor cells of neuroblastic tumours. Advance in the molecular classification of the various clinical subtypes of neuroblastoma. Improvement of the treatment of patients with high-risk neuroblastoma through the study of preclinical pharmacology.



### Translational research on central nervous system tumours

Dr. Ofelia Cruz and Dr. Andrés Morales

Development and evaluation of new treatment protocols. Definition of prognostic characteristics of the various paediatric gliomas. Characterisation of molecular changes involved in childhood brain tumours (gliomas, DIPG, medulloblastomas, ependymomas and others).

### Leukaemia and non-malignant blood disorders

Dr. Mireia Camós

The main goal of this research line is to achieve a better knowledge of the etiopathogenesis and molecular bases of paediatric blood disorders and to find ways to translate new diagnostic, prognostic and therapeutic tools for these disorders to clinical practice. Research has been started on the role of the regulatory pathways of haematopoietic stem cells in infants under the age of 12 months with acute leukaemia.

### Translational research on Ewing's sarcoma

Dr. Jaume Mora

Study of the origin of Ewing's sarcoma and phenotypic and genotypic characterisation of the various clinical subtypes. Research on the existence of tumoral stem cells or progenitor cells. Improvement of the treatment of patients with Ewing's sarcoma through the study of preclinical pharmacology.

### Integral treatment of patients with retinoblastoma

Dr. Guillermo Chantada

Integral treatment of retinoblastoma patients, with special emphasis on treatment with intra-arterial chemotherapy (IAC). Treatments with different protocols of systemic, induction or post-surgery chemotherapy according to histological criteria of risk and treatment with chemotherapy. Medium- and long-term monitoring of patients with RTB background and especially of those treated with IAC.

### **Projects**

- Translational research program in diffuse intrinsic pontine gliomas. Hospital Sant Joan de Déu Esplugues HSJD. April 2014 – April 2017. Pl: Angel Montero-Carcaboso.
- Genetic and epigenetic study of the regulatory molecular pathways of haematopoietic progenitor cells in paediatric leukaemias with rearrangement of the MLL gene. Fundación CRIS de Investigación para Vencer el Cáncer. March 2014
   March 2017. Pl: Mireia Camos.
- Evaluation of the calcium-sensing receptor and PTHrP as new therapeutic targets in neuroblastoma. Analysis of the expression and function of the GCM transcription factors in these developmental tumours. (CELLEX). Fundació Privada CELLEX. January 2014 – January 2014. Pl: Carmen de Torres.
- Biological studies group for paediatric acute lymphoblastic leukaemia (LAL): harmonisation and standardisation of diagnosis and follow-up of minimal residual disease and promotion of cooperative research. Fundación Sandra Ibarra de Solidaridad Frente al Cáncer. January 2014 January 2014. Pl: Mireia Camos.
- 2014SGR1398 Developmental tumours research group. Agaur Agència de Gestió d'Ajuts Universitaris i de Recerca. January 2014 – December 2016. Pl: Jaume Mora.
- Translational research programme on diffuse intrinsic pontine. Contrato Miguel Servet I. Instituto de Salud Carlos III. January 2014 January 2019. Pl: Angel Montero-Carcaboso.
- Translational research program in diffuse intrinsic pontine. Proyecto asociado a contrato Miguel Servet I. Instituto de Salud Carlos III. January 2014 – December 2016. Pl: Angel Montero-Carcaboso.
- Search, validation and clinical translation of new therapeutic targets based on the study of genomics and integrative proteomics in Ewing's sarcoma. Asociación Española Contra el Cáncer. October 2013 – September 2018. Pl: Jaume Mora.
- Study of molecular pathways regulating haematopoietic progenitor cells in paediatric leukaemias with rearrangement of gene MLL. Hospital Sant Joan de Déu - Esplugues HSJD. March 2013 – February 2016. Pl: Mireia Camos.



- Preclinical study of the effectiveness of inhibitor TG101348 in ex vivo cells of acute lymphoblastic leukaemia: evaluation of the disease in vivo in immunodeficient mice. Fundación para la Investigación Biomédica del Hospital Universitario la Princesa (FIBHUP). February 2013 – February 2014. PI: Mireia Camos.
- Study of molecular pathways regulating haematopoietic progenitor cells in paediatric leukaemias with rearrangement of gene MLL. Instituto de Salud Carlos III. January 2013 – December 2015. Pl: Mireia Camos.
- Molecular mechanisms involved in the development of paediatric leukaemias. Fundación Científica de la Asociación Española Contra el Cáncer (AECC); Fundación Instituto Mar de Investigaciones Médicas. September 2012 – August 2015. Pl: Mireia Camos.
- CHD5, PAFAH1B1 and NME1: Markers for prognosis and prediction of therapeutic response in neuroblastoma. Chemoresistance mechanisms. Hospital Sant Joan de Déu - Esplugues HSJD. April 2012 – March 2015. Pl: Cinzia Lavarino.
- CHD5, PAFAH1B1 and NME1: Markers for prognosis and prediction of therapeutic response in neuroblastoma. Chemoresistance mechanisms. Instituto de Salud Carlos III (ISCIII). January 2012 – December 2015. Pl: Cinzia Lavarino.
- Limited distribution of drugs in tumoral microenvironment as the cause of chemoresistance in neuroblastoma. Fundación Banco Bilbao Vizcaya Argentaria. January 2012 December 2015. Pl: Angel Montero-Carcaboso.
- Limited distribution of drugs in tumoral microenvironment as the cause of chemoresistance in neuroblastoma. Call for proposals: National R&D&I Programme, Fundamental Research Projects Subprogramme 2011; Category A: Young Researcher. Ministerio de Ciencia e Innovación. January 2012 December 2015. Pl: Angel Montero-Carcaboso.
- Neuroblastoma NEN. Associació de familiars i amics de pacients amb neuroblastoma. January 2012-. Pl: Cinzia Lavarino.
- Research on Ewing's sarcoma Asociación Pablo Ugarte. Asociación Pablo Ugarte. May 2011-. Pl: Jaume Mora.
- Neuroblastoma Chemo. Chemotherapy of neuroblastoma. Marie Curie Fellowship PIRG08-GA-2010-276998 European Commission. March 2011 – March 2015. Pl: Angel Montero-Carcaboso.
- Evaluation of the calcium-sensing receptor as a new tumour-suppressing gene and therapeutic target in neuroblastoma. Fundació Privada CELLEX. January 2011 April 2014. Pl: Carmen de Torres.
- Preclinical and translational pharmacology in neuroblastoma. Call for proposals: Grants for oncology researchers 2010;
   Category B: Return. Fundación Científica de la Asociación Española Contra el Cáncer (AECC). October 2010 January 2014. Pl: Jaume Mora.

### Clinical trials

- Open single-arm study to evaluate the long-term safety and efficacy of romiplostim in thrombocytopaenic paediatric
  patients with immune thrombocytopaenic purpura (ITP). AMGEN. October 2014-. Pl: Ruben Berrueco.
- Open randomised active comparator-controlled clinical trial to evaluate the safety, efficacy, and pharmacokinetic and pharmacodynamic properties of oral rivaroxaban during 30 days of treatment, in children with diverse manifestations of venous thrombosis. Bayer Pharma AG. September 2014-. Pl: Ruben Berrueco.
- Multi-centre randomised open active comparator-controlled clinical trial to evaluate the efficacy and safety of rivaroxaban at a dose adjusted to the age and weight of children with acute venous thromboembolism. Bayer Pharma AG. September 2014-. Pl: Ruben Berrueco.
- Multi-centre open single-arm two-part phase I/IIA study to determine the safety, tolerability and pharmacokinetics of oral dabrafenib in children between the ages of 12 months and 18 years with advanced solid tumours and positive BRAF V600 mutation. Glaxosmithkline. September 2014-. PI: Jaume Mora.
- Multi-centre open phase I study to evaluate the pharmacokinetics and safety of naloxegol in paediatric patients between the ages of 6 months and 18 years receiving treatment with opioids. Astrazéneca Farmacéutica Spain. Astrazéneca (Gabinete de prensa). July 2014-. Pl: Jaume Mora.
- Uncontrolled single-centre phase II clinical trial of dinutuximab (CH 14.18) with the cytokines GM-SCF (granulocyte-macrophage colony-stimulating factor) and IL-2 in patients with high-risk neuroblastoma who are not candidates for other immunotherapy trials. Fundació Privada per a la Recerca i la Docència Sant Joan de Déu. May 2014-. Pl: Jaume Mora.
- Project for updating the study on congenital haemophilia in Spain (PUCHS). Retrospective non-interventionist multi-centre study of the prevalence of haemophilia in Spain. Novo Nordisk Pharma. May 2014-. Pl: Teresa Toll.



- Multi-centre open phase I increasing-dose study of a single group, with monitoring of efficacy, to evaluate vemurafenib (ro5185426) in children and adolescents with surgically incurable and unresectable melanoma in stage iiic or iv presenting BRAF V600 mutations. F. Hoffmann- La Roche Ltd; Hospital Sant Joan de Déu - Esplugues HSJD; Quintiles. February 2014-. Pl: Ofelia Cruz.
- Formation of a Spanish cohort of childhood cancer survivors: SPAIN-CCSS cohort. January 2014-. PI: Héctor Salvador.
- Randomised open comparative combined phase 1/2 dose-finding study to evaluate the efficacy and safety of plerixafor together with standard regimes for mobilisation of haematopoietic stem cells in peripheral blood, and subsequent
  harvest by apheresis, versus only standard regimes for mobilisation in paediatric patients between the ages of 2 and
  18 years with solid tumours meeting requirements for autologous transplantations. January 2014-. Pl: Susana Rives.
- Observational prospective study of the expression of ABCB1/P-glycoprotein as a factor for the biological stratification of non-metastatic osteosarcoma of the extremities. Grupo Español de Investigación en Sarcoma. January 2014-. Pl: Jaume Mora.
- Phase II study of ipilimumab in children and adolescents (from 12 to <18 years) with unresectable malignant melanoma
  in stage III or stage IV, previously treated or untreated. Bristol-Myers Squibb International Corporation (BMSIC); Hospital
  Sant Joan de Déu Esplugues HSJD. November 2013-. Pl: Ofelia Cruz.</li>
- Rare sarcomas register: A tool to help to evaluate the number of cases of each subtype and their therapeutic orientation by the Spanish Research Group on Sarcomas (GEIS). Grupo Español de Investigación en Sarcoma. November 2013-. Pl: Jaume Mora.
- Prospective multi-centre phase II trial with gemcitabine and rapamycin as second-line treatment of metastatic osteo-sarcoma. GEIS 29. January 2013-. Pl: Jaume Mora.
- Monoclonal chimeric recombinant CH 14.18 antibody. April 2013-. Pl: Jaume Mora.
- Phase I/II study of sunitinib in young patients with advanced digestive stroma tumour. Cetir Centre Mèdic; Hospital Sant Joan de Déu - Esplugues HSJD; Pfizer, S.L.U. April 2013-. PI: Ofelia Cruz.
- Controlled randomised open multi-centre phase III study to evaluate the safety and efficacy of oral LDE225 versus temozolomide in recurrent medulloblastoma patients with activation of the Hh pathway. Hospital Sant Joan de Déu Esplugues HSJD; Novartis Farmacéutica. April 2013-. Pl: Ofelia Cruz.
- Multi-centre adaptive randomised open phase IB study of the pharmacokinetics and pharmacodynamics of oseltamivir (Tamiflu®) in the treatment of influenza in immunocompromised patients between the ages of 0 and 18 years, with
  confirmed influenza infection. F. Hoffmann- La Roche; Hospital Sant Joan de Déu Esplugues HSJD. January 2013-.
  Pl: Ruben Berrueco.
- Active comparator-controlled randomised partly masked phase IV study to evaluate the pharmacokinetics and pharmacodynamics, safety and tolerability of fosaprepitant in paediatric patients for the prevention of emetogenic chemotherapy-induced nausea and vomiting (CINV). Hospital Sant Joan de Déu Esplugues HSJD; Merck, Sharp & Dohme de España. October 2012-. Pl: Jaume Mora.
- Database of ADVATE (AHEAD) results in haemophilia A. SynteractHCR Benelux. July 2012-. Pl: Teresa Toll.
- Intergroup study for children and adolescents with non-Hodgkin's B lymphoma or lymphoblastic B-cell leukaemia;
   evaluation of effectiveness and safety of rituximab in high-risk patients. Hospital Sant Joan de Déu Esplugues HSJD;
   Sociedad Española de Hematología y Oncología Pediátricas. July 2012-. Pl: Veronica Celis.
- Randomised open comparative multi-centre phase II study of bevacizumab treatment in paediatric patients with recently diagnosed supratentorial high-grade glioma. F. Hoffmann-La Roche. April 2012-. Pl: Ofelia Cruz.
- Multi-centre paediatric register of disease in essential thrombocythaemia (ET). Shire Pharmaceuticals Iberica. May 2011-. Pl: Teresa Toll.
- Prospective multi-centre uncontrolled phase II clinical trial of intensive chemotherapy, surgery and radiotherapy in tumours of the Ewing's sarcoma family in children, adolescents and adults. Ministerio de Sanidad y Política Social. January 2010 – June 2015. PI: Jaume Mora.
- Post-authorisation observational study of the safety of FEIBA (factor VIII anti-inhibitor coagulant complex). Uncontrolled open non-interventionist observational cohort study of FEIBA in haemophilic patients with inhibitor. Estudio FEIBA. January 2010-. Pl: Teresa Toll.
- First intergroup international study of classic Hodgkin's lymphoma in children and adolescents. Euronet-PHL-C1 January 2009-. Pl: Ofelia Cruz.
- Observational post-authorisation study of Factor IX Grifols (high purity double inactivated human factor IX concentrate) in prophylaxis or treatment of haemophilia B patients. October 2006-. Pl: Teresa Toll.



### **Publications**

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- Francis JH, Schaiquevich P, Buitrago E, Del Sole MJ, Zapata G, Croxatto JO, Marr BP, Brodie SE, Berra A, Chantada GL, Abramson DH. Local and systemic toxicity of intravitreal melphalan for vitreous seeding in retinoblastoma: a preclinical and clinical study. Ophthalmology 2014. 121: 1810-1817. IF: 6,170(Q1).
- Grigorovski N, Lucena E, Mattosinho C, Parareda A, Ferman S, Catalá J, Chantada G. Use of intra-arterial chemotherapy for retinoblastoma: results of a survey. Int J Ophthalmol 2014. 7: 726-730. IF: 0,500(Q4).
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### Supervised theses

 Retrospective analysis of pediatric malignant bone sarcoma (OS and ES) managed at Hospital Sant Joan de Déu. Cohort study from 1994 to 2014. Università degli studi di Ferrara, Facoltà di Medicina e Chirurgia. Tesi di specializzazione. Doctoranda: Caterina Radice. Director: Dr. Jaume Mora. December 2014.



# Adult-age disorders originating in the foetal period or in the early years of life

Study of the biological bases of the consequences of anomalies, diseases and treatments in childhood. Specifically studied are the relation between growth retardation and endocrine-metabolic changes, the future consequences of prenatally diagnosed anomalies and their prevention. Some of the members of the group, which is led by Dr. Ibáñez, belong to the Centre for Biomedical Network Research on Diabetes and Associated Metabolic Disorders (CIBERDEM) financed by the Carlos III Health Institute.

- 1. Early detection of risk groups:
- Identification of new genetic and environmental factors predisposing the absence of post-natal weight and height recovery in children with low birth weight (LBW). Cohort of newborns.
- Identification of new genetic and environmental factors predisposing quick recovery of weight and/or development of overweight in the first 12 months of life. Candidate genes: TNF, MCR4, among others. Cohort of newborns.
- Detection of early markers of cardiovascular risk and chronic inflammation in paediatric patients with LBW background [adipokines: total adiponectin, high molecular weight (HMW) adiponectin, visfatin, osteocalcin, TNF, osteopontin, vaspin, carotid artery diameter] and its relation to the development of total and visceral adiposity. Cohort of schoolchildren.
- Determination of prevalence of insulin resistance and metabolic syndrome in paediatric patients with LBW. Cohort of schoolchildren.
- Determination of effects of growth hormone treatment on subcutaneous and visceral fat deposits in patients with LBW without post-natal weight and height recovery. Cohort of schoolchildren.
- 2. Early prevention of endocrine/metabolic alterations associated with quick and excessive post-natal weight recovery.
- Adoption of environmental measures (basically alimentary measures) to avoid quick weight increase in the first 4 months
  of life. This objective includes the comparison of the effects of breastfeeding to those of the two commercial isocaloric
  formulas (standard and protein-enriched) on the post-natal growth pattern, body composition [measured by a dual-energy absorptiometry technique (DXA) and visceral fat (ultrasound scan and magnetic resonance)], insulin resistance
  (homeostasis model assessment), and the markers of chronic inflammation and cardiovascular risk (adipokines).
- Adoption of preventive therapeutic measures (by administration of insulin sensitizers [metformin] with or without antiandrogens) aimed to prevent and/or modulate endocrine/metabolic changes associated with post-natal growth recovery, specifically including insulin resistance, excessive centrally-distributed visceral fat and other changes forming the metabolic syndrome such as hypertension, and the changes of the lipid profile and chronic inflammation markers in pre-puberal children with LBW without spontaneous recovery of weight and height treated with growth hormone.



### Research team

Coordinator	Dra. Lourdes Ibáñez
Researchers	Thais Agut, Ana Alarcón, Asteria Albert, Lluís Amat, Israel Blasco, José M.ª Boguñá, Cristina Boix, Miquel Borrás, Sergi Cabré, Justo Callejo, Marta Camprubí, Cristina Carrasco, Paula Casano, Montserrat Castañón, Marta Díaz, Rubén Díaz, Silvia Ferrero, Alfredo García-Alix, M.ª Dolores Gómez-Roig, Eduardo González, Margarita Ibáñez, Isabel Iglesias, Martín Iriondo, Montse Izquierdo, Josep Jiménez-Chillarón, Lucas Krauel, Josep M.ª Lailla, María Jesús Leal, Carles Lerin, Marina Llobert, Isabel Miró, Julio Moreno, Marta Olivares, Miriam Pérez, Pilar Poo, Jordi Prat, Marta Ramon, Silvia Ribó, Ana Riverola, Juan Rodó, David Rodríguez, Joan Sabriá, Cristina Salvador, Giorgia Sebastiani, Xavier Tarrado, Anna Torres, Antonio Vela
Post-doctoral researchers	Laura Martínez , David Sánchez-Infantes, Silvia Velazquez
Pre-doctoral researcher	Adriano Bonforti
Laboratory technicians	Judith Cebrià
Assistants	Marta Aragó, Beatriz de Novoa, Abel López-Bermejo, Laura Bosch, Maria Victoria Marcos, Edurne Mazarico

### Research lines

#### Childhood diabetes

Dr. Josep Jiménez-Chillarón and Dr. Rubén Díaz

The "foetal origin of adult disorders hypothesis" postulates that an adverse intrauterine environment may affect the growth of the foetus by introducing permanent changes in gene expression in key cells and/or tissues. Such changes endure after birth and may contribute to the development of chronic and complex disorders typical of adults such as Type 2 diabetes or obesity. Our laboratory's goal is to achieve an understanding of the molecular mechanisms associating nutrition during intrauterine development with the risk of chronic illnesses as an adult, focusing especially on diabetes and obesity.

### Physiological and pathological conditions in newborns and their consequences for subsequent development

Dr. Alfredo García-Alix and Dr. Martín Iriondo

Genetic potential and foetal environment may have irreversible consequences for a person's development and they may be the origin of disorders in the adult. The study of factors that influence the various stages of life: periconceptional, intrauterine, perinatal and postnatal will allow advances to be made in our knowledge of the conditioning factors which may interfere with correct development. Moreover, the follow-up of the nutritional and health-related interventions carried out on babies up to their adolescence and adulthood will permit medical teams to develop better treatments and preventive strategies.

### Foetal medicine: foetal well-being markers

Dr. María Dolores Gómez-Roig

We consider it necessary to make a deeper study of the condition of the foetus precisely to be able to evaluate it at any point in the course of gestation. We have methods allowing us to determine the foetus's well-being but when these methods indicate that it may be in a risk situation, we lack precise diagnostic tests to quantify the foetal condition as would be required to make a precise diagnosis and to suitably adapt the obstetric procedure to be followed.

### Intrauterine growth restriction and postnatal changes

Dr. Lourdes Ibáñez Toda

Foetal growth restriction may have irreversible consequences. The study of the various stages between intrauterine life and adolescence will allow advances to be made in the prevention of this disorder and in the treatment and prevention of the complications which may be derived from it.



### **Projects**

- Improving the life of children with diabetes. Fundación Banco Bilbao Vizcaya Argentaria. November 2014 November 2015. Pl: Ruben Díaz.
- Evaluation of cardiovascular risk in the first two years of life in children born large or small for their gestational age.
   Fundación Salud 2000. May 2014 April 2017. Pl: Lourdes Ibáñez.
- Programme for intensification of research activity in the Spanish National Health System 2013. INT13/00095. Instituto de Salud Carlos III. February 2014 – February 2015. Pl: Lourdes Ibáñez.
- Early biomarkers of the safety and efficacy of nutritional support in extremely preterm infants (EPI). PI13/01562. Instituto de Salud Carlos III. January 2014 December 2016. PI: Isabel Iglesias.
- Combined Maternal-Foetal and Neonatal Medicine Group, Hospital Clínic de Barcelona and Hospital Sant Joan de Déu. Agaur - Agència de Gestió d'Ajuts Universitaris i de Recerca. SGR 2014. 2014SGR928. January 2014 – December 2016. Pl: Maria Dolores Gómez-Roig.
- Effect of prenatal and perinatal changes on postnatal development. Disorders of foetal origin. Agaur Agència de Gestió d'Ajuts Universitaris i de Recerca. SGR 2014. 2014SGR512. January 2014 – December 2016. Pl: Lourdes Ibáñez.
- A multidisciplinary research programme for the development of new diagnostic approaches and intervention measures
  to reduce prenatal brain damage using growth restriction as a model. CEREBRA Fetal Research Programme. Pl: Eduard Gratacós.
- Research personnel training, candidate: Luís Miguel Río. Ministerio de Ciencia e Innovación (MINECO). 2013 2017.
   PI: Carles Lerín.
- IRBETAINE-CIG Molecular mechanisms underlying the development of insulin resistance: role of betaine supplementation. European Commission. July 2013 August 2015. Pl: Carles Lerín.
- Ramon y Cajal researcher, Dr. Carles Lerín. Ministerio de Ciencia e Innovación (MINECO). July 2013 January 2016.
   PI: Carles Lerín.
- Unraveling Novel Molecular Mechanisms Underlying the Development of Insulin Resistance. European Foundation for the Study of Diabetes. July 2013 – October 2014. Pl: Carles Lerín.
- Neuroprotection and regeneration/repair by combined therapy (hypothermia + allopurinol) in an animal model of hypoxic-ischaemic brain damage. Sociedad Española de Neonatología. April 2013 March 2014. Pl: Marta Camprubí.
- Metabolic and biochemical effects of betaine on insulin sensitivity and physical exercise. Ministerio de Ciencia e Innovación (MINECO). January 2013 January 2017. Pl: Carles Lerín.
- Maternal-Child Health and Development Network (SAMID). Instituto de Salud Carlos III. Enero 2013 December 2016. Pl: Maria Dolores Gómez-Roig.
- Fire Squadron Grant 2012 Newborns. Hospital Sant Joan de Déu Barcelona. May 2012 April 2015. Pl: Isabel Iglesias.
- Neuropsychological rehabilitation after moderate and severe childhood TBI, a randomized study with parent-supported intervention, children with robotic intervention and control group. Fundació La Marató de TV3. February 2012 – February 2015. PI: Mª Pilar Poo.
- Non-genomic inheritance of diabetes in a mouse model of neonatal overnutrition: potential role of epigenetic mechanisms. Instituto de Salud Carlos III. January 2012 January 2017. Pl: Josep Jiménez-Chillarón.
- Genetic determinants of prenatal and postnatal growth: association with early markers of cardiovascular and metabolic syndrome risk. Instituto de Salud Carlos III. January 2012 – December 2015. Pl: Lourdes Ibáñez.
- Metabolic and biochemical effects of betaine on insulin sensitivity and physical exercise. Ministerio de Ciencia e Innovación. January 2012 December 2015. Pl: Carles Lerín.
- Prognostic factors of brain injury in foetuses with early restricted intrauterine growth. Instituto de Salud Carlos III. January 2012 December 2015. Pl: Antonio Vela.
- Non-genomic inheritance of diabetes in a mouse model of neonatal overnutrition: potential role of epigenetic mechanisms. Instituto de Salud Carlos III. January 2012 August 2015. Pl: Josep Jiménez-Chillarón.



- Perinatal nutrition in males programmes lipogenic gene expression in their descendants through epigenetic mechanisms. Ministerio de Ciencia e Innovación. January 2012 December 2015. Pl: Josep Jiménez-Chillarón.
- Magnesium sulphate in continuous versus discontinuous regime in the framework of watchful waiting in severe pre-eclampsia: randomised clinical trial. Ministerio de Sanidad y Política Social. January 2012 December 2015. Pl: Joan Sabrià.
- Evaluation of prenatal exposure to antidepressants and anxiolytics by their determination in alternative biological matrices. Instituto de Salud Carlos III. January 2012 December 2015. Pl: Maria Dolores Gómez-Roig.
- Miguel Servet Contracts. Instituto de Salud Carlos III. 2015 2015. Pl: Josep Jiménez-Chillarón.
- Experimental study of the effect of fibre-rich diet administration on various diets. Sara Borrell Postdoctoral Training Contracts. Instituto de Salud Carlos III. Candidate: Sánchez-Infantes Sánchez, Carlos. 2011 2014. Pl: Lourdes Ibáñez.
- Study to determine the suitability of preparing a practical clinical guide on hypoxic-ischaemic encephalopathy. Agencia Informació, Avaluació i Qualitat en Salut. December 2011-. Pl: Alfredo Garcia-Alix.
- Influence of postnatal nutritional support on extreme premature methylome. Alter Farmacia, S.A.; Asociación Española de Pediatría. September 2011 – December 2014. Pl: Isabel Iglesias.
- Río Hortega Contract, candidate: Nuria Sanz. Instituto de Salud Carlos III. April 2011 March 2014. PI: Lourdes Ibáñez.
- Fund for scientific advance and innovation in children's diabetes. Fundació Caixa d'Estalvis i Pensions de Barcelona. January 2011-2015. Pl: Ruben Díaz.
- Low molecular weight heparin (LMWH) for prevention of complications derived from placental insufficiency in at-risk patients without thrombophilia: randomised multi-centre study. Ministerio de Sanidad y Política Social. January 2011 – December 2015. Pl: Maria Dolores Gómez-Roig.
- Intrauterine growth restriction and postnatal endocrine/metabolic changes. Instituto de Salud Carlos III. January 2011
   December 2014. Pl: Lourdes Ibáñez.
- Diagnostic and prognostic value of the heart function study on the perinatal result and its association with markers of myocardiac cell injury and heart dysfunction in cord blood in intrauterine growth restriction foetuses. Instituto de Salud Carlos III. January 2010 – June 2014. Pl: Josep Mª Laïlla.
- Group on experimental diabetes. Agència de Gestió d'Ajuts Universitaris i de Recerca. 2009 2014. Pl: Josep Jiménez-Chillarón.
- Effect of prenatal and perinatal changes on postnatal development. Agència de Gestió d'Ajuts Universitaris i de Recerca. 2009 2014. Pl: Lourdes Ibáñez.
- Neonatal cerebral infarction: a multidisciplinary study of pathogenic factors, new diagnostic and prognostic indicators, and impact on neurodevelopment and quality of life. Instituto de Salud Carlos III. October 2009 – January 2014. Pl: Alfredo Garcia-Alix.
- Diabetes special fund CIDI (Fund for Scientific Advance and Innovation in Childhood Diabetes). Obra Social Sant Joan de Déu. November 2008-. Pl: Beatriz De Novoa.
- Foetal origin of adult diabetes: epigenetic change-mediated Beta-cell failure. Fundación Salud 2000. July 2008 December 2014. Pl: Josep Jiménez-Chillarón.
- Multi-centre study on postnatal growth restriction in extreme preterm infants (<1500 gr) in Spanish Neonatal Intensive</li>
   Care Units. Follow-up to the age of 2 years. Bebe Due España. January 2005 December 2018. Pl: Martin Iriondo.

### Clinical trials

- Treatment with recombinant growth hormone (rGH) in short patients born small-for-gestional-age (SGA) followed at Hospital Sant Joan de Déu: Analysis of early predictors of good response useful in clinical practice - WI191603. Fundació Privada per a la Recerca i la Docència Sant Joan de Déu. November 2014-. Pl: Lourdes Ibáñez.
- Identification of circulating microRNAs in short children born small for gestational age: Relationship with pre- and postnatal growth and metabolic parameters. October 2014-. Pl: Abel López-Bermejo. Investigator: Lourdes Ibáñez.
- Double-blind placebo-controlled randomised multi-centre study on two parallel groups to evaluate the efficacy and safety of sildenafil IV in the treatment of neonates with persistent pulmonary hypertension of the newborn (PPHN) or hypoxic respiratory insufficiency at risk of PPHN, with long-term follow-up to investigate the evolution of its development 12 and 24 months after completion of the treatment under study. Parexel Internacional. May 2014-. Pl: Julio Moreno.



- Randomised, open, active-controlled, multinational, dose-escalation trial investigating safety, tolerability, pharmacokinetics and pharmacodynamics of a single dose of long-acting growth hormone (NNC0195-0092) compared with daily dosing of Norditropin® SimpleXx® in children with growth hormone deficiency. Novo Nordisk. January 2014-. Pl: Lourdes Ibáñez.
- Obesity. Sanofi-Aventis. January 2014 December 2015. Pl: Marta Ramon-Krauel.
- AEST0017-EXPERTKIDS Advantages of a bolus calculator in the control of preprandial and postprandial glycaemia and in the flexibility of the meals of paediatric patients treated with multiple daily insulin injections. Roche Diagnostics. November 2013-. PI: Marta Ramon-Krauel.
- Cardiovascular Risk Markers in 6-yr-old Children Born Small for Gestational Age (SGA) and Postnatal Catch-up Growth\_Relationship with Weight and Length Gain, Abdominal Fat Distribution and Type of Feeding in the First Months of Life. WI176617. Pfizer. April 2013-. PI: Lourdes Ibáñez.
- Prospective, open, randomised clinical trial with two groups of patients to evaluate the efficacy and safety of the combination of ethinyl estradiol and levonorgestrel versus the combination of low doses pioglitazone, spironolactone and metformin in adolescents with ovarian hyperandrogenism and hyperinsulinism: effects on ovulatory function, chronic inflammation parameters, markers of cardiovascular risk and of development of Type 2 diabetes. Fundació Privada per a la Recerca i la Docència Sant Joan de Déu. January 2013-. Pl: Lourdes Ibáñez.
- Follow-up study until attainment of adult size in patients included in the phase III Study with Omnitrope© on treatment of Spanish children with growth hormone deficit. Sandoz Farmacéutica. October 2012-. PI: Marta Ramon-Krauel.
- GHLiquid-3676 (NNH-SOM-2012-01). NordiNet<sup>®</sup> International outcome study (IOS). Novo Nordisk Pharma. October 2012-. Pl: Lourdes Ibáñez.
- Urogynaecologic dysfunctions in women with surgical genital prolapse. Impact of vaginal surgery on urinary stress incontinence. May 2012-. Pl: Lluís Amat.
- Retrospective study on the influence of GH treatment onset age on height gain in children born SGA. GH-RAST Study.
   Pfizer. May 2012-PI: Lourdes Ibáñez.
- Effects on markers of cardiovascular risk of addition of metformin to the treatment with growth hormone of prepuberal
  patients with background of low birth weight for gestational age without postnatal height recovery. January 2012-. Pl:
  Paula Casano.
- Descriptive, multi-centre, cross-sectional epidemiologic study of the reference values of IGF-1, IGFBP3 and ALS in a
  healthy Spanish paediatric population, according to chronological age, sex and puberal stage, as per Protocol no. IPSINC-2011-01, in which their characteristics are defined. Ipsen Pharma. October 2011-. Pl: Ruben Díaz.
- Benefits of strict glycaemic control on the prognosis of critically ill paediatric patients. Prospective randomised clinical trial. Hospital Sant Joan de Déu Barcelona. September 2011-. Pl: Lourdes Ibáñez.
- Epidemiologic study of the early diagnosis of invasive candidiasis in very low-weight preterm newborns. CANDI-NEO Study. Astellas Pharma. June 2011-. Pl: Ana Alarcon.
- Phase II, randomised, parallel-group, placebo-controlled, double-blind clinical trial to evaluate the safety and efficacy of dietary supplementation with tryptophan in weight reduction and its neuropsychological effects on obese adolescents. Ministerio de Sanidad y Política Social. January 2011 – December 2014. Pl: Marta Ramon-Krauel.
- Effects on markers of cardiovascular risk of addition of metformin to the treatment with growth hormone of prepuberal patients with background of low birth weight for gestational age without postnatal height recovery. January 2010-. Pl: Paula Casano.
- Resuscitation of extremely low-weight newborns by a comprehensive monitoring system: study of influence of the fraction of inspired oxygen. January 2010-. Pl: Marta Thió.
- Pilot study of the effects of growth hormone on body adiposity and visceral fat in children with low birth weight for gestational age. Pfizer. June 2009-2014. Pl: Lourdes Ibáñez.
- European Increlex® [injectable mecasermin (rDNA derived)] Growth Forum database on growth restriction: Registry of European patients to monitor the long-term efficacy and safety of Increlex. Eu-IGFD. February, 2009-. PI: Rubén Díaz.
- Endocrine metabolic effects and effects on visceral adiposity of metformin administration in low doses in prepuberal children with low birth weight for gestational age, spontaneous postnatal weight and height recovery, and risk markers. Instituto de Salud Carlos III. January 2009 January 2014. Pl: Lourdes Ibáñez.
- International Cooperative Study on Growth. October 2007-. Pl: Rubén Díaz.
- Genetics and Neuroendocrinology of Short Stature International Study. June 2007-. Pl: Rubén Díaz.



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- Agut T, Muchart J, Delgadillo V, García-Alix A. Rombencefalosinapsis, una rara alteración del desarrollo del cerebelo de fácil diagnóstico. An Pediatr (Barc) 2014. 81:e3-4. IF: 0,722(Q3).
- Bassols J, Moreno-Navarrete J, Carreras-Badosa G, Diaz M, Prats-Puig A, Palomer AM, de Zegher F, Ibáñez L, Fernandez-Real JM, Lopez-Bermejo A. Placental Sprouty 2 (SPRY2): Relation to Placental Growth and Maternal Metabolic Status. Neonatology 2014. 106: 120-125. IF: 2,369(Q1).
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### Supervised theses

- Diagnostic value of vascular indices studied with three-dimensional power Doppler and analysed with the VOCAL programme, in foetuses with intrauterine growth restriction. Universitat de Barcelona. Thesis presented: 17/12/2014. Doctoral candidate: Anna Torres Soto. Directors: María Dolores Gómez-Roig, Antonio Vela.
- Determination of the use of cervical ultrasound scans with three-dimensional power Doppler (VOCAL system) in the prediction of the behaviour of pregnant women with risk of early delivery. Universitat de Barcelona. Thesis presented: 27/10/2014. Doctoral candidate: Raul De Diego Burillo. Director: Maria Dolores Gómez-Roig.

### **Networks**

- CIBERDEM: Centre for Biomedical Network Research on Diabetes and Associated Metabolic Disorders. Pl: Lourdes Ibáñez.
- Maternal-Child Health and Development Network (SAMiD). Carlos III Health Institute. 2009-2013. Pl: Josep M. Laïlla.



# Infectious diseases and systemic inflammatory response in paediatrics

The research group on infectious diseases is oriented towards the study of the clinical, molecular and epidemiologic aspects of the main paediatric infectious diseases, including vaccine-preventable diseases (such as pneumococcal disease or papillomavirus infection) and vertically transmitted infections (such as HIV-1 or hepatitis C). The group also focuses on the early diagnosis and identification of infectious diseases by molecular methods. The multidisciplinary character of the group's members favours the comprehensive study of our patients' infections.

### Research team

Coordinator Line coordinator Researchers	Clàudia Fortuny, Carmen Muñoz-Almagro Jordi Antón Laia Alsina, Eva del Amo, Rosa Bou, Pedro Brotons, Joan Calzada, Cristina Esteva, Mariona Fernández de Sevilla, Victòria Fumadó, Juan José García-García, Eva Gargallo, Amadeu Gené, Susanna Hernández, Estíbaliz Iglesias, Iolanda Jordán, Teresa Juncosa, Cristian Launes, Mª Anunciación Martín, Antoni Noguera, Mónica Piquer, Ana María Plaza, Silvia Ricart, Judith Sánchez, Palmira Santin, Laura Selva, Vicenç Torrente, Mireya Urrea, Asunción Vicente, Hector de Paz, Olga Domingez, Anna Esteve, Maria Teresa Giner, Rosa Jiménez, Jaime Lozano
Research assistant	Irene Latorre
Assistant	Carlos Cisneros

### Research lines

### Molecular epidemiological surveillance of vaccine-preventable diseases

Dr. Carmen Muñoz Almagro

Human beings' first contact with many microorganisms takes place in childhood, when the child has not been infected or has not developed disease. Vaccination early in life has proven to be an effective instrument in combating infectious diseases. To evaluate the best vaccination strategies in a specific population, a good molecular characterisation of the microorganisms in circulation in the respective community is fundamental, since microorganisms diversify genetically to adapt themselves in the best possible way to a specific environment. The most active research line of our group at present is the molecular epidemiological surveillance of pneumococcal disease. Since the late 1980s, we have been studying the evolution of the pneumococcus serotypes and clones producing invasive disease in our population, and since 2008 the surveillance of the child population of Sierra Leone has been added to our study, applying innovate diagnostic and capsular typing techniques based on molecular methods.

### HIV

Dr. Claudia Fortuny

Study of the factors associated with vertically transmitted infections, with special emphasis on HIV infection: long-term follow-up of healthy patients exposed to HIV and to antiretroviral drugs to determine whether exposure to these drugs during the gestational and neonatal periods affects neurologic or weight-height development in any way, whether they are associated with carcinogenesis and whether they are a risk factor for other disorders.



### Systemic inflammatory response in the paediatric age

Dr. Jordi Antón

Research on the immune mechanisms in the following groups of disorders: congenital immunodeficiencies, secondary immunodeficiencies, autoimmune diseases and allergic disorders. Specifically, studies on the inflammatory response in severe invasive pneumococcal disease, an analysis of phenotypes and genotypes of variable common immunodeficiency, and an analysis of the signalling pathways of the Toll-like receptors in hereditary and non-hereditary inflammatory diseases have been started.

### **Projects**

- Development of new genetic diagnosis techniques involving high-performance sequencers and their applicability to the diagnosis of osteogenesis imperfecta. Sociedad Española de Reumatología Pediátrica. December 2014-December 2016. Pl: Rosa Bou.
- Evaluation of somatic mosaicism in the NOD2 gene in seronegative juvenile idiopathic arthritis. Sociedad Española de Reumatología Pediátrica. December 2014-December 2016. Pl: Estibaliz Iglesias.
- Utility of 256-channel multi-slice computed tomography to evaluate cardiac involvement in Kawasaki disease. Sociedad Española de Reumatología Pediátrica. December 2014-December 2016. Pl: Joan Calzada.
- Analysis of autoinflammatory mechanisms mediated by the NF-kB pathway and the inflammasome/caspase-1/IL-1 axis in juvenile idiopathic arthritis with negative antinuclear antibodies. Societat Catalana de Reumatologia. June 2014 June 2016. Pl: Estibaliz Iglesias.
- Study of the primary and secondary defects of the IL12-IFNg-TNFa pathway with susceptibility to intracellular microorganism infection. Hospital Sant Joan de Déu Barcelona. March 2014 February 2017. Pl: Laia Alsina.
- Analysis of autoinflammatory mechanisms mediated by the NF-kB pathway and the inflammasome/caspase-1/IL-1 axis in juvenile idiopathic arthritis with negative antinuclear antibodies. 2nd Honourable mention. Beca Mutual Mèdica. January 2014 – December 2015. PI: Estibaliz Iglesias.
- Analysis of autoinflammatory mechanisms mediated by the NF-kB pathway and the inflammasome/caspase-1/IL-1 axis in juvenile idiopathic arthritis with negative antinuclear antibodies. Sociedad Española de Reumatología. January 2014 – December 2015. Pl: Estibaliz Iglesias.
- Defects in innate immunity and coinfection with respiratory virus: the perfect storm for developing invasive pneumococcal disease in children? Instituto de Salud Carlos III. Pl13/01729. January 2014 – December 2016. Pl: Carmen Muñoz-Almagro.
- Study of autoinflammatory disease genes in patients with JIA. Obra Social Sant Joan de Déu. January 2014 December 2014. Pl: Jordi Antón.
- Longitudinal study of mitochondrial DNA mutations in children exposed to HIV (infected and non-infected) and to antiretroviral drugs. Instituto de Salud Carlos III. Pl13/01738. January 2014 December 2016. Pl: Clàudia Fortuny.
- Study group on immune dysfunction diseases in paediatrics (GEMDIP) 2014SGR1531. Agaur Agència de Gestió d'Ajuts Universitaris i de Recerca. January 2014 December 2016. Pl: Jordi Antón.
- Consolidated group on infectious diseases in the paediatric age. Consolidated research group on infectious diseases in the paediatric age. 2014SGR505. Agaur - Agència de Gestió d'Ajuts Universitaris i de Recerca. January 2014 – December 2016. Pl: Carmen Muñoz-Almagro.
- Identification of prognostic factors in muscle biopsy for the diagnosis of patients with juvenile dermatomyositis. Sociedad Española de Reumatología. January 2014 – December 2015. Pl: Estibaliz Iglesias.
- Validation of the single daily dose of isoniazid at 10 mg/kg weight in newborns under the age of 3 months. Instituto de Salud Carlos III. PICI14/00228. January 2014 – December 2016. Pl: Antoni Noguera.
- RESPOC. Fast, cost-effective, user-friendly point of care (POC) instrument for detection of respiratory pathogens, including Streptococcus pneumoniae. European Commission. December 2013 – May 2016. Pl: Carmen Muñoz-Almagro.
- Molecular diagnosis of food allergy to shellfish in the paediatric population. Sociedad Española de Inmunología Clínica, Alergia y Asma Pediátrica. November 2013 – November 2015. Pl: Olga Dominguez.



- Identification of prognostic factors in muscular biopsy in the diagnosis of patients with juvenile dermatomyositis. Societat Catalana de Reumatologia. June 2013 June 2015. Pl: Estibaliz Iglesias.
- Study of the primary and secondary defects of the IL-12/IFN-gamma/TNF-alpha pathway with susceptibility to infection by intracellular micro-organisms. Instituto de Salud Carlos III (ISCIII). PI12/01990. January 2013 – December 2015. PI: Laia Alsina.
- Validation of the Minimally Invasive Autopsy (MIA) tool for cause of death investigation in developing countries. Bill & Melinda Gates Foundation. December 2012 – December 2015. Pl: Carmen Muñoz-Almagro.
- SHARE-Single HUB and Access Point for Paediatric Rheumatology in Europe (SHARE). European Commission. September 2012 August 2015. Pl: Jordi Antón.
- Incidence of somatic mutations of the NLRP3 gene in patients with clinical diagnosis compatible with Cryopyrin-associated periodic syndromes. Societat Catalana de Reumatologia. June 2012 May 2014. Pl: Jordi Antón.
- Support technician at the Sequencing Unit. Instituto de Salud Carlos III (ISCIII). CA11/00447. Beneficiary: Cristina Esteva. April 2012 April 2015. Pl: Carmen Muñoz-Almagro.
- Use of dried-blood spot (DBS) samples for detection and molecular surveillance of Streptococcus pneumoniae in developing countries. Hospital Sant Joan de Déu Esplugues HSJD. April 2012 March 2015. Pl: Carmen Muñoz-Almagro.
- Correlation between the clinical and immunologic phenotypes of paediatric patients with common variable immunodeficiency. Sociedad Española de Inmunología Clínica, Alergia y Asma Pediátrica. January 2012 – December 2014. Pl: Mónica Piquer.
- Effectiveness of 13-valent pneumococcal conjugate vaccine in the prevention of invasive pneumococcal disease in children. A matched case-control study. Instituto de Salud Carlos III (ISCIII). Pl11/02081. January 2012 – December 2015. Pl: Juan José García-García.
- Predoctoral training grants in health research. Beneficiary: Eva del Amo. Instituto de Salud Carlos III (ISCIII). FI11/00720.
   September 2011 September 2015. Pl: Carmen Muñoz-Almagro.
- Impact of the administration of systemic glucocorticoids on the inflammatory response and clinical evolution of patients with moderate-severe bronchiolitis. EC10-176. Ministerio de Sanidad y Política Social. January 2011 – June 2014. Pl: lolanda Jordán.
- Reference laboratory for molecular epidemiologic monitoring of meningococcal disease, invasive pneumococcal disease and pertussis. Agència de Salut Pública de Catalunya. January 2011 December 2015. Pl: Carmen Muñoz-Almagro.
- Intensification for healthcare activity. Fundación Godia. Pl: Carmen Muñoz-Almagro.

### Clinical trials

- β-SPECIFIC 4 patients: Paediatric efficacy and safety study with canakinumab as first-line treatment. Open study on the efficacy and safety of dose reduction or dose interval lengthening of canakinumab (ACZ885) in patients with systemic juvenile idiopathic arthritis (SJIA). November 2014-. PI: Rosa Bou.
- Open trial registering subjects aged 6 to 18 years with pain requiring treatment with extended-release opioid, to evaluate the safety and efficacy of tapentadol ER versus morphine ER, followed by an open extension. November 2014-.
   PI: S Navarro Vilarrubí.
- Prospective, multi-centre, single-arm study to evaluate the efficacy, safety and pharmacokinetics of denosumab in children with osteogenesis imperfecta. October 2014-. Pl: Rosa Bou.
- Retrospective study of food-allergic patients (milk and/or eggs and/or vegetables) treated with omalizumab as sole treatment or associated with oral immunotherapy based on a multi-centre register (OmaBase). August 2014-.Pl: Ana Ma Plaza.
- Long-term extension study to evaluate the safety and efficacy of tocilizumab administered subcutaneously to patients with polyarticular juvenile idiopathic arthritis and systemic juvenile idiopathic arthritis. June 2014-. Pl: Rosa Bou Torrent.
- Randomised, double-blind, placebo-controlled study of canakinumab in patients with hereditary periodic fevers (TRAPS, HIDS or FMFrc) with randomised withdrawal/frequency reduction of the dose and subsequent long-term open treatment phase. Novartis Farmacéutica. May 2014-. Pl: Jordi Antón.



- Tolerance to 2 highly hydrolysed children's milk formulas based on rice proteins and casein in children with allergy to cow's milk proteins. Biosearch. May 2014-. Pl: Ana Ma Plaza.
- Validation of the daily single dose of isoniazid at 10 mg/kg of weight in newborns aged under 3 months. April 2014-. PI: Antoni Noguera.
- Spanish Register of Uveitis Associated with Juvenile Idiopathic Arthritis. Sociedad Española de Reumatología. April 2014-. Pl: Jordi Antón.
- CEntroS Project for Early Assistance for Respiratory Allergy (CESAR Project). Stallergenes Ibérica. March 2014-. Pl. Ana M.ª Plaza.
- Continued access to darunavir/ritonavir (DRV/rtv) for children aged 3 years or more and adolescents infected by HIV-1.
   March 2014-. Pl: Clàudia Fortuny.
- Phase 2/3, multi-centre, open, multi-cohort, two-part study to evaluate the pharmacokinetics, safety and antiviral activity of elvitegravir (EVG) administered with a base regime (BR) containing a protease inhibitor reinforced with ritonavir (IP/r) in paediatric subjects infected by HIV-1, previously treated with antiretrovirals. Gilead Sciences; Hospital Sant Joan de Déu Barcelona. February 2014-. Pl: Clàudia Fortuny.
- Tigencycline Evaluation Surveillance Trial. Pfizer. January 2014-. Pl: Amadeu Gené.
- Double-blind randomised multi-centre comparative clinical trial to evaluate the effectiveness, safety and pharmacokinetics of daptomycin in comparison to the active reference treatment in paediatric patients with acute haematogenous osteomyelitis caused by gram-positive organisms. December 2013 -. Pl: Juan José García-García.
- Phase III, randomised, double-blind, placebo-controlled study to determine the efficacy, safety and tolerability of lebrikizumab in adolescent patients with uncontrolled asthma treated with inhaled corticosteroids and a second control drug.
   F. Hoffmann- La Roche; Hospital Sant Joan de Déu Barcelona. November 2013-. Pl: Ana Mª Plaza.
- Multi-centre long-term follow-up study of HLH patients who have been treated with NI-0501, an anti-interferon gamma monoclonal antibody. Novimmune. November 2013-. PI: Laia Alsina.
- Phase III, multi-centre, open clinical trial to evaluate the pharmacokinetics, efficacy and safety of abatacept administered subcutaneously (s.c.) in children and adolescents with polyarticular juvenile idiopathic arthritis and inadequate response (IR) to biological or non-biological disease-modifying antirheumatic drugs (DMARDs). Bristol-Myers Squibb International Corporation (BMSIC); Hospital Sant Joan de Déu Esplugues HSJD. September 2013-. Pl: Jordi Antón.
- Multi-centre, randomised, placebo-controlled, double-blind study on parallel groups to evaluate the safety, efficacy and pharmacokinetics of belimumab, an anti-BLyS human monoclonal antibody, plus standard therapy, in paediatric patients with systemic lupus erythematosus (SLE). Glaxosmithkline. September 2013-. Pl: Jordi Antón.
- Phase Ib, multi-centre, open study to investigate the pharmacokinetics, pharmacodynamics and safety of tocilizumab after subcutaneous administration to patients with polyarticular juvenile idiopathic arthritis. Roche Farma. July 2013-. PI: Jordi Antón.
- Phase 1/2, two-stage, open study on a single group to determine the safety, pharmacokinetics and efficacy of telaprevir in combination with peginterferon alfa-2b and ribavirin in paediatric subjects aged 3 to 17 years infected by genotype 1 hepatitis C virus. Hospital Sant Joan de Déu Barcelona; Vertex Pharmaceuticals Incorporated. June 2013-. Pl: Clàudia Fortuny.
- Comparative evaluation of the safety and efficacy of daptomycin versus standard treatment in paediatric patients aged 2 to 17 years with bacteraemia caused by Staphylococcus aureus. PharmaNet GmbH. May 2013-. Pl: Antoni Noguera.
- Multi-centre, single-arm, open pilot study to explore the safety, tolerability, pharmacokinetics and efficacy of multiple intravenous administrations of NI-0501, an anti-interferon gamma monoclonal antibody (anti-IFN), in paediatric patients with reactivated primary haemophagocytic lymphohistiocytosis. Novimmune. April 2013-. PI: Laia Alsina.
- PASS Protocol IG1004 post-authorisation safety study with Flebogamma DIF 100 mg/ml and Flebogamma DIF 50 mg/ml. Instituto Grifols. March 2013-. Pl: Laia Alsina.
- Phase III contact follow-up trial comparing the diagnostic functioning of C-Tb versus QuantiFERON®-TB Gold In-Tube, in combination with a randomised double-blind safety analysis in different parts of the body with C-Tb versus 2 TU of Tuberculin PPD RT23SSI (PPD). Statens Serum Institute. February 2013-. PI: Antoni Noguera.
- Multi-centre, double-blind, randomised, placebo-controlled study on parallel groups to evaluate the safety and tolerability of 10 mg of bilastine administered once daily to children aged 2 to 11 years with allergic rhinoconjunctivitis or chronic urticaria. Faes Pharma. February 2013-. Pl: Ana Mª Plaza.
- Tigencycline Evaluation Surveillance Trial. PFIZER INC. January 2013-. PI: Amadeu Gené.



- Phase IB, open, randomised, adaptive, multi-centre study on the pharmacokinetics and pharmacodynamics of oseltamivir (Tamiflu®) in the treatment of influenza in immunocompromised subjects aged 0 to 18 years, with confirmed influenza infection. January 2013-. Pl: Ruben Berrueco.
- Multi-centre, randomised, blind-observer, active control study to evaluate the security, tolerability, efficacy and pharmacokinetics of ceftaroline versus a comparator in paediatric subjects with acute bacterial infection of the skin and skin structures. Cerexa Inc; Hospital Sant Joan de Déu Barcelona. October 2012 – July 2014. Pl: Juan José García-García.
- Paediatric Granulomatous Arthritis Outcome Regist. August 2012-. Pl: Jordi Antón.
- Use of omalizumab in real clinical practice in Spain after 5 years of experience. EXPERT 5 Study. Novartis Farmacéutica. May 2012-. Pl: Ana Mª Plaza.
- EPOCA Multinational study of the epidemiology, treatment and outcomes of paediatric arthritis. February 2012-. Pl: Jordi Antón.
- Open extension study to evaluate the long-term safety of etanercept in children and adolescents with extended oligoarticular juvenile idiopathic arthritis, enthesitis-related arthritis or psoriatic arthritis, who previously took part in Protocol 0881A1-3338-WW (B1801014). Pfizer. January 2012-. Pl: Jordi Antón.
- Pharmacovigilance in patients with juvenile idiopathic arthritis (PHARMACHILD) under treatment with biological drugs and/or methotrexate. Register of the Pediatric Rheumatology International Trials Organization (PRINTO)/Pediatric Rheumatology European Society (PRES). January 2012-. Pl: Jordi Antón.
- International, multi-centre, prospective, single-arm, open study to evaluate the safety, efficacy and pharmacokinetics of atazanavir (ATV) powder potentiated with ritonavir (RTV) liquid with an optimised combination of nucleosides in children infected by HIV, untreated or previously treated with antiretrovirals, aged from 3 months to 8 years (Pediatric Atazanavir International Clinical Evaluation: the PRINCE II study). Bristol-Myers Squibb International Corporation (BMSIC). December 2011-. PI: Clàudia Fortuny.
- Short cycle therapy (SCT) (5 days on/2 days off) in young people infected by HIV-1 (PENTA 16). Fondazione Penta; Hospital Sant Joan de Déu Barcelona. December 2011-. Pl: Clàudia Fortuny.
- Evaluation of early treatment in children with juvenile idiopathic arthritis: retrospective analysis. September 2011-. Pl: Jordi Antón.
- Phase III, randomised, double-blind, placebo-controlled study on parallel groups to evaluate the efficacy and safety during 48 weeks of orally inhaled tiotropium bromide (2.5 µg and 5 µg once daily) administered with the Respimat<sup>®</sup> inhaler to adolescents (aged 12 to 17 years) with persistent moderate asthma. September 2011-. PI: Ana Mª Plaza.
- Multi-centre, randomised, double-blind study with dual simulation to evaluate two doses of adalimumab versus methotrexate (MTX) in paediatric patients with chronic plaque psoriasis (Ps). Abbott Laboratories. March 2011-. Pl: Ma Asunción Vicente.
- HIDS study: Open, multi-centre pilot study on the efficacy and safety of treatment with canakinumab for 6 months in patients with active Hyper-IgD syndrome. Novartis Farmacéutica, S.A. February 2011 – August 2014. Pl: Jordi Antón.
- Multi-centre, longitudinal post-commercialisation observational register of long-term efficacy and safety of Humira<sup>®</sup> (adalimumab) in children with moderately to severely active polyarticular or polyarticular-course juvenile idiopathic arthritis (JIA). (STRIVE STUDY). Abbott Laboratories. May 2010-. Pl: Jordi Antón.
- Continued access to etravirine in previously treated children and adolescents infected by HIV-1. Janssen Cilag. April 2010-. Pl: Clàudia Fortuny.
- Modulation of systemic inflammatory response in critically ill children after glutamine supplementation. January 2010-.
   Pl: lolanda Jordán.
- Open extension study with canakinumab (ACZ885) in patients with systemic juvenile idiopathic arthritis and active systemic manifestations. Novartis Farmacéutica. June 2009-. Pl: Jordi Antón.
- Open, multi-centre trial on multiple-dose administration pharmacokinetics and on safety and efficacy during 48 weeks
  of maraviroc in combination with an optimised base treatment designed for subjects aged 2 to 18 years infected by
  HIV-1 with CCR% tropism who previously received treatment with antiretrovirals. Pfizer. April 2009-. PI: Clàudia Fortuny.
- Spanish Cohort of HIV Mother-Infant Pairs (HIV-MIP). January 2008-. Pl: Clàudia Fortuny.
- Evaluation of treatment satisfaction of allergic children who have received an antihistamine treatment. OSCAR study.
   July 2007-. Pl: Ana Ma Plaza.



### **Publications**

- Alsina L, Colobran R, de Sevilla MF, Català A, Viñas L, Ricart S, Plaza AM, Lois S, Juan M, Pujol-Borrel R, Martínez-Gallo M. Novel and atypical splicing mutation in a compound heterozygous UNC13D defect presenting in Familial Hemophagocytic Lymphohistiocytosis triggered by EBV infection. Clin Immunol 2014. 153: 292-297. IF: 3,992(Q2).
- Alsina L, Israelsson E, Altman MC, Dang KK, Ghandil P, Israel L, von Bernuth H, Baldwin N, Qin H, Jin Z, Banchereau R, Anguiano E, Ionan A, Abel L, Puel A, Picard C, Pascual V, Casanova JL, Chaussabel D. A narrow repertoire of transcriptional modules responsive to pyogenic bacteria is impaired in patients carrying loss-of-function mutations in MYD88 or IRAK4. Nat Immunol 2014. 15: 1134-1142. IF: 24,973(Q1).
- Alsina L, Llobet-Agulló P, Soler-Palacín P. Ampliación del cribado neonatal a la detección de inmunodeficiencias combinadas graves. Un imperativo moral. An Pediatr (Barc) 2014. 81: 273-274. IF: 0,722(Q3).
- Alvaro M, García-Paba MB, Giner MT, Piquer M, Domínguez O, Lozano J, Jiménez R, Machinena A, Martín-Mateos MA, Plaza AM. Tolerance to egg proteins in egg-sensitized infants without previous consumption. Allergy 2014. 69: 1350-1356. IF: 5,995(Q1).
- Baroja-Mazo A, Martín-Sánchez F, Gomez AI, Martínez CM, Amores-Iniesta J, Compan V, Barberà-Cremades M, Yagüe J, Ruiz-Ortiz E, Antón J, Buján S, Couillin I, Brough D, Arostegui JI, Pelegrín P. The NLRP3 inflammasome is released as a particulate danger signal that amplifies the inflammatory response. Nat Immunol 2014. 15: 738-748. IF: 24,973(Q1).
- Basmaci R, Bidet P, Yagupsky P, Muñoz-Almagro C, Balashova NV, Doit C, Bonacorsi S. Major Intercontinentally Distributed Sequence Types of Kingella kingae and Development of a Rapid Molecular Typing Tool. J Clin Microbiol 2014. 52: 3890-3897. IF: 4,232(Q1).
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### Supervised theses

 Serotype diversity of the PMEN clones in Catalonia, a geographical area with low coverage of 13-valent pneumococcal conjugate vaccine (PCV13). Universidad de Barcelona. Presentation on 20/06/2014. Doctoral candidate: Natalia Peris Guisado. Director: Carmen Muñoz-Almagro.



# Low-prevalence genetically-based neurological disorders in paediatrics

This research group investigates inborn errors of intermediary and energy metabolism, neurometabolic disorders affecting the central nervous system, and neuromuscular and neurogenetic disorders. Its studies are patient-oriented since it deals mainly with diagnostic and treatment aspects, although it also investigates more basic aspects involving cell cultures and the search for new biochemical/genetic markers and pathophysiological mechanisms. The group belongs to the Centre for Biomedical Network Research on Rare Diseases (CIBERER).

Several research lines relating to the diagnosis, treatment and study of the pathophysiological mechanisms of genetically-based rare diseases have been under way since 2005. The progress achieved up to now has allowed Hospital Sant Joan de Déu to consolidate its position as a reference centre for several of these disorders, including for example phenylketonuria. Additionally, our Hospital's Neuropaediatrics Service is a national reference for the study and treatment of rare diseases in the paediatric age. The situation at present is very appropriate for the development of various lines of research in collaboration with other reference centres and basic research centres.

### Research team

Coordinator	Dr. Jaume Campistol, Dr. Rafael Artuch
Researchers	Judith Armstrong, Mercedes Casado, Jaume Colomer, Héctor Díez, Carme Fons, Àngels García-Cazorla, Rosa Gassió, Maria Julieta, Cecília Jiménez-Mallebrera, Loreto Martorell, Raquel Montero, Andrés Nascimiento, Mª del Mar O'Callaghan, Aida Ormazabal, Carlos Ortez, Belén Pérez, Mercè Pineda, Pilar Poo, Mercedes Serrano, Cristina Sierra
Laboratory lead researchers	Aroa Fernández, Jordi Genovès, Edgar Gerotina, Juan Moreno, Montserrat Naudó, Tania Pardal, Rosa Maria Puig, Montserrat Quintana, M. Ángeles Rodríguez, Alba Tristán, Nuria Brandi, Andrea Palacio, Marc Turon, Laura Calleión

### Research lines

### PKU and other intermediary metabolism defects

Dr. Jaume Campistol

The fact that our hospital is a reference centre for phenylketonuria in Catalonia has allowed us to carry out an in-depth study of the pathophysiological mechanisms involved in this disorder and to try out new treatments aimed to improve its metabolic control and neurological prognosis. On the basis of these studies, we have reached the conclusion that some neuropsychological and neurological changes are associated, on the one hand, with metabolic control, and on the other, with antioxidant deficiencies. We have begun new treatments (with tetrahydrobiopterin) on our phenylketonuria patients, which have provided a better metabolic control and the possibility of freeing our patients from the special diet they were following. The follow-up of this treatment will be an important subject of study in the next three years. In connection with other intermediary metabolism defects, our work on metabolism disorders of homocysteine and other amino acids, which is primarily focused on characterising new disorders and new phenotypic presentations, may be noted.



### Mitochondrial energy metabolism and ataxias

Dr. Rafael Artuch

In this research line we have analysed the clinical and biochemical aspects of mitochondrial encephalomyopathies in childhood caused by changes in oxidative phosphorylation, studying as well the effects of treatment with various therapies. This line of research has been possible thanks to stable collaborations with reference centres within the framework of the Centre for Biomedical Network Research on Rare Diseases (CIBERER) network, and thanks to the performance of research projects financed by FIS. We have carried out a research line for the diagnosis of primary and secondary deficiencies of coenzyme Q. This line has been possible thanks to the three FIS projects that have been consecutively obtained for research on this subject.

### Applied research in neuromuscular disorders

Dr. Cecília Jiménez-Mallebrera

Our research lines are focused at present on two main areas: 1. Muscular dystrophies, including Duchenne muscular dystrophy (DMD) and congenital muscular dystrophies (CMD), with special attention to the role of the extracellular matrix and of collagen VI in muscular dystrophies, and to the study of fibrosis and the proliferation of adipose tissue. 2. The second group of disorders which we investigate are those connected with mitochondrial myopathies of nuclear origin, with special emphasis on the mitochondrial DNA depletion syndromes. 3. Lastly, as a cross-sectional activity, we are working on the development of biomarkers in serum and tissues (soluble factors and microRNA) for the diagnosis of these disorders and the monitoring of clinical trials. In both cases, by applying high-performance techniques such as biochips, bioinformatics and cellular models, the gene expression footprint of patients' muscle has been determined in comparison to healthy muscle, allowing new pathophysiological mechanisms and diagnostic markers to be identified for these disorders.

### Neurometabolic disorders with expression in the CNS

Dr. Àngels García-Cazorla

We have been studying these metabolic deficiencies since 2003 while serving various hospital centres in Spain, Portugal, Greece, Argentina, Turkey and India, among other countries. Basically, we study dopamine and serotonin defects and quite recently we have also turned our attention to GABA. From the clinical standpoint, our patients present severe encephalopathies which are detected by specifically studying this neurotransmitter in cerebrospinal fluid (CSF). Our main focus is diagnosis within a very clear therapeutic approach since many of these disorders have a treatment that can improve or normalise the patient's clinical condition. Moreover, some aspects of translational research are now also an important part of our research with the inclusion of studies of CSF proteomics and of cell lines with tyrosine hydroxylase (a limiting enzyme in dopamine synthesis) deficiency, which are analysed by various cell biology and electrophysiology techniques. We have been able to add these new procedures to our research thanks to the establishment in recent years of the laboratory for the study of neuronal synapse in neuropaediatric disorders, primarily for the purpose of studying synaptic metabolism.

### Movement disorders of genetic and neurometabolic origin

Dr. Belén Pérez-Dueñas

The Research Group on Paediatric Neurosciences forms part of the Integral Unit for the Study of Movement Disorders Caused by Rare Diseases. This unit, which is directed jointly by Hospital Sant Joan de Déu and Hospital Clínic de Barcelona, has been designated as a Reference Integral Unit by the Spanish National Health System.

This line is focused on research on rare diseases of genetic and neurometabolic origin which occur with movement disorders in childhood. Such movement disorders can occur in isolated form or in association with other neurodevelopmental problems, and they are a major cause of physical disability in children. The research on this group of disorders is addressed to clinical characterisation, identification of new biomarkers, and molecular studies to identify new genetic defects.

Two consecutive FIS projects have been carried out in the last 5 years with their focus on the study of defects of the genes responsible for the transport, synthesis and processing of vitamins. Thiamine and cerebral folate deficiencies affect the developing central nervous system and may produce clinical conditions of acute and/or progressive encephalopathy, mitochondrial energy deficiency and cerebral myelination disorders. Their identification is a priority since the early administration of high doses of these vitamins may bring about an immediate recovery from symptoms and revert brain lesions. Thanks to these projects, we have established blood and cerebrospinal fluid biomarkers for their identification. Indeed, thanks to these findings, our hospital has become a reference centre in this field and we have taken part in the identification of new phenotypes associated with genetic defects.



### Neuronal development disorders: Rett syndrome

Dr. Judith Armstrong and Dr. Mercè Pineda

The Rett Syndrome (RTT) Research Group at Hospital Sant Joan de Déu has long experience with this disorder from both the clinical and genetic standpoints. This research line has been based on the detection of mutations of the genes connected with the disorder in the patients, and on the search for new genes and the improvement of the techniques for detecting and locating new target tissues for the diagnosis of this disorder. Various therapeutic trials have also been conducted and an internationally validated age-unrelated checklist or clinical evaluation scale has been developed that has allowed phenotype-genotype correlations to be established in these patients. Likewise, we have started a research line aimed to detect targets for pharmacological therapy in parallel in cell lines, iP S cells and transgenic mice, in which two recurrent mutations in Rett patients – c.763C>T (p.Arg255X) and c.916C>T (p.Arg306Cys) – are studied. Gene, protein and pharmacological therapy studies have been promoted in connection with this disorder since 2007, and genetic diagnosis will be essential for their performance. Our research teams belong to the European Research Board of the RettDatabase Network, and to the IRSF Research Council.

### **Projects**

- Severe childhood neurological disorders. Fundación Banco Bilbao Vizcaya Argentaria. November 2014 November 2015. Pl: Rafael Artuch.
- Identification of populations showing high linear correlations between biochemical variables. SAF2013-50139-EXP.
   Ministerio de Ciencia e Innovación (MINECO). September 2014 August 2015. Pl: Rafael Artuch.
- Cellular model for the study and treatment of excitatory/inhibitory synaptic unbalance in Rett syndrome. Obra Social Sant Joan de Déu. September 2014 – August 2016. Pl: M. Àngels García-Cazorla.
- Study of defects of thiamine transport and metabolism associated with recurrent childhood encephalopathies. Fl grant: Beneficiary: Juan Darío Ortigoza. Agaur - Agència de Gestió d'Ajuts Universitaris i de Recerca. May 2014 – April 2017. Pl: Belén Pérez-Dueñas.
- Study of defects of thiamine transport and metabolism associated with recurrent childhood encephalopathies. Hospital Sant Joan de Déu Barcelona. March 2014 – March 2017. Pl: Belén Pérez-Dueñas.
- Exome sequencing for discovery of candidate genes in Rett and Rett variants. Associació Catalana de la Síndrome de Rett - ACSR. January 2014-. Pl: Judith Armstrong Morón.
- Research Group on Paediatric Neurosciences and Metabolism. SGR 2014. 2014SGR1150. Agaur Agència de Gestió d'Ajuts Universitaris i de Recerca. January 2014 – December 2016. Pl: Jaume Campistol.
- Role of collagen VI and biglycan in muscle homeostasis: regulation of muscle fibre size and metabolism. Implications for muscular dystrophies. PI13/00837. Instituto de Salud Carlos III. January 2014 – December 2016. PI: Cecilia Jiménez-Mallebrera.
- Research activity intensification programme in the Spanish National Health System 2013. INT13/00212. Instituto de Salud Carlos III. January 2014 – January 2015. Pl: Rafael Artuch.
- MHealth4Ped Innovating the mHealth resources (a mobile health application) to facilitate the self-management and independence of patients and their carers in chronic paediatric disorders. Ministerio de Ciencia e Innovación (MINECO). October 2013 – September 2014. Pl: Mercedes Serrano.
- Reina Sofía Foundation for Rett Syndrome. Fundación Reina Sofía. May 2013-. Pl: Judith Armstrong.
- Role of collagen VI in muscle homeostasis: regulation of muscle fibre size and of glucose and fatty acid metabolism.
   Hospital Sant Joan de Déu Barcelona. April 2013 April 2016. PI: Cecilia Jiménez-Mallebrera.
- Inherited NeuRoMetabolic Diseases INFORMATION NETWORK. InNerMeD-I-Network. European Commission. April 2013 September 2015. Pl: M. Àngels García-Cazorla.
- Biomarkers of cerebral neurotransmission alteration in paediatric encephalopathies of genetic origin: studies on patients and on a cellular mode. Instituto de Salud Carlos III (ISCIII). January 2013 December 2015. PI: M. Àngels García-Cazorla.
- Post FSE (Río Hortega) contract Marta Molero. Instituto de Salud Carlos III. January 2013 December 2014. Pl: Rafael Artuch.
- Study of defects in the transport and metabolism of thiamine associated with recurrent encephalopathies in childhood.
   Instituto de Salud Carlos III (ISCIII). January 2013 December 2015. PI: Belén Pérez-Dueñas.



- Study of biochemical markers of dopaminergic and serotonergic neurotransmission in relation to neurological and neuropsychological changes in phenylketonuria. Instituto de Salud Carlos III (ISCIII). January 2013 December 2015. Pl: Jaume Campistol.
- Study of RNA in CSF in Rett patients; new diagnostic approaches. Fondo Biorett. January 2013 December 2015. Pl: Judith Armstrong.
- Programme for Intensification of Research Activity in the Spanish National Health System 2012. Instituto de Salud Carlos III (ISCIII). January 2013 January 2014. PI: Rafael Artuch.
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   January 2012 March 2015. Pl: Rafael Artuch.
- Río Hortega Contract, candidate: Mireia Tondo. Instituto de Salud Carlos III (ISCIII). January 2011 January 2014. Pl: Rafael Artuch.
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- Application of Global Gene Expression Analysis and Functional Genomics to the Study of the Physiopathology, Treatment and Diagnosis of Pediatric Myopathies. Instituto de Salud Carlos III (ISCIII). April 2010 April 2016. PI: Cecilia Jiménez-Mallebrera.
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### Clinical trials

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   September 2014-. PI: Andrés Nascimento.
- Observational, Ambispective Natural History Study of Patients with Mucopolysaccharidosis Type IIIA (MPS IIIA) or Sanfilippo Syndrome Type A. July 2014-. Pl: Mercè Pineda.
- Phase III, multi-centre, double-blind, prospective, randomised, controlled, multiple-treatment study to evaluate the efficacy and safety of Dysport in the paediatric treatment of upper limb spasticity. May 2014-. Pl: Xenia Alonso.
- Prospective, cross-sectional, longitudinal study with additional retrospective review of clinical records to evaluate the clinical and biochemical characteristics and evolution of the disorder in mucopolysaccharidosis type IIIB patients. INC Research UK Limited. March 2014-. Pl: Ma del Mar O'Callaghan.
- Phase IV, open, single-cohort study of long-tern neurocognitive (NC) results in children aged 4-5 years with phenylke-tonuria treated with sapropterin dihydrochloride (Kuvan®) for 7 years. Merck KGaA. February 2014-. Pl: Jaume Campistol.
- Register of patients with Niemann-Pick disease, type C. February 2011-. Pl: Mercè Pineda.
- Retrospective review of the clinical records of deceased patients with mucopolysaccharidosis type IIIB. January 2014-.
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- Retrospective observational study of hyperammonaemia in organic acidaemia decompensation episodes treated with a control arm (ammonium sequestrant). Orphan Europe. December 2012-. Pl: M. Àngels García-Cazorla.
- International disease register with data on manifestations, interventions and results in patients with tuberous sclerosis complex (TOSC). Novartis Farmacéutica. November 2012-. Pl: Jaume Campistol.
- Multi-centre, open, long-term follow-up study to evaluate the safety and efficacy of brivaracetam as adjuvant treatment in paediatric patients with epilepsy. October 2012-. Pl: Francesc Xavier Sanmartí.
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### Supervised theses

- Capillary electrophoresis applications in inborn errors of metabolism diagnosis. Universitat Autònoma de Barcelona. Presentation on 05/05/2014. Doctoral candidate: Mercedes Casado Rio. Director: PI: Rafael Artuch.
- Dopamine metabolism biomarkers in childhood neurological changes. Universitat de Barcelona. Presentation on: 05/05/2014. Doctoral candidate: Marta Molero Luis. Director: Pl: Rafael Artuch.
- Fibroblasts from patients with myopathies: a method to establish primary cultures from skin biopsies and their applications. Universitat de Barcelona. Presentation on 30/06/2014. Director: Pl: Cecilia Jiménez-Mallebrera.

### **Networks**

- Centre for Biomedical Network Research on Rare Diseases (CIBERER). Ministry of Economy and Competitiveness.
   Carlos III Health Institute.
- European Treat-NMD Network.



# Etiopathogeny and treatment of severe mental disorders

Schizophrenia, the most paradigmatic mental disorder, affects about 1% of the population and is one of the disorders of this type that causes the greatest disability. It has been estimated that severe mental disorders affect 2.8% of the population. Engaged in research on people who suffer severe mental disorders, our group is formed by a multidisciplinary team (with members from the spheres of psychiatry, psychology, nursing, biology, social work, etc.). Ours is a broad field of study, covering subjects ranging from gene expression factors to psychosocial interventions. We belong to the Centre for Biomedical Network Research on Mental Health (CIBERSAM), financed by the Carlos III Health Institute.

### Research team

Coordinator	Judith Usall
Line coordinators	Susana Ochoa, Luis San, Belén Ramos
Researchers	José Ángel Alda, Hilari Andrés, Belén Arranz, Gildas Brebion, Emma Casas, Daniel Cruz, Ruth Cunill, Montse Dolz, Gemma Escartín, Gemma Escuder, Aida Farreny, Alexandrina Foix, Mar García, Sergio Herrera, Marcia Irazabal, Fernando Lacasa, María Ángeles Mairena, Francisco Martínez, Josep Lluis Matalí, Trini Peláez, María Dolores Picouto, Bernardo Sánchez, Eduardo Serrano, Christian Stephan-Otto, Sonia Vilamala, Antonio Manuel Alba, Adela Berrozpe, Mar Alvarez, Marta Carulla, Daniel Muñoz, Juan Jairo Ortiz, Anna Sintes
Trainee researchers	Gemma Riquelme, Èlia Vila, Elena Rubio, Núria del Ccho
Pre-doctoral researchers	Anna Butjosa, Montserrat Fusté, Elena Huerta, Raquel López, Christian Núñez, Sara Siddi, Jordina Tor, Raquel Pinacho, Regina Vila
Assistants	Raúl Alelú, Marta Coromina, Jorge Cuevas, Maria Jose Escandell, Lourdes Fañanas, Mar Fatjó, Isidre Ferrer, Grace Gill, Carla Jané, Juan Carlos Leza, Jose Ramon Martin, Javier Meana, Eva Miquel, Marta Pardo, Beatriz del Pino, Marta Puig, Stephanie Sammut, Núria Sebastián, Sarabel Solis, Carles Soriano, Salvador Soto, Charles Spence, Teresa Tarragó, Elsa Valdizán, Judit Villén

### Research lines

### Clinical, cognitive and psychosocial bases of severe mental disorders

Dr. Susana Ochoa

The evaluation of the clinical, psychosocial and neuropsychological characteristics presented by people with severe mental disorders will allow us to more suitably identify the treatment needs in each case. Our research line has the goal of evaluating various clinical, social and neuropsychological aspects, among others, of people who are beginning to experience the first episodes of severe mental disorder and, in this respect, it is necessary to possess suitable measuring instruments in order to be able to make correct evaluations. Likewise, we seek to determine the clinical, social or neuropsychological operating variables which have the greatest effect on a poor evolution of the disorder in order to be capable of preventing deterioration. Another of our aims is to study the clinical, social and neuropsychological differences of the various severe mental disorders and of first psychotic episodes. Lastly, we focus on the development of appropriate measuring instruments to evaluate patients suffering from severe mental disorders.



# Molecular psychiatry

Dr. Belén Ramos

The research conducted by our group focuses on achieving an understanding of how the regulation of gene expression may contribute to the pathophysiology of severe psychiatric disorders by controlling important processes for normal neuronal development which could affect the patients' neuronal connectivity. Additionally, this research seeks to identify in such disorders new molecular changes in the brain which could contribute to the functioning of the neuron-glia microcircuits. We focus mainly on the study of the Sp4 and Sp1 transcription factors in the context of psychotic disorders, in various biological substrates (post-mortem brain and peripheral cells) and in different stages of the disorder, as well as their association with the severity of negative symptoms in the case of schizophrenia studies. Additionally, we are conducting an investigation which has the aim of identifying new altered cell programmers in the brains of schizophrenia patients by means of proteomic techniques. We study how altered molecular markers in these disorders are regulated by (a) pharmacological treatments in vivo and in vitro in rodents, and by (b) physiological signals of response to neuronal activity in rat neuronal cultures and (c) in a murine pharmacological model of psychosis.

### Mental health interventions

Dr. Judith Usall

Current pharmacological and psychological treatments are not effective in all people who suffer schizophrenia. Our research group conducts clinical trials on the treatment of resistant schizophrenia or schizophrenia with predominant negative pharmacological or psychological symptoms. Four clinical trials have been conducted independently of the pharmaceutical industry, with financing from both public administrations and private foundations (Stanley Foundation). Gender- and sex-sensitive psychopharmacology is also taken into account in the research carried out. We are preparing to start new projects that will allow new pharmacological and psychosocial treatments to be developed and evaluated.

### Mental disorders in childhood and adolescence

Dr. Luis San

The importance of mental disorders for patients suffering from them and for society at large has been clearly recognised in recent decades. Evidently, the ultimate goal of the research in child and adolescent psychiatry is to improve clinical practice. Consequently, it is necessary to potentiate the relationship between these two perspectives both to optimise day-to-day practice and to prioritise research that answers questions with a bearing on the improvement of diagnoses and treatments. To do this it is necessary to promote research that involves various basic and clinical disciplines. Of special importance are developmental neuropsychology, genetics, neuroimaging, neurobiology, therapeutics, epidemiology and prevention.

# **Projects**

- Research Fellowship: Christian Núñez Leánez. Ministerio de Ciencia e Innovación (MINECO). July 2014 March 2015.
   PI: Christian Núñez.
- Post-residency grants 2014 PSSJD Elena Rubio. Parc Sanitari de Sant Joan de Déu. May 2014 May 2016. Pl: Josep Maria Haro.
- Río Hortega research training contract. Instituto de Salud Carlos III (ISCIII). May 2014 May 2016. Pl: Josep Maria Haro. Beneficiary: Elena Rubio.
- Unusual psychic experiences and jumping to conclusions in the clinical and general populations. Parc Sanitari de Sant Joan de Déu - Serveis de Salut Mental. February 2014 – February 2015. Pl: Gildas Brebion.
- Metacognitive training (MCT) effectiveness in people with long-evolution psychosis treated in community rehabilitation services. Parc Sanitari de Sant Joan de Déu -Serveis de Salut Mental. February 2014 – February 2015. Pl: Mar García Franco.
- Effectiveness of the metacognitive training programme in the improvement of the social and occupational inclusion of people with a first psychotic episode. Fundació Caixa d'Estalvis i Pensions de Barcelona. February 2014 – January 2016. Pl: Susana Ochoa.
- Grant for research fellowships abroad 2013-14. Universitat de Barcelona. January 2014 December 2014. Pl: Sara Siddi.
- Effectiveness of metacognitive training for people with first psychotic episodes. Obra Social Sant Joan de Déu. January 2014 – December 2014. Pl: Susana Ochoa.



- Prolactin levels in patients with a first psychotic episode without antipsychotic treatment with secondary sexual and reproductive effects. Cross-sectional and follow-up study after three months. Parc Sanitari de Sant Joan de Déu - Serveis de Salut Mental. September 2013 – January 2015. Pl: Núria del Cacho.
- Evaluation of treatment needs of users of the psychosocial rehabilitation services from the standpoint of users, their families and service professionals. Parc Sanitari de Sant Joan de Déu. February 2013 – December 2015. Pl: Sonia Vilamala.
- Multimedia adaptation of REPYFLEC cognitive remediation treatment for persons with schizophrenia. OSSJD Obra Social Sant Joan de Déu. January 2013-. Pl: Aida Farreny.
- Predoctoral PFIS research training contract. Instituto de Salud Carlos III. September 2012 August 2014. Pl: Josep Maria Haro. Beneficiary Raquel Pinacho.
- Transcriptional regulation by psychoactive drugs in rat neurons and astrocytes. Collaboration agreement with IPROTE-OS. November 2012-. Pl: Belén Ramos.
- Observational study of prospective cohort of patients with persistent symptoms of schizophrenia to describe the course and burden of the disorder. F. Hoffmann- La Roche Ltd. September 2012-. Pl: Josep Maria Haro.
- Proteomics in Severe Psychiatric Disorders. Industex Obra Social Sant Joan de Déu. September 2012-. Pl: Belén Ramos.
- Sexual, reproductive and osteopaenic side effects in hyperprolactinaemia from use of antipsychotics. Gender differences. Parc Sanitari de Sant Joan de Déu. May 2012 June 2014. Pl. Judith Usall.
- Clinical and neurobiological determinants of second episodes of schizophrenia. Longitudinal study of first psychotic episodes. Instituto de Salud Carlos III. January 2012 – December 2015. Pl: Judith Usall.
- Effectiveness of metacognitive training (MCT) on symptoms, metacognition, and social and neuropsychological functioning in persons with short-evolution psychosis. Instituto de Salud Carlos III. January 2012 December 2014. Pl: Susana Ochoa.
- Multi-centre longitudinal study on clinical, cognitive and neuroimaging characteristics in children and adolescents with Psychosis Risk Syndrome. Instituto de Salud Carlos III. January 2012 December 2015. Pl: Montserrat Dolz.
- Prevalence of sleep disorders in children and adolescents with recent diagnosis of attention deficit hyperactivity disorder and their relation to iron metabolism. Instituto de Salud Carlos III. January 2012 – December 2014. Pl: José Ángel Alda.
- Study of hallucinations from a neurofunctional and cognitive standpoint. Instituto de Salud Carlos III. January 2011 December 2014. Pl: Gildas Brebion.
- Hallucinations and source memory impairment in schizophrenia patients and non-clinical individuals. Instituto de Salud Carlos III. January 2010 January 2016. Pl: Gildas Brebion.
- RETICS BioBanks PSSJD Brain Bank. Instituto de Salud Carlos III. January 2010 December 2014. Pl: Mercedes Roca Casasus.

# Clinical trials

- Multi-centre, flexible-dose, open extension study with a duration of 104 weeks to evaluate the long-term safety and
  efficacy of lurasidone in paediatric patients with schizophrenia and patients with irritability associated with autistic disorder. July 2014-. Pl: Luis San.
- Multi-centre, fixed-dose, placebo-controlled, double-blind, parallel, randomised study with a duration of 6 weeks to evaluate the efficacy and safety of lurasidone in adolescent patients with schizophrenia. June 2014-. Pl: Luis San.
- Cross-sectional study with retrospective review of patients with persistent symptoms of schizophrenia to estimate the
  use of medical resources and the burden of the disorder. F. Hoffmann- La Roche. September 2013-. Pl: Belén Arranz.
- Healthcare- and social cost of handling the attention deficit hyperactivity disorder. Shire Pharmaceuticals Iberica. December 2012-. Pl: José Ángel Alda.
- Phase 4, open, multi-centre study of safety during 2 years of treatment with lisdexamfetamine dimesylate in children and adolescents aged 6 to 17 years with attention deficit hyperactivity disorder (ADHD). Shire Pharmaceuticals Iberica. August 2011-. Pl: José Ángel Alda.



- Clinical and neuropsychological factors associated with the response to second-generation antipsychotics in children and adolescents diagnosed with a first episode of early onset schizophrenia spectrum. Ministerio de Sanidad y Política Social. January 2011 – November 2014. Pl: Luis San.
- A 6-month double-blind, placebo-controlled study of efficacy of raloxifene as an adjuvant treatment for negative symptoms of schizophrenia in postmenopausal women. The Stanley Medical Research Institute. January 2011 December 2014. Pl: Judith Usall.

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# **Networks**

 Centre for Biomedical Research on Mental Health (CIBERSAM). Ministry of Economy and Competitiveness (MINECO). Instituto Carlos III.



# Impact, risk and prevention of mental disorders

Mental disorders are the group of illnesses with the greatest impact on the population's health in the most economically-developed countries, as has been stated by the World Health Organisation and in the Global Burden of Disease study. Between 20% and 30% of all people suffer a mental disorder at some point in their life. In many cases, this disorder is highly incapacitating. Our interdisciplinary group, which includes psychiatrists, psychologists, statisticians, sociologists and basic researchers, studies the factors that provide protection against or increase the risk of mental disorders, and treatments for the people who suffer them, for the purpose of improving preventive and therapeutic strategies.

In recent years, aware of the importance of mental health in the achievement of a physically, mentally and socially healthy ageing process, we are devoting special attention to the study of health histories in order to determine the factors which favour active healthy ageing and at exactly which moment in time it is necessary to intervene in order to improve the course of each individual's health. We seek to translate all this knowledge into healthcare innovations which can be easily incorporated into our healthcare and social support systems.

Our group forms part of the Centre for Biomedical Network Research on Mental Health (CIBERSAM), financed by the Carlos III Health Institute and it is recognised as a consolidated research group by the Government of Catalonia (AGAUR – Agency for Administration of University and Research Grants).

# Research team

Coordinator	Josep Maria Haro
Line coordinators	Beatriz Olaya, Jordi Navarra
Researchers	Ai Koyanagi, Rubén Moreno, Carla Obradors, Stefanos Tyrovolas, Claudia Caprile
Pre-doctoral researchers	Elvira Lara, Noé Garin, Ziggi Santini, Íñigo Romero, Ramón Nogueira, Philipp Edmund Schustek, Laura Puigcerver, Víctor Gómez
Laboratory technician	Joel García
Statistician	Jaume Aguado, Maria Victoria Moneta
Support personnel	Marta Hernández

# Research lines

# **Epidemiology**

Dr. Josep M. Haro

This research line seeks to determine the impact (prevalence and disability) of mental illnesses in the general population and the healthcare received by the people who suffer them. Epidemiologic studies are necessary for the planning and management of resources, as well as to evaluate the existence and impact of factors associated with the occurrence of mental disorder. The various projects of the line are focused on the adult, child-adolescent, and elderly populations. Additional goals are to determine the populational prevalence of mental illnesses in the adult and child-adolescent populations; to study the socio-demographic characteristics and risk factors associated with mental illnesses; to analyse how the healthcare services care for the people with mental health problems; to determine the impact of mental health problems on quality of life and disability; and to analyse the relation between ageing and neuropsychiatric illnesses.



# Prevalence and co-morbility of mental disorders in the various age groups

Dr. Beatriz Olaya

This research line is focused on determining the impact (prevalence and disability) of mental illnesses in the general population and the healthcare received by the people who suffer them. Epidemiologic studies are necessary for the planning and management of resources, and to evaluate the existence and impact of factors associated with the occurrence of mental disorder. The various projects of this research line are focused on the adult, child-adolescent, and elderly populations.

# Basic processes of perception, attention and action

Dr. Jordi Navarra

This research line seeks to describe specific normal and dysfunctional (for example schizophrenia) perception and attention processes. Specifically, it studies the cerebral mechanisms which allow us to describe the cognitive and neurophysiological bases of adaptation to the asynchrony between signals of different sensory modalities, to reduce the asynchrony between sensory information (visual and auditory, for example) on a specific event, to investigate the filter and integration mechanisms of sensory information in schizophrenia, to code sensory information in an integrated or independent way, to describe the role of the perception of faces in the selection and inhibition of bilingual languages, to select one language or another according to the context, to study the role of the integration of sensory-motor information during the performance of movements in phenylketonuria, and to coordinate sensory and motor information during the performance of a movement.

# **Projects**

- Sant Boi Ageing Study. Ajuntament de Sant Boi. November 2014 October 2015. Pl: Josep Maria Haro.
- Pre-doctoral grants. University teacher training 2013: Elvira Lara Pérez. Ministerio de Educación. September 2014 –
   September 2018. Pl: Josep Maria Haro.
- Post-residency grant 2014 PSSJD: Elena Rubio. Parc Sanitari de Sant Joan de Déu. May 2014 May 2016. Pl: Josep Maria Haro.
- Río Hortega research training contract. Beneficiary: Elena Rubio Abadal. Instituto de Salud Carlos III. May 2014 May 2016. Pl: Josep Maria Haro.
- Neuropsychiatric disorders in the elderly. Instituto de Salud Carlos III. March 2014 March 2019. Pl: Ai Koyanagi.
- Doctor training contracts. Beneficiary: Laura Puigcerver. Ministerio de Ciencia e Innovación (MINECO). January 2014
   January 2018. Pl: Jordi Navarra.
- The role of variability in neuronal activity in perception, decisions and trust. Ministerio de Ciencia e Innovación (MINE-CO). January 2014 – December 2016. Pl: Ruben Moreno.
- Support for research groups 2014. Impact and risk factors of mental disorders. Agair Agència de Gestió d'Ajuts Universitaris i de Recerca. January 2014 – December 2016. Pl: Josep Maria Haro.
- Contracting grant I3 Jordi Navarra. Ministerio de Ciencia e Innovación (MINECO). November 2013 November 2016.
   PI: Jordi Navarra.
- Motor changes underlying attention deficit hyperactivity disorder (ADHD): diagnostic implications. Fundación Alicia Koplowitz. October 2013 – November 2015. Pl: Jordi Navarra.
- Functional connectivity and decoding in neuronal circuits of the primary visual cortex and the hippocampus. Agaur Agència de Gestió d'Ajuts Universitaris i de Recerca. April 2013 – March 2016. Beneficiary: Ramon Nogueira Mañas. Pl: Ruben Moreno.
- MARATONE Mental Health Training through Research Network in Europe. European Commission. April 2013 March 2017. Pl: Josep Maria Haro.
- European Innovation Partnership on Active and Healthy Ageing EIP AHA Committee. European Commission. March 2013-. PI: Josep Maria Haro.
- Impact of chronic mental disorders and of psychiatric disorders on disability and quality of life in elderly patients. Ministerio de Educación. March 2013 March 2017. Beneficiary: Noé Garín Escrivà. Pl: Josep Maria Haro.



- Health condition, quality of life and well-being in ageing: a longitudinal study. Instituto de Salud Carlos III. January 2013
   December 2015. Pl: Josep Maria Haro.
- Spatial Recoding of Sound. Ministerio de Ciencia e Innovación (MINECO). January 2013 December 2015. Pl: Jordi Navarra.
- Post-doctoral contracts IISC III Sara Borrell. Instituto de Investigación Sanitaria Carlos III. 2013-2015. Pl: Josep Maria Haro.
- Observational study of a prospective cohort of patients with persistent symptoms of schizophrenia to describe the course and burden of the disorder. F. Hoffmann-La Roche. September 2012-. Pl: Josep Maria Haro.
- Basque Government pre-doctoral grant: Íñigo Romero Arandia. Fundació Privada per a la Recerca i la Docència Sant Joan de Déu; Gobierno Vasco Departamento de Educación e Universidades. January 2012 – December 2015. Pl: Íñigo Romero.
- Provision of support on the design, application and analysis of research projects based on neuroimaging techniques, which generally share the goal of identifying the neurofunctional bases of various mental processes. Ministerio de Ciencia e Innovación (MINECO). January 2012 – December 2014. Pl: Josep Maria Haro.
- An age-friendly city for a successful ageing. Fundació Caixa d'Estalvis i Pensions de Barcelona. December 2011 January 2014. Pl: Josep Maria Haro.
- Computational Neuroscience. Ministerio de Ciencia e Innovación (MINECO). July 2011 July 2016. Pl: Ruben Moreno.
- CoNeuron. Drawing neuronal circuits without seeing them. European Commission. March 2011 March 2015. Pl: Ruben Moreno.
- Post-FSE contract (Río Hortega). Beneficiary: Montserrat Fuste. Instituto de Salud Carlos III. January 2011 January 2014. Pl: Josep Maria Haro.
- Roadmap for Mental Health Research in Europe (ROAMER). European Commission. 2011-2015. Pl: Josep Maria Haro.
- Lilly collaboration agreement. Eli Lilly and Company Limited. December 2010-. Pl: Josep Maria Haro.
- Pre-doctoral grants for research training 2010. Instituto de Salud Carlos III. September 2010 August 2014. Pl: Josep Maria Haro. Beneficiary: Raquel Pinacho.
- COST Time In Mental activity: theoretical, behavioural, bioimaging and clinical perspectives (TIMELY). European Commission. April 2010 April 2014. Pl: Jordi Navarra.
- Pre-doctoral grants for research training 2009. Beneficiary: Jaime Perales. Instituto de Investigación Sanitaria Carlos III.
   2010-2014. Pl: Josep Maria Haro.
- Centre for Biomedical Network Research on Mental Health (CIBERSAM). Instituto de Salud Carlos III (ISCIII). January 2008-. Pl: Josep Maria Haro.

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# Supervised theses

 Health and ageing: active ageing in older adults and health related quality of life in people dementia. Universitat Pompeu Fabra. Doctoral candidate: Jaume Perales. Director: Josep Maria Haro.

# **Networks**

Centre for Biomedical Research on Mental Health (CIBERSAM). Ministry of Economy and Competitiveness (MINECO).
 Carlos III Health Institute.



# Research and innovation in surgery

This group is engaged in research on the illnesses in which surgical treatment occurs at some point in the care process. Due to its multidisciplinary character, this group is formed by a team of people from different spheres of medicine (including experts in general and digestive surgery, traumatology, gynaecology, urology, image diagnosis, endocrinology and nutrition, among others), who are coordinated to focus their skills on the various areas of interest to the group's research. The group has a wide-ranging scope of study, including pathophysiological, epidemiological and risk-related factors as well as the critical analysis of the various aspects of surgical therapeutics.

# Research team

Coordinator Line coordinators	David Parés  Juan Castellanos, Manuel Céspedes, Jaime Jimeno
Line Coordinators	Juan Castellanos, Manuel Cespedes, Jaime Jimeno
Researchers	Rosa Cambra, Manel Carreras, Josep M Casulleras, Isaac Cebrecos, Jordi Comajuncosas, Raúl de Diego, Enric Domínguez, Laia Estalella, Lluis Font, Josep-Ramón Méndez, Laura García, Andres E. Gerding, Pere Gris, Judit Hermoso, Oscar Izquierdo, Carlos Jordán, Lucas Krauel, Jose Luís López-Negre, Jose Manuel Ledesma, Montserrat Margarit, Eva Martinez, Gabriela Monroy, Rolando Orbeal, Jose Maria Rodríguez, Nuria Rojo, Sergi Romero, Ana Sánchez, Joan Urgellés, Arnau Valls, Helena Vallverdú

# Research lines

## Functional pathology of the digestive system and of the abdominal wall

Dr. David Parés

This line is focused on functional disorders of bowel habit (faecal incontinence), benign anorectal pathology (haemorrhoids, fistulas, anal fissures) and their diagnosis by 3D endoanal ultrasound scan, and clinical and quality-of-life aspects in inguinal hernia.

# Study of hepatobiliary, endocrine system and mammary disorders

Dr. Jaime Jimeno

Most of the studies in this research line are focused on aspects of care quality in laparoscopic cholecystectomy and on the pathology of the parathyroid gland.

# Locomotor system disorders

Dr. Juan Castellanos

This line encompasses all types of research in orthopaedic surgery and traumatology, centred to a large extent on aspects involving the control and study of infection in traumatology and on the microsurgical treatment of various locomotor system pathologies.

# Uro-gynaecological and pelvic floor surgery

Dr. Manuel Céspedes

Post-delivery disorders of the pelvic floor (urinary incontinence) and surgical disorders of the urethra.



# **Projects**

- Effect of external neurolysis of the peripheral nerves on the occurrence of ulcers in diabetic polyneuropathy. Parc Sanitari de Sant Joan de Déu. February 2014 February 2015. Pl: Oscar Izquierdo.
- Prospective randomised study of the utility of a change of position of the umbilical trocar on the incidence of surgical wound infection in laparoscopic cholecystectomy. Parc Sanitari de Sant Joan de Déu. February 2014 – February 2015.
   Pl: Judit Hermoso.
- Relation between serum levels of progesterone, estradiol and relaxin and the occurrence of faecal incontinence symptoms during pregnancy and the post-delivery period. Instituto de Salud Carlos III). January 2014 December 2016. Pl: Eva Maria Martínez.
- Support for research groups 2014. Surgery Research and Innovation Group. Agència de Gestió d'Ajuts Universitaris i de Recerca. January 2014 – December 2016. Pl: David Parés.
- Impact of the use of information and communication technologies (ICTs) in the management of the surgery waiting list: a randomised clinical trial. Parc Sanitari de Sant Joan de Déu. February 2013 December 2015. Pl: David Parés.
- Effect of electromagnetic fields on adhesion and formation of S. epidermidis biofilm on various metals. Mutual Mèdica de Catalunya i Balears. November 2011 – December 2014. Pl: Luis Font.

# Clinical trials

 Low molecular weight heparin (LMWH) for the prevention of complications derived from placental insufficiency in atrisk patients without thrombophilia: randomised multi-centre study. ACNC0005. September 2011-. Pl: Raul De Diego.

# **Publications**

- Carnuccio P, Jaime Jimeno Fraile, Parés D. Laparoscopic right colectomy: a systematic review and meta-analysis of observational studies comparing two types of anastomosis. Tech Coloproctol 2014. 18:5-12. IF: 1,344(Q3).
- Comajuncosas J, Hermoso J, Gris P, Jimeno J, Orbeal R, Vallverdú H, López Negre JL, Urgellés J, Estalella L, Parés D.
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- Correa J, Lopez-Negre JL, Barrio C, Parés D. ¿Cómo podemos mejorar la atención de los pacientes con patología anorrectal benigna?. Aten Primaria 2014. 46:582-583. IF: 0,894(Q3).
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- Parés D. Factors influencing clinical results in colon surgical resection: surgeon, volume of cases and now day of the week?. Am J Surg 2014. 207:1003. IF: 2,406(Q1).
- Parés D, Jimeno J, Orbeal R. Reingreso hospitalario en cirugía general y digestiva: ¿existe asociación con la edad de los pacientes?. Gastroenterol Hepatol 2014. 37:269-270. IF: 0,832(Q4).
- Secanell M, Orrego C, Vila M, Vallverdú Helena, Mora N, Oller A, Bañeres J. Implementación de un listado de verificación de prácticas seguras en cirugía: experiencia de la fase inicial de la puesta en marcha de un proyecto colaborativo en hospitales de Catalunya. Med Clin (Barc) 2014. 143:17-24. IF: 1,252(Q3).



# Healthcare technologies and results in primary care and mental health (PRISMA)

This research team conducts projects relating to the field of epidemiology, analysis of the effectiveness and suitability of treatments, mental health determinants, and economic effects on society. Analyses are made of both illnesses and the treatments applied to them in specific contexts.

- 1. Evaluation of the prevalence of mental illnesses and of the needs of the people who suffer them, in both the general population and specific populations (primary care, prison care).
- 2. Evaluation of the effectiveness of intervention in primary care: anti-depressive treatment, psycho-education, pharmaceutical intervention, etc.
- 3. Description of the population for which the primary care physicians prescribe antidepressant medications and description of the treatment pattern.
- 4. Evaluation of how health determinants influence the presentation and/or evolution of mental illnesses.
- 5. Economic evaluation of the impact of mental illnesses on society.
- 6. Evaluation of interdisciplinary cooperation in primary care.

# Research team

Coordinator	Antoni Serrano-Blanco
Line coordinators	Luisa Baladón, Ana Fernández, Maria Rubio, Juan Vicente Luciano
Researchers	Jaume Autonell, Ignacio Aznar, Vanessa Barneda, Alexia Camuñas, Eugenia Cardeñosa, Albert Feliu, Rita Fernández, Montserrat Gil, Laura González, Anna Maria Jové, Juan Manuel Mendive, Maria Antonia March, Jose Bruno Montoro, Maria Teresa Peñarrubia, Enric Vicens, Mireia Vives
Assistants	Martin Knapp, Paul McCrone, Antonio Cuesta-Vargas, Luis Salvador-Carulla

# Research lines

# Innovative interventions in fibromyalgia

Dr. Juan Vicente Luciano

Fibromyalgia (FM) is a chronic syndrome characterised by multifocal pain and other associated somatic symptoms including fatigue, insomnia, cognitive problems and psychological disorders. Its high prevalence, severe functional deterioration and high healthcare cost cause FM to be considered a severe public health problem. Although the pathogenesis of FM is unknown at present, it is probably produced by an interaction of biological, behavioural and psychological mechanisms.

The FM syndrome poses a major challenge to healthcare professionals due to the absence of optimum treatments. The effectiveness of pharmacological treatments is usually limited and the most promising effects have been found in non-pharmacological treatments (for example, aerobic exercise, health education, relaxation). Nevertheless, there exists



a lack of empirical evidence with respect to the cost-effectiveness of these treatments. Bearing all this in mind, in 2007 we began a research line addressed to evaluating the effectiveness and cost-effectiveness of the various treatments for FM with the collaboration of Prof. M. Knapp and Dr. Francesco D'Amico of the Personal Social Services Research Unit (PSSRU – London School of Economics and Political Science, UK) and with Dr. Javier García-Campayo (Hospital Miguel Servet, Zaragoza, Spain): (1) Psycho-education implemented in general practice vs. usual care; (2) Cognitive behaviour therapy vs. recommended pharmacological therapy vs. usual care; (3) Therapy acceptance and commitment group vs. FDA recommended pharmacological treatment; and (4) Mindfulness-based stress reduction (MBSR) vs. usual care (research project recently financed by ISCIII, Miguel Servet contract).

## New technologies and mental health

Dr. Luisa Baladón

In recent years we have been witnessing the gradually progressive introduction of new health technologies which will transform healthcare in a not too distant future. This research group has taken part in innovation projects that incorporate the use of the new technologies in the detection, follow-up and treatment of mental disorders. In this this line, we have participated in the following projects:

- Help for Mood (www.help4mood.info): European project (7th EU Framework Programme), which has the goal of assisting the follow-up and treatment of depression patients at home by a sensor system and a computer avatar that interacts with the patient.
- MADep: a national project (Acció10) that develops a website for the performance of depressed patient follow-up tasks
  in the home. It includes an alarm system that is activated when it detects that the evolution of the patient's depression
  may lead to a relapse.
- Computer psychotherapy: a national project led by Dr. Javier García-Campayo (redIAPP) which provides online psychotherapy services to depressed patients in primary care.

### Economic evaluation of healthcare services

Dr. Antoni Serrano-Blanco

Resources are limited and healthcare needs are growing. It is the responsibility of managers, planners, clinicians and patients to use healthcare resources as efficiently as possible. Health economy studies generate evidence with respect to the efficiency of healthcare services in order to provide help for the decision-making process. Our group has incorporated the economic evaluation of all the therapeutic interventions in which we have taken part, which allows us to determine their level of efficiency, that is to say, the degree to which their healthcare goals have been achieved, while measuring the accompanying costs of these interventions. Another type of studies in which we have participated is that of determining the economic costs of illnesses and establishing the factors that influence them.

# Prevention of common mental illnesses

Dr. Ana Fernández

Major depression is the most common mental illness and its treatment is carried out mainly at the primary care level. This group has taken part in the PREDICT-CCRT project, which has developed and evaluated the first preventive intervention for major depression carried out by primary care physicians in Spain. This group is working at present on the development of new applications for this intervention.

# Pharmacoepidemiology and cooperative treatment in primary care

Dr. María Rubio

This research line is focused on evaluating the effectiveness and efficiency of various therapeutic alternatives and interventions for improving these treatments. The projects are set within the framework of primary healthcare and are mainly centred around the pharmacological approach and multidisciplinary care.

Some of the most representative projects of this line include:

- NO-INICIADORES (NON-STARTERS) project (the problem of not starting pharmacological treatment: evaluation with mixed methods. FIS PI14/00052): This project's goal is to determine the prevalence and economic consequences of not starting pharmacological treatment in primary care, and to establish the motivations of non-starter patients.
- INFAP project (FIS PI11/01345): The goal of this project is to evaluate the cost-effectiveness of the treatment of light-to-moderate major depression in primary care on watchful waiting in comparison to the use of antidepressants.
- ATDOM project (COFB grant): This is a clinical and economic evaluation of the integration of a pharmacist into a primary-care home assistance team.
- QUALIFAR project (CAMFIC grant): This project's goal was to determine the barriers to and facilitators of cooperation between family physicians and community pharmacists.



 PRODEFAR project (Pl070546): This project evaluated the cost-effectiveness of a pharmaceutical intervention aimed to improve adherence to antidepressant treatment in primary care.

# **Projects**

- Unfulfilled needs in elderly persons hospitalised for the first time in an acute psychiatric unit: Relation to quality of life and use of healthcare and social resources. Parc Sanitari de Sant Joan de Déu. February 2013 – December 2015. Pl: Antoni Serrano-Blanco.
- Preventive activities and health promotion in primary care. Instituto de Salud Carlos III. January 2013 December 2016.
   Pl: Antoni Serrano-Blanco.
- Genetic, practitioner- and patient-related factors and their interaction as associated with the therapeutic success of an intervention to prevent major depression in primary care. PredictD-EVAL study. Pl12/02755. Instituto de Salud Carlos III. 2013-2015. Pl: Juan Bellón.
- Cost-effectiveness of a non-pharmacological intervention vs. pharmacology (fluoxetine, escitalopram or venlafaxine) in major depression in Spanish primary care (INFAP study). Instituto de Salud Carlos III. January 2012 – December 2015. Pl: Antoni Serrano-Blanco.
- Research on healthcare services and health results. Agaur Agència de Gestió d'Ajuts Universitaris i de Recerca. September 2009 December 2014. Pl. Antoni Serrano-Blanco.
- A Computational Distributed System to Support the Treatment of Patients with Major Depression (Help4Mood). Pl: Colin Matheson (University of Edinburgh). Seventh Framework Programme Theme ICT-2009.5.1 (Personal Health Systems); EU STREP 248765. 2010-2014.
- Mental Health Training Through Research Network In Europe (MARATONE) Period: 2013 to 2017. Funded by 7MP European Union FP7-PEOPLE-2012-ITN (316795). Pl: Ludwig-Maximilians (Universitaet Muenchen). Researchers: CIBER consortium for the Mental Health thematic area, Fondazione IRCCS Istituto Neurologico Carlo Besta, Instytut Psychiatrii i Neurologii, King's College London, Deutsche Lufthansa AG, London School of Economics and Political Science (Martin Knapp), National Suicide Research Foundation, Parc Sanitari Sant Joan de Déu (JM Haro, A. Serrano-Blanco, S. Ochoa), Siemens AG, Schweizer Paraplegiker-Forschung AG, Universität Leipzig, Oulun Yliopisto.
- RETICS (redIAPP). Ministerio de Sanidad y Consumo, Instituto de Salud Carlos III, Red (RD12/0005/008). 2013-2017.
   Node de Salut Mental i Atenció Primària (grup PRISMA-CAT). Pl. Antoni Serrano-Blanco.
- The problem of non-starting of pharmacological treatment: evaluation by mixed methods. Instituto de Salud Carlos III.
   January 2015 January 2017. Pl: Maria Rubio.
- Clinical and economic evaluation of the integration of a pharmacist into a multidisciplinary home-care team. Beca del Colegio Oficial de Farmacéuticos de Barcelona. January December 2015. Pl: Maria Rubio.
- Study of the typology and costs of interventions associated with containment in acute psychiatric crises in the hospital environment. Ferrer. January 2013 December 2015. Pl: Antoni Serrano-Blanco.
- OBERTAMENT project on combating the stigma against mental illness. Obertament. 2012-2016. Pl: Antoni Serrano-Blanco, Maria Rubio.

# Clinical trials

- Post-injection syndrome in schizophrenia patients receiving olanzapine long-acting injection. Lilly. June 2014-. Pl: Antonio Serrano-Blanco.
- European non-interventionist (ENI) study in schizophrenia patients treated with long-acting injectable (LAI) antipsychotics (ALTO). H. Lundbeck A/S. January 2014 November 2014. Pl: Antonio Serrano-Blanco.
- Observational, multi-centre, open-label, prospective study and 6 weeks of follow-up to evaluate the variation of severity
  of the illness of schizophrenia patients requiring, as per usual clinical practice, treatment with extended-release injectable paliperidone palmitate on hospitalisation in the acute unit due to relapse. Janssen Cilag. May 2013-. Pl: Antonio
  Serrano-Blanco.



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# Awards

November 2014: 2nd Prize Integrated Care for the poster Rubio M, Bosmans E, Peñarrubia MT, March M, Trave P, Fernández A, Bellón JA, Serrano-Blanco A. Cost-effectiveness and cost-utility of a community pharmacist intervention in patients with depression (PRODEFAR study). Second World Congress on Integrated Care "21st Century Integrated Care: serving citizens, patients and communities" 2014, Sydney, Australia, Nov 2014.

# Supervised theses

 Barriers to and facilitators of communication and cooperation between the primary care physician and the community pharmacist. University: UAB. Faculty of Medicine. Doctorate programme: Medicine. Directors: Carlos Martin Cantera and Maria Rubio. Doctoral candidate: Ana Maria Jové. Presentation: June 2014.



# Emerging groups and groups under training

# Clinical research

This is a mutilidisciplinary group of researchers, all of whom work with high-prevalence illnesses. These are disorders with a high morbility-mortality that form a steadily growing part of all hospitals' activity. The group is composed of specialists with long clinical experience who deal regularly with illnesses of this type.

This research group has recently taken up a new line involving critical patients. The common goal of the group is to conduct clinical research, striving to make new clinical findings in order to improve and simplify diagnostic and/or therapeutic techniques. It also seeks to increase the epidemiological research carried out on our area in order to expand the knowledge about the incidence, prevalence and risk factors of high-prevalence illnesses.

# Research team

Coordinator	Luis Lores
Line coordinators	Ernest Bragulat, Antoni Callén, Jordi Graells, Vicenç Díaz de Brito, Alejandra Fernández, César Romero
Researchers	Maria Aiguabella, Mireia Albuixech, Elisabeth Arellano, Nuria Berrocal, Patricia Boronat, Anna Capellà, Xavier Casas, Francisco Castro, Toni Cruz, Gemma Donaire, Ana Escrig, Olga Farré, Rafaelle Fiorillo, Lluis Font, Arantxa Garcia, Diego Gauna, Paola Gómez, Araceli González, Diana Gutierrez, Rosana Hernando, Soledad Herrera, Oscar Izquierdo, Mireia Junyent, Jaime Llopis, Francisco Lopez, Pablo Marchena, Xavier Martret, Patricia Miro, Gerard Navarrete, Joan Nicolás, Rosa Mª Ojeda, Teresa Pascual, Carles Paytubi, Sandra Pérez, Edwin Percy Pesantes, Berthy Rivero, Bernabé Robles, Yobanni Rodriguez, Julián Rodríguez-Larrea, Elisabeth Rovira, Laura Santos, Marta Serrano, Mireia Vila, Mª Jose Vives

# Research lines

# Chronic-degenerative neurological disorders

Antoni Callén

This is a study of personal networks as a strategy to be used against the stress felt by the carers of dementia patients: it analyses the interpersonal relation networks of such carers. The goal is to document the carers' overload and the stress generated as a result of it in order to provide the necessary tools to allow them to cope with their task. Other aspects are the application of the new technologies to patients with cognitive deterioration: Location-Based Extensible and Generic Platform for Ambient Assisted Living (LEGAAL) ICT 4 for Healthy Ageing; the application of the new technologies to foster healthy independent ageing; the monitoring of vital functions; the analysis of the risk of falls as a preventive measure; the promotion of healthy habits; and the geolocation of dementia patients to avoid the risk of their getting lost.

# **Emerging processes of respiratory disorders**

Luis Lores Obradors

This research work is focused on the studies of prevalence of obesity-hyperventilation syndrome and prevalence of COPD in the area of reference, as well as on multiple clinical trials and observational studies on patients with COPD, and on chronic bronchial disorders.



# **Chronic heart disorders**

César Romero

Work is conducted along four research lines: cardiac arrhythmias, heart failure, coronary atherothrombotic disease, and cardiovascular risk factors.

## Urgent care processes and pathologies

Ernest Bragulat

Three research lines are underway: chest pain; prevalence of DVT in mental health patients, and triage at the Sant Joan de Déu Barcelona Healthcare Park.

## Epidemiological research on non-melanoma skin cancer

Jordi Graells

Within the general lines described for this research group, special emphasis is placed on epidemiological research on non-melanoma skin cancer, the risk factors associated with the occurrence of new skin neoplasias, and the relations and synergies between primary care and specialised care.

## Severe infectious processes

Vicenc Díaz de Brito

Four research lines are being followed: 1) Nosocomial infection and infection associated with social-healthcare centres, 2) Infection by multi-resistant microorganisms or highly complex infections, 3) High-prevalence respiratory infections, and 4) Prosthetic osteoarticular and infection.

# Processes and pathologies of critical patients

Alejandra Fernández

Work is carried out along three main research lines: 1) Cardiovascular aspects of ultrasound scan in cardiac arrest, 2) Tracheostomy improvement techniques with ultrasound scans, and 3) Handling of chronic patients in critical care units.

# **Projects**

- Impact of strengthening basic hygiene measures on multi-resistant microorganisms in long-term centres and private residences. Parc Sanitari Sant Joan de Déu (PSSJD), social-healthcare centres and private residences in the area of influence of PSSJD. Beneficiary: Amara Ródenas. Fundació Mutuam Conviure 2013. 2014 2015. Pl: Vicenç Díaz de Brito.
- Study of personal networks as a strategy against stress in carers of Alzheimer patients. Parc Sanitari Sant Joan de Déu.
   2013 2014. Pl: Jaime Llopis.

# Clinical trials

- Observational, cross-sectional, multi-centre descriptive study of the clinical profile of COPD patients treated with double bronchodilation. DOBRO Study. December 2014-. Pl: Xavier Casas.
- Open extension study to evaluate the long-term safety and tolerability of dupilumab in asthma patients who took part in the prior clinical trial on dupilumab in asthma. November 2014 -. Pl. Luis Lores.
- Prospective, multi-centre, randomised, open study with a duration of 12 weeks to evaluate the efficacy and safety of
  glycopyrronium (50 microgrammes once daily) or of the combination of fixed doses of indacaterol and glycopyrronium
  bromide (110/50 microgrammes once daily) on the symptoms and the state of health of patients with moderate chronic
  obstructive pulmonary disease (COPD) who switch from any standard treatment regime for COPD. September 2014 -.
  Pl: Luis Lores.
- Titan study. National study on quality of oral anticoagulation in non-valvular atrial fibrillation. June 2014-. Pl: César Romero.



- Dose-determination, randomised, double-blind, placebo-controlled study to evaluate dupilumab in patients with moderate-to-severe uncontrolled asthma. January 2014-. Pl. Luis Lores.
- Comparative, randomised, double-blind, double-simulation study with parallel groups on fluticasone propionate / formoterol fumarate (Flutiform®) 250/10 μg (2 inhalations twice daily) and on Flutiform® 125/5 μg (2 inhalations twice daily) vs. formoterol fumarate dihydrate (Atimos®) 12 μg (1 inhalation twice daily) on patients with chronic obstructive pulmonary disease (COPD). November 2013-. Pl: Luis Lores.
- Randomised, double-blind, double-simulation, active product-controlled evaluation study on the efficacy, safety and tolerability of aclidinium bromide / formoterol fumarate, administered twice daily, in comparison to salmeterol / fluticasone propionate, administered twice daily, in the 24-week treatment of symptomatic patients with chronic obstructive pulmonary disease (COPD). August 2013-. Pl: Luis Lores.
- ESOPO study. Evaluation of a programme of remote support for patients with COPD and frequent exacerbations on quality of life and the evolution of the disorder. July 2013-. Pl: Luis Lores.
- Multi-centre, randomised, double-blind, placebo-controlled study on parallel groups with 12 weeks of active treatment to evaluate the efficacy, safety and tolerability of QVA149 (indacaterol maleate / glycopyrronium bromide) in patients with COPD with moderate-to-severe airflow limitation. June 2013-. Pl: Luis Lores.
- Multi-centre, randomised study with duration of 52 weeks to evaluate the remote monitoring of patients by means of
  the EXACT questionnaire with results reported by the patient on the reduction of hospitalisations due to exacerbations
  in chronic obstructive pulmonary disease patients in comparison to patients controlled as per the usual clinical practice.
  May 2013-. Pl: Luis Lores.
- Randomised, double-blind, placebo-controlled, multi-centre study on ciprofloxacin in a dose of 32.5 mg dry inhalation powder for inhalation twice daily with intermittent administration, during 28 days with another 28 days of rest, or during 14 days with another 14 days of rest, in comparison to placebo, on evaluation of the time until the first pulmonary exacerbation and the frequency of exacerbations in patients with bronchiectasis not due to cystic fibrosis. March 2013-. Pl: Luis Lores.
- Evaluation of the clinical effects of inhibition of cholesteryl ester transfer protein (CEPT) with evacetrapib in patients with high risk of vascular events ACCELERATE study. January 2013-. Pl: Pablo Marchena.
- Cross-sectional and longitudinal international evaluation of asthma control (LIAISON). August 2012-. PI: Luis Lores.
- Multi-centre, randomised, active-control comparative study of the efficacy and safety of betrixaban in extended treatment vs. Enoxaparin<sup>®</sup> as usual treatment for prevention of venous thromboembolism in patients with medically acute disorder. August 2012-. Pl: Pablo Marchena.
- Study of prognostic factors and prevalence of post-thrombotic syndrome (PTS) in Spain in patients with deep vein thrombosis (DVT). August 2012-. Pl: Pablo Marchena.
- Study of the safety and efficacy of an inhaled combination of inhaled fluticasone propionate/salmeterol vs. inhaled fluticasone propionate in the treatment of adolescents and adults with asthma. February 2012-. Pl: Luis Lores.
- Opportunities for intravenous to oral sequencing and early discharge in gram-positive infections requiring glycopeptide or lipopeptide treatment. SEQUENCE study. February 2012-. Pl: Vicenç Díaz de Brito.
- Open, prospective, randomised, phase IV clinical trial to evaluate the utility of measuring nitric oxide in exhaled air in the therapeutic handling of adult patients with light asthma. January 2012-. Pl: Luis Lores.
- Study of clinical results to compare the effect of inhaled fluticasone furoate/vilanterol powder, 100/25 mg, versus placebo, on the survival of patients with moderate chronic obstructive pulmonary disease (COPD) and with background or high risk of cardiovascular disorder. July 2011-. Pl: Luis Lores.
- Clinical trial of two strategies for making therapeutic decisions in the study of tuberculosis contacts: standard strategy, based on the tuberculin test alone, versus the combination of the tuberculin test and QuantiFERON-TB-Gold in-Tube. April 2011-. Pl: Luis Lores.
- Clinical effectiveness and secondary histological changes in treatment with omalizumab in allergic asthma patients in GINA (Global Initiative of Asthma) stage V. December 2009-. Pl: Luis Lores.

Castellanos J, González-Cuevas A, Sierra JM, García-Nuño L, Diaz-Brito V, Soriano A, Font-Vizcarra L. Adherence
of S. epiderdimis on different metals: a comparative in vitro study. J Appl Biomater Funct Mater 2014. 30:141-4. IF:
0,905(Q4).



# Research Group on Nursing, Education and Society (GIEES)

The Research Group on Nursing, Education and Society (GIEES) is engaged in four different spheres of research (social action, healthcare methodology, educational innovation, and identity traits). Each of these spheres is covered by a group of professors who carry out their research activity on one same focus of interest: the analysis of social inequalities and the situation of vulnerability; the evaluation of nursing care plans; the development and analysis of innovative teaching methodologies; and the identity traits of our profession.

# Research team

Coordinator	Núria Roca, Juan Roldán
Line coordinators	Maria José Morera, Anna Ramió, Juan Roldán
Researchers	Marta Callarisa, Anna Cano, Rosa Gaya, Mar Godall, Amèlia Guilera, Mariona Farrés, Barbara Hurtado, Marina Heredia, Esther Insa, Laura Martínez, Dolors Miguel, Carlos Nebot, Àngels Pedrola, Olga Rodrigo, Júlia Roura, Dolores Royo, Laura Serradesanferm, Carme Vega
Assistants	Ana Merino, Ana Pérez, Joan Uribe

# Research lines

# **Social Action**

Dr. Núria Roca

Social inequalities and the situation of vulnerability in which steadily increasing numbers of people find themselves make it necessary to implement policies that will improve people's lives. The goal of the research group on social action is to conduct research that provides knowledge about the structural conditions of inequality and that allows proposals for improvement to be made.

# **Identity traits**

Dr. Anna Ramió

This sphere aims to strengthen the research in the field of the identity traits of the healthcare professions (and especially those of male and female nurses) and of the social-healthcare organisations. The identity of the professions and organisations is based on the values and attitudes of a collective that, together with its abstract knowledge and its skills, carries out and specifies its social contribution. The investigation in this field seeks to expand the knowledge of and reflect upon these essential fundamental aspects around which the humanised care of people by the social-healthcare professions and organisations pivots.

# **Educational innovation**

Dr. Maria-José Morera

The concern for the quality of teaching and the start-up of initiatives for changes in the organisation of education and in the methodological practices of instruction give innovation and change a fundamental role in the overall process of adaptation to the existing social demands. The Research Group on Educational Innovation studies the teaching methodologies that promote change, innovation and improvement in education. Its main goals are research centred on improvement



of teacher training; organisational culture and governance of educational centres; and the development of educational strategies that strengthen the training of students according to the context and needs of today's world.

# Healthcare methodology

Dr. Juan Roldán Merino

This sphere seeks to strengthen research in the field of the care of people with health problems, in order to promote the health, well-being and quality of life of people of all ages and in all personal situations. We consider that research is an essential activity that will allow us to answer the questions posed by nursing practice, and that it is a basic instrument for the performance of our profession. Research will not only assure a high standard of nursing intervention for all citizens but also entails an added value for us nursing professionals ourselves, for the community and for the selfsame healthcare system.

# **Projects**

- The Teaching Action Plan in undergraduate nursing studies. Campus Docent Sant Joan de Déu Fundació Privada.
   February 2013 January 2015. Pl: Núria Roca.
- Training of the collective of women of Maghrebi origin in Sant Vicenç dels Horts. Campus Docent Sant Joan de Déu Fundació Privada. November 2013 November 2017. Pl: Laura Martínez.
- Hospitality as a value. Meanings and construction in the students of Campus Docent Sant Joan de Déu Fundació Privada (EUI agreement). Campus Docent Sant Joan de Déu – Fundació Privada. December 2012 – December 2016.
   Pl: Laura Martínez, Amèlia Guilera.
- Study of the attitudes and behaviours attached to the institutional values of the Hospitaller Order of Saint John of God, Aragon-San Rafael province. Campus Docent Sant Joan de Déu – Fundació Privada; OHSJD-Provincial Curia. May 2012 – May 2017. Pl: Anna Ramió, Amèlia Guilera and Laura Martínez.
- Mobility of students and its impact on schooling in the metropolitan region of Barcelona: types, processes and trends.
   Ministerio de Economía y Competitividad. January 2013 December 2017. Pl: Sílvia Carrasco. Investigator: Núria Roca.
- Improving the therapeutic relation in nursing care through evidence. A research study-participative action in acute psychiatry units. COIB. December 2014 December 2016.
- Pl: Antonio Rafael Moreno. Investigator: Juan Roldán-Merino.
- Medicated life. Healthcare policies, antidepressant consumption, and vital worlds of Catalan youth. Ministerio de Economía y Competitividad. 2013-2015. Pl: Ángel Martínez. Investigator: Carme Vega.
- Evaluation of critical thought in hospitalisation nursing professionals, according to the Alfaro-LeFevre 4-circle model. COIB. September 2014- December 2016. PI: Esperanza Zurigel. Investigator: Juan Roldán-Merino.
- Adaptation of the Spanish language and study of reliability and validity of the Scoring Scale for Nursing Skills in Crighton Simulation (C-SEI). COIB. September 2014-December 2016. PI: Mariona Farrés.
- International Researchers Group on Mental Health Nursing Care. Campus Docent-Fundació Privada. 2013-2018. Pl: Juan Roldan-Merino.
- Physiological immaturity of the newborn: Multi-phase study by the mixed method. COIB. January 2014- December 2016. Pl: M. Eulalia Juve. Investigator: Bárbara Hurtado.
- Influence of nursing interventions on adherence to treatment with antituberculosis drugs in the paediatric population. COIB. January 2014 December 2016. Pl: Eva M Guix. Investigator: Bárbara Hurtado.
- Carers 2.0: effectiveness of a support programme for non-professional carers of chronic patients. Universitat Rovira i Virgili. January 2013 – December 2015. Pl: Mar Lleixà. Investigator: Juan Roldán Merino.
- Application of the patient- and family-centred care model to hospitalised children diagnosed with acute bronchospasm.
   A commitment to hospital efficiency. COIB. September 2011 December 2014. Pl: Marta Fernández. Investigator: Núria Roca.



- Benito LI, Binefa G, Lluch T, Vidal C, Mila N, Puig M, Roldan J. Defining the role of the nurse in population-bases cancer screening programs: a literature review. Clin J Oncol Nurs. 2014; 18(4): e77-e83. IF: 0,945(Q2).
- Falco-Pegueroles A, Lluch-Canut T, Roldan-Merino J, Goberna-Tricas J. Guardia-Olmos J. Ethical conflict in critical care nursing: Correlation between exposure and types. Nursing ethics. 2014. IF: 1,093(Q2).
- Roldán-Merino J, Lluch-Canut T, Menarguez-Alcaina M, Foix-Sanjuan A, Haro JM. Psychometric evaluation of a new instrument in Spanish to measure self-care requisites in patients with schizophrenia. Perspect Psychiatr Care. 2014; 50: 93-101. IF: 0,712(Q4).
- Zuriguel E, Lluch MT, Falco A, Puig M, Moreno C, Roldan J. Critical thinking in nursing: Scoping review of the literature. International J of Nursing Practice. 2014. IF: 0,532(Q4).

# **Books**

- Aguilar M, Coscolla R, Belzunegui A, Benavent E, Martínez L y Roca N. L'Acció social des de les entitats d'Església: els eu paper en la cohesió social a Catalunya. Barcelona: Fundació Pere Tarrés. Ed. Claret; 2014.
- Fernandez E [coord], Vega C [coord], Ara A, Foix J, Gaibar V, Muela J. Participación en salud: estrategias individuales
  y colectivas frente a los procesos de salud, enfermedad, atención. [Monografía en internet]. Esplugues de Llobregat:
  Ediciones San Juan de Dios; 2014. Disponible en: http://www.santjoandedeu.edu.es/edicionessanjuandedios/catalogo/profesionalidad/participacion-en-salud-estrategias-individuales-colectivas-frente-procesos.
- Ferre-Grau C, Sequeira C, Roldan-Merino JF, Lluch-Canut MT, Lleixa-Fortuno M, Montesol-Curto P, Puig-Llobet M, Falco-Pegueroles M. Projeto internacional para promover a investigacao em emfermagem de saude mental. En: Sequeira C, Carvalho JC i Sa L. (Eds.). IV Congresso Internacional ASPESM: Padroes de Qualidade em Saude Mental. Porto: ASPESM; 2014. p. 2017-226.
- Guilera A, Martínez L, Ramió A, GIEES (Grup d'investigació en infermeria, educació i societat). Conviure amb la malaltia.
   Barcelona: ed. Mediterrània, S.L.: Obra Social Sant Joan de Déu; 2014.
- Rodrigo O, Cais J y Monforte C. Caracteristicas de la profesion enfermera en el contexto español a partir de la experiencia de las enfermeras docentes. En: Libro del 3er Congreso Ibero-Americano de Investigacion Cualitativa. Badajoz: el Congreso; 2014 V.2.
- Roldan J (coord), Lluch MT (coord). Diseños de Proyectos de Investigación en Enfermería de Salud Mental y Adicciones. [Monografía en internet]. Esplugues de Llobregat: Ediciones San Juan de Dios; 2014. Disponible en: http://www.santjoandedeu.edu.es/edicionessanjuandedios/catalogo/profesionalidad/disenosproyectos-investigacion-enenfermeria-salud-mental-adicciones/28.

# Supervised theses

 Evaluation of positive mental health and of the self-care requirements in hospitalised patients diagnosed with schizophrenia, as per the Dorothea Orem Nursing Theory. Universitat de Barcelona (UB). Presentation: 07/07/2014. Doctoral candidate: Dolors Miguel Ruiz. Directors: Juan Francisco Roldán Merino, Maria Teresa Lluch Canut.

# Presented theses

- Management of communal resources in the communities of San Andrés and Almarza. [Doctoral thesis]. Barcelona:
   Universitat de Barcelona. Department of Social and Cultural Anthropology; 2014. Doctoral candidate: Laura Martínez.
- Evaluation of positive mental health and of the self-care requirements in hospitalised patients diagnosed with schizophrenia, as per the Dorothea Orem Nursing Theory. Universitat de Barcelona (UB). Presentation: 07/07/2014. Doctoral candidate: Dolors Miguel Ruiz. Directors: Juan Francisco Roldán Merino, Maria Teresa Lluch Canut.



# Influence of the milieu on the well-being of children and adolescents

Group focused on research in the following spheres:

Study of the epidemiologic and clinical factors involved in childhood accidents. Differential diagnosis of child abuse. Early detection and secondary prevention of social-healthcare problems in adolescence: drugs, sexuality and violence. Impact of external agents (radiation, pollution, etc.) on child health. Improvement of paediatric patient care in the physician's consultation room: presence of parents, analgesia, differentiated care by age (children / adolescents...).

# Research team

Coordinator	Carles Luaces, Jordi Pou
Researchers	Gemma Claret, Ana Isabel Curcoy, Sergi Navarro, Marta Simó, Victoria Trenchs

# **Projects**

- Treatment of pain and anxiety based on the interaction of social robots with children to improve the patient's experience.
   TIN2012-38416-C03-03. Ministerio de Ciencia e Innovación. January 2013-February 2015. PI: Carles Luaces.
- Identification of children, adolescents and young adults visiting the emergency department with low risk of acute appendicitis: impact of the APPY1 test on clinical and economic results. MKTP14-001. Sponsor's name: Venaxis, Inc., 1585 South Perry Street, Castle Rock, CO 80104, USA. Pl: Juan González del Castillo. Investigator: Dr. Victoria Trenchs.

# **Publications**

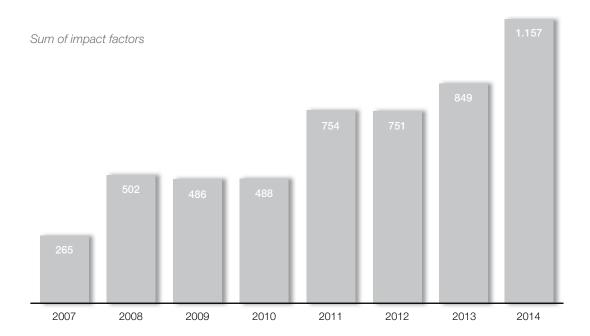
- Almario Hernández AF, Trenchs Sainz de la Maza V, Sangorrin Iranzo A, Luaces Cubells C. Neumoparótida, a propósito de un caso. An Pediatr (Barc) 2014. 81: -0. IF: 0,722(Q3).
- Astete JA, Batlle A, Hernandez-Bou S, Trenchs V, Gené A, Luaces C. Blood culture diagnostic yield in a paediatric emergency department. Eur J Emerg Med 2014. 21: 336-340. IF: 1,500(Q2).
- Díaz Sabogal D, Curcoy Barcenilla AI, Trenchs Sainz de la Maza V, Giménez Roca C, Luaces Cubells C. Malalties de transmissió sexual a urgències pediàtriques. Pediatr Catalana. 2014; 74(4):159-62. IF: 0,722(Q3).
- Bilbao N, Domingo A, Muchart J, Alamar M. Tumor edematoso de Pott: una entidad olvidada? An Pediatr (Barc) 2014. 80:337-338. IF: 0,722(Q4).
- Garcia-Marcos L, Valverde-Molina J, Pavlovic-Nesic S, Claret-Teruel G, Peñalba-Citores AC, Nehme-Álvarez D, Korta-Murua J, Sánchez-Etxaniz J, Alonso-Salas MT, Campos-Calleja C, Fernández-Villar A, Rodríguez-Suarez J; BCOST group. Pediatricians' attitudes and costs of bronchiolitis in the emergency department: a prospective multicentre study. Pediatr Pulmonol. 2014; 49(10): 1011-9. doi: 10.1002/ppul.22906. IF: 2,297(Q1).



- Giménez Roca C, Martínez Sánchez L, Calzada Baños Y, Trenchs Sainz de la Maza V, Quintilla Martínez JM, Luaces Cubells C. Evaluación de los indicadores de calidad en intoxicaciones pediátricas en un servicio de urgencias. An Pediatr (Barc) 2014. 80: 34-40. IF: 0,722(Q3).
- Hernández-Bou S, Trenchs V, Alarcón M, Luaces C. A febrile very young infants with urinary tract infection and the risk for bacteremia. Pediatr Infect Dis J 2014. 33: 244-247. IF: 3,135(Q1).
- Hernández-Bou S, Garcia-Garcia JJ. Utilidad de la procalcitonina para la prescripción antibiótica y la sospecha de bacteriemia en urgencias. Respuesta de los autores. An Pediatr.2014;81:62-3 - Vol. 81 Núm.1 DOI: 10.1016/j.anpedi.2013.12.001. IF: 0,722(Q3).
- Huici-Sanchez M, Escuredo-Argullos L, Trenchs-Sainz de la Maza V, Luaces-Cubells C. Enfermedad cerebrovascular en pediatría. Experiencia de un servicio de urgencias. Rev Neurol 2014. 59: 106-110. IF: 0,926(Q4).
- Martínez Sánchez L, Almario Hernández AF, Escuredo Argullós L, Maçao P, Trenchs Sainz de la Maza V, Luaces Cubells
   C. Uso de antídotos en un servicio de urgencias pediátricas. An Pediatr (Barc) 2014. 81: 220-225. IF: 0,722(Q3).
- Muñoz-Santanach D, Trenchs Sainz de la Maza V, González Forster E, Luaces Cubells C. Niños con traumatismo craneal leve en urgencias: ¿es necesaria la radiografía de cráneo en pacientes menores de 2 años?. Neurocirugia (Astur)
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- Trenchs Sainz de la Maza V, Curcoy Barcenilla AI, en representación del Grupo de Trabajo de Malos Tratos y Situaciones de Riesgo de la Sociedad Española de Urgencias de Pediatría (SEUP). Registro multicéntrico de maltrato en urgencias: casuística de un año. Emergencias 2014; 26 (6): 468-71 IF: 2,583(Q1).



# Impact factor



# Activities

- I Jornada eSalud Mental. January 23
- 4ª Jornada Síndrome de Rett: De la investigació a la assistència en l'edat adulta. March 8.
- VIII Curs d'Avaluació Econòmica i Política Sociosanitària. April 7 11.
- I Fórum Internacional d'Innovació Infermera: una resposta al futur. May 15 and 16.
- Comunicar forma part de la ciència que fem. Fem-ho bé!. Sr. Àlex Argemí. June 3.
- Curs d'Atenció al pacient agitat en salut mental. Últims resultats d'investigació en Pràctica Clínica, Política Sociosanitària i Economia de la Salut. June 6 and 7.
- Debat: Catalunya envelleix: estem preparats per afrontar el repte?. October 1.
- X Jornada de Recerca en Salut Mental. November 13.
- Diabetis tipus 1: estem lluny d'una cura?. November 29.



# Scientific seminars

- The role of population activity in sensory processing. Dr. Iñigo Romero. January 14
- Unidad de Investigación Clínica: actualización de proyectos y servicios. Sr. Joana Claverol. February 11
- How to protect results that cannot be patented? The keys of COPYRIGHT. Sr. José María del Valle. March 11.
- Basic concepts of ethics in research. Dr. Robles. March 20.
- In vivo models generation of Diffuse Intrinsic Pontine Glioma at Hospital Sant Joan de Déu. Dr. Angel Montero Carcaboso. March 25.
- Emotional Intelligence Program for caregivers of people with Severe Mental Disorders. Sra. Berrozpe. April 3.
- Why PK/PD Modeling and Simulation Strategies are essential in Pediatric drug development and treatment. Sra. Maria Igarreta and Sra. Nerea Leal. April 8.
- Infant proB ALL with MLL-AF4 rearrangement: cell or origin, secondary events and disease models. Dr. Pablo Menéndez. April 22.
- European Funding Oportunities 2014-2015. Sra. Roser Arnalte. May 5.
- Paediatric and Adult Gilomas: Similar morphology, different biology. Dra. Teresa Ribalta. May 6.
- Utility of experimental paradigms in defining neuropsychiatric entities. Sra. Puigcerver and Sra. Caprile. May 8.
- Tulips, Windmills and Pneumococcal vaccination. Dr. Karin Elberse. May 15.
- Can gender be disregarded in Mental Health research? Dra. Judith Usall. May 22.
- A novel proteomic signature of postmortem cerebellum in schizophrenia. Dra. Gemma Riquelme and Dra. Elia Vila. June 6.
- Prognostic factors of brain damage in fetuses with restricted intrauterine growth. Dra. Edurne Mazarico. June 17.
- Attention deficit hyperactivity disorder (ADHD). Dr. Alda. July 3.
- Indicators for measuring research and publish in open access. Sra Ana Merino. July 17.
- Collaboration between the primary care physician and the community pharmacist. Dra. Anna M Jové. Septembre 22.
- Next Generation Sequencing: An introduction to Illumina technology and clinical applications. Sr. Toni Lluch and Sra. Ester Castillo. October 7.
- Typology and impact of seclusion and restrain in psychiatry. Dr. Antoni Serrano. October 9.
- Treatment of retinoblastoma with selective oncolytic adenoviruses. Sr. Guillem Pascual Pastó. October 21.
- Glucose transporter 1 (GLUT1) deficiency. Sra. Delia Yubero Siles. November 4.
- Stressful life events and first psychotic episode. Sra. Anna Butjosa. November 11.
- Tools in Translational Research/Cell Therapy held and Gene synthesis and cloning services held. Sr. Christoph Hoefer and Chady Jaber.
- You are WHEN you eat: Neonatal overfeeding reprogrammes the hepatic circadian rhythm in mice. Dr. Josep Jiménez Chillarón. December 2.
- The impact of social networks and social support in mental disorders and their associated burden. Dr. Satini. December 4.
- Signal processing in Neonatology. Dr. Andriy Temko. December 16.
- New therapeutic targets in neuroblastoma: CaSR i PTHrP. Dra. Carmen de Torres. December 16.