

# ALLERGY AND CHILDHOOD RESPIRATORY DISEASES

Leading Researcher:

**M<sup>a</sup> Dolores Hernández**  
PhD



No. Members: 15



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## MAIN RESEARCH LINES

### Innovation in allergy diagnostic methods

New technologies are applied in specific allergy diagnosis, aimed particularly at molecular research of allergens, trying to detect specific molecules that trigger allergic reactions. Therefore, new platforms allow detection of IgE antibodies against multiple molecular allergen components and drugs are used.

### Assessment of new forms allergy treatment effectiveness

Study of safety and efficacy of allergen specific treatments for most common processes in our environment (mites and pollens in adults and in children mites and fungi). Also work on evaluation of new allergen preparations for treatment of bacterial respiratory allergy to prevent recurrent catarrh in childhood preparations.

### Desensitization treatments with food and drug

Development of procedures regularly applied in both children and adults in order to achieve tolerance to essential foods or with risk of producing serious adverse reactions, especially in children and adolescents. The same technology is also applied in cases of drugs allergy.

### Influence of environmental factors in the development of allergic diseases

Influence of tobacco exposure, nutritional factors and lifestyle in development of allergic diseases (especially asthma) is studied.

## SELECTED PAPERS

**Consensus-based approach for severe paediatric asthma in routine clinical practice.** Plaza AM. et al. An Pediatr (Barc), 2015 Oct 26. pii: S1695-4033(15)00362-8.

**Phase I study of subcutaneous allergen immunotherapy with Dermatophagoides pteronyssinus in patients with allergic rhinoconjunctivitis with or without asthma.** Hernández Fernández de Rojas D. et al. Immunotherapy, 2015; 7(2):89-99.

**Risk factors for bronchiolitis, recurrent wheezing, and related hospitalization in preterm infants during the first year of life.** Pérez-Yarza et al. Pediatr Allergy Immunol, 2015 Dec;26(8):797-804. doi: 10.1111/pai.12414. Epub 2015 Jul 1.

**Safety and Efficacy of Pimecrolimus in Atopic Dermatitis: A 5-Year Randomized Trial.** Sigurgeirsson et al. PEDIATRICS, 2015 Apr;135(4):597-606. doi: 10.1542/peds.2014-1990. Epub 2015 Mar 23.

# ALLERGY AND CHILDHOOD RESPIRATORY DISEASES

## SELECTED ACTIVE RESEARCH PROJECTS

Air pollution and respiratory health and allergy: INMA project.

**Angel Mazón Ramos**

RALERGO- Allergy Healthy Routes in VLC

**Dolores Hernández - Rafael Temes Cordovez**

DIVAM - In vitro diagnosis of drug allergy

**Dolores Hernández - Luis A. Tortajada**

COBIOPHAD- Compact biophotonic platform for drug allergy diagnosis

**Dolores Hernández – H2020**



## RELEVANT CLINICAL RESEARCH

Dose-ranging study that investigates the efficacy and safety of sublingual immunotherapy tablets from allergenic extracts of house dust mite in adults with allergic asthma associated with house dust mite.

**Dolores Hernández Fernandez De Rojas**

*Stallergenes S.A*

Open trial to assess tolerability of immunotherapy with avanz<sup>®</sup> salsola.

**Dolores Hernández Fernandez De Rojas**

*Alk-Abello S.A.*

Clinical trial Phase II, multicenter, randomized, double -blind, with subcutaneous immunotherapy at different doses, in parallel and placebo-controlled groups in patients with rhinoconjunctivitis ± asthma sensitized to *Dermatophagoides pteronyssinus*.

**Dolores Hernández Fernandez De Rojas**

*Bial-Industrial Farmacéutica, S.A*

## INDUSTRY COLLABORATIONS

Development of an immune-stimulating bacterial drug for the prevention of recurrent respiratory infections in children and adults - support, advice and development of clinical trial MV130 -SLG - 002.

*Inmunotek S.L.*



# PERIOPERATIVE MEDICINE, ANESTHESIOLOGY AND REANIMATION

Leading Researcher:

**Oscar Díaz  
Cambroneró**

No. Members: **13**

Other relevant  
information:

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## MAIN RESEARCH LINES

The aim of the Research Group is to improve the care and safety of surgical patients throughout the perioperative period, from admission to discharge.

The main lines of research are:

I) Perioperative multimodal rehabilitation: to optimize the already established processes or create new processes that improve the care and recovery of surgical patients throughout their hospital stay. We have developed several projects in this line.

II) Development of tools for monitoring and evaluation of patients after hospital discharge.

III) Patient safety in the surgical environment. Development of habits and practices that promote safety in the surgical environment, for which we have integrated as a group into the SENSAR and are developing multiple education initiatives in order to implement this safety culture.

## SELECTED PAPERS

1. *Serratus plane block: the regional analgesia technique for thoracoscopy?* Broseta AM, Errando C, De Andrés J, et al. *Anaesthesia*, 2015.
2. *Rationale and study design for an individualized perioperative open lung ventilatory strategy (iPROVE): study protocol for a randomized controlled trial.* Ferrando C, Soro M, Canet J, et al. *Trials*, 2015.
3. *Preoperative management of anemia in oncologic surgery.* Díaz-Cambroneró O, Matoses-Jaén S, García-Claudio N, et al. *Revista Española de Anestesiología*, 2015.
4. *Genetic and Clinical Factors Associated with Chronic Postsurgical Pain after Hernia Repair, Hysterectomy, and Thoracotomy: A Two-year Multicenter Cohort Study.* Montes A, Roca G, Sabate S, et al. *Anesthesiology*, 2015.
5. *Perioperative management of direct oral anticoagulant in emergency surgery and bleeding. Haemostasis monitoring and treatment.* Hidalgo F, Gómez-Luque A, Ferrandis R, et al. *Revista Española de Anestesiología*, 2015.
6. *Tecnologías de la información y comunicación aplicadas a la gestión en cirugía ambulatoria.* Argente P. *Cirugía Mayor Ambulatoria*, 2015.
7. *Evaluation of postoperative myocardial injury by heart-type fatty acid-binding protein in off-pump coronary artery bypass grafting surgery.* Carmona P, Mateo E, Montoro A, et al. *Revista Española de Anestesiología*, 2015.
8. *New approaches on diagnosis and treatment of pulmonary embolism.* Gómez-Lacasa A, Ferrandis R, Machado S, et al. *Trends Anaesth Crit Care*, 2014.
9. *Eculizumab for the treatment of pregnancy-related atypical hemolytic uremic syndrome.* Cañigral C, Moscardó F, Castro C, et al. *Ann Hematol*. 2014.
10. *Bridging evidence-based practice and practice-based evidence in periprocedural anticoagulation.* Llau JV, Ferrandis R. *Circulation*, 2013.
11. *The perioperative management of new direct oral anticoagulants: a question without answers.* Ferrandis R, Castillo J, de Andrés J, et al. *Thromb Haemost*, 2013.
12. *Airway pressure curve: a good tool to measure neural inspiratory time?* Ferrandis R, Belda FJ, García-Raimundo M, et al. *Minerva Anestesiol*, 2013.

# PERIOPERATIVE MEDICINE, ANESTHESIOLOGY AND REANIMATION

## SELECTED ACTIVE RESEARCH PROJECTS

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1. Individualized Pneumoperitoneum Pressure in Colorectal laparoscopic surgery (**IPPCollapse**).
2. Optimization of preoperative anemia in patients with colorectal cancer (**Hepcidina**).
3. Analysis of thrombotic/hemorrhagic risk in the perioperative withdrawal of the new direct oral anticoagulants (ACODs).
4. Optimization of the paravertebral thoracic block technique by using ultrasound-guided TC.
5. Individualization of the perioperative ventilatory strategy (**IPROVE**).
6. One-lung ventilation in prone position with single-light tube for thoracoscopic esophagectomies
7. Serratus block analgesia in breast surgery versus standard therapy.
8. Transfusion requirements in cardiac surgery (TRICS).
9. Iron therapy in cardiac surgery.
10. Hemodynamic Monitoring in pediatrics.
11. Postanaesthesia Pulmonary complications after the use of muscle relaxants in Europe (POPULAR).
12. PProtective Ventilation with Higher versus Lower PEEP during General Anesthesia for Surgery in obese Patients (PROBESE).
13. Analysis of a self-assessment eHealth system applied to monitoring ambulatory surgery postoperative patients.
14. Evaluating innovative models for more effective and safe integrated care in the field of outpatient surgery leading to the deployment of more standardized best practices.
15. Prediction of home state in ambulatory surgery.
16. Post-operative residual curarization zero. (PORC 0).

## RELEVANT CLINICAL RESEARCH

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Overall development of research within our group is aimed at clinical level, or even with the purpose of developing multiple education initiatives in order to implement a safety culture in the perioperative period, but there are some studies that have a clear industrial involvement too.

## INDUSTRY COLLABORATIONS

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The *IPPCOLLAPSE* study focuses on the development of algorithms to facilitate the calculation of the abdominal compliance in laparoscopic surgery and thus the laparoscopic insufflation pressure is individualized. We are developing mobile apps for IOS and Android to calculate the abdominal compliance with entering data pressure-volume in our smartphone or tablet manually. This project is supported by private funding (MSD) and it has been granted public funding together with the Polytechnic University of Valencia.

The line of work *Outpatient Surgery*, with the evaluation of patients through self-evaluation eHealth systems after discharge from outpatient surgery units, can allow development, together with industry, of applications that facilitate monitoring patients after hospital discharge.

The group develops, supported by MSD, an international training program in Anesthesiology for the Improvement of surgical conditions in colorectal laparoscopic surgery (CAPE-ISC).



# ART AND SCIENCE in Health-care

## MAIN RESEARCH LINES

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- Innovation and development of teaching methodology in nursery
- Health promotion and measurement tools
- Comfort care requirements in the therapeutic relationship of people with their needs and experiences in health, illness and death

Leading Researcher:

**Esperanza Ferrer**

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No. Members: **16**

Other relevant  
information:

Contact:



# NEUROMUSCULAR PATHOLOGY AND ATAXIAS

Leading Researcher:

Juan J. Vilchez, PhD



No. Members: 15



Contact:

neuromuscular@iislafe.es

## MAIN RESEARCH LINES

### Hereditary and acquired neuropathies study

Genetic characterization of patients with Charcot-Marie-Tooth disease. This study includes genetic mapping, identification of new genes and phenotypic study of particular forms of the disease, especially those related with the GDAP1, SH3TC2 and CMT4-Russe, or CMTXGJB1 genes.

### Clinical studies and therapeutic trials in muscular dystrophies

Clinical, morphological, pathological, immunohistochemical, ultrastructural and molecular characterization of myopathies and asymptomatic hyperCKemia. In addition this research line works on the characterization of distal and scapuloperoneal myopathies, in collaboration with the International Study Group for Distal Myopathies and the Spanish groups promoted by CIBERNED. The research group has participated in an international study on the anoctamin 5 gene responsible for waist dystrophy and distal myopathy.

### Clinical and genetic characterization of congenital myasthenias

Genetic characterization of congenital myasthenias in collaboration with Dr. H. Lochmuller (Munich) laboratory, of and development myasthenia gravis animal model.

#### Collaborations:



## SELECTED PAPERS

**Analysis of the CHCHD10 gene in patients with frontotemporal dementia and amyotrophic lateral sclerosis from Spain.** Dols-Icardo O. et al. Dementia Genetics Spanish Consortium (DEGESCO). Brain. 2015 Dec;138(Pt 12):e400. doi: 10.1093/brain/awv175. Epub 2015 Jul 7.

**The EGR2 gene is involved in axonal Charcot-Marie-Tooth disease.** Sevilla, T. et al. European journal of neurology. 2015 Dec;22(12):1548-55. doi: 10.1111/ene.12782. Epub 2015 Jul 24.

**Muscle imaging in muscle dystrophies produced by mutations in the EMD and LMNA genes.** Díaz-Manera J. et al. Neuromuscul Disord. 2015 Oct 22. pii: S0960-8966(15)00743-9. doi: 10.1016/j.nmd.2015.10.001.

**Targeted screening for the detection of Pompe disease in patients with unclassified limb-girdle muscular dystrophy or asymptomatic hyperCKemia using dried blood: A Spanish cohort.** Gutierrez-Rivas, E. et al. Neuromuscular Disorders. 2015 Jul;25(7):548-53. doi: 10.1016/j.nmd.2015.04.008.

# NEUROMUSCULAR PATHOLOGY AND ATAXIAS

## SELECTED ACTIVE RESEARCH PROJECTS

Study Hypercremia Asymptomatic or Paucisymptomatic.

**Juan Jesus Vilchez Padilla**

Study of Antibodies against membrane neuronal antigens in Opsoclonus myoclonus syndrome, Neuromyotonia and Epilepsy of probable autoimmune cause.

**Luis Bataller Alberola**

Mutational study of a set of patients with Hereditary Motor Distal Neuropathy.

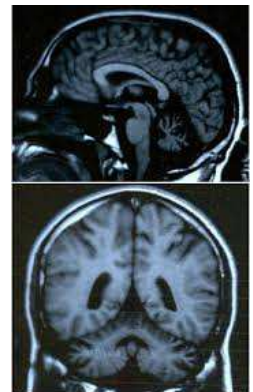
**Teresa Sevilla Mantecon**

Translational Research, Experimental Medicine and Therapeutics  
on Charcot-Marie-Tooth. Treat-Cmt

**Teresa Sevilla Mantecon - Jose Maria Millán Salvador**

Autoimmunity Study in Neuromuscular Syndromes Associated with thymoma.

**Luis Bataller Alberola**



## RELEVANT CLINICAL RESEARCH

Clinical trial in Phase III; randomized, double-blind, placebo-controlled, to evaluate the efficacy and safety of GSK2402968 in patients with Duchenne muscular dystrophy.

**Juan Vilchez Padilla**

Glaxosmithkline, S.A.

Clinical trial in Phase III; randomized, multicenter, double-blind, controlled by placebo and parallel group, to investigate the efficacy, safety and tolerability of two different doses of igpro20 (subcutaneous immunoglobulin) in the treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) -Study PATH.

**Teresa Sevilla Mantecon**

*Csl Behring GmbH*

Randomized European study; double blind, crossover, active-controlled with reference treatment to compare the efficacy and safety of a new intravenous human immunoglobulin at 10%, liquid and ready to use (i10e) with kiovig® in patients with motor multifocal neuropathy.

**Teresa Sevilla Mantecon**

*LFB Biotechnologies*



# JOINT RESEARCH UNIT IN ICTs APPLIED TO BIOMECHANICALS

Leading Researchers:

Enrique Viosca, PhD  
Pedro Vera Luna, PhD



No. Members: 23



Other relevant  
information:



Joint Research Unit  
with IBV Institute  
(Universitat Politècnica  
de València)

Contact:

biomecanica@iislafe.es

## MAIN RESEARCH LINES

**Study of motor and functional recovery of individuals who have suffered an acute stroke.** Study of balance, gait and handling of these patients; effective tele-rehabilitation at home.

**Study of spinal cord injury.** Study of the main causes of iatrogenic spinal cord injury, which facilitates the implementation of preventive measures and early diagnosis.

**Study of immobilization pathology.** Study of immobilization pathology, a common feature in patients with severe physical disabilities (spinal cord injured, patients with brain damage from stroke, TCE, PCI, multiple trauma, etc), including age-related pathologies such as sarcopenia (degenerative loss of muscle mass and strength).

**Study of clinical and functional manifestations of Child Cerebral Paralysis.** Study of the factors that determine the functional capacity during gait and overall mobility.

### **Biomechanical evaluation of implants**

Specifically for orthopedic and dental surgery, instruments and other medical devices.

### **Assessment of in vivo performance of new biomaterials**

Assessment in tissue engineering and regenerative medicine by means of histomorphometric and densitometric studies and biomechanical assays.

### Collaborations

**ciber-66n**  
Centro Investigación Biomédica en Red  
Biotecnología, Biomateriales y Nanomedicina

## SELECTED PAPERS

**Adaptation and validation of the Spanish self-report version of the Spinal Cord Independence Measure (SCIM III).** Aguilar-Rodriguez, M. et al. Spinal Cord. 2015 Jun;53(6):451-4. doi: 10.1038/sc.2014.225. Epub 2014 Dec 16.

**Finite element analysis and cadaveric cinematic analysis of fixation options for anteriorly implanted trabecular metal interbody cages.** Berjano P. et al. Eur Spine J. 2015 Nov;24 Suppl 7:918-23. doi: 10.1007/s00586-015-4277-3. Epub 2015 Oct 9.

**On the Use of Dance as a Rehabilitation Approach for Children with Cerebral Palsy: A Single Case Study.** Morán Pascual P. et al. Stud Health Technol Inform. 2015;217:923-8.

**Woman with sudden neck pain and neurological impairment.** Campoy-Sáenz JA. et al. Semergen. 2015 Nov 27. pii: S1138-3593(15)00318-4. doi: 10.1016/j.semerg.2015.09.010. [Epub ahead of print]

# JOINT RESEARCH UNIT IN ICTs APPLIED TO BIOMECHANICALS

## SELECTED ACTIVE RESEARCH PROJECTS

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Characterization of gait rehabilitation process of persons after a stroke and use of new assessment tools (in collaboration with the European project BNCI-driven robotic physical therapies in stroke rehabilitation of gait disorders). **Enrique Viosca Herrero**

Usability analysis and adaptation of an apparatus for gait rehabilitation (In collaboration with the European project: Development of a raising, walking and exercise device with upper body support for rehabilitation of stroke victims). **Enrique Viosca Herrero**

Objective study of gait in children with CP, before and after the injection of botulinum toxin.  
**Enrique Viosca Herrero**

Clinical validation of biomechanical tests for functional assessment of upper limb with neurological involvement  
**Raquel Marzo Rosello**

Robotic Platform for Rehabilitation and gait training in patients with cerebral palsy.  
**Juan Manuel Belda Lois**

## RELEVANT CLINICAL RESEARCH

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Effect of Allopurinol on the administration for preventing muscle loss in immobilized subjects.  
**Enrique Viosca Herrero**  
*Instituto de Investigación Sanitaria La Fe*

Prospective clinical trial evaluation and efficacy of a transfemoral implantation.  
**Enrique Viosca Herrero**  
*Tequir S.L*

## FUNCTIONAL VALORATION LABORATORY

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The Research Joint Unit has a Functional Validation Laboratory integrated within the Hospital La Fe to provide services of functional and biomechanical assessment.





# BIOMEDICAL IMAGING (GIBI2<sup>30</sup>)

Leading Researcher:

Luis Martí, PhD



No. Members: 28



Other relevant  
information:

Lead the Experimental Radiology and Imaging Biomarkers Platform, that promotes and develops the use of imaging biomarkers extracted from medical images, to optimize diagnostic and therapeutic applications.

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## MAIN RESEARCH LINES

### Development and validation of imaging biomarkers

Aim to optimize the diagnostic and therapeutic efficiency of imaging biomarkers with a multidisciplinary and multimodal approach, and to validate such relationship with the structural, physiological, and molecular biological reality, and thus, control the technical quality of imaging techniques.

### New diagnostic techniques and procedures based on molecular imaging

Combine analysis of molecular information with anatomy, in order to promote improvements in diagnostic systems, develop tools to support clinical decision and enhance pre-and intraoperative planning systems, as well as simulation tools and control in virtual surgery and image-guided therapies.

### Definition and implementation of parametric images with biological, functional and anatomical

Develop methods for the analysis of both in vivo and in vitro composition and structure of biological tissues using techniques based on the measurement of data obtained by functional medical imaging.

### Display of stem cells implants in different organs by functional imaging

Stem cells labelling with visible molecules or nanoparticles by computed tomography, magnetic resonance or multimodality solutions in order to monitor these cells, once introduced, and detect their implantation in the desired organs.

Collaborations:

**ciber-66n**  
Biomedical Research Networking Center  
Bioengineering, Biomaterials, Nanomedicine

## SELECTED PAPERS

**MR Angiography at 3 T of Peripheral Arterial Disease: A Randomized Prospective Comparison of Gadoterate Meglumine and Gadobutrol.** Loewe, C. et al. American Journal of Roentgenology. 2015 Jun;204(6):1311-21. doi: 10.2214/AJR.14.12604.

**Fast inexact mapping using advanced tree exploration on backward search methods.** Salavert J. et al. BMC Bioinformatics. 2015 Jan 28;16:18. doi: 10.1186/s12859-014-0438-3.

**State-of-the-art of bone marrow imaging in multiple myeloma.** Marti-Bonmati, L. et al. Current opinion in oncology. 2015 Nov;27(6):540-50. doi: 10.1097/CCO.0000000000000230.

**ESGAR consensus statement on liver MR imaging and clinical use of liver-specific contrast agents.** Neri E et al. Eur Radiol. 2015 Jul 21.

**A Systematic Approach for Using DICOM Structured Reports in Clinical Processes: Focus on Breast Cancer.** Medina Garcia, R. et al. Journal of Digital Imaging. 2015 Apr;28(2):132-45. doi: 10.1007/s10278-014-9728-6.

# BIOMEDICAL IMAGING (GIBI2<sup>30</sup>)

## SELECTED ACTIVE RESEARCH PROJECTS

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Quantification of inflammation, fat, iron and fibrosis by MR imaging biomarkers in liver transplant patients with recurrent infection with hepatitis C virus.

**Luis Martí Bonmatí**

Development of metallic nanoparticles for imaging and hyperthermal applications in melanoma.

**Teresa Albelda**

Biomechanical tissue modeling applied to computed assisted surgery (sub 3).

**Maximiliano Lloret Llorens - Maximiliano Lloret Larrea**

Evaluation of the radiosensitivity in health personnel working with methods of treatment or medical diagnosis by radiation.

**Alegria Montoro Pastor**

Characterization of biological signatures of glioblastomas using unsupervised prediction models based on structured imaging biomarkers (CURIAM BT +).

**Juan Miguel García Gómez**

## RELEVANT CLINICAL RESEARCH

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Unsupervised glioblastoma tumor components segmentation based on perfusion multiparametric MRI and spatial/temporal constraints.

**Luis Martí Bonmatí**

*Bracco Group*

Implementation and automation of measures of brain atrophy and cervical cord in clinical practice.

**Luis Martí Bonmatí**

*Genzyme*

Brain Repair after stroke: Magnetic field mediated stem cell migration

**Luis Martí Bonmatí**

*Institut de Recerca de l'Hospital Universitari Vall d'Hebron*

## INDUSTRY COLLABORATIONS

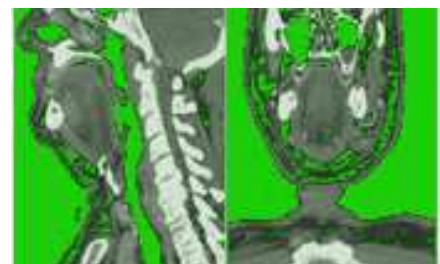
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Reference Site Contract

*PHILIPS Medical Systems Nederland BV*

Audit Radiology Laboratory

*Entidad Nacional de Acreditación (ENAC)*



# CLINICAL AND TRANSLATIONAL RESEARCH IN CANCER

Leading Researcher:

Victoria Castel, PhD



No. Members: 34



Other relevant  
information:

**42 phase I and II  
clinical trials, 4 of  
them promoted by the  
Medical Research  
Institute La Fe and the  
research group.**

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## MAIN RESEARCH LINES

### Translational research in neuroblastoma

Study of neuroblastoma prognostic factors, epigenomics and genomics and new therapeutic targets for neuroblastoma, as well as new drugs for therapeutic targets. Projects in collaboration with SEHOP and SIOPEN.

### Clinical and Translational research in other paediatric cancers

Research on the prognosis, adaptation of treatment to risk factors and new therapeutic and long-term side effects, mainly in different pediatric tumors, including of central nervous system tumors, leukemia / transplant, retinoblastoma and sarcoma.

### Prognostic factors and new therapeutics in adult solid tumors

Development and validation of prognostic and predictive factors in different adult neoplasms (breast cancer, gastrointestinal tumors, tumors of the central nervous system, lung, gastrointestinal, lymphomas and germ cell tumors).

### Genetic predisposition to cancer

Study of hereditary breast and ovarian hereditary cancer (HBOC) genetic predisposition, familial colorectal cancer (Lynch syndrome and familial adenomatous polyposis). This group laboratory (molecular biology lab) is the reference in Valencian Region for mutations in the BRCA1 / 2 genes in HBOC screening.

### Management information systems in cancer

Collaborate with National Registry of Childhood Tumors and NEOS Project of Epidemiology Department of Valencian Regional Health Ministry

## SELECTED PAPERS

**Comparative genetic study of intratumoral heterogenous MYCN amplified neuroblastoma versus aggressive genetic profile neuroblastic tumors.** Berbegall AP et al. *Oncogene*. 2015 Jun 29. doi: 10.1038/onc.2015.200.

**Clinical guideline SEOM: hepatocellular carcinoma.** Sastre J et al. *J. Clin Transl Oncol*. 2015 Dec;17(12):988-95. doi: 10.1007/s12094-015-1451-3. Epub 2015 Nov 25.

**Two independent epigenetic biomarkers predict survival in neuroblastoma.** Yanez, Y. et al. *Clinical Epigenetics*. 2015 Feb 27;7(1):16. doi: 10.1186/s13148-015-0054-8. eCollection 2015.

**Chemotherapy-associated anemia in patients with lung cancer: an epidemiological, retrospective and multicenter study.** Munoz-Langa, J. et al. *Future Oncology*. 2015;11(11):1665-74. doi: 10.2217/fon.15.75.

**Feasibility and Safety of a Modified Outpatient Regimen With Intravenous/Intraperitoneal Chemotherapy for Optimally Debulked Stage III Ovarian Cancer.** Bruixola, G. et al. *International Journal Of Gynecological Cancer*. 2015 Feb;25(2):214-21. doi: 10.1097/IGC.0000000000000330.

# CLINICAL AND TRANSLATIONAL RESEARCH IN CANCER

## SELECTED ACTIVE RESEARCH PROJECTS

EXPO-r-Net: European Expert Paediatric Oncology Reference Network for Diagnostics and Treatment.

**Adela Cañete Nieto**

ENCCA-European Network for Cancer Research in Children and Adolescents.

**Adela Cañete Nieto**

Study of signaling networks in osteosarcomas.

**Jaime Font De Mora Sainz**

The homologous recombination deficiency in sporadic breast cancer.

**Pascual Bolufer Gilabert**

Application of INRG to patients with neuroblastoma: the value of new prognostic groups for therapeutic individualization.

**Victoria Castel Sánchez**



## RELEVANT CLINICAL RESEARCH

Clinical trial in Phase II, nonrandomized treatment, with temozolomide combined with topotecan for neuroblastoma and other pediatric solid tumor in situation of relapse or progression.

**Victoria Castel Sánchez**

*Instituto de Investigación Sanitaria La Fe*

Clinical trial in Phase I / II, multicenter, open-label, to find the doses to assess security, tolerability and efficacy of weekly nab®- paclitaxel in pediatric patients with relapsed or refractory solid tumor.

**Victoria Castel Sánchez**

*Celgene Corporation*

Clinical trial in Phase I / II to evaluate brentuximab vedotin (SGN-35) in pediatric patients with systemic anaplastic large cell lymphoma or Hodgkin lymphoma relapsed or refractory.

**Amparo Verdeguer Miralles**

*Millennium Pharmaceuticals, Inc*

## INDUSTRY COLLABORATIONS

Efficacy of frontline uses of midostaurin and chemotherapy in the treatment of acute myeloid leukemia with mutations in FLT3

*Novartis Pharmaceutical*

Laboratory of Molecular Biology: Molecular biomarkers in cancer.

*Amgen*

From the patient to the laboratory, a bidirectional pathway: Neuroblastoma spread of poor prognosis as a model of individualized therapy

*Asociación Pablo Ugarte*

# CELIAC DISEASE AND GASTROINTESTINAL IMMUNOPATHOLOGY

Leading Researcher:

**Carmen Ribes PhD**



No. Members: 15



Contact:

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## MAIN RESEARCH LINES

### Celiac disease

Study of celiac disease from three different approaches: diagnosis, prevention and treatment. In diagnosis field, immunohistochemistry techniques have been developed in intestinal mucosa to assess complex or low degree of enteropathy patients, demonstrating the effectiveness of a rapid test (serum and whole blood) for the determination of serological markers of coeliac disease. The group collaborates with industry in validation of new serological methods of immunological markers for the disease.

### Hepatocyte transplantations

Develop, in collaboration, a program of hepatocyte transplantation in paediatric patients who are awaiting for whole organ transplantation or as an alternative to it. Efficacy and safety were evaluated and medical treatment protocols (immunosuppression) and follow-up is established.



## SELECTED PAPERS

**Espghan 2012 guidelines for coeliac disease diagnosis: validation through a retrospective spanish multicentric study.** Donat, E. et al. SEGHP Working Group on Coeliac Disease. Journal of Pediatric Gastroenterology and Nutrition. 2015 May 25.

**The HLA-DQ2 genotype selects for early intestinal microbiota composition in infants at high risk of developing coeliac disease.** Olivares, M. et al. Gut. 2015; 64(3): 406-17.

**Nutrition of infants and young children (1-3 years) and its effect on later health: a systematic review of current recommendations (EarlyNutrition project).** Zalewski, BM et al. Critical Reviews in Food Science and Nutrition. 2015 Mar 9:0.

**Systematic review with meta-analysis: early infant feeding and coeliac disease - update 2015.** Szajewska, H et al. Alimentary Pharmacology & Therapeutics. 2015; 41(11): 1038-54.

# CELIAC DISEASE AND GASTROINTESTINAL IMMUNOPATHOLOGY

## SELECTED ACTIVE RESEARCH PROJECTS

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MyCyFFAPP. Innovative approach for self-management and social welfare of cystic fibrosis patients in Europe: development, validation and implementation of a telematics tool. **Carmen Ribes Koninckx**. Coordinator H2020 project.

Long-term study of Docosahexaenoic acid treatment influence on systemic inflammation in the lung and the intestine in patients with cystic fibrosis. **Carmen Ribes Koninckx**

Safety, efficacy, tolerability and pharmacokinetics of rebetol pegintrony in children with chronic hepatitis C. **Carmen Ribes Koninckx**

Clinical study in Phase I/II; in two stages, open, single group, of the safety, pharmacokinetics and effectiveness of Telaprevir in combination Peginterferon alpha-2b and Ribavirin in pediatric subjects of 3-17 years infected with hepatitis virus. **Carmen Ribes Koninckx**

## RELEVANT CLINICAL RESEARCH

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Study of the safety and nutritional capacity of a new hypoallergenic formula for infant with various allergies against the protein of cow milk.

**Carmen Ribes Koninckx**

*Hero España, S.A*

Evaluation of the pharmacokinetics of Boceprevir in pediatric patients with chronic Hepatitis C Genotype 1 (Phase 1B).

**Carmen Ribes Koninckx**

*Merck Sharp & Dohme Corp.*

Clinical trial in Phase III to evaluate the efficacy and safety of Boceprevir in combination with Peginterferon alfa-2B and Ribavirin in pediatric patients with Chronic Hepatitis C Genotype 1.

**Carmen Ribes Koninckx**

*Merck Sharp & Dohme Corp*

## INDUSTRY COLLABORATIONS

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Liver disease associated with cystic fibrosis.

*Laboratorios Ordesa, Numil Nutricion Srl*

Evaluation of DGP POC (Simtomax) diagnostic test for early detection of celiac disease in children.

*Tillotts Pharma Ag*

Evaluation of a new test using energized Elia gliadin peptides.

*Tillotts Pharma Ag*



# JOINT RESEARCH UNIT FOR CEREBROVASCULAR RESEARCH

Leading Researcher:

Enrique Alborch, PhD



No. Members: 10



Other relevant  
information:

JOINT RESEARCH UNIT  
WITH UNIVERSITAT DE  
VALENCIA (Departamento  
de Fisiología)



Contact:

cerebrovascular@iislafe.es

## MAIN RESEARCH LINES

Study of cerebral circulation physiology, pathophysiology and pharmacology of ischemic stroke, functional ingredients for the treatment of hypertension and the pathophysiology of diabetic vasculopathy, the latter two as risk factors for stroke.

### Improvement of circulatory function in experimental ischemic stroke (ICTUS)

Study the hypothesis phytoestrogen genistein protects the brain against ischemic stroke by improving circulatory function in terms of reduced production of thromboxane A2 and platelet-leukocyte aggregates, and preservation of vascular reactivity.

### Antihypertensive effects of lactoferrin hydrolyzates

Evaluate long-term intake effect of a bovine lactoferrin hydrolysate enriched in low molecular weight peptides (LFH<3kDa) on the progression of hypertension in spontaneously hypertensive rats and its in vivo mechanism action.

### Involvement of prostacyclin and potassium channels in diabetes-induced hyporeactivity of rabbit carotid artery to B-type natriuretic peptide

Study on how alloxan-induced diabetes can modify the effects of BNP in rabbit carotid arteries and the mechanisms involved in such actions.

Collaborations:



## SELECTED PAPERS

**An antihypertensive lactoferrin hydrolysate inhibits angiotensin I-converting enzyme, modifies expression of hypertension-related genes and enhances nitric oxide production in cultured human endothelial cells.** Garcia-Tejedor, A et al. Journal of Functional Foods. 2015; 12: 45-54.

**Dairy Debaryomyces hansenii strains produce the antihypertensive casein-derived peptides LHLPLP and HLPLP.** Garcia-Tejedor, A et al. LWT-Food Science and Technology. 2015; 61(2): 550-556.

**In vivo antihypertensive mechanism of lactoferrin-derived peptides: Reversion of angiotensin I-and angiotensin II-induced hypertension in Wistar rats.** Garcia-Tejedor, A et al. Journal of Functional Foods. 2015; 15: 294-300.

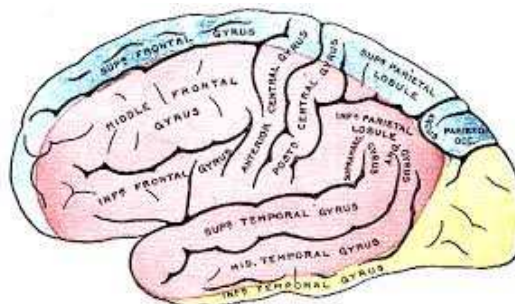
**Unraveling the mechanisms of action of lactoferrin-derived antihypertensive peptides: ACE inhibition and beyond.** Manzanares, P et al. Food & Function. 2015; 6(8): 2440-52.

# JOINT RESEARCH UNIT FOR CEREBROVASCULAR RESEARCH

## SELECTED ACTIVE RESEARCH PROJECTS

Influence of diabetes on the signaling pathways of brain estrogen receptors in experimental acute ischemic stroke: Therapeutic Implications

German Torregrosa Bernabé



## INTELLECTUAL PROPERTY RIGHTS

**PATENT:** APOTRANSFERRIN FOR THE TREATMENT OF BRAIN STROKE

National reg: P201131816

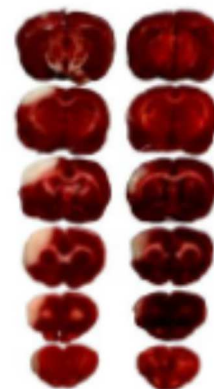
PCT Reg: PCT/EP2012/072195

National phases: USA, JAPAN and EUROPE

Co-ownership:

F.G.TRIALS I PUJOL, UAB, and IIS La Fe (Drs. Alborch and Salom)

Vehicle    ATF



## INDUSTRY COLLABORATIONS

Study of the effect of probiotic on hypertension in SHR rats

Biopolis S.L.



Leading Researcher:

**Rafael Botella PhD**



No. Members: 7



Contact:

[dermatologia@iislafe.es](mailto:dermatologia@iislafe.es)

## MAIN RESEARCH LINES

### **Melanoma, immune response perspective applying gene therapy techniques**

Basic (gene therapy, immune response) and clinical (dermoscopy, clinical trials). research. Identification of mutations that may be relevant for treatment using targeted drugs against molecular targets (BRAF, KIT). Other treatments are aimed at enhancing the host immune response against the tumor (anti-CTLA4).

### **Metabolic profile patients of patients with moderate to severe psoriasis**

Obtain a complete metabolic patients profile and study their modification with different therapies for psoriasis: topical treatment with ultraviolet light, traditional systemic drugs and biological systemic drugs. This line can provide valuable information on the relationship between metabolic syndrome and psoriasis, as well as the ability of new biological drugs to modify different molecules involved production in vascular risk of these patients.

### **PET-CT evaluation of decreased vascular inflammation in patients with moderate to severe psoriasis**

Aim to compare, using the PET-CT, the modification of vascular inflammation occurring in patients with moderate to severe psoriasis treated with anti-TNF drugs with those undergoing conventional treatments.

## SELECTED PAPERS

**Study of the immunophenotype of the inflammatory cells in melanomas with regression and Halo Nevi.** Botella-Estrada, R et al. American Journal of Dermatopathology. 2015; 37(5): 376-80.

**Dermoscopy margin delineation in radiotherapy planning for superficial or nodular basal cell carcinoma.** Ballester Sanchez, R et al. British Journal of Dermatology. 2015; 172(4): 1162-3.

**Update on melanoma epigenetics.** de Unamuno, B; Palanca, S; Botella, R. Current Opinion in Oncology. 2015; 27(5): 420-6.

**New alpha-papillomavirus 4 isolate in a verruca vulgaris with multicentric superficial basal cell carcinoma.** Sabater-Marco, V et al. International Journal of Dermatology. 2015; 54(4): e102-3.

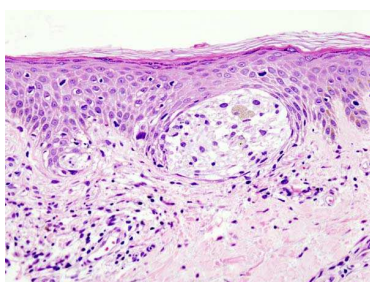
**Epigenetic activation of a cryptic TBC1D16 transcript enhances melanoma progression by targeting EGFR.** Vizoso, M et al. Nature Medicine. 2015; 21(7): 741-50.

### SELECTED ACTIVE RESEARCH PROJECTS

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Molecular features of melanomas with different growth pattern as the basis for stable-foundation of biomarkers for early diagnosis, prognosis, response and implementation of a personalized treatment.

**Rafael Botella Estrada**



### RELEVANT CLINICAL RESEARCH

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Comparison of a simultaneous treatment regimen versus to a sequential treatment regimen with mebutato ingenol gel 0.015% and 0.05% in two areas with actinic keratosis (face/scalp and trunk/limbs).

**Rafael Botella Estrada**

*Leo Pharma A/S*

Double-blind clinical trial of keratolytic capillary gel gv-264 in psoriasis of the scalp.

**Rafael Botella Estrada**

*Laboratorios Viñas, S.A.*

### INDUSTRY COLLABORATIONS

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Study of an electronic brachytherapy for cutaneous basal cell carcinoma.

*Nucletron Operations B.V.*

Metabolic profile in patients with moderate to severe psoriasis and its modification with treatment.

*Pfizer*

Tumoral skin disease in transplant patients at the Hospital La Fe.

*Merck Sharp Dohme España S.A.*

*Vidad Formativa*

# DIGESTIVE and LIVER MEDICINE

Leading Researcher:

Marina Berenguer  
Haym

No. Members: **12**

Other relevant  
information:

Contact:

## MAIN RESEARCH LINES

- Hepatitis C and liver transplantation (clinical, serological and immunological studies)
- Hepatitis B and liver transplantation (clinical and biological studies)
- Viral hepatitis in immunocompetent patient
- Hepatocellular carcinoma and liver transplantation
- Wilson's disease
- Non-cirrhotic portal hypertension
- Immunosuppression complications
- CMV infection after LT

## SELECTED PAPERS

Acute cellular rejection versus recurrent hepatitis C after liver transplantation: Clinical and pathological features driving a rational diagnostic approach. de la Pena-Moral, Jesus M.; Pons, Jose A.; Tome, Santiago; Gude, Francisco; Miras, Manuel; Bermejo, Juan; Ramirez, Pablo; Berenguer, Marina; Varo, Evaristo; Forteza, Jeronimo; Parrilla, Pascual. *Hepatology Research*. 2015 Apr;45(4):423-31. doi: 10.1111/hepr.12369. Epub 2014 Jul 2.

Alterations in carbohydrate metabolism in cirrhotic patients before and after liver transplant.. Ramos-Prol A1, Hervás-Marín D2, Rodríguez-Medina B3, Campos-Alborg V4, Berenguer M3, Moya-Herraiz Á3, Merino-Torres JF5. *Diabetes Res Clin Pract*. 2015 Nov;110(2):123-8. doi: 10.1016/j.diabres.2015.10.002. Epub 2015 Oct 9. Beyond cure: preventing and managing the complications of end-stage liver disease. Berenguer M1, García-Eliz M, Baiguera C, Puoti M. *Curr Opin HIV AIDS*. 2015 Sep;10(5):355-60. doi: 10.1097/COH.0000000000000184.

Distinct phenotype of hepatotoxicity associated with illicit use of anabolic androgenic steroids. Robles-Diaz, M.; Gonzalez-Jimenez, A.; Medina-Caliz, I.; Stephens, C.; Garcia-Cortes, M.; Garcia-Munoz, B.; Ortega-Alonso, A.; Blanco-Reina, E.; Gonzalez-Grande, R.; Jimenez-Perez, M.; Rendon, P.; Navarro, J. M.; Gines, P.; Prieto, M.; Garcia-Eliz, M.; Bessone, F.; Brahm, J. R.; Parana, R.; Lucena, M. I.; Andrade, R. J. *Alimentary Pharmacology & Therapeutics*. 2015 Jan;41(1):116-25. doi: 10.1111/apt.13023. Epub 2014 Nov 13.

Effectiveness and safety of first-generation protease inhibitors in clinical practice: Hepatitis C virus patients with advanced fibrosis. Salmeron, Javier; Vinaixa, Carmen; Berenguer, Ruben; Manuel Pascasio, Juan; Sanchez Ruano, Juan Jose; Angel Serra, Miguel; Gila, Ana; Diago, Moises; Romero-Gomez, Manuel; Maria Navarro, Jose; Testillano, Milagros; Fernandez, Conrado; Espinosa, Dolores; Carmona, Isabel; Antonio Pons, Jose; Jorquera, Francisco; Javier Rodriguez, Francisco; Perez, Ramon; Montero, Jose Luis; Granados, Rafael; Fernandez, Miguel; Belen Martin, Ana; Munoz de Rueda, Paloma; Quiles, Rosa. *World Journal Of Gastroenterology*. 2015 Aug 14;21(30):9163-74. doi: 10.3748/wjg.v21.i30.9163.

Entecavir has high efficacy and safety in white patients with chronic hepatitis B and comorbidities. Buti, Maria; Morillas, Rosa M.; Perez, Juan; Prieto, Martin; Sola, Ricard; Palau, Antonio; Diago, Moises; Bonet, Lucia; Gallego, Adolfo; Garcia-Samaniego, Javier; Testillano, Milagros; Rodriguez, Manuel; Castellano, Gregorio; Gutierrez, Maria L.; Delgado, Manuel; Mas, Antoni; Romero-Gomez, Manuel; Calleja, Jose L.; Gonzalez-Guirado, Agustina; Arenas, Juan I.; Garcia-Buey, Luisa; Andrade, Raul; Gila, Ana. *European Journal Of Gastroenterology & Hepatology*. 2015 Jan;27(1):46-54. doi: 10.1097/MEG.0000000000000195.



Hepatitis B virus quasiespecies evolution after liver transplantation in patients under long-term lamivudine prophylaxis with or without hepatitis B immune globulin. Buti, M.; Tabernero, D.; Mas, A.; Homs, M.; Prieto, M.; Rodríguez-Frías, F.; Casafont, F.; Casillas, R.; Gonzalez, A.; Miras, M.; Herrero, J. I.; Castells, L.; Esteban, R. *Transplant Infectious Disease*. 2015 Apr;17(2):208-20. doi: 10.1111/tid.12360.

High efficacy and safety of triple therapy in HCV genotype 1 and moderate fibrosis: a multicenter study of clinical practice in Spain. Crespo, Javier; Diago, Moises; Cabezas, Joaquin; Berenguer, Marina; Broquetas, Teresa; Angel Serra, Miguel; Morillas, Rosa; Garcia-Samaniego, Javier; Luis Calleja, Jose; Jose Sanchez, Juan; Lens, Sabela; Soto-Fernandez, Susana; Sacristan, Begona; Fernandez, Inmaculada; Lopez-Nunez, Carmen; Buti, Maria; Romero-Gomez, Manuel; Saez-Royuela, Federico; Fernandez, Conrado; Jorquera, Francisco; Sanchez-Antolin, Gloria; Manuel Pascasio, Juan; Cuadrado, Antonio; Hernandez-Guerra, Manuel. *Annals Of Hepatology*. 2015 Jul-Aug;14(4):477-86.

HIV Infection Does Not Worsen Prognosis of Liver Transplantation for Hepatocellular Carcinoma. Agüero F1, Forner A2,3, Manzano C1, Valdivieso A4, Blanes M5, Barcena R6, Rafecas A7, Castells L8,3, Abradelo M9, Torre-Cisneros J10, González-Diéguez L11, Salcedo M12, Serrano T13, Jiménez-Pérez M14, Herrero J15,16,3, Gastaca M4, Aguilera V5,3, Fabregat J7, Del Campo S6, Bilbao I8, Romero CJ9, Moreno A1, Rimola A17,3, Miro JM1; FIPSE investigators. *Hepatology*. 2015 Oct 30. doi: 10.1002/hep.28321. [Epub ahead of print]

Impact of anticoagulation on upper-gastrointestinal bleeding in cirrhosis. A retrospective multicenter study. Cerini, Federica; Martinez Gonzalez, Javier; Torres, Ferran; Puente, Angela; Casas, Meritxell; Vinaixa, Carmen; Berenguer, Marina; Ardevol, Alba; Augustin, Salvador; Llop, Elba; Senosiain, Maria; Villanueva, Candid; de la Pena, Joaquin; Banares, Rafael; Genesca, Joan; Sopena, Julia; Albillos, Agustin; Bosch, Jaume; Hernandez-Gea, Virginia; Carlos Garcia-Pagan, Juan. *Hepatology*. 2015 Aug;62(2):575-83. doi: 10.1002/hep.27783. Epub 2015 Apr 27.

Lead-in period and week 8 as predictive tools for response to boceprevir therapy: a retrospective study of Spanish real clinical practice. Crespo J1, Berenguer M2, Pérez F3, Fernández I4, González O5, Bárcena R6, Buti M7, López J8, Calleja JL9; en representación del grupo de investigadores del estudio LEAD-IN. *Gastroenterol Hepatol*. 2015 Nov;38(9):517-24. doi: 10.1016/j.gastrohep.2015.04.002. Epub 2015 May 12.

Management of HCV in the liver transplant setting. Berenguer, Marina. *Clinics and research in hepatology and gastroenterology*. 2015 Sep; 39 Suppl 1:S115-9. doi: 10.1016/j.clinre.2015.05.004. Epub 2015 Jul 20.

Monosegment ALPPS: A new variant of the techniques for rapid hepatic regeneration. Critical review of the initial results of our series. Montalva Oron, Eva Maria; Maupoey Ibanez, Javier; Banuelos Carrillo, Romulo; Bosca Robledo, Andrea; Orbis Castellanos, Juan Francisco; Moya Herraiz, Angel; Ballester Valles, Carmen; Perez Rojas, Judith; Aparicio Urtasun, Jorge; Lopez-Andujar, Rafael. *Cirugia Espanola*. 2015 Aug-Sep;93(7):436-43. doi: 10.1016/j.ciresp.2015.02.011. Epub 2015 Apr 14. English, Spanish.

Ombitasvir plus paritaprevir plus ritonavir with or without ribavirin in treatment-naïve and treatment-experienced patients with genotype 4 chronic hepatitis C virus infection (PEARL-I): a randomised, open-label trial. Hezode, Christophe; Asselah, Tarik; Reddy, K. Rajender; Hassanein, Tarek; Berenguer, Marina; Fleischer-Stepniowska, Katarzyna; Marcellin, Patrick; Hall, Coleen; Schnell, Gretja; Pilot-Matias, Tami; Mobashery, Niloufar; Redman, Rebecca; Vilchez, Regis A.; Pol, Stanislas. *Lancet*. 2015 Jun 20;385(9986):2502-9. doi: 10.1016/S0140-6736(15)60159-3. Epub 2015 Mar 31.

Ombitasvir/paritaprevir/r, dasabuvir and ribavirin for cirrhotic HCV patients with thrombocytopaenia and hypoalbuminaemia. Forns, Xavier; Poordad, Fred; Pedrosa, Marcos; Berenguer, Marina; Wedemeyer, Heiner; Ferenci, Peter; Shiffman, Mitchell L.; Fried, Michael W.; Lovell, Sandra; Trinh, Roger; Lopez-Talavera, Juan Carlos; Everson, Gregory. *Liver International*. 2015 Nov;35(11):2358-62. doi: 10.1111/liv.12931. Epub 2015 Sep 6.

Outcomes in liver transplantation: Does sex matter?. Sarkar, Monika; Watt, Kymberly D.; Terrault, Norah; Berenguer, Marina. *Journal Of Hepatology*. 2015 Apr;62(4):946-55. doi: 10.1016/j.jhep.2014.11.023. Epub 2014 Nov 27. Review.

Overcoming drug resistance in HSV, CMV, HBV and HCV infection. López-Labrador FX1,2, Berenguer M3,4, Navarro D5,6. *Future Microbiol*. 2015 Nov;10:1759-66. doi: 10.2217/fmb.15.74. Epub 2015 Nov 2.



# DIGESTIVE and LIVER MEDICINE

## SELECTED ACTIVE RESEARCH PROJECTS

Impact of specific immune response against cell cytomegalovirus (cmv) after liver transplant in the aggressive recurrent hepatitis c PI13/01770

PI: VICTORIA AGUILERA SANCHO-TELLO

ISCIIS-FIS. 2014-2016

64130,00€

Quantification of inflammation, GREASE, IRON AND FIBROSIS BY MR imaging biomarkers in transplant patients with recurrent LIVER INFECTION HEPATITIS C VIRUS

PI: LUIS MATÍ BONMATÍ

Co-Investigator: ÁNGEL RUBÍN SUÁREZ

BECA FIS INSTITUTO SALUD CARLOS III 2013-2015

19965,00€

True prevalence of hepatitis C virus (HCV): screening with rapid test in saliva (OraQuick) or with immunoassay from dried blood spots in a Health district.

IP: Marina Berenguer

Referencia: PI15/02010

Entidad financiadora: ISCIIS-FIS

Periodo: 2015-2018

## RELEVANT CLINICAL RESEARCH

- Clinical study randomized and open to evaluate the safety and effectiveness of ombitasvir / abt-450 / ritonavir administered with ribavirin (RBV) in adults with chronic infection hepatitis c virus (HCV) genotype 4 and cirrhotic
- Clinical study phase ii / iii to study the efficacy and safety of combining MK 8742 MK 5172 and in subjects with chronic infection hepatitis c virus with advanced cirrhosis e category b liver failure of child pugh (CP)
- Open-label randomized study to evaluate the safety and efficacy of coadministration of ABT 450 with ritonavir (ABT 450 / R) and ABT 267 in adults with chronic infection Hepatitis C virus (PEARL I)
- Clinical study phase II to investigate the efficacy and safety of combining simeprevir and daclatasvir in patients with chronic infection by virus Hepatitis C genotype 1b or genotype 4.
- Clinical STUDY Phase III, randomized, double-blind, placebo controlled to evaluate the safety and efficacy of S 888711 (LUSUTROMBOPAG) for the treatment of thrombocytopenia in patients with chronic liver disease who undergo invasive procedures scheduled (L-PLUS 2)
- Clinical study, randomized, open, multicenter to evaluate the effectiveness and safety in subjects with elad acute alcoholic hepatitis (HAAG) scoring and failure in LILLE.
- Clinical Study phase III, randomized, double-blind trial to evaluate the safety and efficacy of tenofovir alaninamide 25 mg once a day in front of tenofovir disoproxil fumarate 300 mg once a day for the treatment of hepatitis b HBEAG-positive.
- Clinical study phase II, multicenter, open, to investigate the safety and effectiveness of fixed dose combination sofosbuvir / ledipasvir + ribavirin administered in patients with HCV infection in chronic liver disease advanced or after liver transplant.
- Clinical study, randomized, international, double-blind, placebo-controlled, parallel group to evaluate the effectiveness and safety of oral AVATROMBOPAG a once a day for adults with treatment of disease associated thrombocytopenia hepatic a scheduled before a procedure.
- Between others

# JOINT RESEARCH UNIT IN ENDOCRINOLOGY, NUTRITION AND CLINICAL DIETETICS

Leading Researchers:

**Francisco Merino, PhD**  
**Jose Miguel Soriano,**  
**PhD**



No. Members: 8



Other relevant  
information:

JOINT RESEARCH UNIT  
WITH UNIVERSITAT DE  
VALENCIA (Departamento  
Medicina Preventiva y  
Salud Pública)



Contact:  
[endocrinologia@iislafe.es](mailto:endocrinologia@iislafe.es)

## MAIN RESEARCH LINES

### Paediatric nutrition

Laying the foundations for infant feeding, to avoid micronutrient deficiencies in order to prevent pathologies that may manifest in later ages. Studies on the addition of prebiotics to infant milk formulas may reduce the incidence of certain types of infections and allergic symptoms in healthy infants.

### Inborn errors of metabolism

Lysosomal diseases are a large group of hereditary diseases that generate an intralysosomal deposition of complex molecules that trigger severe and progressive organic and functional alterations in all the affected organs.

### Obesity

The group is involved in various projects in relation to obesity and its comorbidities. It is worth mentioning studies measuring blood pressure by ambulatory monitoring in obese children and adolescents.

### Diabetes

The group leads several research lines in diabetes, both in inpatient and outpatient regimen. It is worth in this field diabetes and transplantation, pancreas transplantation in diabetes, artificial pancreas, blood glucose sensors...

### Endocrine tumors

Mechanisms involved in endocrine tumor pathology, particularly at the pituitary level and neuroendocrine tumors in general.

## SELECTED PAPERS

**Prevalence of bacteria and absence of anisakid parasites in raw and prepared fish and seafood dishes in Spanish restaurants.** Sospedra, I; Rubert, J; Soriano, JM; Mañes, J; Fuentes, MV. Journal of Food Protection. 2015; 78(3): 615-618.

**Short sleep duration is related to emerging cardiovascular risk factors in obese children.** Navarro-Solera, M et al. Journal of Pediatric Gastroenterology and Nutrition. 2015; 61(5): 571-576.

**Alterations in carbohydrate metabolism in cirrhotic patients before and after liver transplant.** Ramos-Prol, A et al. Diabetes Research and Clinical Practice. 2015; 110(2): 123-8.

**Applying extracellular vesicles based therapeutics in clinical trials - an ISEV position paper.** Lener, T et al. Journal of Extracellular Vesicles. 2015; 4: 30087.

**The Extracellular Vesicles of the Helminth Pathogen, Fasciola hepatica: Biogenesis Pathways and Cargo Molecules Involved in Parasite Pathogenesis.** Cwiklinski, J et al. Molecular & Cellular Proteomics. 2015; 14(12):3258-73.

## JOINT RESEARCH UNIT IN ENDOCRINOLOGY, NUTRITION AND CLINICAL DIETETICS

### SELECTED ACTIVE RESEARCH PROJECTS

Study of abnormal carbohydrate metabolism in cirrhotic patients undergoing liver transplantation. Impact of intensive glycemic control during hospitalization after transplantation.

**Juan Francisco Merino Torres**

Nutritional status in patients with chronic pancreatitis (in collaboration with the HGU Alicante).

**Juan Francisco Merino Torres**

Intensification and personalized telematics monitoring in lifestyle modification for the treatment of obesity and cardiometabolic risk prevention (in collaboration with Cintia González Blanco (Hospital Sant Pau, Barcelona)

**Juan Francisco Merino Torres**

Pancreas transplantation as treatment of diabetes mellitus. Evaluation after 10 years of follow up.

**Juan Francisco Merino Torres**

Evolution of cardiovascular risk factors after surgery in obesity.

**Juan Francisco Merino Torres**

### RELEVANT CLINICAL RESEARCH

Protocol H9X-MC-GBDX. Randomized, open and parallel group study in which it is compared the effect on glycemic control in the treatment with Dulaglutide once a week and insulin Glargine in patients with type 2 diabetes and moderate or severe chronic kidney disease.

**Juan Francisco Merino Torres**

*Eli Lilly And Company*

Trial to compare the efficacy and safety of insulin Degludec/Liraglutide versus insulin Glargine in patients with type 2 diabetes mellitus.

**Juan Francisco Merino Torres**

*Novo Nordisk S/A*

### INDUSTRY COLLABORATIONS

Nutritional Research at the Hospital, I + D + i in endocrinology and nutrition.

*Nutricia SRL, Vegenat, Nestle, Abbott, Fresenius*

Treatment of diabetes mellitus in the hospital environment, the role of GLP-1

*Novo Nordisk S/A Pharma*



# JOINT RESEARCH UNIT IN ICTs APPLIED TO HEALTHCARE PROCESS RE-ENGINEERING

Leading Researchers:

Bernardo Valdivieso,  
PhD

Vicente Traver, PhD



No. Members: 20



Other relevant  
information:



Joint Research Unit  
with ITACA Institute  
(Universitat Politècnica  
de València)

Contact:

erpss@iislafe.es

## MAIN RESEARCH LINES

### Proactive management of chronic conditions (Integrated Care)

Development of home healthcare and chronic patients remote management, palliative care and caregivers through the application of IT to integrated management thereof. Study of change and maintenance users behavior to adopt healthy lifestyles, strengthening it through different techniques, adherence to treatment, conducting healthy activities, etc.

### Active and healthy aging

Active research in the EIP-AHA initiative (European Innovation Partnership: Active and Healthy Ageing) including Prescription and Adherence action work groups at regional level, Falls Prevention, Prevention of functional decline and frailty, Integrated Care, Independent Living and Age-Friendly Environments. **3-Stars Reference Site**

### Health 2.0

Improving healthcare information delivery and quality taking advantage of new technologies: enhancing development of tools for communication and sharing information based on new web 2.0 technologies.

### Big Data Analysis and Business Intelligence

The aim is to exploit the information available in hospital information systems (more than 20MM of data including patients, processes, diagnostic tests, pharmaceutical prescription, and soon "omics" data) with an approximation of Big Data and Data Mining, applied to population health and disease management for decision-making in research, and improvement of healthcare processes. Development of predictive models and implementation of clinical decision support system tools.

## SELECTED PAPERS

**Telemedicine in Inflammatory Bowel Disease: Opportunities and Approaches.** Peris Aguas, M et al. Inflammatory Bowel Diseases. 2015; 21(2): 392-9.

**Operative definition of active and healthy ageing (AHA): Meeting report. Montpellier October 20–21, 2014.** Bousqueta, J et al. European Geriatric Medicine. 2015; 6(2): 196-200.

**Operational definition of Active and Healthy Ageing (AHA): a conceptual framework.** Bousquet, J et al. The journal of nutrition, health & aging. 2015; 19 sep(9):1-6.

**Automatic generation of computable implementation guides from clinical information models.** Boscá, D et al. Journal of Biomedical Informatics. 2015; 55: 143-52.

**Cloud computing for context-aware enhanced m-Health services.** Fernandez-Llatas, C et al. Methods in Molecular Biology. 2015; 1246: 147-55.

## Collaborations:



# JOINT RESEARCH UNIT IN ICTs APPLIED TO HEALTHCARE PROCESS RE-ENGINEERING

## SELECTED ACTIVE RESEARCH PROJECTS

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EIP-AHA: European Innovation Partnership on Active and Healthy Ageing **Bernardo Valdivieso**

Beyond SILOS: Learning from integrated eCare practice and promoting deployment in European regions  
**Bernardo Valdivieso**

CRONICSALUD: Design and evaluation of an intervention supported by technology for the management of chronic low-complexity patients **Bernardo Valdivieso**

Mobile interactive patient services: Stimulating the interaction of public health (MIPS) **Bernardo Valdivieso**

BASECLINICA: Collaborative platform of clinical case management for research and training of health professionals **Vicente Traver**

EMPOWERING HOSPITAL-EMPH **Bernardo Valdivieso**

## RELEVANT CLINICAL RESEARCH

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- Randomized clinical trial to evaluate a model of integrate chronic disease management supported by Information and Communication Technologies.  
**Bernardo Valdivieso**  
*Instituto de Investigación Sanitaria La Fe*
- Development, validation and application in clinical routine of a predictive model to identify complex chronic patients in Health Department of La Fe.  
**Bernardo Valdivieso**  
*Instituto de Investigación Sanitaria La Fe*
- Clinical impact of telemedicine on the Crohn's Disease and Ulcerative Colitis: Study TECCU.  
**Mariam Aguas**  
*Instituto de Investigación Sanitaria La Fe*

## INDUSTRY COLLABORATIONS

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GECHRONIC: Randomized clinical trial to evaluate a model of integrate chronic disease management supported by Information and Communication Technologies.  
*IIS La Fe, Soluciones Tecnológicas para la Salud y el Bienestar, Accenture, VitalAire*

FASYS: Absolutely safe and healthy factory.  
*Soluciones Tecnológicas para la Salud y el Bienestar, S.A.*

Evaluation of professional satisfaction with the use of electronic tablets in hospital at home.  
*Ferrer Farma S.A./ Grunethal Pharma S.A*

Leading Researcher:

Esther Zorio Grima

No. Members: **13**

Other relevant  
information:

Contact:

## MAIN RESEARCH LINES

- An epidemiologic and pathologic comprehensive study of sudden cardiac death (SCD) based upon forensic series from our county.
- Cardiogenetic approach of the screening offered to families with SCD due to cardiomyopathies and suspected channelopathies.
- Advanced ECG recording and image studies in cardiomyopathies, also including postmortem advanced heart imaging.
- Advanced functional research concerning channelopathies (in silico functional prediction of mutated channels, transgenic animals and IPs with RyR2 mutations)
- Pathophysiologic mechanisms underlying arrhythmogenic cardiomyopathies and endometrosis, including Wnt pathway and miRNAs.
- Intercellular communication among epicardial fat, coronary arteries and myocardium in coronary artery disease. Role of miRNAs.

## SELECTED PAPERS

- Neco P,...,Zorio E,..., Gomez AM. Paradoxical effect of increased diastolic Ca<sup>2+</sup> release and decreased sinoatrial node activity in a mouse model of catecholaminergic polymorphic ventricular tachycardia. *Circulation* 2012;126:392-401.
- Domingo D, ..., Molina P,..., Zorio E. The Non-ventricular, clinical and functional features of the RyR2<sup>R420Q</sup> mutation causing Catecholaminergic Polymorphic Ventricular Tachycardia. *Rev Esp Cardiol* 2015;68:398-407
- Domingo D, López R, Arnau MA, ..., Zorio E. Una nueva mutación en el gen del receptor de la rianodina (RyR2 C2277R) como causa de taquicardia ventricular catecolaminérgica polimórfica. *Rev Esp Cardiol* 2015;68:71-3.
- Jiménez-Jáimez J, ..., Grima EZ, ..., Tercedor L. Diagnostic Approach to Unexplained Cardiac Arrest (from the FIVI-Gen Study). *Am J Cardiol*. 2015;116:894-9
- Braza-Boils A, Marí-Alexandre J, Molina P, Arnau MA,...,Domingo D,...,Giner J,..., Zorio E. Deregulated hepatic microRNAs underlie the association between nonalcoholic fatty liver disease and coronary artery disease. *Liver Int* 2016;36:1221-9.
- Ortiz-Genga MF, ..., Zorio E, ..., Molina M, ... Monserrat, L. Truncating FLNC mutations are associated with high-risk dilated and arrhythmogenic cardiomyopathies. *JACC* ( in press).
- Marí-Alexandre J..., Gilabert-Estellés J, ..., Braza-Boils A, Sandoval J. **miRNAs Regulation and Its Role as Biomarkers in Endometriosis**. *Int J Mol Sci*. 2016;13;17(1).
- Braza-Boils A..., Marí-Alexandre J...Estellés A, Gilabert-Estellés J,...Peritoneal fluid modifies the microRNA expression profile in endometrial and endometriotic cells from women with endometriosis. *Hum Reprod*. 2015; 30:2292-302
- Marí-Alexandre J...Estellés A, Braza-Boils A, Gilabert-Estellés J. MicroRNAs and angiogenesis in endometriosis. *Thromb Res*. 2015;135 Suppl 1:S38-40.



## SELECTED ACTIVE RESEARCH PROJECTS

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- PI14/01477, INSTITUTO DE SALUD CARLOS III, ARRHYTHMOGENIC CARDIOMYOPATHY
- ANR-13-BSV1-0023-03, AGENCE NATIONALE DE LA RECHERCHE, CATECHOLAMINERGIC POLYMORPHIC VENTRICULAR TACHYCARDIA
- DPI2015-69125-R, MINECO, COMPUTATIONAL SIMULATION OF CHANNELOPATHIES
- DPI2015-70821-R, MINECO, ADVANCED IMAGING IN ARRHYTHMOGENIC CARDIOMYOPATHY
- PI14/01309, INSTITUTO DE SALUD CARLOS III, BIOMARKERS IN ENDOMETRIOSIS

## RELEVANT CLINICAL RESEARCH

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Genotype-phenotype correlations in myocardiopathies

Genotype-phenotype correlations in channelopathies

Epidemiologic evaluation of SCD causes from a gender perspective

Exome approach to inherited cardiac diseases

New ECG criteria for arrhythmogenic cardiomyopathy with LV involvement

Biomarkers in endometriosis

## INDUSTRY COLLABORATIONS

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None active

With Genzyme and Shire we are looking for a collaboration to study Fabry disease in SCD victims  
(as long as inclusion criteria are met)

# GASTROINTESTINAL ENDOSCOPY

## MAIN RESEARCH LINES

- Design and development of gastrointestinal endoscopy prototypes
- Transmission of electromagnetic waves through human gastrointestinal tissue as a tool for early diagnosis
- *In vivo* histologic diagnosis of colonic epithelial lesions.
- Design, development and implementation of new information and communication tools in digestive endoscopy.
- Colorectal cancer early diagnosis and prevention.
- Inflammatory bowel diseases.

## SELECTED PAPERS

- S Carballal L, et al. Real-life chromoendoscopy for neoplasia detection and characterization in long-standing IBD. Gut 2016 (published online, DOI: 10.1136/gutjnl-2016-312332)
- Vicente Pons Beltrán et al. Evaluation of different bowel preparations for small bowel capsule endoscopy: a prospective, randomized, controlled study. Digestive diseases and sciences. 56 - 10, pp. 2900 - 2905. 10/2011. ISSN 1573-2568
- Vicente Pons Beltrán et al. Intestinal preparation prior to capsule endoscopy administration. World journal of gastroenterology : WJG. 14 - 37, pp. 5773 - 78. (China): 07/10/2008. ISSN 1007-9327
- Vicente Pons Beltrán et al. Evaluation of postsurgical recurrence in Crohn's disease: a new indication for capsule endoscopy?. Gastrointestinal endoscopy. 66 - 3, pp. 533 - 573. 09/2007. ISSN 0016-5107
- A Fornes-Leal et al. Dielectric characterization of healthy and malignant colon tissues in the 0.5–18 GHz frequency band. Phys Med Biol 61 (2016) 7334–46
- Bustamante-Balen M et al. Prevalence of non-polypoid colorectal neoplasms in symptomatic patients scheduled for colonoscopy: a study with total colonic chromoscopy. J Clin Gastroenterol 2010;44:280-5. A. FI: 2.75
- Bustamante-Balen M et al. Assessing the reproducibility of the microscopic diagnosis of sessile serrated adenoma of the colon. Rev Esp Enf Dig 2009;101:258-64
- Argüello L et al. The appropriateness of colonoscopy at a teaching hospital: magnitude, associated factors and comparison of EPAGE and EPAGE-II criteria. Gastrointest Endosc 2012; 75: 138-145. A.
- Jover R et al. Clinical Practice Guidelines: Quality of colonoscopy in colorectal cancer screening. Endoscopy 2012; 44(4): 444-451.
- Fernandez-Esparrach, G et al. Endoscopic ultrasound-guided fine-needle aspiration and trucut biopsy in the diagnosis of gastric stromal tumors: a randomized crossover study. Endoscopy 2010; 42: 292-299.

Leading Researcher:

Vicente Pons Beltrán

No. Members: 9

Other relevant  
information:

Contact:

pons\_vicbel@gva.es

# GASTROINTESTINAL ENDOSCOPY

## SELECTED ACTIVE RESEARCH PROJECTS

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ENDOWORM SYSTEM FOR ENTEROSCOPY IN HUMAN BEINGS. IP: VICENTE PONS BELTRAN  
Institute of Health Carlos III. EUR 53.845

WIBEC. WIRELESS IN-BODY ENVIRONMENT COMMUNICATIONS. IP (HOSPITAL LA FE): VICENTE PONS BELTRAN  
Marie Skłodowska-Curie Actions. Innovative Training Networks. H2020-MSCA-ITN-2015. EUR 3.957.045,03

MOLECULAR AND HISTOLOGIC CHARACTERIZATION OF COLON SERRATED LESIONS: DEVELOPMENT OF AN  
INDIVIDUALIZED RISK PROFILE WITH IMPLICATIONS FOR COLORECTAL CANCER SCREENING. IP: MARCO  
BUSTAMANTE.

DEVELOPMENT AND VALIDATION OF A WEB-BASED LEARNING TOOL ON THE USE OF NARROW BAND IMAGING  
TECHNOLOGY FOR THE *IN VIVO* PREDICTION OF COLON POLYP HISTOLOGY. IP: MARCO BUSTAMANTE

THE EUROPEAN POLYP SURVEILLANCE TRIAL (EPoS). IP: RODRIGO JOVER

## RELEVANT CLINICAL RESEARCH

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## INDUSTRY COLLABORATIONS

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Leading Researcher:

**Francisco Martínez,  
PhD**



No. Members: **11**



Contact:  
[genetica@iislafe.es](mailto:genetica@iislafe.es)

## MAIN RESEARCH LINES

### **Neurodevelopmental disorders and genetic basis of congenital malformations**

Detection of genomic rearrangements in patients with neurodevelopmental disorders associated with congenital anomalies, analysis of their potential impact at the phenotypic level, analysis of the function and expression pattern of the genes, and screening mutations in candidate genes.

### **Reproductive problems**

Mutation screening of two candidate genes involved in chromosomal instability, SYCP3 and AURK-B. The results show the relationship between chromosomal instability and infertility.

### **Disorders of sexual development**

This research line focuses on finding the causes of disorders of sexual development in children (ambiguous genitalia, intersex conditions) and adults (gender identity disorder).



## SELECTED PAPERS

**TAF1 Variants Are Associated with Dysmorphic Features, Intellectual Disability, and Neurological Manifestations.** O'Rawe, JA et al. American Journal of Human Genetics. 2015; 97(6): 922-32.

**A novel missense mutation in the NSDHL gene identified in a Lithuanian family by targeted next-generation sequencing causes CK syndrome.** Preiksaitiene, E et al. American Journal of Medical Genetics Part A. 2015; 167(6): 1342-8.

**Infectious and Immunologic Phenotype of MECP2 Duplication Syndrome.** Bauer, M et al. Journal of Clinical Immunology. 2015; 35(2): 168-81.

**Novel mutations of NFIX gene causing Marshall-Smith syndrome or Sotos-like syndrome: one gene, two phenotypes.** Martinez, F et al. Pediatric Research. 2015; 78(5): 533-9.

**Silver-Russell syndrome caused by epigenetic alteration in a child conceived by intrauterine insemination from donor sperm.** Arcos-Machancoses, JV et al. American Journal of Medical Genetics Part A. 2015; 167(11): 2861-4.

## SELECTED ACTIVE RESEARCH PROJECTS

Pilot study of massive sequencing focused in sequences of high interest to the genetic diagnosis of intellectual disability.

**Francisco Martinez Castellano**

Search and identification of new genetic and epigenetic causes in autism spectrum disorders: design and implementation of a high-resolution array with key elements of the epigenetic machinery.

**Carmen Orellana Alonso**

## SERVICES OF ADVANCED CLINICAL AND DIAGNOSTIC RESEARCH

The Genetics Translational Research Group of IIS La Fe provides to the medical community diagnostic studies on the genetic origin of neurodevelopmental disorders:

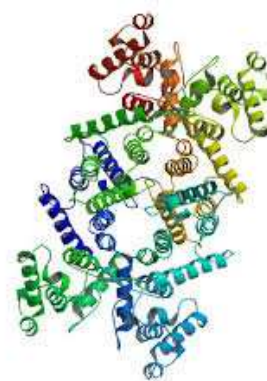
- Mental disability/mental retardation
- Autism spectrum disorders
- Congenital disorders

These procedures, which require cytogenetic techniques, molecular cytogenetics and molecular genetics, are performed by highly qualified staff for the correct interpretation of the results and the subsequent genetic counselling of patients

The research group in genetics consists of a multidisciplinary group of professional with a broad expertise in this field.

### Services:

- ✓ Clinical Interpretation of the cgh-array results
- ✓ Screening for subtelomeric rearrangements/MLPA (Multiplex ligation-dependent probe amplification)
- ✓ Study of balanced subtelomeric translocations/FISH
- ✓ Screening of microdeletions and microduplications/MLPA
- ✓ Expertise in designing customized MLPA probes
- ✓ Uniparental disomy
- ✓ Chromosomal mosaicism
- ✓ X-Chromosome inactivation



# HAEMATOLOGY AND HEMOTHERAPY

Leading Researcher:

**Miguel A. Sanz, PhD**



No. Members: 35



Other relevant  
information:

**25 phase I and II  
active clinical Trials,  
and 38 in phase III.**

Contact:

[hematologia@iislafe.es](mailto:hematologia@iislafe.es)

## MAIN RESEARCH LINES

### Cytogenetic and molecular disease characterization

Cytogenetic and molecular characterization of oncohematologic diseases (leukaemia, myelodysplasia syndromes, multiple myeloma and chronic lymphoproliferative disorders), and benign hematologic diseases (immune thrombocytopenic purpura, thrombotic thrombocytopenic purpura and acquired aplastic anemia) in order to study prognostic factors and therapeutic targets, and the development of in vitro and in vivo models for the study of drugs with potential activity in these diseases

### New progenitor sources

Studies of new progenitor sources for hematopoietic transplants and grafts; and adoptive immunotherapy.

### Hemotherapy

Optimizing the use of allogeneic blood in surgery, improvement of hemovigilance system and research in therapeutic apheresis.

### Cell therapy and regenerative medicine

#### Collaborations:



## SELECTED PAPERS

**An international consortium proposal of uniform response criteria for myelodysplastic/myeloproliferative neoplasms (MDS/MPN) in adults.** Savona, MR et al. Blood. 2015; 125(12): 1857-65.

**Critical analysis of the stringent complete response in multiple myeloma: contribution of sFLC and bone marrow clonality.** Martinez-Lopez, J et al. Blood. 2015; 126(7): 858-62.

**Maternal and fetal outcomes in pregnant women with acute promyelocytic leukemia.** Sanz, MA et al. Annals of Hematology. 2015; 94(8): 1357-61.

**Bloodstream infections in adult patients undergoing cord blood transplantation from unrelated donors after myeloablative conditioning regimen.** Sanz, J et al. Biology of Blood and Marrow Transplantation. 2015; 21(4): 755-60.

**Outcome of graft failure after allogeneic stem cell transplant: study of 89 patients.** Ferra, C et al. Leukemia & Lymphoma. 2015; 56(3): 656-62.

# HAEMATOLOGY AND HEMOTHERAPY

## SELECTED ACTIVE RESEARCH PROJECTS

Multiple Myeloma: risk groups based on new biomarkers and evaluation of therapeutic interventions in curative intent with high sensitivity techniques for EMR.

**Javier de la Rubia Comos**

Molecular characterization of specific forms of acute myelogenous leukemia (AML) by complete exome sequencing.

**Miguel Ángel Sanz Alonso**

Study of the expression and activity modifiers mechanisms of B-MYB in myeloid malignancies. Identification of genes and implications in leukemogenesis.

**Miguel Ángel Sanz Alonso**

MDS-RIGHT, Providing the right care to the right patient with myelodysplastic syndrome at the right time. **H2020 project.**

**Guillermo Sanz Santillana**

HARMONY, Healthcare Alliance for Resourceful Medicines Offensive against Neoplasms in Hematology. **IMI2 project.**

**Guillermo Sanz Santillana**

## RELEVANT CLINICAL RESEARCH

Clinical trial in Phase Ib, to dose-finding of panobinostat (LBH589) orally in combination with an induction therapy with idarubicin and cytarabine and with a consolidation treatment with high-dose of cytarabine in adult patients aged 65 years or less with acute myeloid leukemia (AML).

**Miguel Ángel Sanz Alonso** - *Novartis Farmaceutica, S.A*

Clinical trial in phase I/II; national, open, multicenter, of panobinostat in combination with idarubicin and cytarabine in patients age  $\geq 65$  years with acute myelogenous leukemia (AML) newly diagnosed.

**Miguel Ángel Sanz Alonso** - *Fundación Pethema*

Pilot trial in phase II; multicenter, no randomized, to evaluate the efficacy and safety of dasatinib after allogeneic stem cell transplantation in patients with Philadelphia positive acute lymphoblastic leukemia (bcr-abl +) de novo.

**Guillermo Sanz Santillana** - *Grupo Español de Trasplante Hematopoietico (GETH)*

## INDUSTRY COLLABORATIONS

A prospective multicenter european registry for newly diagnosed patients with myelodysplastic syndromes of ipss low and intermediate-1 subtypes

*Radboud University Nijmegen Medical Center*

Study for the validation of a personalized medicine ex vivo test in acute lymphoblastic leukemia.

*Vivia Biotech*

Determination of the alteration 5Q - in patients diagnosed with MDS.

*Celgene S.L*





# HAEMOSTASIS, THROMBOSIS, ARTHROESCLEROSIS AND VASCULAR BIOLOGY

Leading Researcher:

**Francisco España, PhD**



No. Members:



Other relevant  
information:

**Best in Class award in  
the category  
*Personalized Medicine*  
2013 for the Unit of  
Risk Assessment of  
Family Sudden Death**

Contact:  
[hemostasia@iislafe.es](mailto:hemostasia@iislafe.es)

## MAIN RESEARCH LINES

### Pathophysiology of blood coagulation system

Explore the functionality of mutations or polymorphisms present in the genes coding for the protein C system and for other components present in plasma involved in the risk of thrombosis.

Identification of novel molecules with anticoagulant and/or cytoprotective activity in the protein C pathway: exploring their clinical usefulness.

Identification of diagnosis and prognostic markers of cancer, thrombosis and cancer-associated thrombosis: towards the personalized medicine.

### Collaborations:



### Pathophysiology of platelets and pharmacological aspects

Study in depth the pathophysiology of platelets, pharmacological aspects and their contribution to the generation of thrombin, besides of performing biochemical, functional and proteomic studies of platelets and their modulation by blood cells.

## SELECTED PAPERS

Martos L, Bonanad S, Ramón LA, Cid AR, Bonet E, Corral J, Miralles M, España F, Navarro S, Medina P. A simplified assay for the quantification of circulating activated protein C. Clin Chim Acta 2016; 459: 101-4.

Navarro-Fernandez J, de la Morena-Barrio ME, Padilla J, Miñano A, Bohdan N, Águila S, Martínez-Martínez I, Sevivas TS, de Cos C, Fernández-Mosteirín N, Llamas P, Asenjo S, Medina P, Souto JC, Overvad K, Kristensen SR, Corral J, Vicente V. Antithrombin Dublin (p.Val30Glu): a relatively common variant with moderate thrombosis risk of causing transient antithrombin deficiency. Thromb Haemost 2016; 116(1): 146-54.

de la Morena-Barrio ME, Martínez-Martínez I, de Cos M, Wypasek E, Roldán V, Undas A, Lefebvre D, Sevivas T, España F, Jaeken J, Corral J, Vicente V. Hypoglycosylation is a common finding in antithrombin deficiency in the absence of a SERPINC1 gene defect. J Thromb Haemost 2016; 14:1549-60.

Moscardó, Antonio; Latorre, Ana; Santos, Maria Teresa; Bonanad, Santiago; Valles, Juana. Platelet function in malignant hematological disorders. Curr Opin in Oncology 2015; 27: 522-31.

Moscardó, A.; Valles, J.; Latorre, A.; Jover, R.; Santos, M. T. The histone deacetylase sirtuin2 is a new player in the regulation of platelet function. J Thromb Haemost 2015; 13(7): 1335-44.

Medina P, Navarro S, Bonet E, Martos L, Vayá A, Estellés A, Bertina RM, Vos H, España F. Functional analysis of two haplotypes of the human endothelial protein receptor gene (PROCR). Arterioscl Thromb Vasc Biol 2014; 34 (3): 684-90.

Moscardó A, Vallés J, Latorre A, Santos MT. The association of thromboxane A2 receptor with lipid rafts is a determinant for platelet functional responses. FEBS Lett 2014; 588: 3154-9

Navarro S, Medina P, Bonet E, Corral J, Martínez-Sales V, Martos L, Rivera M, Roselló-Lletí E, Alberca I, Roldán V, Mira Y, Ferrando F, Estellés A, Vicente V, Bertina RM, España F. Association of the thrombomodulin gene c.1418C>T polymorphism with thrombomodulin levels and with venous thrombosis risk. Arterioscl Thromb Vasc Biol 2013; 33: 1435-40.

Deguchi H, Elias DJ, Navarro S, España F, Griffin JH. Elevated serum amyloid A is associated with venous thromboembolism. Thromb Haemost 2012; 128: 410-6.

Medina P, Bonet E, Navarro S, Martos L, Estellés A, Ferrando F, Vicente V, Bertina RM, España F. Effects of oral anticoagulant therapy and haplotype 1 of the endothelial protein C receptor gene on activated protein C levels. Thromb Haemost 2012; 107: 448-457.

# HAEMOSTASIS, THROMBOSIS, ARTHROESCLEROSIS AND VASCULAR BIOLOGY

## SELECTED ACTIVE RESEARCH PROJECTS

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Identification and functional analysis of plasma microRNAs involved in arterial and venous thrombosis.

**Francisco España Furió**

Identification and functional analysis of plasma microRNAs involved in arterial and venous thrombosis.

**Francisco España Furió**

Identification of diagnosis and prognostic markers of cancer-associated thrombosis: towards the personalized prevention of complications in oncologic patients.

**Pilar Medina Badenes - Francisco España Furió**

Identification of novel molecules with anticoagulant and/or cytoprotective activity in the protein C pathway: exploring their clinical usefulness.

**Silvia Navarro Rosales**

Clinical usefulness of an assay on gold nanoparticles for the identification of markers of cancer in urine.

**Pilar Medina Badenes**

Development of an assay for the determination of inorganic poluphosphates in plasma as new risk factor of thrombotic disease.

**Silvia Navarro Rosales**

## RELEVANT CLINICAL RESEARCH

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Clinical trial; randomized, crossover, open, in two-part, to evaluate the pharmacokinetics, efficacy and safety profile of free recombinant FVIII plasma protein formulated with sucrose (BAY 81-8973) with hemophilia-A severe, previously treated with prophylactic therapy. **Saturnino Haya Guaita - Bayer Healthcare**

Clinical trial in Phase II/III; open and multicentric to evaluate the efficacy, safety and pharmacokinetics of pegylated recombinant factor VIII (bax 855) administered for prophylaxis and treatment of bleeding in patients with severe hemophilia pretreated. **Saturnino Haya Guaita - Baxter Innovations GmbH**

Clinical trial; in two parts, double-blind, randomized, placebo and open controlled group to investigate the efficacy, safety and tolerability of eltrombopag, an agonist of the thrombopoietin receptor, in pediatric patients with chronic immune thrombocytopenic purpura (idiopathic) (pti) already treated. **Maria de los Ángeles Dasi Carpio - Glaxosmithkline, S.A.**

## INDUSTRY COLLABORATIONS

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Determining immunoglobulin G subtypes in patients with inhibitors.  
Instituto Grifols S.A.

Does bleed less Hemophilia B or Hemophilia A? Significance of thrombin generation assay to predict the severity of hemorrhagic phenotype of hemophilia and to know the real pharmacokinetics of rFIX.  
Empresa farmacéutica Pfizer.

Study comparative of costs of home treatment vs hospital treatment in patients with haemophilia.  
Bayer Hispania

# HEART REGENERATION AND TRANSPLANT

Leading Researcher:

José A. Montero, PhD



No. Members: 35



Contact:  
cirugia\_cardiaca@iislafe.es

## MAIN RESEARCH LINES

### **Adult stem cells for myocardial infarction treatment. Preclinical studies**

Analysis of the ability of mesenchymal and hematopoietic precursor cells to repair the infarcted myocardium. An experimental myocardial infarction rat model development allows testing the integration capacity of transplanted human cells and monitoring in vivo functional recovery.

### **Study of metabolic disorders associated with hypoxia situations**

The lack of oxygen and nutrients into the cell causes changes in the number and composition of exosomes, vesicles secreted by cells that play a key role in intercellular communication. The group studies these processes using genetically modified animals, infarction models and cell lines.

### **Valvular pathology**

Knowledge of mechanisms involved in valvular degeneration and evaluation of therapeutic implications, through imaging techniques by studying different valve disorders and by means of valve interstitial cell cultures of patients.

### **Assessment and prevention of reperfusion-induced injury**

Analysis of microvascular obstruction and intra-infarction haemorrhage causes and creation of an animal model to experiment with different drugs and possible strategies to reduce this injury

### **Primary angioplasty in acute myocardial infarction with ST-segment elevation**

Assessment of coronary disease pattern of patients referred to the Hemodynamics Laboratory in the acute phase of myocardial infarction, and different factors involved in the prognosis of these patients.

### **Collaborations:**

**TerCel**  
Red de Terapia Celular

  
**PRINCIPE FELIPE**  
CENTRO DE INVESTIGACION

## SELECTED PAPERS

**Angiotensin receptor neprilysin inhibition compared with enalapril on the risk of clinical progression in surviving patients with heart failure.** Packer, M et al. Circulation. 2015; 131(1): 54-61.

**Glucose starvation in cardiomyocytes enhances exosome secretion and promotes angiogenesis in endothelial cells.** Garcia, NA et al. Plos One. 2015; 10(9): e0138849.

**Incidence of Development of Obesity After Heart Transplantation According to the Calcineurin Inhibitor.** Lopez-Vilella, R et al. Transplantation Proceedings. 2015; 47(1): 127-9.

**Involvement of the-420C > G RETN polymorphism in myocardial fibrosis in patients with hypertrophic cardiomyopathy.** Hernandez-Romero, D et al. Journal of Internal Medicine. 2015; 278(1): 50-8.

# HEART REGENERATION AND TRANSPLANT

## SELECTED ACTIVE RESEARCH PROJECTS

HECATOS. Hepatic and Cardiac Toxicity Systems Modelling. FP7 project.

**Jose Vicente Castell Ripoll - Pilar Sepúlveda Sanchís**

Evaluation of the effect of the expression of HIF-1alpha on mesenchymal cells and their contribution to myocardial regeneration and maintenance of hematopoietic progenitors. .

**Pilar Sepúlveda Sanchís**

Implementation of enzyme technology in the development of textile dressings with healing action for application in the medical field - CELLTEX.

**Pilar Sepúlveda Sanchís**

EPINANOSKIN. Obtaining a biocompatible scaffold of nanofibers for improving the regeneration of the epidermis in a dermal equivalent.

**Pilar Sepúlveda Sanchís**

Study of metabolomic profile of patients undergoing acute ischemia.

**Pilar Sepúlveda Sanchís**

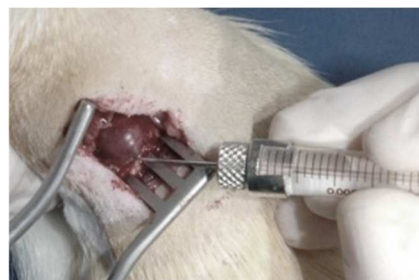


## RELEVANT CLINICAL RESEARCH

Clinical trial in Phase III; open, randomized, multicenter, stratified, active comparator and parallel-group, comparing treatment with 177 Lu-dota0-tyr3-octreotide acetate versus long-acting octreotide in patients with midgut carcinoid tumors, unresectable, progressive and positive for somatostatin receptors.

**Pilar Bello Arques**

*Advanced Accelerator Applications*



## INDUSTRY COLLABORATIONS

Project NANONATURAL: functionalization of biocompatible nanofibers veils by adding natural active ingredients for use in the treatment of bruises and wounds

*AITEX*

Study of the efficacy of cell therapy developed by CTX in a model of acute myocardial infarction in immunosuppressed rats

*Coretherapix SLU*

New therapies for the treatment of heart failure based on the use of stem cells derived heart. Collaborative project with the Oxford University.

*Nhsbt-Blood and Transplant*

# EXPERIMENTAL HEPATOLOGY AND LIVER TRANSPLANTATION

Leading Researcher:

Jose V. Castell, PhD



No. Members: 19



Other relevant  
information:

Applicacell Biotech, S.L.,  
is an IIS La Fe Spin-off,  
that provides R&D  
services and efficacy-  
oriented clinical trials to  
Pharmaceutical,  
Cosmetical and  
Biotechnological  
enterprises.

Contact:

hepatologia\_experimental  
@iislafe.es

## MAIN RESEARCH LINES

### **Metabolism and hepatotoxicity of drugs**

Development of new strategies based on the use of hepatic cell models for drug metabolism and hepatotoxicity studies in pharmaceutic development.

### **Development of strategies aimed at reactivating the expression of genes characteristic of adult liver phenotype**

Development of cell models by genetic engineering to reactivate transcription factors that modulate multiple genes in adult liver, such as drug biotransformation enzyme genes. In this line, adenoviral vectors encoding transcription factors have been developed and optimal combinations for the functional reactivation of P450 enzymes in HepG2 cells have been defined.

### **Direct and indirect reprogramming of fibroblasts to hepacytes/hepatoblasts**

Development of a human liver cell model through direct and indirect conversion of fibroblasts to iHEP. Moreover, pluripotent adult stem cells residing in the liver are being characterized to implement cell therapy in different liver diseases.

### **Etiology of non-alcoholic fatty liver: transcriptional mechanisms involved**

Study new transcriptional programs involved in the non-alcoholic fatty liver disease both of metabolic and iatrogenic (induced by drugs) origin.

## SELECTED PAPERS

### **Transplantation of hESC-derived hepatocytes protects mice from liver injury.**

Tolosa, L et al. Stem Cell Research & Therapy. 2015; 6(1): 246.

### **A score model for the continuous grading of early allograft dysfunction severity.**

Pareja, E et al. Liver Transplantation. 2015; 21(1): 38-46.

### **Growth-promoting and tumourigenic activity of c-Myc is suppressed by Hhex.**

Marfil, V et al. Oncogene. 2015; 34(23): 3011-22.

### **High-content screening of drug-induced mitochondrial impairment in hepatic cells: effects of statins.** Tolosa, L et al. Archives of Toxicology. 2015; 89(10): 1847-60.

### **Human neonatal hepatocyte transplantation induces long-term rescue of unconjugated hyperbilirubinemia in the Gunn rat.** Tolosa, L et al. Liver Transplantation. 2015; 21(6): 801-11.

### **LC-MS untargeted metabolomic analysis of drug-induced hepatotoxicity in HepG2 cells.** Garcia-Canaveras, JC et al. Electrophoresis. 2015 Jun 1.

# EXPERIMENTAL HEPATOLOGY AND LIVER TRANSPLANTATION

## SELECTED ACTIVE RESEARCH PROJECTS

HECATOS. Hepatic and Cardiac toxicity systems modelling.

**Jose Vicente Castell Ripoll - Pilar Sepulveda Sanchis**

INNOVALIV. Innovative strategies to generate human hepatocytes for treatment of metabolic liver diseases: Tools for Personalized Cell Therapy.

**Jose Vicente Castell Ripoll**

Search metabonomic patterns for rapid assessment of the quality of the donor liver, previous to implantation, and subsequent monitoring of the post-transplant evolution.

**Agustín Lahoz Rodriguez**

Induction of Myc activity by HHEX homeoprotein: basis and applications to cancer and reprogramming phenomena.

**Bernardo Roque Bort Martí**

EUTOXRISK21. AN INTEGRATED EUROPEAN 'FLAGSHIP' PROGRAM DRIVING MECHANISM-BASED. **H2020 project.**

**Jose Vicente Castell Ripoll**

## RELEVANT CLINICAL RESEARCH

Effectiveness of n-acetylcysteine in the preservation solution for liver transplantation.

**Rafael Lopez Andújar**

*Instituto de Investigación Sanitaria La Fe*

Biomechanical tissue modeling applied to computer assisted surgery (Subproject 4)

**Rafael Lopez Andújar**

*Instituto de Investigación Sanitaria La Fe*

## INDUSTRY COLLABORATIONS

Study of drug metabolism and hepatotoxicity (DENDRIA Project)

*Noscira S.A. y Faes Pharma, S.A.*

Agreement for Scientific Collaboration between LEITAT and the Experimental Hepatology Unit

*Acondicionamiento Tarrasense – LEITAT*

Planning and guided liver biopsies and monitoring the evolution of tumor masses (oncotic Project)

*Hospital Clínica Benidorm - Centro Medico Salus Baleares, S.L.*

### Collaborations:

Joint Research Unit in Experimental  
Hepatology



VNIVERSITAT  
DE VALÈNCIA

Joint Research Unit on Molecular Mechanisms  
(Chemical and Biological) of Adverse Drug Reactions



UNIVERSIDAD  
POLITECNICA  
DE VALENCIA



# INFLAMMATORY BOWEL DISEASE

Leading Researcher:

Pilar Nos, PhD



No. Members: 15



Contact:  
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## MAIN RESEARCH LINES

### Characterization of cytokine expression in patients with inflammatory bowel disease

Expression characterization of different cytokines at different stages of Crohn's disease and ulcerative colitis, and correlation of these patterns with mucosal healing.

### Enzyme catalase as therapeutic option in Crohn's disease

Antioxidant defences (superoxide dismutase, catalase and glutathione peroxidase) characterization in patients with inflammatory bowel disease to clarify oxidative damage origin.

### Oxidative stress and mitochondrial function in patients with Crohn's disease: pathogenic and therapeutic implications

Characterization of apoptotic ability of immune cells with inflammatory bowel disease patients and its impact on disease pathogenesis. Studies on prevention of postoperative recurrence in Crohn's disease, being pioneer in biologic drugs treatment.

### Telecommunication and information technologies

Clinical impact in management, monitoring and self-control Crohn's disease or ulcerative colitis patients. This is an emerging work line for the research group in collaboration with Telemedicine Unit of University and Polytechnic Hospital La Fe.

### Collaborations:



## SELECTED PAPERS

**Identification of risk loci for Crohn's disease phenotypes using a genome-wide association study.** Alonso, A et al. *Gastroenterology*. 2015; 148(4): 794-805.

**Two-week, high-dose proton pump inhibitor, moxifloxacin triple *Helicobacter pylori* therapy after failure of standard triple or non-bismuth quadruple treatments.** Gisbert, JP et al. *Digestive and Liver Disease*. 2015; 47(2): 108-13.

**Fecal Calprotectin in Ileal Crohn's Disease: Relationship with Magnetic Resonance Enterography and a Pathology Score.** Cerrillo, E et al. *Inflammatory Bowel Diseases*. 2015; 21(7): 1572-9.

**Rectal cancer threatening or affecting the prostatic plane: is partial prostatectomy oncologically adequate?. Results of a multicentre retrospective study.** Frasson, M et al. *Colorectal Disease*. 2015; 17(8): 689-97.

**Usefulness of the Log Odds of Positive Lymph Nodes to Predict and Discriminate Prognosis in Gastric Carcinomas.** Calero, A et al. *Journal of Gastrointestinal Surgery*. 2015; 19(5): 813-20.

# INFLAMMATORY BOWEL DISEASE

## SELECTED ACTIVE RESEARCH PROJECTS

Clinical impact of telemedicine in Crohn's disease and ulcerative colitis: Study Teccu.

**Mariam Aguas Peris**

Protein and genetic analysis of catalase and other antioxidants enzymes in Crohn's disease: therapeutic impact.

**Belén Beltrán Niclós**

Study of genetic polymorphisms in the catalase gene in patients with Crohn's disease.

**Belén Beltrán Niclós**

Peroxisome proliferator-activated receptor gamma (PPAR- $\gamma$ ) in the regulation of innate immunity (defensins) and acquired (catalase) in Crohn's disease.

**Belén Beltrán Niclós**

WiBEC. Wireless in-body environment communications. **H2020 project.**

**Pilar Nos Mateu**

## RELEVANT CLINICAL RESEARCH

Clinical trial; randomized, double-blind, with parallel and placebo controlled groups to evaluate the efficacy and safety of NNC0114- 0006 in subjects with active Crohn's disease.

**Belén Beltrán Niclós**

*Novo Nordisk A/S*

Clinical trial in Phase III; multicenter, randomized, double-blind, with parallel and placebo controlled group to evaluate the efficacy and safety of expanded allogeneic stem cells (EASC) derived from adipose tissue for the treatment of perianal fistulizing Crohn's disease after a period of 24 weeks. Study ADMIRE-CD.

**Belén Beltrán Niclós - Joaquín Ernesto Hino- josa De Val**

*Tigenix, S.A.U.*

Open trial, multicenter to evaluate the impact of Adalimumab in the quality of life, the use of health care and cost of ulcerative colitis patients in similar clinical practice conditions.

**Pilar Nos Mateu**

*Abbvie Deutschland Gmbh & Co. Kg*

## INDUSTRY COLLABORATIONS

Research in Colon proctology

*Covidien Ag; Johnson & Johnson S.A*

Research in Inflammatory Bowel Disease

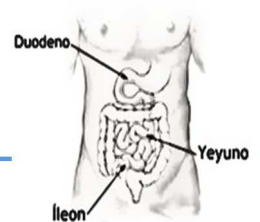
*Shire Pharmaceuticals Iberica S.L, Abbvie Farmaceutica Slu, Geteccu, Merck Sharp Dohme España,S.A., GETEII, Otsuka Pharmaceutical S.A.*

Collaboration Agreement for stays of training in endoscopy and Inflammatory Bowel Disease IBD Forendo

*Merck, Sharp & Dhome*

Design and development of new panels of biomarkers for diagnosis and treatment of Crohn syndrome and related inflammatory diseases.

*Making Genetics S.L*



# MYOCARDIAL DYSFUNCTION AND HEART TRANSPLANT

Leading Researcher:

José M. Rivera, PhD



No. Members: 17



Contact:

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@iislafe.es

## MAIN RESEARCH LINES

### Cellular and molecular basis of myocardial damage

Studies on the kinetics of nucleocytoplasmic transport and gene expression in human cardiomyocytes, associated with ventricular dysfunction in heart failure (HF).

### Genomics and heart failure

Analysis of the changes in the transcriptome of patients with ischemic and dilated cardiomyopathy using advanced tools (RNA-Seq).

### Biomarkers

Determination of serum markers (natriuretic peptides) associated with cardiac morbidity and mortality. Determination of circulating endothelial cells, endothelial microparticles and progenitor cells. The group is pioneer in the use of biomarkers in heart failure of the heart transplant graft (sialic acid, fibrinogen, PCR, von Willebrand factor, etc).

### Immunomodulators

Research on immunomodulatory drugs (modulate the immune response in patients with cardiac allograft), focusing on all pharmacological groups that are currently on the market and in others to be marketed in the near future (biological immunosuppressive -Belatacept).

### Collaborations:



## SELECTED PAPERS

**Gene expression network analysis reveals new transcriptional regulators as novel factors in human ischemic cardiomyopathy.** Herrer, I et al. BMC Medical Genomics. 2015; 8: 14.

**The Adipokine Chemerin Induces Apoptosis in Cardiomyocytes.** Rodriguez-Penas, D et al. Cellular Physiology and Biochemistry. 2015; 37(1): 176-92.

**ATP synthase subunit alpha and LV mass in ischaemic human hearts.** Rosello-Lleti, E et al. The Journal of Cellular And Molecular Medicine. 2015; 19(2): 442-51.

**RNA Sequencing Analysis Identifies New Human Collagen Genes Involved in Cardiac Remodeling.** Gil-Cayuela, C et al. The Journal of The American College of Cardiology. 2015; 65(12): 1265-7.

**Patients with Dilated Cardiomyopathy and Sustained Monomorphic Ventricular Tachycardia Show Up-Regulation of KCNN3 and KCNJ2 Genes and CACNG8-Linked Left Ventricular Dysfunction.** Ortega, A et al. PLoS One. 2015; 10(12): e0145518.

# MYOCARDIAL DYSFUNCTION AND HEART TRANSPLANT

## SELECTED ACTIVE RESEARCH PROJECTS

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Nucleo-cytoplasmic transport and gene expression changes in heart failure. Commissioning of a new therapeutic strategy.

**Jose Miguel Rivera Otero.**

Nucleo-cytoplasmic kinetics of human cardiomyocytes transport in heart failure. Cellular and gene expression analysis.

**José Miguel Rivera Otero**

RETICS. 12/0042/0003 RD. Incorporation January 2013. Spanish Cardiovascular RED. Node La Fe.

**Jose Miguel Rivera Otero**

Genetic study of the treatment in terminal heart failure: ACE inhibitors, beta-blockers and aldosterone antagonist.

**Ignacio José Sánchez Lázaro**

## RELEVANT CLINICAL RESEARCH

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Clinical study Phase I; multicenter, double-blind and randomized, to establish the safety and clinical benefit of Vytorin (Ezetimibe / Simvastatin) versus simvastatin monotherapy in patients with high risk of acute coronary syndrome.

**Antonio Salvador Sanz**

*Merck Sharp & Dohme De España. S.A.*

Clinical trial; randomized, double-blind, multicenter, to evaluate the safety and efficacy of BAY 94-8862 in patients who come to hospital emergency due to a worsening of chronic heart failure with left ventricular systolic dysfunction, accompanying with diabetes mellitus type 2, compared with Eplerenone.

**Luis Almenar Bonet**

*Bayer Healthcare Ag*

Clinical trial; multicenter, randomized, double-blind, parallel-group of 6-12 month duration, to assess the safety of chronic oral administration of Ivabradine with modified release formulation versus Ivabradine of immediate release formulation in patients with chronic heart failure and left ventricular systolic dysfunction.

**Luis Almenar Bonet**

*Laboratorios Servier, S.L.*

## INDUSTRY COLLABORATIONS

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International study of comparative health effectiveness with medical and invasive approaches

*IDIPAZ*

Clinical trial; Single-center, prospective, randomized of immunosuppression with tacrolimus or cyclosporine with MMF in cardiac transplantation and its effects on renal function.

*Astellas Pharma S.A.*

Assessment of the evolution of patients with pulmonary valve insufficiency as a sequel after surgery for congenital heart disease

*Laboratorios Menarini, AstraZeneca Farmaceutica Spain, S.A*

# NANOMEDICINE AND SENSORS

## MAIN RESEARCH LINES

### Nanomedicine

1 – Nanomaterials development for controlled release and image applications, for example by NMR or by the use of fluorophores. Drug controlled release studies are conducted on cellular and animal models. The developed nanomaterials only show release in the presence of certain physical, chemical or biochemical stimuli.

2 - Development of nanomaterials as sensors. Mesoporous materials capped with oligonucleotides as nanoscopic gates are synthesized for the detection of pathogens.

The designed systems show a selective release of a dye or a fluorophore in the presence of DNA. The aim of this methodology is the detection of pathogens such as *Mycoplasma pneumoniae*, tuberculosis, Ebola, papilloma, hepatitis C, etc.

3 –Nanomaterials development based on superparamagnetic iron oxide nanoparticles for medical magnetic resonance imaging applications.

### Sensors

1 –Biosensors development applied to diagnosis and prognosis. Development of sensor devices based on innovative technologies aimed at the prevention and diagnosis of human diseases and pathologies in a personalized way.

2 - Development of determinants to improve the diagnosis of drug allergy. Developing systems and operating procedures for establishing specific IgE levels expressed by a patient allergic to a drug (amoxicillin and other antibiotics) using human blood serum samples.

3 –Sensors development based on holistic approximations using HPLC-MS, NMR and electronic tongues for the detection of certain pathologies such as prostate cancer, bladder cancer, interstitial cystitis, neurogenic and overactive bladder, etc.

### Metabolomic and proteomic biomarkers in urological cancers

1- Identification of urinary metabolomic biomarkers for non-invasive diagnosis and monitoring of bladder cancer patients.

2- Study of metabolic pathways and their cellular reprogramming during bladder carcinogenesis.

3- Identification of urinary metabolomic biomarkers for non-invasive diagnosis and monitoring of prostate cancer patients.

4-Use of trained dogs for the detection and signaling of urinary samples of patients with prostate cancer

Leading Researcher:

José Luis Ruiz Cerdá

Ramón Martínez  
Máñez

No. Members: 19

Contact:

Jose.L.ruiz@uv.es  
rmaez@qim.upv.es

# NANOMEDICINE AND SENSORS

## SELECTED PAPERS

Lluís Pascual, Inmaculada Campos, José-Luis Vivancos, Guillermo Quintás, Alba Loras, M. Carmen Martínez-Bisbal, Ramón Martínez-Máñez, Francisco Boronat, José Luis Ruiz-Cerdà. Detection of prostate cancer using a voltammetric electronic tongue. *Analyst* 2016, 141(15), 4562-4567.

Patricia Zaragoza, Jose Luis Ruiz-Cerdà Guillermo Quintás, Salvador Gil, Ana M. Costero, Zacarias León, José-Luis Vivancos and Ramón Martínez-Máñez. Towards the potential use of <sup>1</sup>H NMR spectroscopy in urine samples for prostate cancer detection. *Analyst* 2014, **139**, 3875

## SELECTED ACTIVE RESEARCH PROJECTS

Fetal brain arborization non-invasive test. Ángel Maquieira Catalá, José Morales Roselló

Constitución de una "plataforma de Smart drug Discovery". Miguel Ángel Miranda Alonso, José Vicente Castell Ripoll.

Modelización 3D de hipertermia en tejidos celulares mediante nanopartículas magnéticas.  
Javier Ibáñez Civera, José Tomás Cucarella

Nanomateriales inteligentes, sondas y dispositivos para el desarrollo integrado de nuevas herramientas aplicadas al campo biomedico. Ramón Martínez Máñez, Félix Sancenón Galarza

Desarrollo de equipos y dispositivos electrónicos como sistema de detección y actuación basados en nuevas tecnologías electrónicas. Aplicación al área biomédica. Eduardo García Breijo

Gated sensing materials and devices for the detection of infectious diseases and urological cancer  
Ramón Martínez Máñez, José Luis Ruiz Cerdá, Javier Pemán

Gated nanodevices for targeted release in senescence and cancer related diseases  
Ramón Martínez Máñez, Juan B. Salom Sanvalero, Ricardo Prat Acín

Señalización mediante el olfato de perros de muestras urinarias de pacientes con cáncer de próstata y su análisis metabolómico mediante Resonancia Magnética Nuclear. José Luis Ruiz-Cerdá

Development and application of new chemometric strategies for metabolomic analysis. Guillermo Quintás Soriano

Análisis multiplataforma en la detección de cáncer de próstata de acuerdo a la carga tumoral. José Luis Ruiz-Cerdá

Acción preparatoria: Caplengua. Detección de cáncer de próstata (CaP) mediante lenguas electrónicas. Una aproximación en el diagnóstico precoz. José Luis Ruiz-Cerdá

Estudio espectroscópico multiplataforma (RMN, HPLC) como alternativa no invasiva de indicador de agresividad tumoral en pacientes con CaP. José Luis Ruiz-Cerdá

Desarrollo de un estudio piloto para la detección no invasiva de cáncer de vejiga: identificación de marcadores metabólicos urinarios. Guillermo Quintás Soriano

Identificación de metabolitos específicos del metabolismo tumoral vesical a través del análisis metabolómico de muestras tisulares vesicales mediante HR-MAS RMN y UPLC-MS. José Luis Ruiz-Cerdá



# MOLECULAR, CELL AND GENOMICS BIOMEDICINE

Leading Researcher:

José María Millán  
Salvador, PhD



No. Members: 18



## Other relevant information:

Patent: *Method for obtaining data that can be used for the diagnosis and prognosis of neurosensory hypoacusia*

National Reg: P201132013

PCTReg: PCT/ES2012/070869

National phases: EEUU,  
CANADA y EUROPA

Co-ownership: FPS, SAS, APH  
Poniente, and IIS La Fe (Dr.  
Herminio Pérez Garrigues).

Contact:  
neurosensoriales  
@iislafe.es

## MAIN RESEARCH LINES

### **Identification of variants in genes that lead to inherited diseases**

Which affect vision, hearing, and some neuromuscular diseases by screening for mutations in the genes identified as responsible for these diseases, as well as determining the pathogenic nature of all (e.g. Usher syndrome or deafness).

### **Determination of the molecular and cellular mechanisms of neurosensory diseases development of the nervous system and cell pluripotency**

The research group works on aspects related to cellular pathophysiology and biology, molecular biology and structural biology as well as in disease models.

### **Development of experimental neurodegenerative models**

E.g. rd10 mice, porcine retinal cultures, *C.elegans*,... for the research of diseases affecting hearing or vision, to determine the role of different genes in cell pluripotency and development.

Specifically, regarding the research on Hearing / Vision, the research group focuses on:

- Evaluation of the efficacy and safety of prostheses and drugs in the areas of otolaryngology and ophthalmology
- Electrophysiological and molecular studies of embryonic eye development
- Morphofunctional studies of the optic nerve

The group has an important/comprehensive database for Usher syndrome, retinitis pigmentosa, Age-related macular degeneration (AMD), X-linked retinitis, oculocutaneous albinism, sensorineural deafness, Meniere's disease, Huntington's disease, spinal muscular atrophy and Duchenne's muscular dystrophy among

## SELECTED PAPERS

**Predicting proliferative vitreoretinopathy: temporal and external validation of models based on genetic and clinical variables.** Rojas, J et al. The British Journal of Ophthalmology. 2015; 99(1): 41-8.

**Management and return of incidental genomic findings in clinical trials.** Ayuso, C et al. Pharmacogenomics Journal. 2015; 15(1): 1-5.

**Clinical Aspects of Usher Syndrome and the USH2A Gene in a Cohort of 433 Patients.** Blanco-Kelly, F et al. JAMA Ophthalmology. 2015; 133(2): 157-64.

**IP3 signalling regulates exogenous RNAi in *Caenorhabditis elegans*.** Nagy, AI et al. EMBO Reports. 2015; 16(3): 341-50.

**Long-term visual outcomes for a treat and extend anti-vascular endothelial growth factor regimen in eyes with neovascular age-related macular degeneration.** Mrejen, S et al. Journal of Clinical Medicine. 2015; 4(7): 1380-402.

# MOLECULAR, CELL AND GENOMICS BIOMEDICINE

## SELECTED ACTIVE RESEARCH PROJECTS

MECHAGGRENAMICS - Mechanisms of cell dysfunction by aggregation dynamics of polyq-containing proteins.

**Rafael Vazquez Manrique**

Molecular genetic study of genes involved in Usher syndrome and other candidates genes (PDZD7, NCAM2 and MRPL39). Expression studies of the USH genes.

**Jose Maria Millán Salvador**

Molecular mechanisms of protein aggregation in vitro and in vivo models of Huntington disease.

**Rafael Vazquez Manrique**

Modulation effect of hypoxia inducible factor (HIF) on retinal degeneration in retinitis pigmentosa.

**Regina Rodrigo Nicolás**

Study of genetic splicing variants identified in patients with Usher of the Valencian community from nasal ciliated cells.

**Teresa Jaijo Sanchís**

## RELEVANT CLINICAL RESEARCH

Clinical trial in phase II; randomized, double-blind and placebo-controlled, to evaluate the effect of V0251 in acute vertigo.

**Herminio Pérez Garrigues**

*Pierre Fabre Medicament*

Cochlear implants, nucleus®, for patients with severe tinnitus and asymmetric hearing loss

**Constantino Morera Pérez**

## INDUSTRY COLLABORATIONS

Agreement for the validation of cochlear implants.

*Cochlear Europe Limited*

Research, development and validation in innovative technologies for implantable hearing solutions

*Med-El Elektromedizinische Geraete Gesellschaft M.B.H.*

Preparation of 8 biological samples (4 DNAs and 4 ECD controls) for future sequencing platform NGS

*Genycell Biotech, S.L.*

### Collaborations:



Joint Research Unit in Neurology  
and Molecular Genetics

Leading Researcher:

**Máximo Vento, PhD**



No. Members: **23**



Other relevant  
information:

**Dr. Vento is honorary  
member of the  
American Pediatric  
Society (USA; 2007)**

Contact:  
[perinatologia@iislafe.es](mailto:perinatologia@iislafe.es)

## MAIN RESEARCH LINES

### Experimental studies in animal models related to oxygen metabolism:

- Pregnant mice model of fetal-to-neonatal transition in different environmental oxygen concentrations. Own ad hoc camera design with enhanced systems to manipulate mice, rapid achievement of targeted inspiratory fractions of oxygen (FiO<sub>2</sub>), security pressure valve, and software allowing design of FiO<sub>2</sub> profiles.
- Hypoxia-reoxygenation-hypothermia model in newborn piglets. New validated biomarkers for oxidative damage in different tissue especially in brain that can be determined in tissue (brain), cerebrospinal fluid, plasma and urine.

### Fetal and genetic oxygenation studies

- Oxygenation studies during foetal to neonatal transition in the delivery room during neonatal resuscitation and postnatal adaptation.
- Validation and evaluation of new biomarkers of brain damage in situations of asphyxia in biological fluids (plasma, urine, CSF) using UPLC-MS / MS.
- Randomized controlled multicentre Spanish trial on the use of hypothermia + topiramate/placebo in newborn infants with birth asphyxia evolving to hypoxic ischemic encephalopathy.
- Randomized controlled multicentre International trial on the use of higher vs. lower inspiratory fraction of oxygen to resuscitate extremely low birth weight infants.
- Screening for toxic environmental substances in donated human milk in the Milk Bank of the Newborn Division of the University & Polytechnic Hospital La Fe.

### Collaborations:



## SELECTED PAPERS

**Postnatal development of fetuses with a single umbilical artery: differences between malformed and non-malformed infants.** Vicente Arcos-Machancoses, J et al. World Journal Of Pediatrics. 2015; 11(1): 61-6.

**Changes in Perinatal Care and Outcomes in Newborns at the Limit of Viability in Spain: The EPI-SEN Study.** Garcia-Munoz, RF et al. Neonatology. 2015; 107(2): 120-9.

**Urinary Lipid Peroxidation Byproducts: Are They Relevant for Predicting Neonatal Morbidity in Preterm Infants?.** Kuligowski, J et al. Antioxidants & Redox Signaling. 2015; 23(2): 178-84.

**Factors influencing gastrointestinal tract and microbiota immune interaction in preterm infants.** Collado, MC et al. Pediatric Research. 2015; 77(6): 726-31.

**Neonatal assessment in the delivery room - Trial to Evaluate a Specified Type of Apgar (TEST-Apgar).** Ruediger, M et al. BMC Pediatrics. 2015; 15: 18.

## SELECTED ACTIVE RESEARCH PROJECTS

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Efficacy of oro-pharyngeal mother's milk: late-onset sepsis in LBW infants

**Máximo Vento Torres**

TORPIDO-2. Targeted oxygenation in the resuscitation of premature infants: effects on developmental outcome- the torpido2 study

**Máximo Vento Torres**

Randomized controlled trial regarding the use of hypothermia + topiramate / placebo in asphyctic newborn infants evolving to hypoxic ischemic encephalopathy.

**Máximo Vento Torres**

ALBINO. Effect of allopurinol in addition to hypothermia for hypoxic-ischemic brain injury on neurocognitive outcome. H2020 project.

**Máximo Vento Torres**

## RELEVANT CLINICAL RESEARCH

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Clinical trial; multicenter, randomized, double-blind and placebo-controlled, comparing the use of early moderate total body hypothermia with topiramate or placebo in asphyxiated newborns evolving from hypoxic ischemic encephalopathy moderate to severe.

**Máximo Vento Torres**

*Instituto de Investigación Sanitaria La Fe*

Resuscitation of extremely low weight newborn through a comprehensive monitoring system: Study of the influence of the inspiratory oxygen fraction.

**Máximo Vento Torres**

*Dr. Máximo Vento Torres*

Clinical trial; multicenter, randomized, placebo-controlled, double-blind, two parallel group, to evaluate the efficacy and safety of Sildenafil IV in the treatment of infants with persistent pulmonary hypertension of the newborn (PPHN) or hypoxic respiratory failure and at risk for PPHN.

**Máximo Vento Torres**

*Pfizer Inc.*

## INDUSTRY COLLABORATIONS

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Evaluation on the predictive value of a novel neuronal damage derived biomarker (CDP-CHOLINE) in a randomized control trial or early hypothermia plus topiramate or placebo.

*Laerdal Foundation*

CANDI-NEO study on fungal infection in the perinatal period.

*Astellas Pharma*

Oxygen Nomogram Development in the Perinatal Period.

*Non-restricted Educational Grant: Masimo Inc (USA)*

Leading Researcher:

**Salvador Aliño, PhD**



No. Members: **11**



Contact:

[farmacogenetica@iislafe.es](mailto:farmacogenetica@iislafe.es)

## **MAIN RESEARCH LINES**

### **Pharmacogenetics of immunosuppressive drugs in organ transplantation**

Genotyping of the most important single nucleotide polymorphisms (SNPs) in the genes responsible for the transport and metabolism of drugs, in order to find correlations with blood levels achieved with immunosuppressive drugs and more recently, with some data on effectiveness and safety of treatment, in field of renal, heart, liver and lung transplantation.

### **Pharmacogenetics of anticancer drugs in breast cancer**

Correlating the polymorphisms in genes related to the administered drugs with the effectiveness and safety of these treatments. The research group has begun a project with the same objective but applied to colon cancer.

### **Pharmacogenetics in heart failure**

Pharmacogenetic studies in heart failure patients treatments, with beta-blockers, ACE inhibitors and aldosterone antagonists.

### **Pharmacogenetics Panels developed:**

- Immunosuppressants (especially those used for solid organ transplantation: renal, heart, liver and lung)
- Adult Oncology: Breast Cancer and Acute Myeloid Leukemia (Colon cancer in development)
- Heart Failure (beta-blockers, ACE inhibitors and aldosterone antagonists)

## **SELECTED PAPERS**

**Impact of Single Nucleotide Polymorphisms (SNPs) on Immunosuppressive Therapy in Lung Transplantation.** Ruiz, J et al. International Journal of Molecular Sciences. 2015; 16(9): 20168-82.

**A systematic review and meta-analysis of the impact of WT1 polymorphism rs16754 in the effectiveness of standard chemotherapy in patients with acute myeloid leukemia.** Megías-Vericat, JE et al. The Pharmacogenomics Journal. 2015 Dec 8.

**Association of SNPs with the efficacy and safety of immunosuppressant therapy after heart transplantation.** Sanchez-Lazaro, I et al. Pharmacogenomics. 2015; 32(4): 1841-2.

**Positive impact of ABCB1 polymorphisms in overall survival and complete remission in acute myeloid leukemia: a systematic review and meta-analysis.** Megías-Vericat, JE et al. The Pharmacogenomics Journal. 2015 Oct 27.

### SELECTED ACTIVE RESEARCH PROJECTS

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Contracts for technical support in research from the National Health System.

**Maria Jose Herrero Cervera**

Hepatic gene therapy by injection of DNA by catheterization in tight vascular territory: preclinical model in pig and human "ex vivo".

**Salvador F. Aliño**

Comprehensive, Integrative and Genomic Approach to the Understanding and Treatment of Cancer and Leukemia

**Miguel Angel Sanz - Salvador Aliño**

Pharmacogenetics in Breast Cancer and in acute myeloid leukemia.

**Salvador Aliño**

### RELEVANT CLINICAL RESEARCH

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Prospective study on the utility of pharmacogenetics in assessing efficacy and safety of immunosuppressive drugs in organ transplantation

**Salvador Aliño**

*Instituto de Investigación Sanitaria La Fe*



### INDUSTRY COLLABORATIONS

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Study of the use of methoxy polyethylene glycol-epoetin beta in the treatment of anemia associated with chronic renal failure in the context of clinical practice.

*Roche Farma, S.A.*

Study of the use of orphan drugs in a tertiary hospital.

*Fundación Genzyme, Shire Pharmaceuticals Ibérica S.L, Sanofi Aventis S.A*

Implementation and impact in dispensing and storage of drugs in unit dose.

*Roche Farma, S.A., Boehringer Ingelheim España*





Instituto de  
Investigación  
Sanitaria La Fe

RESEARCH GROUP

# PRIMARY CARE

## MAIN RESEARCH LINES

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- Improving health care for chronic conditions and palliative care seeking the best feasible strategy in clinical practice
- Control and treatment of cardiovascular risk factors

Leading Researcher:

**Antonio Maiques  
Galán**

No. Members: **15**

Contact:



# REPRODUCTIVE MEDICINE

Leading Researcher:

**Antonio Pellicer, PhD**



No. Members: **14**



Other relevant  
information:

**Dr. Pellicer is  
President of the  
Infertility Institute of  
Valencia (IVO)**

Contact:  
**medicina\_reproductiva  
@iislafe.es**

## MAIN RESEARCH LINES

### Endometriosis

- Discovery and validation of endometriosis specific metabolites in urine, serum and tissue non-invasive markers.
- Detection of nerve fibers
- Use of dopaminergic derivatives in the treatment of endometriosis TRV

### Fertility preservation

- Techniques for ovarian tissue cryopreservation and oocyte vitrification
- Detection of unknown metastatic disease in breast cancer patients
- Activation and in vitro oocytes maturation
- Fertility preservation in leukemia patients
- Uterus transplant

### In Vitro fertilization

- Study of factors related to ovaries response in low-responder patients
- Prevention of ovarian hyperstimulation
- Telomere length in umbilical cord blood with intrauterine growth restriction (IUGR) and from assisted reproductive techniques (ART) as markers of fetal programming and reproductive harm

### Preimplantation Genetic Diagnosis (PGD)

Establish and implement a successful preimplantation genetic diagnosis program, capable of preventing the transmission of monogenic diseases. In addition, work in the successful transfer of a single embryo.



## SELECTED PAPERS

**Oocyte donation outcome after oncological treatment in cancer survivors.** Munoz, E et al. Fertility and Sterility. 2015; 103(1): 205-13.

**Fertility preservation for age-related fertility decline.** Donnez, J et al. Lancet. 2015; 385(9967): 506-7.

**Monozygotic twinning after assisted reproductive technologies: a case report of asymmetric development and incidence during 19 years in an international group of in vitro fertilization clinics.** Tocino, A et al. Fertility and Sterility. 2015; 103(5): 1185-9.

**Thirty-five years later, the first assisted reproductive technology program opens in Cambodia.** de Ziegler, D et al. Fertility and Sterility. 2015; 103(5): 1146-9.

**Understanding mammalian germ line development with in vitro models.** Martinez-Arroyo, AM et al. Stem Cells and Development. 2015; 24(18): 2101-13.

# REPRODUCTIVE MEDICINE

## SELECTED ACTIVE RESEARCH PROJECTS

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Improved security and new strategies in Fertility Preservation of oncological patients.

**Edurne Novella Maestre**

Inhibition of angiogenesis in endometriotic lesions through the use of dopamine agonists as nontoxic and efficacious in the treatment of endometriosis in human therapeutics.

**Antonio Pellicer**

Comparison of follicular viability after application of 3 methods for core separation before ovarian cryopreservation.

**César Díaz García**

Local interaction with the dopaminergic system vascular endothelial growth factor and its receptor 2 (VEGF/VEGFR2) in the regulation of angiogenesis in the corpus luteum under physiological conditions.

**Antonio Pellicer Martinez**

## RELEVANT CLINICAL RESEARCH

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Clinical trial; prospective, randomized and controlled. Preparation of antral follicles, prior to ICSI IVF, in patients with low ovarian response.

**César Díaz García**

*Instituto de Investigación Sanitaria La Fe.*

Providing techniques of traditional Chinese medicine to improve the results of IVF treatments: Acupuncture in embryo transfer.

**Mónica Romeu Villarroya**

*Instituto de Investigación Sanitaria La Fe.*

Clinical trial in Phase IIIB; multicenter, randomized, double-blind, of hydroxyprogesterone caproate injection, 250 mg/ml, compared to the vehicle, to prevent preterm birth in women with a prior spontaneous preterm birth.

**Alfredo Perales Marín**

*Hallogic, Inc.*

## INDUSTRY COLLABORATIONS

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Non-Invasive monitoring of fetal heart rate and uterine contractions by means of surface electrodes.  
*GE Healthcare Bio-Sciences, SA.*

Screening of tumor cell detection for improving safety in preserving fertility in oncological patients.  
*Merck S. L.*

Multicenter study in 11 National Hospitals "Determination of tyrosine kinase soluble FMS-LIKE 1 (sFlt-1) and placental growth factor (PIGF) as possible markers in predicting early preeclampsia"  
*Laboratorios Roche.*

# DIGESTIVE SURGERY

Leading Researcher:

Matteo Frasson

No. Members: **20**

Contact:

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gmail.com

Investigacioncdlfe@  
gmail.com

Telephone:

+34-633236008

## MAIN RESEARCH LINES

- ZERO ANASTOMOTIC LEAK: risk factors for anastomotic leak after colon and cancer resection, biomarkers for early diagnosis, intraoperative tools to prevent anastomotic leak, pre and intra- operative techniques to decrease its frequency.
- COLORECTAL CANCER: the use of imaging for preoperative staging, surgical technique advances to improve oncological results, pathological staging of early and advanced colorectal cancer to select patients for further treatments, innovative tools for early diagnosis (in collaboration with UPV).
- ESOPHAGEAL and GASTRIC CANCER: prognostic factors for response to preoperative treatment in gastric cancer, evaluation of the quality of surgery in esophageal cancer resection
- INFLAMMATORY BOWEL DISEASE: accuracy of Magnetic Resonance Enterography in the preoperative assessment of Crohn's Disease patients, gene therapy with IL10 gene in Crohn's disease.
- SURGICAL TECHNIQUE: usefulness of a supra-aponeurotic mesh for the prevention of postoperative hernia, results of the Dor technique in patients with gastro-esophageal reflux, results after surgery for achalasia .

## SELECTED PAPERS

- Dielectric characterization of healthy and malignant colon tissues in the 0.5-18 GHz frequency band. Fornes-Leal A, Garcia-Pardo C, Frasson M, Pons Beltrán V, Cardona N. Phys Med Biol. 2016 Oct 3;61(20):7334-7346.
- Risk Factors for Anastomotic Leak After Colon Resection for Cancer: Multivariate Analysis and Nomogram From a Multicentric, Prospective, National Study With 3193 Patients. Frasson M, Flor-Lorente B, Rodríguez JL, Granero-Castro P, Hervás D, Alvarez Rico MA, Brao MJ, Sánchez González JM, García-Granero E; ANACO Study Group. Ann Surg. 2015 Aug;262(2):321-30.
- Selective approach for upper rectal cancer treatment: total mesorectal excision and preoperative chemoradiation are seldom necessary. Marinello FG, Frasson M, Baguena G, Flor-Lorente B, Cervantes A, Roselló S, Espí A, García-Granero E. Dis Colon Rectum. 2015 Jun;58(6):556-65.

Preoperative chemoradiation may not always be needed for patients with T3 and T2N+ rectal cancer. Frasson M, García-Granero E, Roda D, Flor-Lorente B, Roselló S, Esclapez P, Faus C, Navarro S, Campos S, Cervantes A. Cancer. 2011 Jul 15;117(14):3118-25.

# DIGESTIVE SURGERY

## SELECTED ACTIVE RESEARCH PROJECTS

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Multicentric studies leaded by our group:

- APPRO study : RCT to study the best technique to perform abdomino-perineal rectal amputation for low rectal cancer
- ANACARE study: large multicentric Spanish observational study to investigate risk factors for anastomotic leak after rectal resection
- EDEN study: large multicentric Spanish observational study to assess the accuracy of blood biomarkers in predicting anastomotic leak.

## RELEVANT CLINICAL RESEARCH

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- GHOST ileostomy: a new technique to avoid ileostomy in rectal cancer patients. A prospective, multicentric study
- ANACO study: risk factors for anastomotic leak after colon cancer resection. A multicentric study leaded by our group, the biggest published so far about this important issue.
- CT-virtual colonoscopy in the preoperative assessment of patients with colon cancer: evaluation of its accuracy as a new tool for patients' selection to preoperative chemotherapy.
- MRI- enterography in patients with Crohn's disease: a new tool to select patients for surgery avoiding useless and expensive medical treatment
- PEACE study: RCT to study the usefulness of a mesh to prevent laparotomy hernia, one of the most important long-term complications in colorectal cancer patients

Moreover the group is collaborating to many multicentric European (FOXTROT, Birmingham; HIP, Leicester), and National (Vikingo; VEGF, Barcelona; CCR-IV, Barcelona) projects on colorectal cancer and Crohn's disease (Vedolizumab-4003 RCT).

## INDUSTRY COLLABORATIONS

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- CIRO2 project: in collaboration with AIMPLAS, the aim of this study is the production of a tool to measure O2 saturation in the bowel wall just moments before the anastomosis. This could guarantee the appropriate vascularization of the stumps, resulting in a decreased risk of anastomotic leak.
- WIBEC project: European consortium of hospitals, university of engineer and industries to study Intracorporeal Wireless Communication. Financed by a Marie-Curie EU grant.
- STUDER project: in collaboration with the Universidad Politecnica de Valencia and some industries, the aim is to study the accuracy of electromagnetic waves to diagnose colorectal cancer.



# RESPIRATORY INFECTIONS

Leading Researcher:

**Rosario Menéndez,**  
PhD



No. Members: **19**



Other relevant  
information:

**Dr. Rosario Menéndez**  
is Member of the  
**Microbiology**  
**Tuberculosis and**  
**Pulmonary Infections**  
**Program Committee.**

Contact:  
infecciones\_respiratorias@  
iislafe.es

## MAIN RESEARCH LINES

### Study of the inflammatory response in lower respiratory tract infections

Study the inflammation, stability, risk factors and prognosis in both community-acquired pneumonia (CAP) and in patients with chronic obstructive pulmonary disease (COPD).

### Epidemiological, molecular and genetic basis of the lower respiratory tract infections

Study the role of genetic polymorphisms in severe initial presentation (cardiac and inflammatory biomarkers as predictors of cardiac events and mortality in CAP) and, especially, its possible impact on determining if there is an appropriate response to treatment during respiratory infection.

### Non-cystic fibrosis bronchiectasis

Chronic airway inflammation is possibly one of the most important pathophysiological factors of NCFB and is a major cause of functional impairment and disease progression.

### Research in the Intensive Care Unit

Immunological basis in the development of Ventilator-associated pneumonia (VAP).

Application of molecular biology techniques (PCR) for early etiologic diagnosis of VAP and VAT.

Multi-resistant bacteria and pulmonary infection in critically ill patients: usefulness of surveillance cultures; usefulness of epidemiological surveillance; and clinical and microbiological characterization.

### Collaborations:



## SELECTED PAPERS

**Blood culture contamination rate in an intensive care setting: Effectiveness of an education-based intervention.** Ramirez, P et al. American Journal of Infection Control. 2015; 43(8): 844-7.

**Predicting in-hospital treatment failure ( $\leq 7$  days) in patients with COPD exacerbation using antibiotics and systemic steroids.** Crisafulli, E et al. COPD-Journal of Chronic Obstructive Pulmonary Disease. 2015; 9:1-11.

**Bacteraemia and antibiotic-resistant pathogens in community acquired pneumonia: risk and prognosis.** Torres, A et al. European Respiratory Journal. 2015; 45(5): 1353-63.

**Microbiology and outcomes of community acquired pneumonia in non cystic-fibrosis bronchiectasis patients.** Polverino, E et al. Journal of Infection. 2015; 71(1): 28-36.

**Red blood cell distribution width [RDW] and long-term mortality after community-acquired pneumonia. A comparison with proadrenomedullin.** Bello, S et al. Respiratory Medicine. 2015; 109(9): 1193-206.

# RESPIRATORY INFECTIONS

## SELECTED ACTIVE RESEARCH PROJECTS

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Usefulness of antibiotic therapy in exacerbations of chronic obstructive pulmonary disease (COPD) without purulence in sputum: Clinical trial; randomized, controlled, double-blind of efficacy and safety.

**Rosario Menéndez Villanueva**

Muscle electrostimulation in critical patient undergoing sedation and mechanical ventilation. Effect on muscle weakness acquired in intensive care unit and its clinical consequences.

**Paula Ramírez Gallego**

Study Neumonac. Influence of vaccination on the etiology, serotype and complications of NAC.

**Rosario Menéndez Villanueva**

Influence of the degree of immunocompetence in presentation and prognosis in patients with severe community acquired pneumonia (CAP).

**Rosario Menéndez Villanueva**

PNEUMOSIP– a cost-effective solution for the rapid diagnostic of pneumonia. SME instrument-H2020 project.

**Rosario Menéndez Villanueva**

## RELEVANT CLINICAL RESEARCH

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Clinical trial in phase II; randomized, double-blind, placebo-controlled, multicenter, parallel group, adaptive, sequential group, to determine the efficacy and safety of bt086 as adjunctive therapy in cases of severe community acquired pneumonia (scap).

**Paula Ramírez- Biotest Ag**

Clinical trial; multicenter, randomized and double-blind for evaluating the efficacy and safety of oral solitromicina (cem-101) compared to oral moxifloxacin in the treatment of adult patients with bacterial pneumonia acquired in the community.

**Rosario Menéndez Villanueva - Cempra Pharmaceuticals, Inc.**

Clinical trial in phase II; open and multicenter, to evaluate tolerability, safety, efficacy and pharmacokinetic/pharmacodynamic (PK / PD) of POL7080 in treating patients with acute exacerbation of bronchiectasis not associated with cystic fibrosis caused by *Pseudomonas aeruginosa* infection that require intravenous therapy.

**Rosario Menéndez Villanueva - Polyphor Ltd**

## INDUSTRY COLLABORATIONS

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Influence of immunocompetence in presentation and prognosis in hospitalized patients with severe sepsis caused by pneumonia.

**Grifols Inc**

Immune and inflammatory response in pneumonia by *Staphylococcus aureus* resistant to methicillin treated with linezolid or vancomycin.

**Pfizer Slu**

Effect of use of chlorhexidine sponge on biofilm formation on endoluminal and exoluminal surfaces of external ventricular drains.

**3M Deutschland GmbH**

# JOINT RESEARCH UNIT IN MULTIPLE SCLEROSIS AND NEUROREGENERATION

Leading Researchers:

Bonaventura Casanova,  
PhD  
José M. García Verdugo,  
PhD



No. Members: 15



Other relevant  
information:

JOINT RESEARCH UNIT  
WITH UNIVERSITAT DE  
VALENCIA (Neurobiología  
Comparada Group)



Contact:

esclerosis\_multiple@iislafe.es

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## MAIN RESEARCH LINES

### Clinical studies in multiple sclerosis

Prospective follow-up of 1,200 multiple sclerosis and other demyelinating diseases patients through different clinical study techniques; the role of IgM bands in determining the response to the different treatments is being reassessed.

### Studies of biological fluids biomarkers

Study of lipid-specific IgM oligoclonal bands in the CSF and correlation with clinical, immunological, and imaging features for different phenotypes of demyelinating diseases of central nervous system.

Analysis of immune response in patients with multiple sclerosis according to their pattern of oligoclonal bands in CSF and lymphocyte activation measured by the expression of cytokines in serum.

Cell studies to further understand the pathogenesis of demyelinating diseases of central nervous system (CNS): antigen specificity of activated T lymphocytes in CSF and peripheral blood; cooperation between T and B lymphocytes; follow-up of the cell exchange between CNS and PNS (peripheral nervous system).

### Studies of neuroimaging biomarkers

Studies using MRI to characterize lesions, volume and assess atrophies in patients with MS. Furthermore, OCT is used for the study of alterations of the retina and optic nerve in optical neuritis within multiple sclerosis, recurrent optic neuritis and optic neuromyelitis, for development of neural repair cell-based therapies.

Collaborations:   

## SELECTED PAPERS

**Ultrastructural pathology of anaplastic and grade II ependymomas reveals distinctive ciliary structures--electron microscopy redux.** Alfaro-Cervelló, C et al. Ultrastructural Pathology. 2015; 39(1): 23-9.

**Assessment of the reproducibility of oligoclonal IgM band detection for its application in daily clinical practice.** Espino, M et al. Clinica Chimica Acta. 2015; 438: 67-9.

**Antibodies to MOG and AQP4 in adults with neuromyelitis optica and suspected limited forms of the disease.** Hoeftberger, R et al. Multiple Sclerosis Journal. 2015; 21(7): 866-74.

**Meox2/Tcf15 heterodimers program the heart capillary endothelium for cardiac fatty acid uptake.** Coppiello, G et al. Circulation. 2015; 131(9): 815-26.

**Whole-epigenome analysis in multiple myeloma reveals DNA hypermethylation of B cell-specific enhancers.** Agirre, X et al. Genome Research. 2015; 25(4): 478-87.

# JOINT RESEARCH UNIT IN MULTIPLE SCLEROSIS AND NEUROREGENERATION

## SELECTED ACTIVE RESEARCH PROJECTS

Clinical phenotype and physiopathogeny in the demyelinating processes of the central nervous system caused by somatic hyper mutations in the genes encoding monoclonal antibodies intrathecal IgM production.

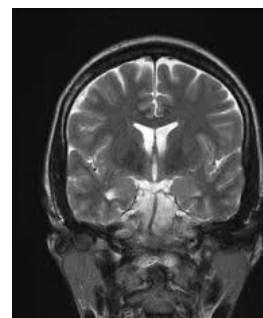
**Bonaventura Casanova Estruch**

Analysis of the myelination process in striatal, effects of EGF and IGF-1.

**Jose Manuel Garcia Verdugo**

Brain repair after stroke: magnetic-field mediated stem cell migration.

**Sara García Gil-Perotín**



## RELEVANT CLINICAL RESEARCH

Clinical trial; randomized, double-blind, placebo controlled group and parallel group, to dose-finding to evaluate the efficacy, safety, tolerability and pharmacokinetics of biib033 in patients with relapsing forms of multiple sclerosis when used simultaneously with avo- nex® .

**Bonaventura Casanova Estruch**

*Biogen Idec Research Limited*

Clinical trial in Phase II; multicenter, randomized, double-blind, parallel and placebo controlled group, to dose-finding to evaluate the safety and efficacy of 3 different oral doses of mt-1303 administered over a period of 24 weeks in patients with relapsing-remitting multiple sclerosis.

**Bonaventura Casanova Estruch**

*Mitsubishi Tanabe Pharma Corporation (Mtpc)*

Clinical trial; randomized, double-blind, parallel and placebo controlled group to evaluate the efficacy, safety, tolerability and pharmacokinetics of biib033 in patients with a first episode of acute optic neuritis.

**Bonaventura Casanova Estruch**

*Biogen Idec Research Limited*

## INDUSTRY COLLABORATIONS

Involvement of the atrophy of the subventricular zone in the development of disability progression in multiple sclerosis.

*Novartis Farmacéutica S.A.*

Analysis of the immune response in MS patients according to their oligoclonal bands pattern in LCR and the lymphocyte activation measured by the expression of cytokines in serum.

*Fundación Biogen IDEC*

RM patterns from brain and spinal cord in relation to the presence of neural autoantigens recognized by immunoglobulin M present in the cerebrospinal fluid of multiple sclerosis patients.

*Almirall*

# SEVERE INFECTION

Leading Researcher:

Javier Pemán, PhD



No. Members: 15



Other relevant  
information:

Award "For Women in  
Science" considered  
the "Nobel for  
women" awarded to  
María Ángeles Tormo  
(2013)

Contact:

infeccion\_grave@iislafe.es

## MAIN RESEARCH LINES

### In vitro susceptibility study of yeast and filamentous fungi to antifungal agents by standard and commercialized methods

Determination of different methods usefulness to determine the susceptibility of filamentous fungi and yeasts to new antifungal agents

### Establishment of predictive scores of invasive fungal infection in critically ill patients

A prospective multicenter study in six Spanish Intensive Care Units is being developed to determine detection of *Candida* germ-tube antibodies usefulness in critically ill patients with candidemia.

### New strategies for the treatment of fungal biofilms-associated infections

Focus on the study of kinetics of biofilm growth as well as cytoarchitecture and matrix composition of the biofilm formed by the different *Candida* species both in presence and absence of antifungal agents alone or combined for new therapeutic strategies. The combination of antifungals, with different mechanism of action, and anti-biofilm substances might be a more efficient alternative than the antifungal monotherapy against *Candida* spp. biofilms.

### Biobank of respiratory samples for patients undergoing lung transplant

A research project using new techniques of mass sequencing has been designed to learn how the microbiota affects the graft viability in LT receptors from the University and Polytechnic Hospital La Fe (HUP).

## Collaborations:

**RETIC-RIS** | Red Española de Investigación en

## SELECTED PAPERS

**Multicenter study of epidemiological cutoff values and detection of resistance in candida spp. To anidulafungin, caspofungin, and micafungin using the sensitive yeastone colorimetric method.** Espinel-Ingroff, A et al. Antimicrobial Agents and Chemotherapy. 2015; 59(11): 6725-32.

**A simple prediction score for estimating the risk of candidaemia caused by fluconazole non-susceptible strains.** Cuervo, G et al. Clinical Microbiology and Infection. 2015; 21(7): 684.e1-9.

**Daptomycin plus fosfomycin versus daptomycin monotherapy in treating MRSA: protocol of a multicentre, randomised, phase III trial.** Shaw, E et al. BMJ Open. 2015; 5(3): e006723.

**Virological failure to raltegravir in Spain: incidence, prevalence and clinical consequences.** Santos, JR et al. Integrase Resistance Study Group in Spain INI-VAIN Study Group. The Journal of Antimicrobial Chemotherapy. 2015; 70(11): 3087-95.

**Candida tropicalis bloodstream infection: Incidence, risk factors and outcome in a population-based surveillance.** Fernández-Ruiz, M et al. The Journal of Infection. 2015; 71(3): 385-94

## SELECTED ACTIVE RESEARCH PROJECTS

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New strategies for the treatment of fungal biofilm-associated infections

**Emilia Cantón Lacasa**

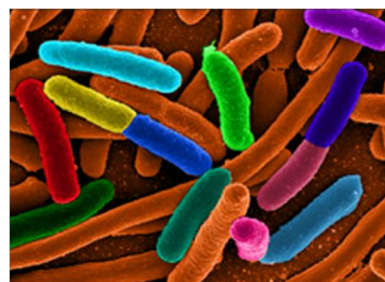
Fungal infections in patients with cystic fibrosis.

Impact on functional and clinical evolution.

**Amparo Solé**

Predisposing factors for CMV infection in lung transplanted patients.

**Amparo Solé**



## RELEVANT CLINICAL RESEARCH

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Clinical trial in phase II; multicenter, randomized, double-blind, placebo controlled to investigate the efficacy and safety of 10 or 20 mg / day of aerosolized liposomal cyclosporine (L-CSA) versus placebo in preventing aerosolized bronchiolitis obliterans syndrome (sbo) in lung transplant patients.

**Amparo Solé Jover**

*Pari Pharma GmbH*

Clinical trial in Phase III, double-blind, multicenter, randomized, placebo-controlled trial to evaluate repeated courses of Aztreonam for inhalation solution (75 mg of Aztreonam powder and solvent for nebuliser solution) in patients with bronchiectasis not associated with Cystic Fibrosis and Infection Endobronchial Gram-negative (AIR-BX2).

**Amparo Solé Jover**

*Gilead Sciences Inc.*

Clinical trial; randomized, multicenter, comparing the efficacy of the combination of daptomycin and Fosfomycin against the monotherapy with daptomycin for the treatment of methicillin-resistant *Staphylococcus aureus* bacteremia in hospitalized patients.

**Miguel Salavert Lleti**

*Miquel Pujol Rojo (Servicio Infecciosos H. Bellvitge)*

## INDUSTRY COLLABORATIONS

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Detection value of galactomannan antigen of *Aspergillus* in the diagnosis of invasive aspergillosis. Multicenter study.

*Pfizer Internacional*

Epidemiology of multiresistant bacteria in units of critical patients.

*BioMérieux España S.A.*

Epidemiology and risk factors for *S. aureus* infections in respiratory patients.

*Pfizer nacional*