IGTP

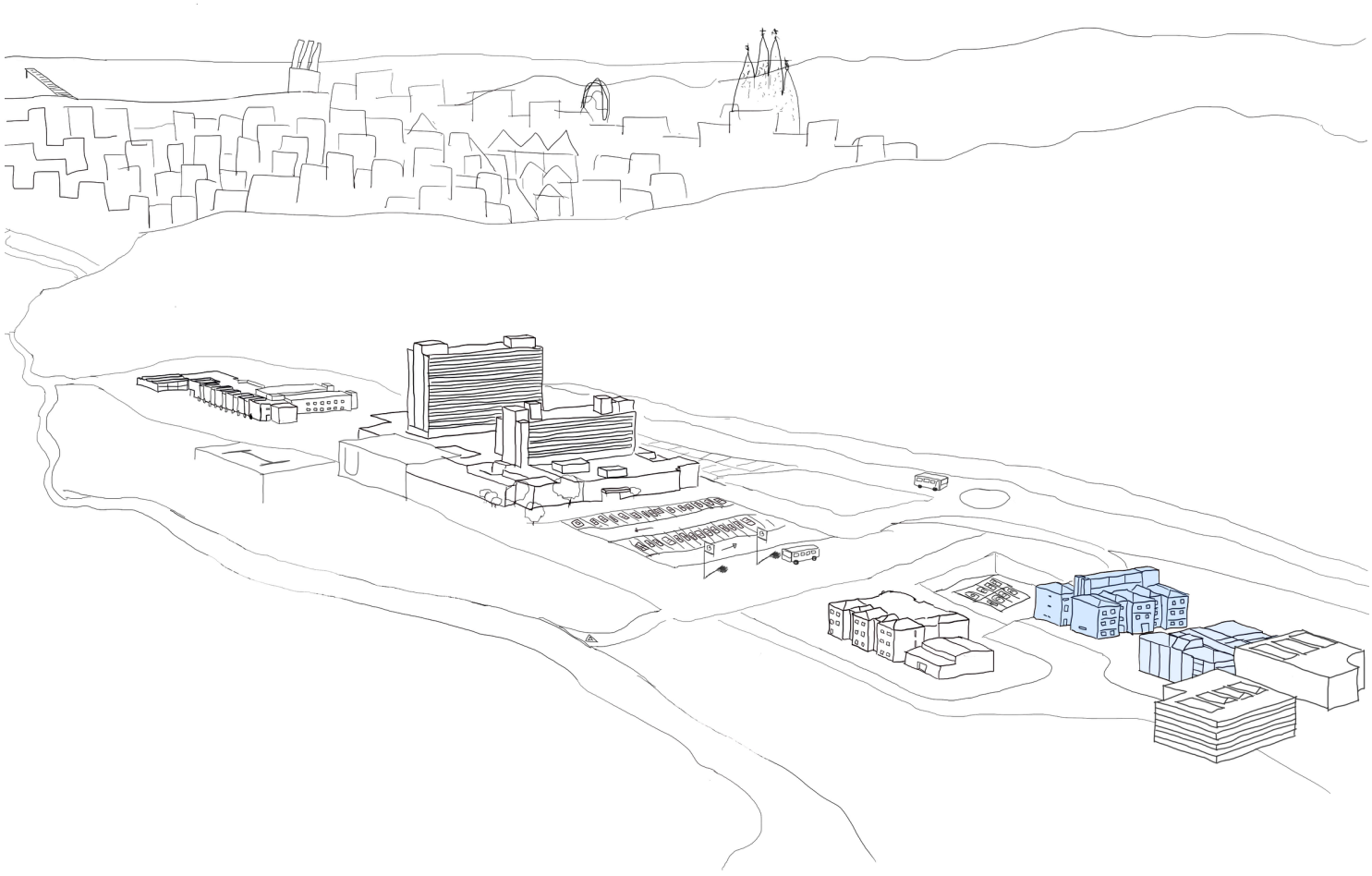
Germans Trias i Pujol Research Institute

2018

ANNUAL REPORT

Index

IGTP
Institut de Recerca Germans Trias i Pujol



Generalitat de Catalunya
UAB Universitat Autònoma de Barcelona
ICO Institut Català d'Oncologia
Ajuntament de Badalona
IDIAP Jordi Gol
IrsiCaixa Institut de Recerca de la Sida
Germans Trias i Pujol Hospital
INSTITUT GUTTMANN HOSPITAL DE NEUROREHABILITACIÓ
CONSORCI SANITARI DEL MARESME
BANC DE SANG I TEIXITS
Institut Català de la Salut
Josep Carreras LEUKAEMIA Research Institute

Annual Report 2018

1. INTRODUCTION

Without doubt, 2018 has been an excellent year for the IGTP and all the institutions included within it. It has been a good year in terms of maintaining our standards of quality in scientific production, obtaining new projects and developing innovation activities.

The institution has seen an increase in registrations of clinical trials in 2018, with 470 to be exact, which continues a steady increase in annual numbers. This increase has had a direct impact on turnover (an increase of 0.8 M€) and together with an increase of incoming overheads from projects this has strengthened the position of the institute. This year it has continued to register an increase in publications, more than 800, with more than 4300 impact factor points. In terms of scientific quality, nearly a quarter of these are in the first decile (24%) and 51% i the first quartile. The high scientific output per principal investigator has also been maintained at 4.9% articles/PI.

During recent years the Innovation and Business Development Unit has been created and leveraged, first under the leadership of Dr Núria Martí, now Director of Innovation at BioCat, and currently under Jaume Ruiz. The IGTP Innovation structure has continued to enjoy the support of ITEMAS of the ISCIII. During 2018 the culture of innovation has also been activated in the hospital, with the appointment of Dr Oriol Estrada as Director of Innovation of the HUGTiP, with Dr Daniel Moreno joining the team. It is worth highlighting the commitment to carry out one of the BioCat training programmes, D-Health, in the Respiratory Service in 2019. The Unit has supported the valorizing of more than 60 ideas and projects during 2018, with 5 new patents and a new spin-off company. Biointaxis will develop gene therapy for Friedrich's ataxia, it is led by Dr Antoni Matilla. The Business Development Unit has obtained nearly 1 M€ in competitive calls since 2014.

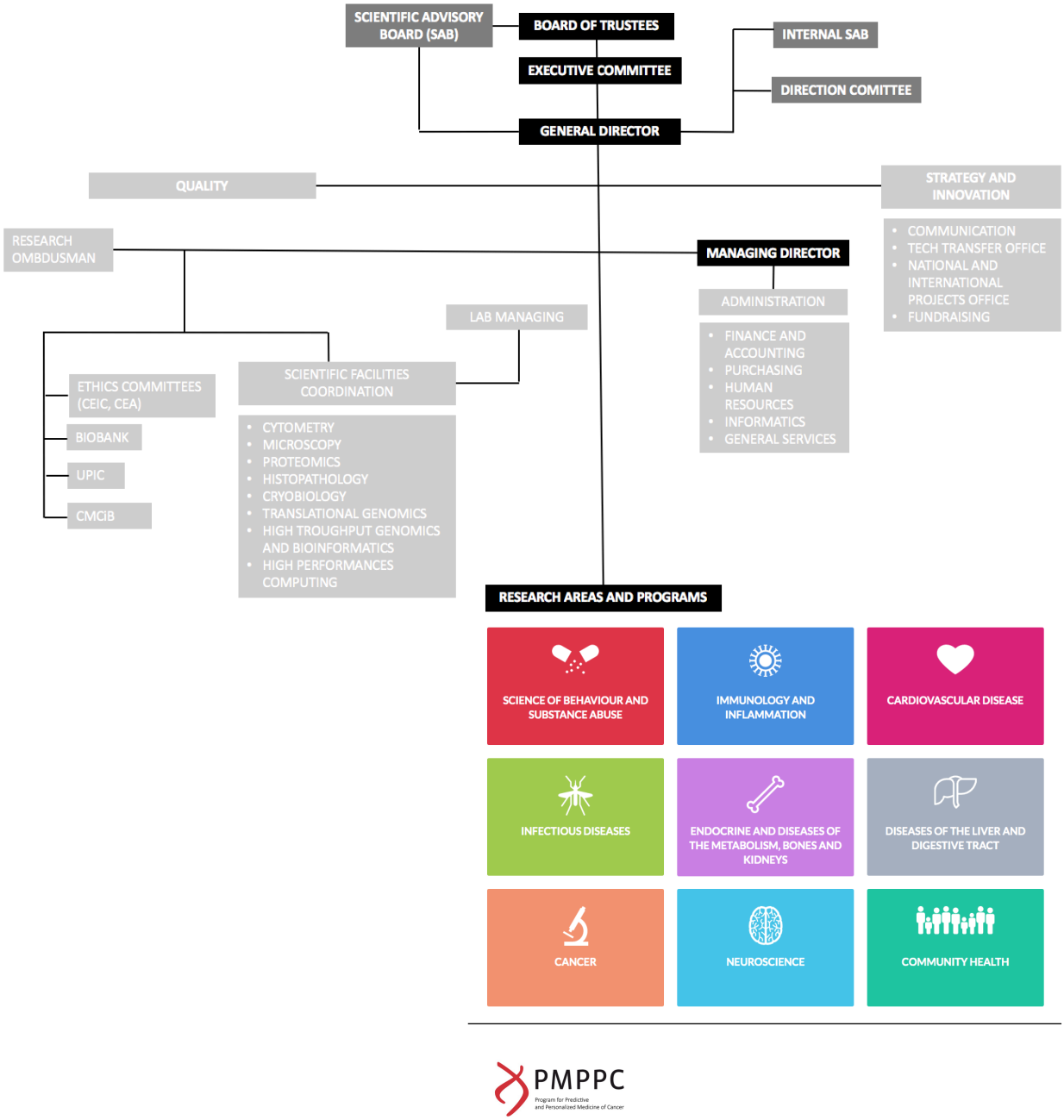
Additionally, one of the great institutional milestones in 2018 has been the CMCiB starting to function as a service to Catalonia researchers, but also for those in the rest of Europe. The prevision is to have 3T NMR and other state-of-the-art bioimaging equipment available during next year. The supplier/partner is Canon Medical, which will supply a full-time bioimaging engineer who will carry out primary bioimaging research as well as providing support for all CMCiB projects during the next five years. The centre is already executing experiments worth over 1 M€ for researchers, from Can Ruti Campus and elsewhere, for the 2019-2020 period. Other multinational companies have also visited with a view to carrying out research and training activities at the CMCiB. Discussions are advancing to define a common working plan with the CRESA at Torrelameu, part of the IRB, in order to consolidate a Catalan Experimental Centre with two sites, one at Can Ruti and the other in Lerida.

During 2018 the periodic evaluation process for the IGTP as an accredited centre of excellence by the ISCIII has been formalized. The external scientific advisory board met in June 2018 and reported to the Board of Trustees of the IGTP.

The ESAB appraised the considerable amount of work carried out to reorganize and improve performance of the IGTP in recent years and recommended that the strategy of improving scientific excellence and promotion of innovation continue.

Dr. Manel Puig Domingo, **IGTP Director**

2. ORGANIZATIONAL CHART



3. RESEARCH AREAS AND GROUPS

3.1. Research areas and groups

The IGTP has 36 clinical, basic and translational research groups organized around the clinical areas of the Germans Trias i Pujol University Hospital. The Programme for Predictive and Personalized Medicine of Cancer (PMMPC) is predominantly centred on cancer, but includes research into different medical areas. In the last two years the IGTP has completed a process of analysis, identification, validation and monitoring of the scientific activity of the research groups. This has resulted in a rationalization and restructuring of the areas and the group descriptions detailed below.

1. MEDICAL COMPLICATIONS OF SUBSTANTIAL ABUSE

This is a clinical research group focused on the complications that arise from alcohol and drug abuse, particularly opiates and cocaine. The group is financed by public agencies and Themes networked funding by the Ministry of Health (RETICS-ISCIII), in this case the Addictive Disorders Network (RTA).

Group leader: **Dr Robert Muga Bustamente**

Research lines:

1. **Medical Complications associated with alcohol abuse:** To characterize comorbidity of patients requesting treatment for disorders due to alcohol abuse: Alcoholic hepatopathology, immunological alterations, malnutrition, cardiovascular risk, neurological risk and HIV infection, amongst other pathologies being studied.
2. **Monitoring HIV and hepatitis B and C virus in patients with disorders due to alcohol or drug abuse:** To establish diagnostics, clinical evaluation and access to treatment of viral infection in users of alcohol and drugs. To analyze the risk of developing diseases such as cancer, AIDS or liver cirrhosis; and also risk of death due to infections.
3. **Mortality associated with disorders due to alcohol and drug abuse**: To describe the long-term evolution of patients who abuse drugs and alcohol and detail the causes of death in function of comorbidity when they seek treatment**.**

2. IMMUNOPATHOLOGY

The Immunopathology research group is within the Immunology Service of the Germans Trias Hospital. It is an experienced interdisciplinary team that is highly motivated to carry out translational research and give support to clinical teams who are developing their own research projects to examine the mechanisms of the immune response. In the laboratory there are advanced immunopathology diagnostics services (including: autoimmunity, allergies, immunochemistry, cellular immunology and immunodeficiency, amongst others), histocompatibility and various panels for immune monitoring of immune-mediated illnesses and immunological treatments (immune-modulating drugs, monoclonal antibodies, cellular therapies and other immunotherapeutic procedures). Since 2008, the group has been developing new immune tolerance-inducing therapies.

Group leader: **Dr Eva Mª Martínez Cáceres**

Research lines:

1. **Innovation and Diagnostic Immunology.** The aim of this line of research is to identify new biomarkers for diagnostics or monitoring response to treatment and to implement functional immune-phenotypic panels for patients with immune-mediated illnesses and/or in treatment with therapies that target the immune system.
2. **Clinical Epidemiology Research.** The objective is to better understand the immunopathology of immuno-mediated illnesses, the predictive value and pathogenicity, diagnostic and/or prognostic values of serological and genetic cellular markers available.
3. **Immune therapies inducing tolerance. T**he objective is to develop therapeutic strategies to re-establish immunological tolerance to autoantigens (in autoimmune diseases), to allergens (in severe allergies) and to alloantigen (in transplant). At the moment the group is concentrating on autoimmune diseases of the central nervous system (multiple sclerosis).
4. **Neuroimmunology: Cellular tolerance therapy in multiple sclerosis. Research line codirected by Dr C Ramo, Head of the Multiple Sclerosis Unit in the Department of Neuroscience.** The group has developed a tolerogenic cell product made from autologous dendritic cells obtained from monocytes in the peripheral blood of patients.

3. IMMUNOLOGY OF DIABETES

The multidisciplinary Immunology of Diabetes Group at the IGTP is part of the Immunology Section of the Germans Trias i Pujol University Hospital (HUGTiP). It is made up of researchers, endocrinologists, pediatricians and technicians; the group works to understand more about the causes of type 1 diabetes.

Group leader: **Dr Marta Vives-Pi**

Research lines:

1. **Immunotherapies for the prevention and treatment of type 1 diabetes**
   The line of research aims to stop the autoimmune response using innovative therapies to re-establish the cellular tolerance of the insulin-producing cells.
   This line of research is funded by Instituto de Salud Carlos III and Fundació La Marató de TV3.
2. **Pathogenic mechanisms of autoimmunity**
   This line of research aims to identify the mechanisms of the specific immune responsible for destruction of insulin-producing beta cells, with special atention to prenatal environmental factors.
3. **Pediatric type 1 diabetes: tolerance, spontaneous remission and biomarkers**
   The aim of this line is to explore mechanisms of tolerance restablishment in children at the onset of the disease, and to define new biomarkers of remission.

4. HEART DISEASE

The objective of the Heart Institute is to carry out research that will increase the development of new treatments for heart disease by better understanding its origins and progression. This way will improve the quality of life for heart patients.

The Heart Institute combines health care with research. The team includes cardiologists, surgeons, nurses, administrative staff and researchers from multidisciplinary backgrounds (eg. biology, veterinary science, biotechnology and pharmacy) all dedicated full time to the task.

The Heart Failure Research group and the Heart Regeneration Research Group (ICREC), based at the IGTP and led by Dr Antoni Bayés Genís is focussed on two principal areas: one purely clinical and one more translational. On the clinical side, the group searches for biomarkers for diagnostics and prognostics for heart failure and develops technology related to Telemedicine. On the basic/translational side, the group is interested in studying the potential for regeneration of different types of stem cells (derived from adipose cardiac tissue and blood or umbilical cord, amongst other sources) and in therapeutic approaches based on engineering tissues to safeguard and restore myocardium damaged during infarction. The ICREC group is made up of researchers experienced in cell techniques and decellurization, repopulation and implantation of biological meshes. The ICREC group also counts on highly skilled personnel with experience of mouse and pig models of myocardial infarction.

Group leader: **Dr Antoni Bayés Genís**

Research lines:

1. **Cardiac Regeneration**
2. **Hearth Failure**
3. **Coronary Surgery Research**
4. **Acute Coronary Syndrome**
5. **Coronary Imaging**

5. EXPERIMENTAL TUBERCULOSIS UNIT

The Unitat de Tuberculosi Experimental (Experimental Tuberculosis Unit, UTE), was founded by Dr Pere-Joan Cardona in 1997. It is located in the Can Ruti Campus as a unit of the IGTP and the CRP-TB Consortium of the CIBERES net, funded by the Spanish Government; and linked to the University (Microbiology and Genetics Department, Faculty of Medicine, Universitat Autonòma de Barcelona).

Group leader: **Dr Pere Joan Cardona**
Emerging Group leader: **Dr Cristina Vilaplana**

Research lines:

1. Experimental modelling of TB (**PI: Dr Pere-Joan Cardona).** This research line is devoted to the design, development and characterization of new experimental models (in vitro, in vivo and in silico). a) To study and better understand TB course: TB infection and progression to active disease. b) To better mimic TB in humans. c) To study the influence of comorbidities in TB (as does within the H2020 EU-funded Consortia TBVAC2020 (Grant nº643381).

2. **Evaluation of new prophylactic and therapeutic strategies against TB (PI: Dr Pere-Joan Cardona)**. The study of the immunopathology of the TB infection led Dr Cardona to propose a new hypothesis (the Dynamic Hypothesis) to explain the Latent Tuberculosis Infection, and the design, patent and development of RUTI®, a therapeutic vaccine to shorten the chemotherapy of latent tuberculosis infection. RUTI® was evaluated in a successful Phase II Clinical Trial in SouthAfrica, and has also proved both a prophylactic and a post-exposure effect, generating 2 other patents.

3. **Study of the role of inflammation in TB and its modulation through Host-Directed Therapies (HDT) (PI: Dr Cris Vilaplana).** This research line was created thanks to the Miguel Servet 1 personal contract awarded to Dr Vilaplana (CP13/00174), and includes: 1) Study of TB lesions obtained in surgery: in search of best biomarkers correlating with TB pathology, clinical features, MDR cases and prognostic. In collaboration with the National Center of Tuberculosis and Lung Diseases (NCTLD) of Georgia. 2) Evaluation in animal models and in clinical trials of repurposed drugs with anti-inflammatory effect (mainly common NSAIDs as ibuprofen and aspirin, statins and others).

6. INNOVATION IN RESPIRATORI INFECTIONS AND TUBERCULOSIS DIAGNOSIS

The research group is co-led by two Principal Investigators. **Dr José Domínguez** (MSc, PhD) is a "Miguel Servet" senior researcher and **Dr Cristina Prat-Aymerich** (MD, PhD) is a medical microbiologist. This co-leadership gives a complementary clinical-basic translational perspective to the group's activity. The group is working in the field of the respiratory infections and tuberculosis, improving the understanding of the host-pathogen interaction, and exploring new approaches in the diagnosis and therapies.

Joint Group Leaders: **Dr José Domínguez & Dr Cristina Prat-Aymerich**

Research lines:

1. **Host-pathogen interaction.** Regarding respiratory infections, research focuses explore the microbial mechanisms of adaptation to the respiratory tract and related aspects of clinical presentation with phenotypic and genotypic traits of microorganisms; including bioinformatics approaches. The objective is to identify differential factors that will allow the design of diagnostic tools to distinguish colonization from infection. The group is also participating in the ASPIRE consortium
2. **Immune response characterization.** Evaluation of the diagnostic and prognostic importance of inflammation markers in infectious diseases. The study the host immune response to different antigens specific of Mycobacterium tuberculosis to better characterize the latency state and the search for new biomarkers useful for identifying infected individuals with a higher risk of progressing to disease. The group is involved in the VacTrain Consortium founded by the FP7 programme**.**
3. **Intracellular resistance model.** Establishment of a model of intracellular persistence in alveolar macrophages permits the group to carry out trials for S. aureus protection with gentamicin and microscopy and transcriptome studies and explore the impact of tobacco smoke in the persistence of M. tuberculosis and its potential interaction with the anti-TB drugs.
4. **Diagnostic technology innovation.** Use of molecular, metabolomics and immunology techniques for developing and testing diagnostic technologies and for studying mutations associated with resistance to first and second line anti-tuberculosis drugs. The group is also involved in two European consortiums with these purposes: "TB-prognosis" Consortium, funded by IRSES-FP7, and "StopTB/HIV at one" consortium, funded by EDCTP. We also participate in various trials carried out at the hospital for respiratory infections.
5. **New therapeutic approaches.** The group is carrying out studies of novel therapeutic elements using susceptibility studies in vitro; and conventional S. aureus and M. tuberculosis drugs, by means of new administration, principally via nanoparticles, which release antibiotic at the site of infection, and are tested in the cellular model. The TARMAC consortium, funded by CIBERES, CIBER-BBN and SEPAR, is developing this study.

7. CLINICAL VIROLOGY AND NEW DIAGNOSTIC APPROACHES

The Research Group on Clinical Virology and New Diagnostic Approaches promotes multidisciplinary translational research to improve the diagnostics, prognostics and management of infections caused by

viruses and other pathogens that impact on clinical applications and public health. The Group is integrated with the Clinical and Experimental Microbiology Group, in the Microbiology Service at Hospital Universitari Germans Trias i Pujol.

Group Leader: **Dr Elisa Martró**

Research lines:

1. **Hepatitis C (HCV).** The research activity of the Group in this line focusses on the study of HCV genetic variability. 1) The prediction of response to antiviral treatments (baseline genetic diversity and resistance-associated substitutions. 2) The prediction of the progression of hepatic fibrosis and 3) The characterization of the molecular epidemiology of HCV (description of new subtypes, characterization of transmission events and networks).
2. **Other Viral Infections.** The Group also studies other clinically relevant viruses at the genetic level in order to improve their diagnosis, and to characterize their molecular epidemiology and clinical associations including cancer. These viruses include the Hepatitis B virus, the human Papillomavirus (VPH), the *Molluscum contagiosum* virus.
3. **Other infectious diseases**. The Group collaborates in the development and validation of molecular assays for the diagnosis of other infectious diseases, particularly in the field of sepsis, as a rapid microbiological diagnosis is crucial for patient survival.
4. **Epidemiology of Sexually Transmitted Infections.** The Group collaborates with the CEEISCAT (Centre for Epidemiological Studies of Sexually Transmitted Infections and AIDS in Catalonia). They have optimized various diagnostic techniques adapted for minimally invasive sampling (especially urine, saliva, and fingerpick blood) for the screening of STI in vulnerable populations attending alternative testing centres, contributing to their epidemiological characterization with public health applications.

8. INFECTIOUS AND RESPIRATORY DISEASE RESEARCH GROUP

This multidisciplinary group made up of researchers of the Infectious Diseases and International Health Unit of the Germans Trias Hospital and of the Pneumology Services at the Parc Tauli Hospitals has various lines of research. These include clinical research, microbiology and molecular biology. The general aim of the group is to carry out clinical and translational research on infectious and respiratory diseases.

Group Leaders: **Dr Miquel Sabria and Dr Maria Luisa Pedro-Botet**

Research lines:

1. **Infectious Diseases.** Research into community acquired and nosocomial Pneumonia; bacteraemias and infectious endocarditis; primary immunodeficiencies; Chagas disease and other tropical diseases.
2. **International Health.** Research into epidemiological, clinical, therapeutic and preventive aspects of Legionnaires' Disease, molecular and phenotypic epidemiology of Legionella, development of new detection, diagnostic and typing methods for Legionella
3. **Chronic Obstructive Pulmonary Disease (COPD).** Description of the bronquial microbioma and bronquial inflammatory response associated with the particular clinical variants of different patient cohorts.

4. **Cancer.** The group acts as a Corporate Research Program Coordinator (PCI) for Lung Cancer in the Instituto Carlos III On-line Network for Respiratory Disease, CIBERES Enfermedades Respiratorias. The project includes the creation of a biobank for tumour tissue, non-tumour tissue and peripheral blood from patients with Stage I or II non-small cell lung cancer in order to be able to detect new predictive and prognostic biomarkers.

9. PLASMODIUM VIVAX AND EXOMES RESEARCH (PVREX)

The group brings their expertise in malaria and exosome research with a very strong motivation to produce translational impact. The group uses a series of molecular and cellular biology technologies combined with immune-epidemiological studies in endemic regions of vivax malaria (i) to study the biology of the parasite, (ii) to unveil mechanistic insights into anaemia and splenomegaly, and (iii) to discover new antigens for vaccinations. In addition, the group is pioneering the use of reticulocyte-derived exosomes as a new vaccine and platform against malaria. To this end, Dr del Portillo has co-founded INNOVEX THERAPEUTICS SL, the first Spanish Spin-off devoted to the use of exosomes as new therapeutic agents and diagnostic tools.

Join Group leaders: **Dr Hernando del Portillo & Dr Carmen Fernandez**

Research lines:

1. **Reticulocyte-derived exosomes as a new vaccine and platform against *Plasmodium vivax* malaria.** The group has published the first report of immune responses elicited by exosomes derived from reticulocytes opening new avenues for the development of rex as a new vaccine and platform against malaria.
2. **Antigen discovery.** They have identified vaccine-protective antigens associated with reticulocyte-derived exosomes in experimental infections of a reticulocyte-prone rodent malaria model and are presently identifying parasite antigens associated with rex in natural infections of malaria patients. In addition, through global transcriptional analysis, they have identified *P. vivax* antigens whose expression is dependent on an intact spleen. To determine which antigens are associated with clinical protection, they have modified vectors for soluble expression of malaria proteins in the wheat germ cell-free system and are testing them in multiplex assays with immune sera of children from prospective longitudinal cohort studies in Brazil and PNG.
3. **Role of the spleen, cyto-adherence and pathology**. The group has implemented intravital microscopy and magnetic resonance imaging in a rodent malaria model with tropism for reticulocytes. Noticeably, experimental infections in this model induce remodelling of the spleen facilitating cyto-adherence and macrophage-clearance escape. They have obtained evidence demonstrating that a similar mechanism occurs in P. vivax, as there is cyto-adhesion of *P. vivax*-infected reticulocytes to the ICAM1 endothelial receptor and to cryostat sections of human spleens.
4. **Functional gene studies and in vitro culture of *P. vivax*.** The group is functionally characterizing P. vivax genes through heterologous transfection in *P. falciparum* as presently there is no continuous *in vitro* culture of *P. vivax* blood stages. To this end, they have constructed different vectors to stably express transgenes in *P. falciparum* in all the asexual blood stages at different levels. Using one of such vectors, they have over-expressed virulent genes of *P. vivax* in *P. falciparum* and have

demonstrated that members of particular variant proteins are ligands of the endothelial ICAM1 receptor, involved in severe malaria. They are trying to establish a continuous in vitro culture system for *P. vivax* to try implementing homologous transfection technology and reverse genetics approaches for this parasite species.

5. **Biomarker discovery.** Using mass-spectrometry to identify new markers for identifying P. vivax asymptomatic carriers with the ultimate goal of developing POC diagnostic devices easily deployable in the field to contribute to the elimination of vivax malaria.
6. **Exosome-vaccines against neglected tropical diseases.** Many parasitic diseases include diseases related to poverty such as the malaria caused by *Plasmodium vivax*, Chagas disease caused by *Trypanosoma cruzi* and fascioliasis caused by *F. hepatica*. The group hypothesizes that exosomes derived from these three human infections act in inter-cellular communication facilitating the establishment of infections and that the parasite-specific proteins associated with these exosomes will identify new antigens for vaccination. The use of human reticulocyte-derived exosomes will serve as a new vehicle for antigen delivery and presentation to develop vaccines against these neglected tropical diseases.

10. AIDS BASIC AND CLINICAL RESEARCH

Research into infections with HIV on the Can Ruti Campus are carried out at the IrsiCaixa AIDS Research Institute and Fight AIDS Foundation (FLS). IGTP, IrsiCaixa and FLS investigators work together on many research projects under the terms of collaborative agreements.

Group leader: **Dr. Bonaventura Clotet, President of the Fight AIDS Foundation and Director of IrsiCaixa.**

IrsiCaixa research lines:

- Prevention, eradication and functional cure
- Microbiome
- New treatments and resistance to antivirals
- Inmunopathogenesis
- Other diseases

Fight Aids Foundation research lines:

- Clinical virology and the genome of the microbiota
- Aging and complications associated with HIV and antiretrovirals
- Clinical pharmacology
- Co-infection with hepatitis and cohorts
- Co-infection with Human Papilloma Virus and opportunistic infections
- Immunology and vaccines
- Pyschology
- Dietetics

11. GLOBAL HEALTH AND EPIDEMIOLOGY OF STDs

A multidisciplinary team of professionals carries out the duties of the CEEISCAT using both formal epidemiological tracking systems and specific observational studies that make up the Integrated Epidemiological Surveillances System for HIV/AIDS/STDs in Catalonia (SIVES). An essential and key aspect of the work is interaction with different national and international professional networks in clinical work, microbiology and epidemiology and also with NGOs that work with the target populations of the studies.

Group Leader: **Dr Jordi Casabona**

Research lines:

1. Modelling and new methods of monitoring outbreaks of HIV and sexually transmitted diseases (STDs).
2. Evaluation of preventive interventions for HIV and STDs and measures to prevent and control them.
3. Implementation studies for operational research in early diagnosis of HIV.
4. Biological behavioural and structural determinants of the acquisition and propagation of communicable diseases in the immigrant population.
5. Metrics and social networks applied to the study of HIV and STDs.

12. ACQUIRED PNEUMONIAS IN THE COMMUNITY

The GEMPAC (Maresme Research Group for Community Acquired Pneumonia) physically located at the Maresme Health Consortium, which covers primary health care in the Maresme region and is centred in the Mataró Hospital. It has a collaborative agreement with the IGTP for research activities. The group has made important contributions in the areas of incidence, microbiology, prognostic risk factors, costing, diagnostic errors and the value of inflammatory markers for the prediction of pneumonia and aetiological orientation.

Research Lines:

1. **Population study on acute COPD**
   Community study of diagnostic error for COPD, study of incidence of exacerbation of COPD, case-controlled study of risk factors for acute-prone phenotypes with the importance of oral hygiene, disphagia, diet (antioxidantes and vitamin D levels).
2. **Study of risk factors for pneumonia in respiratory patients (asthma and COPD)**

Community study of risk factors for pneumonia in asthmatic patients with COPD and the importance of the use of broncodilatotors and oral hygiene. Study of the impact of biological markers and immunoglobulins in prognosis of community acquired pneumonia

3. **Study of infectious comorbidity in patients admitted to hospital for acute COPD**
   Study of the prevalence of infections in patients admitted to hospital for acute COPD for Clostridium difficile microbacteria infections and the impact of flu epidemic
4. **Study of risk factors for community acquired pneumonia**
   Study of risk factors for community acquired pneumonia such as treatment with Benzodiazepine, dysphagia,oral hygiene, occupation etc.

13. ENDOCRINE THYROID AND OBESITY

The Endocrine and Obesity Research group is coordinated by Prof Manuel Puig-Domingo, who is currently Head of the of Endocrinology and Nutrition Service at Germans Trias Hospital, Professor of Endocrinology at the Germans Trias Unit of the Faculty of Medicine of Autonomous University of Barcelona, and Scientific Director of Germans Trias Research Institute.

Group Leader**: Dr Manel Puig Domingo**

Research lines:

1. **Molecular phenotyping of pituitary tumours and its application to personalized medicine.** The group has been working in recent years to achieve results regarding the potential usefulness of different molecular and genetic markers that could be used to explain the biological and clinical behaviour of pituitary adenomas, while at the same time identifying biomarkers and bioimaging markers that could predict therapeutic responses. The ultimate goal is to translate these findings to clinical practice by including them in the therapeutic algorithms.
2. **Thyroid pathology.** The group has also been working for many years on the evaluation of thyroid function in relation to iodine nutrition and its consequences during pregnancy. Additionally, the group also carries out thyroid cancer research, as part and founder of a Catalan consortium for the study of thyroid cancer.
3. **Obesity.** Since 2010, different research activities have been initiated to study the complications of Obesity and its potential reversal after therapeutic bariatric surgery. Adipose tissue of different topographies is being collected and studied for epigenetic changes.

14. OBESITY AND TYPE II DIABETES: ADIPOSE TISSUE BIOLOGY

The group searches for molecules secreted by white and brown adipose tissue involved in the inflammatory state that occurs during the obesity. They also evaluate the capability of these molecules to inhibit/activate the brown adipose tissue and to modulate the properties of subcutaneous white adipose tissue, which is replaced by thermogenic beige adipose tissue (browning) in obesity. The goal of this group is to decipher why the excess of fat is inhibiting the normal activation and function of brown adipose tissue and browning, and to search for novel pharmacological approaches to treat obesity and related diseases.

Group Leader: **Dr David Sanchez-Infantes**

Research lines:

1. **Novel cytokines involved in the inhibition/activation of brown adipose tissue function and browning.** The group searches for molecules secreted by white and/or brown adipose tissue involved in the inflammatory state that occurs during obesity. The goal of this group is to decipher why the excess of fat inhibits the normal activation and function of brown adipose tissue and browning, and to search for novel pharmacological approaches to treat obesity and related diseases.

15. KIDNEY AFFECTNG DISEASES

The Kidney-affecting Diseases Research Group (REMAR) aims to deepen in the knowledge of the aetiopathogenic mechanisms of the diseases that affect kidneys, and to boost the translational research for the benefit of renal patients.

Group Leader: **Dr Josep Bonet**

Research lines:

1. **Urine exosomes in Transplanted patients.** Renal biopsy is the gold standard procedure to diagnose most of renal pathologies. However, this invasive method is of limited repeatability and often describes an irreversible renal damage. The identification of specific biomarkers in the urinary exosomes can help replacing this technique by a less invasive diagnostic.
2. **Morbid Obesity and renal disease.** Morbid Obesity plays an important role in promoting chronic kidney disease. Our group has participated in the development of several studies related to MO. We are currently interested in the study and definition of specific genes involved in this pathology.
3. **Proteomics and glomerular disease.** Investigating new urinary markers by proteomics is one of the most important challenges in the forthcoming years, as it will allow classifying more specifically and effectively primary renal diseases.
4. **Mesenchymal Stem Cells in Kidney Transplant.** The aim of this research is to develop a strategy to optimize the induction of tolerance in clinical transplantation. Based on previous work on the interactions of MSC with other cells, we aim to generate regulatory cells in vitro for therapeutic applications.
5. **Peritoneal Dialysis**

16. INNOVATION FOR VESCILES AND CELLS FOR APPLIATIONS IN THERAPHY (IVECAT)

The IVECAT group is interested in the different aspects of nano-vesicles such as exosomes and in different cells types such as Dendritic Cells and Mesenchymal Stem Cells, from basic research to clinical application. The main focus are transplantation and renal related diseases.

Group Leader: **Dr Francesc Borràs**

Research lines

1. **Exosomes:** new tools in biomarker definition for renal and neurological disorders Renal biopsy is the gold standard procedure to diagnose most of renal pathologies. However, this invasive method is of limited repeatability and often describes an irreversible renal damage. -The identification of specific biomarkers in the urinary exosomes can help replacing this technique by a less invasive diagnostic.
2. **New strategies for the induction of Tolerance in Transplantation:** Organ transplantation from unrelated donors is often the treatment of choice for solid organ end stage disease, but a major drawback is the allo-immune response generated against donor antigens expressed in the graft, in particular Human Leukocyte Antigens (HLA), which leads to the rejection of the transplanted organ. Our group is interested in the development of both cell and cell-free approaches as promising therapeutic options for transplantation.

17. ENDOCRINE REGULATORY GENOMICS

The endocrine system consists of a collection of distinct cell identities organized in tissues and shaped into functional organs. These highly specialized tissues ensure the physiological equilibrium of an organism and its possibility, throughout life, to interact with the environment. How do these cell populations preserve their identity? Which molecular mechanisms are required to maintain their phenotype stable for decades? How are gene regulatory networks altered in pathological conditions? The group combines molecular genetics and bioinformatic approaches to understand the regulatory mechanisms that control function and cell fate of the endocrine tissues central to diabetes.

Group Leader: **Dr Lorenzo Pasquali**

Research lines:

1. **Unmasking the regulatory networks, in the insulin-producing pancreatic beta-cells, that prelude the onset of different forms of diabetes.**
2. **Identifying the regulatory changes underlying the loss of cell fate in neoplastic conditions such as in the neuroendocrine tumours.**

18. SARCOPENIA AND FRAGILITY RESEARCH GROUP

The "Sarcopenia, Frailty and Dependence Study Group" is an emerging research group in the Maresme Health Consortium (CSdM). The group's mission is to generate useful scientific knowledge to improve care for the elderly (especially those pre-frail and frail), to prevent functional decline and disability and keep them functionally autonomous and independent as long as possible.

Group Leader: **Dr Mateu Serra Prat**

Research lines:

1. **Endocrinology of Aging**

   This line explores the endocrine changes that occur in aging and their impact on fragility and functional decline.

2. **Polypharmacy in the elderly**

   The group is interested in evaluating the safety of medication in the aged population and determining the risk factors for secondary effects of medication in this group. They also evaluate the effectiveness of interventions aimed at a safer and more rational use of medication in poly-medicated elderly people.

3. **Rehabilitation, physical exercise and analysis of movement**

   The group aims to characterize balance and speed in the elderly (with static and dynamic baropodometry and posture) and evaluate the impact of alterations on the apparition of accidental falls.

4. **Anorexia and nutrition in the elderly**

   The group studies nutritional status and eating habits as risk factors for fragility as well as the effectiveness and safety of nutritional interventions (protein supplements, vitamin D etc) aimed at improving the nutritional status and functional capacity of the individual.

19. DIGESTIVE INFLAMATORY AND PATHOLOGY GROUP

The Inflammatory Intestinal Disease Unit is a multidisciplinary group that carries out translational research. The Unit has carried out cutting-edge research over the last 25 years, which has meant that it has reached a level of excellence in intestinal healthcare and has set a national and international benchmark for the treatment of ulcerative colitis and Crohn's disease. In recent years, the Unit has established new lines of research in the field of irritable bowel syndrome and the improvement of therapeutic endoscopy. Understanding, innovating, explaining and training are important and integrated parts of our scientific task with a view to transferring our results to clinical practice. The team combines experts in different skills to ensure that research questions are tackled from the most experimental side (IGTP) to the most clinical side (HUGTP). The research lines are based on innovative research tools, which allow us to generate new hypotheses aimed at the development of a more personalized medicine, better therapies and improved patient management.

Group Leader: **Dr Eugeni Domenech**

Research Lines:

1. **Physiopathology of intestinal inflammatory disease and therapeutic innovation**
2. **Genetic and functional characterization of phenotypes relevant to clinical**
3. **Loss of response to cortioco-steroids in ulcerative colitis.** The objective of this line of research is to use systems biology to understand corticosteroid treatment failure. Researchers will propose new therapeutic tools to combat cortico-refractionary responses. They will determine miRNA profiles that can predict the response to therapy.
4. **Neurogastroenterology and Research in endoscopic therapies.**This line of research aims to optimize probiotic treatments for irritable bowel syndrome. Pre-clinical studies will be carried out to improve endoscopic treatment with patches for long-term release of cytostatic or anti-inflammatory drugs.

20. INNATE IMMUNITY

The Innate Immunity group has been active since 2009 and studies Innate Immunity in health and disease. The group conducts research on three important aspects of human pathology: liver disease, atherosclerosis and bacterial infection.

The aim of this group's research is to define the role of Innate Immunity proteins as prognostic or diagnostic biomarkers of disease. They are also generating knowledge for the development of new pharmacological agents that modulate Innate Immune responses. In this context, research interests are at present mostly centred on the role of macrophage protein CD5L in the control of immune homeostasis and inflammatory disease.

Group Leader: **Dr Maria-Rosa Sarrias**

Research Lines

1. **Role of innate immunity in liver disease**
   The main objective is to study microenvironment interactions in the setting of liver disease. Functional studies are focussed on the intercommunication between two key liver cell types, macrophages and hepatic stellate cells, with hepatocytes. With a more clinically oriented goal, we are exploring the potential of several Innate Immunity proteins as biomarkers for the improvement of patient management. Both approaches will lead to a better understanding of the complex mechanisms underlying liver disease.
2. **The role of CD5L and CD36 in the physiology of macrophages in atherosclerosis**
   Under persistent hyperlipidemic conditions, a series of changes in the vessel wall may lead to atherosclerosis, a chronic inflammatory condition in which macrophages play a key role. Complications of atherosclerosis such as plaque rupture and thrombosis are the most common causes of death in Western societies. The group aims to determine the contribution of CD5L and its cellular receptor CD36 to key events of macrophage physiology in the context of atherosclerosis.
3. **The role of CD5L in bacterial infection**
   The Innate Immune response is the first line of defence against invading pathogens. We are devoted to understand the complex interplay between host defence and pathogen evasion. Our studies include the role of CD5L in modulating macrophage responses to bacterial products, from inflammatory molecules (eg LPS) to whole organisms, such as Escherichia coli or Mycobacterium tuberculosis. This line of research opens the door to the discovery of new therapeutic targets.

21. HIGHER DIGESTIVE TRACT MOTILITY RESEARCH GROUP

The Higher Digestive Tract Motility Research Group is a group based at the Mataró Hospital. The goal of the group is to study the physiology of gastrointestinal motility and the pathophysiology of diseases associated with alterations of gastrointestinal motility, which are prevalent diseases with a high impact on health and quality of life of the population. The group combines basic and clinical researchers organized around a General Hospital and the Department of Physiology at the UAB and translates its research activities into clinical practice (Clinical Guidelines and Position Statements).

Group Leader: **Dr Pere Clavé**

Research lines:

1. **Oropharyngeal dysphagia, risk factors and treatment.** Oropharyngeal dysphagia (OD) is a common disorder that affects more than 50% of elderly people in hospital and patients who have suffered ictus or other neurological illnesses. Our objective is to develop neurohabilitation strategies using pharmacological stimulation strategies, electrical intrapharingeal or transcutaneous stimulation, transcranial magnetic stimulation (rTMS) and electrical transcranial stimulation.
2. **Oropharyngeal dysphagia, malnutrition and pneumonia.** Oropharyngeal dysphagia can cause two groups of complications of great clinical importance. The general objective is to study the risk factors for pneumonia from aspiration, malnutrition and dehydration in patients with oesophageal dysphagia. The group develops protocols to reduce the incidence of these complications of OD using a protocol of stimulation.
3. **Colorectal motility.** The general objective of this line is to increase understanding of constipation in different elderly phenotypes in Catalonia. Specifically, this involves the study of prevalence, risk factors, physiopathology and impact on quality of life of constipation in the elderly to their fragility and improving treatments.
4. **Gastro-oesophageal Motility.** The general objective is to broaden understanding of gastro-intestinal and vesical motility in order to discover its relation to appetite control in different population groups such as the robust elderly, fragile elderly, obese individuals and obese individuals who have undergone bariatric surgery.
5. **In vitro intestinal Motility.** This research line centres on the study of human gastrointestinal pathologies which progress with severe disruption to gastrointestinal motility but currently have no specific treatment: diverticular disease and postoperative paralytic ileus.

22. TRANSLATIONAL ENDOSCOPY

The Translational Research in Endoscopy Group (TER Group), comprises members of the Digestive Endoscopy Unit of University Hospital Germans Trias (HUGTIP), and the Institute of Research Germans Trias (IGTP) and aims to translational research the field of endoscopy, oriented to obtain clinical applicability, developing and optimizing new treatment techniques in endoscopy.

The activity of the research lines has resulted in significant contributions that have increased knowledge in gastrointestinal endoscopy. Studies have led to diagnostic and therapeutic innovations to improve the clinical management of patients suffering from diseases of the digestive tract and the development of new medical devices.

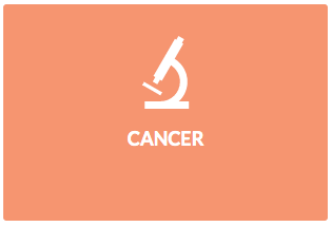
Group Leader: **Dr Vicente Lorenzo-Zuñiga**

Research lines:

1. **Experimental Endoscopy.** We have developed experimental models to reproduce daily clinical practice in gastrointestinal endoscopy.
2. **Experimental Therapy.** Endoscopic shielding technique to prevent complications arising from thermal damage after endoscopic resection. Utility of platelet-rich plasma (PRP) in endoscopic resection

Development an endoscopic platform to perform drug delivery for topical treatment of inflammatory colitis and colonic neoplasms**.**

3. **Bioengineering.** Development of hydrogels "Bi-Bio" bio-absorbable-biodegradable to prevent thermal damage complications after endoscopic mucosal resection and accelerate mucosal healing. Development of hydrogels "Tri-Bio" bio-absorbable-biodegradable-bioactive that act as platforms releasing drugs such as topical treatment of inflammatory or tumorous lesions of the colon. Development of biodegradable stents by using 3-D printer using a combination of various polymers. Development of test strips that allow the diagnosis of gallstones, as a strategy to prevent recurrent choledocholithiasi. Development of flexible needle puncture, allowing the transtumoral cannulation (Tran-Tumor-Cannulation -TTC Needle Needle). Development of delivery system biodegradable stents with endoscopic guidance (Endotri-BDStent-Deployment System -EBD System). Development of applications for smartphones to improve the quality of bowel preparation
4. **Clinical Endoscopy.** Development of clinical practice guidelines (EPAGE II: European Panel for the Appropriateness of Gastrointestinal Endoscopy)
5. **Bowel Cleansing.** Various studies have been performed to improve the quality of bowel preparation and patient satisfaction**.**
6. **Optical Diagnosis.** The group has carried out trials with better endoscopes in order to be able to use a histological approach without obtaining tissue.



23. EPIGENETICS OF CELL DIFFERENTIATION AND CANCER

The main focus of the group's research is the characterization of the molecular mechanisms underlying cancer cell programs and the identification of molecular markers with clinical applications. The other main line is the characterization of the epigenetic changes, which take place normally during muscle lineage-commitment, cell activation and terminal differentiation, which can be altered in muscle pathologies such as muscular dystrophies and rhabdomyosarcomas.

Group Leader: **Dr Miguel Angel Peinado**

Research Lines (led by Dr MA Peinado)

1. **Chromatin architecture in cell differentiation and cancer. Cell properties are determined by programs regulating gene expression**
2. **The role of repeat elements in genome structure and function**
3. **Clinically oriented research on the epigenetic changes involved in human cancer, with a special focus on colorectal cancer**

The group has created Aniling, a spin-off of the IGTP focused on the improvement of next generation genomic technologies to integrate molecular data into biologically and clinically meaningful information. The team have also developed bioinformatic tools to facilitate the access to molecular data generated with the most advanced technologies to scientists and clinicians (http://maplab.cat).

Research Lines (led by Dr Monica Suelves)

4. **DNA methylation dynamics during muscle lineage-commitment, cell activation and terminal differentiation**
5. **Role of HDAC11 in muscle regeneration**
6. **Epigenetic changes in muscle pathologies**

24. CANCER GENETICS AND EPIGENETICS

The group studies tumours from the intestinal tract (i.e. colon, and stomach) that sometimes develop when the cell machinery preserving the integrity of the genome is not working properly. When these corrector genes (mutators) are inactivated, the mutations that occur in all normal cells accumulate in large numbers because they are not repaired. This work includes studies into mutator genes that are not inactivated by mutations (mutator mutations) but by epigenetic silencing and other processes associated with aging. The studies have clinical applications for hereditary cancers. Molecular diagnosis of the deficient mutator genes

determines which members of families will be affected in the future. Identification of tumours with this kind of genomic instability is also useful to detect familial cancer patients and to predict survival.

Group Leader: **Dr Sergio Alonso**

Research Lines

1. **Molecular mechanisms for gastrointestinal cancer pathogenesis.** Our research aims to understand better the mechanisms of genomic instability as a "remote control", and cancer epigenetics as an "ultraremote control" mechanisms underlying tumorigenesis.
2. **Epigenetic biomarkers for cancer susceptibility and metastatic spread.** We are currently analyzing the impact of the alterations in patterns of DNA methylation in genome disruption and studying the applications of these epigenetic somatic alterations for gastrointestinal cancer diagnosis and prognosis.
3. **Genomics and epigenomics of colorectal cancer prediction.** We are starting new projects to discover cancer susceptibility and resistance genes by using genomic and epigenomic approaches.

25. ENDOCRINE TUMOURS

The group's research aims to understand the molecular landscape of endocrine tumours and identify biomarkers with clinical applications (diagnostics, prognostics, response to therapy) and novel therapeutic targets. They focus on thyroid cancer and pituitary adenomas. These tumours have a low prevalence, so they have established a network of national and international clinical collaborators, to speed the advance towards clinically essential information.

Group Leader: **Dr Mireia Jordà**

Research Lines:

1. **Molecular pathogenesis of distant metastatic differentiated thyroid cancer.** Differentiated thyroid cancer (DTC) is usually associated with an excellent prognosis, but the main cause of death is distant metastases. Distant metastatic DTC (dmDTC) presents an interpatient heterogeneity in terms of outcome. Research is focussed on the DNA methylation signatures of these tumours.
2. **Kallikreins, new players in thyroid cancer: regulation, function and clinical use.** In recent years, kallikreins (KLKs) have emerged as important cancer biomarkers. We are currently assessing the clinical utility of KLKs and the functional implications in thyroid cancer.
3. **Molecular pathogenesis of pituitary adenomas.** With the Endocrinology and Nutrition Service at Germans Trias i Pujol Hospital, the group investigates the pathogenesis of pituitary tumours and identies prognostic markers, predictors of response and new therapeutic strategies.
4. **Development of molecular assays for clinical settings.** The final objective of our translational projects is the implementation of our findings in clinical settings. Thus, we are developing molecular tools based on our results compatible with any pathology laboratory.

26. CANCER BIOLOGY AND PRECISION MEDICINE

The group was among the first to perform a large scale screening for epidermal growth factor receptor (EGFR) mutations in lung adenocarcinoma patients. They now focus on demonstrating that as soon as a tumour driver genetic alteration is blocked with a specific targeted therapy, a chimera of compensatory signalling pathways is immediately activated, making the tumour independent of the initial driver oncogene and causing resistance to monotherapy. They also investigate the development of quantitative assays and biomarkers to help patient stratification in future clinical trials. The ultimate aim is to integrate advancements in molecular biology with clinical trials, taking research from the "bench-to-bedside".

Group Leader: **Dr Rafael Rosell**

Research Lines

1. Co-activation of receptor tyrosine kinases in EGFR mutant NSCLC cells and patients
2. Proviral integration site for Moloney murine leukemia virus-1 (PIM1) kinase in EGFR mutant NSCLC
3. Heat shock protein 90 (HSP90) inhibitors to overcome innate resistance to EGFR mutant NSCLC
4. Co-targeting PIM1 or Src to beat the limitations of single MET inhibition
5. Defeating the signalling that mediates streaming and metastasis in early stage tumours treated with adjuvant chemotherapy
6. Combinations with cyclin D-dependent kinase (CDK) 4/6 inhibitors in KRAS mutant NSCLC and not only
7. Landscape in KRAS mutant lung cancers and therapeutic principles
8. PAK [p21 (RAC1) activated kinase] inhibitors and combinatorial approaches in lung cancer cell lines
9. Novel approaches for the treatment of head and neck squamous cell carcinoma
10. Towards widespread clinical application of blood-based diagnostic tools. The European Liquid Biopsies Academy
11. Implementation of liquid biopsy as a tool for cancer diagnosis and follow up in our patients.

27. BADALONA APPLIED RESEARCH GRUP IN ONCOLGY (B-ARGO)

The Group Badalona applied research group in oncology (B•ARGO) is a new transversal organization of the basic, translational and clinical research that has been carried out for many years at the IGTP and the Germans Trias University Hospital (HUGTiP). It has been set up to coordinate and increase the research effort on translational cancer at the IGTP in conjunction with clinical care professionals at the HUGTiP and the Catalan Institute of Oncology (ICO) Badalona, also carrying out cancer healthcare at the hospital.

The multidisciplinary group is made up of over 30 professionals working on the different aspects of research. B•ARGO is concentrates its work in **three main areas**:

1. Thoracic tumours, sarcoma and tumours of the nervous system, with an emphasis on radiotherapy research.
2. Reproductive tumours of breast, germinal cell and gynaecological origin and tumours of the head and neck.

3. Digestive, urological neuroendocrine tumours and tumours of the skin and carcinomas of unknown primary (CUP).

Group Leader: **Dr Ricard Mesía**

28. HEREDITARY CANCER

The group investigates genetic diseases that confer a high predisposition to develop cancer. They study the genetics of these cancer syndromes, the molecular basis of the associated clinical manifestations and in particular, the molecular pathogenesis of the associated tumours. Among the different cancer syndromes, our group is focused in the Neurofibromatoses (NFs) and related diseases like the RASopathies. The group also performs the genetic diagnostics of Neurofibromatoses and RASopathies and participates of the CSUR of Phakomatoses Germans Trias i Pujol University Hospital - Institut Català d'Oncologia (HGTiP-ICO). Finally, the group is also committed to the development of new tools for the genetic diagnostics of hereditary cancer jointly with the Hereditary Cancer Program at ICO.

Group Leader: **Dr Eduard Serra**

Research Lines

1. **Cancer genomics and integrative biology**
   Genomic analyses at different levels (genomics, transcriptomics, epigenomics) and use different types of materials (primary tumours, primary cell lines, selected cell types, in vitro and in vivo models, iPSCs, etc) to investigate on tumour formation, development and dissemination, upon the integration of all this information by using bioinformatics.
2. **Stem cell and iPSC-based models for cancer and regeneration**
   Research into the identity and behaviour of the cell type that originates benign tumours of the peripheral nervous system (PNS) associated to the NFs. Generation of iPSCs directly from NF-associated benign tumour cells and development of tumoroid models, from iPSCs or directly from tumours. We want to use iPSCs also to understand the formation of cells of the PNS and use them with regeneration purposes.
3. **Molecular pathogenesis of the Neurofibromatoses and related diseases**
   Investigation of the molecular basis of the Neurofibromatoses and RASopathies and their associated clinical traits. Research into the clinical presentations of patients visited at the Phakomatoses CSUR HGTiP-ICO or other clinical settings, or by using models that facilitate experimental approaches.
4. **Innovation for the genetic diagnostics**
   Together with the Hereditary Cancer Program at ICO we are constantly trying to improve the genetic diagnostics of hereditary cancer. We try to develop cost-effective strategies that efficiently allow the identification and interpretation of disease-causing mutations using genomic and bioinformatics techniques.

29. RESISTANCE CHEMOTHERAPY AND PREDICTIVE BIOMARKERS

This group works on the molecular processes through which tumour cells develop resistance to chemotherapy during the treatment of colorectal cancer (CRC) and melanoma (MLN) patients. By identifying the factors responsible for this chemoresistance, the researchers aim to discover biomarkers that will improve the selection of effective treatments for patients and lead to the development of new therapeutic strategies.

Group Leader: **Dr Eva Martínez Balibrea**

Research lines:

1. **Predictive biomarkers for treatment selection**
   Study of the somatic genetic polymorphisms within genes involved in pharmacodynamics and pharmacokinetics processes affecting the effectiveness of a given chemotherapeutic drug or its related toxicity. Secondly, the study of tumour gene and/or protein expression patterns that could be associated with resistance to chemotherapy and that could serve as clinical biomarkers to select treatments.
2. **Development and study of in vitro models of acquired resistance to chemotherapy**
   The study of changes in patterns of gene or protein expression and DNA-methylation associated with resistance acquisition by using high-throughput techniques. Secondly the elucidation of the mechanisms responsible for resistance acquisition to chemotherapeutics and define new putative predictive biomarkers. Thirdly, the identification of new ways of therapeutic intervention able to revert this chemoresistance.

30. CHILDHOOD LIVER ONCOLOGY (C-Log)

The group forms part of the Gastroenterology department of the hospital (HUGTiP), it is also part of the CIBERehd. The cLOG research lines based on increasing the molecular knowledge of the underlying mechanisms responsible for hepatocarcinogenesis and tumour progression. We use the latest omics and sequencing technologies in order to identify diagnostic/prognostic biomarkers and key molecular pathways for improving the clinical management and treatment of children suffering from liver cancer.

Group Leader: **Dr Carolina Armengol**

Research lines:

1. **Collection of biological samples from liver cancer patients**
   Collection of biospecimens from national childhood liver cancer patients. Currently collecting 70-805 of these samples in Spain. Participation in the H2020 ChiLTERN project also permits collection of samples from European paediatric patients with liver cancer enrolled in the first international clinical trial (PHITT).
2. **New insights into hepatoblastoma (HB) through proteomic profiling.**
   Performance of proteomic studies of HB and identification of new prognostic markers.
3. **Study to prospectively validate the use of biomarkers in clinical practice.**

The present ongoing study is part of the European ChiLTERN project, aimed at examining the expression/presence of a panel of biomarkers.

4. **Comprehensive molecular characterization of hepatoblastoma.**
   Integration of RNA-sequencing, genomic, epigenomic and transcriptomic data with the aim of increasing the molecular knowledge of HB.
5. **Establishment of pre-clinical models of childhood liver cancer.**
   Development of new translational models of childhood liver cancer based on the establishment of orthotopic Patient-Derived Xenografts (PDXs) and organoid cultures.

31. LEUKEMIA RESEARCH

Research into leukaemia on the Can Ruti Campus is carried out in the Josep Carreras Leukaemia Research Institute (IJC) on its Campus ICO-Germans Trias i Pujol. The CMI groups work in complete coordination with other groups and institutions on the campus, which whom they share basic facilities and support services. The mission of the IJC is to research the basic, epidemiological, preventive and transferable clinical aspects of leukemia pathologies and of other malignant blood diseases.

Group Leader: **Dr. Manel Esteller**, Director elect of the Josep Carreras Leukemia Research Institute, and Dr**. Francesc Solé,** Scientific Director, IJC Campus ICO-GTiP

RESEARCH LINES:

- Acute Lymphoblastic Leukemia (ALL)
- Barcelona Endothelia Team (BET)
- Chromatin, Metabolism and Cell Fate
- 3D Chromatin Organization
- Endocrine Regulatory Genomics
- Functional Cytomics
- Genetics and Epigenetics in Myeloid Neoplasias
- Immunohematology and Glycobiology
- Iron Metabolism: Regulation and Disease
- Leukemia Stem Cell Group
- Lymphoid Neoplasias
- Multiple Myeloma Group
- Myelodysplastic Syndromes
- Regulatory Genomics
- Stem Cell Biology, Developmental Leukemia and Immunotherapy
- Stem Cell Transplantation

32. VASCULAR PATHOLOGY OF THE BRAIN

The research area of cerebral vascular pathology at the Germans Trias Institute was set up in 2005 by the Clinical Director of the Department of Neuroscience and director of the Germans Trias i Pujol Hospital to promote translational research.

Group Leader: **Dr Antoni Dávalos**

Research lines:

1. Endovascular treatment of acute ictus: clinical trials REVASCAT, DAWN
2. Reperfusion intravenous therapies and neuroprotection: clinical trials DIAS-3/4, WAKE-UP, TANDEM
3. New treatments for secondary prevention of ictus: clinical trials SOCRATES, NAVIGATE-ESUS
4. Futile Rechanneling in Ischemic Acute Stroke (FURIAS): Study of new RM imaging markers for predicting future recanalization in patients undergoing vascular therapy in the acute phase of ictus.
5. Use of the RACE pre-hospital clinical scale to determine the level of specialization offered to patients with acute ictus in function of its severity and to organize new referral circuits for patients.
6. Asymptomatic cerebral atherosclerosis (AsIA Study): population study of prevalence of asymptomatic intracraneal estenosis and its relation to vascular risk, cardiovascular risk and risk of dementia.
7. Study of intracranial plaques (PROYECTO CRYPTICAS): Study using new HRMR sequences of intracraneal atherosclerotic plaques in atherothrombic ictus and cryptogenic ictus.
8. Neuroplasticity, cognitive function and neuroimaging in ischemic cerebral ictus: study of cognitive prognostics, structural changes in white matter, functional RM and cognitive alternations in acute ictus.
9. Neurotoxicity of iron in cerebral ischemia
10. STR01-STROKECHIP: Validation of a panel of biomarkers for precocious diagnostic of ictus and differentiation from analogous conditions and from ischemic ictus and haemorrhagic ictus.
11. Influence of grades of physical activity previous to ictus on functional prognostic, haemorrhagic transformation and arterial rechanneling in acute occlusion of the median cerebral artery.

33. CELLULAR AND MOLECULAR NEUROBIOLOGY

The objective of the group is to foster basic and translational research in the stroke field. Our goal is to generate knowledge, test it into preclinical models of stroke and translate it to the clinical arena in order to provide a better life for stroke patients.

Group Leader: **Dr Teresa Gasull Dalmau**

Research lines:

1. **New generation therapies to protect the brain after stroke**
   As the result of our research, apotransferrin, a protein naturally present in the blood, is being developed as a new therapy for stroke. In an experimental stroke model, we have recently identified a novel candidate for the treatment of stroke that exerts actions at the frontier of neuroprotection and neuro-repair. A proteomic approach in in vitro studies has identified novel potential target candidates downstream the N-methyl-D-aspartate (NMDA) receptor. Its potential to prevent stroke damage is currently being further evaluated using in vivo preclinical studies.

2. **Biomarkers for successful and differential diagnosis of stroke subtypes and personalized therapy**
   We have recently found a biomarker in the blood for ischemic stroke patients at admission. Specific posttranslational modifications of this and other biomarkers are being re-examined to reach an improved specificity and sensitivity to diagnose stroke subtypes and differentiate ischemic or hemorrhagic events. Blood biomarkers are under evaluation to personalize and improve the therapeutic benefit of apotransferrin in selected stroke patients.
3. **In vivo molecular bioimaging to assess pathological hallmarks of stroke**
   In vivo molecular imaging of apoptosis, inflammation, BBB disruption, and homing of traceable adoptive cells in the brain ischemic areas are used to assess pathological hallmarks after experimental stroke.

34. NEUROMUSCULAR AND NEUROPEDIATRIC RESEARCH GROUP

The multidisciplinary research group includes clinicians from the hospital neurology and paediatric services and specialized basic researchers in the laboratory. The main objective is to find treatments for neuromuscular and neuropediatric diseases that have no cure yet. As well as working on the management of patients, the researchers are constructing a powerful patient database, have broad expertise in genetic, transcriptomic and proteomic techniques for studying the pathogenicity of the disease at the molecular level and is experienced in testing treatments in vitro, in vivo and in patients.

Group Leader: **Dr Gisela Nogales**

Research lines:

1. **Myotonic distrophy type I**
   The most prevalent dystrophy in adult. We are working currently in two research areas in this disease: 1) testing the therapeutic value of antisense for these patients in vitro; 2) identifying new biomarkers for diagnosis, symptoms prevention, or treatment follow-up.
2. **Myotonic Distrophy type II**
   Myotonic dystrophy type II has a similar genetic defect than myotonic dystrophy type I, with lower prevalence and a milder presentation. Recently a non-classic debut symptomatology has been identified

revealing that many cases remain undiagnosed. We are working on better diagnosis, segmentation and prognosis with a view to better treatments.

3. **McArdle Disease or Glycogenosis type V**
   McArdle disease is a metabolic disease with genetic causes. We are optimizing the genetic diagnosis strategies for this disorder and evaluating exercise intervention for patients Exercise can have a serious impact in the well-being and improve patients' quality of life.

35. NEUROGENETICS

The Neurogenetics Research Group provides genetic diagnoses for the Neurology and Paediatrics Services. Scientific research focusses on the genetic and molecular mechanisms underlying neurodegenerative processes. It uses multidisciplinary strategies to identify genes, proteins and other gene products involved in the function and dysfunction of the nervous system by using next-generation RNA and DNA sequencing, functional assays, biochemical, proteomics, and molecular neurosignaling studies. An important objective of the group is to identify and implement treatments for various neurodegenerative diseases. It uses gene therapy technology based on adeno-associated virus vectors (AAV), screenings of drug compounds and genetic libraries, and in vitro and in vivo preclinical testing of new therapeutic candidates.

Group Leader: **Dr Antoni Matilla**

Research lines:

1. **Identification of the genetic causes and molecular mechanisms underlying hereditary ataxias and paraplegias**
   Identification of the gene and the genetic cause associated with spinocerebellar ataxia type 37 (SCA37). Characterization of the underlying molecular mechanisms. Study of the genetic defects underlying neurodegeneration in ataxias and spastic paraplegias. Identification of mechanisms underlying neurodegeneration in spinocerebellar ataxia type 1 (SCA1).
2. **Therapeutic treatments in a mouse model of Friedreich's Ataxia**
   Gene therapy with vectors based on adeno-associated virus (AAV) in a mouse model of Friedreich's ataxia. Restoration of frataxin deficits and mitochondrial function with adeno-associated vector on a mouse model for Friedreich's ataxia
3. **Therapeutic treatments in a mouse model of mucopolysaccharidosis IIIB (Sanfilippo syndrome B) type**
   Evaluation of the substrate reduction strategy to decrease GAGs content in a mouse model of Sanfilippo B Syndrome. Evaluation of modulation of autophagy and neuroimmunomodulators as therapeutic treatments in a mouse model for Sanfilippo B Syndrome
4. **Identification of neurosignalling mechanisms and potential therapeutic targets**
   Determination of the role of protein phosphatase PP2A and its inhibitor Anp32a in neurodegeneration. Identification of genetic and chemical modulators of autophagy in Sanfilippo B cell models. Identification of molecular mediators of mitochondrial dysfunction in cellular models of Friedreich's ataxia, spinocerebellar ataxia, and Alzheimer's disease by genetic and chemicals screenings
5. **Genetic diagnosis of more than 400 neurological diseases**

Development and implementation of next-generation sequencing technologies and bioinformatics tools to identify and characterize genetic causes underlying neurological diseases.

36. GENOMICS AND TRANSCRIPTOMICS OF SYNNUCLEOPATHIES

Synucleinopathies encompass three diseases that are characterized by abnormal α-synuclein oligomerization and deposition in specific brain areas: Parkinson's disease (PD), dementia with Lewy bodies (DLB) and Alzheimer's disease (AD)

Research focuses on the molecular characterization of Lewy body diseases, including both genomic and transcriptomic research. The group characterized the first molecular subgroup of DLB, which has opened new avenues in the research of Lewy body diseases and revealed the possible existence of a new therapeutic target for at least one specific subgroup of DLB patients.

Neurodegenerative disorders are characterized by a high grade of heterogeneity. The goal is to identify these different mechanisms for defining different disease subgroups. This is essential for better diagnosis and more personalized treatments. The group has file four patents.

Group Leader: **Dr Katrin Beyer**

Research Lines

1. **Molecular characterization of Lewy body diseases**
   Search for genetic variation (2) Expression analysis of genes involved in the pathogenesis of Lewy body disorders and of alternative splicing (3) Analysis of miRNAs expression changes in brain and blood. (4) 3'UTR variation analysis of genes involved in the pathogenesis of Lewy body disorders. (5) Functional and integrated analyses
2. **Identification of diagnostic biomarkers for dementia with Lewy bodies**
   Translation of findings made in post-mortem brain samples to blood and saliva to identify peripheral diagnostic biomarkers for Lewy body disease for clinical use.
3. **Establishment of cell and animal models suitable for testing of results**
   Implementation of the *Octodon degus* animal model. For AD and DLB.

3.2. Strategic research projects

In terms of the “Big Science” initiatives, we are proud of the overall performance of the institute. Specifically, the IGPT has been able to lead forward two strategic projects the GCAT Project of Genomes for Life (http://www.gcatbiobank.org/en_index/) and the Centre of Comparative Medicine and Bioimage (CMCiB).

GCAT genomes for life

IGTP Staff involved in the project:

- Rafael de Cid
- Miguel Angel Peinado
- Manel Puig Domingo

The mission of the former Institute of Predictive and Personalized Medicine of Cancer (IMPPC), now the PPMC Program within the IGTP, is to carry out a research of excellence in cancer prediction and become a reference centre nationally and internationally. The Program on Genomics and Epigenomics of Cancer Prediction, pioneer in its concept and research tasks, is essential to reach these objectives. While genomic studies have recently yielded the identification of genetic variants (polymorphisms) associated with increased cancer risk, the contribution of similar epigenetic variants is essentially unexplored at present. This dynamizing action is the best formula to finance this Program that depends heavily on the existence of a DNA bank that requires considerable investment due to its large scope. The loan requested will permit the creation of a prospective DNA biobank of some 70,000 samples from healthy individuals. This bank will be complemented with 10,000 samples of individuals suffering from common neoplastic pathologies, which will be available through a subcontract of a transversal DNA bank from Neocodex Inc. This subcontract will make it possible to use the samples at time zero in the project for association studies and will provide the informatic infrastructure and the know-how that will facilitate and streamline the creation of the longitudinal DNA bank. The researcher responsible for the Project was Manuel Perucho and is currently Manel Puig Domingo. Both the program and its associated DNA bank are references for the National health System and the samples and the attached information are already available to the scientific community.

Comparative Medicine & Bioimage Centre (CMCiB)

IGTP Staff involved in the project:

- Miquel Angel Gasull Duro
- Sara Capdevila
- Pere Joan Cardona
- Manel Puig Domingo

The scientific activity and technological transfer of the IGTP have been focused in recent years on 5 great areas of medicine: cardiology, digestive, infectious diseases, immunology and neurology. This activity, mainly based on the study of the diseases, their diagnosis and treatment through experimental animal models, has increased so much in the past 5 years that the capacity of the facility for small animals has become insufficient. Additionally, the increasing need to use bigger mammals such as pigs as animal models, due to their high similarity with humans, has also become a challenge, as the current facility doesn't include any suitable area for them and it is necessary to establish collaborations with third parties at high costs. Both difficulties are currently being overcome by establishing priorities in the distribution of resources, with an associated loss of opportunities and competitiveness as an outcome. This further complicates the translational ability of research groups in spite of being in their most productive phase. For this reason, the creation of a new building is planned, including an enlargement of the capacity to host small animals and the inclusion of areas to host big animals, expected to solve the spatial problems; and to improve research capacity by implementing a centralized system of caring for the hosted animals. The creation of this new centre should have an impact on the research and the translationality of the groups involved and provide a stimulus to other emergent groups, which might benefit from this improved capacity. The development of a Centre for Comparative Medicine is a crucial action for the IGTP. The use of small and large animal models for pre-clinical trials and proof of concept studies are key for the development of advanced therapies from the "bench to the bedside".

The Comparative Medicine and Bioimage Centre of Catalonia (CMCiB) has become a reality at the campus. Its activity dedicated to biomedical research and training is already active aiming to become a reference centre for comparative medicine, surgery, bioimaging and computational models in Europe, while at the same time developing alternative research methods. Located on the health and research campus Can Ruti in Badalona the centre is integrated with the campus and the environment. It is close to the

hospital and other research centres at Can Ruti and is a centre of excellence for translational research and continuing education for health professionals

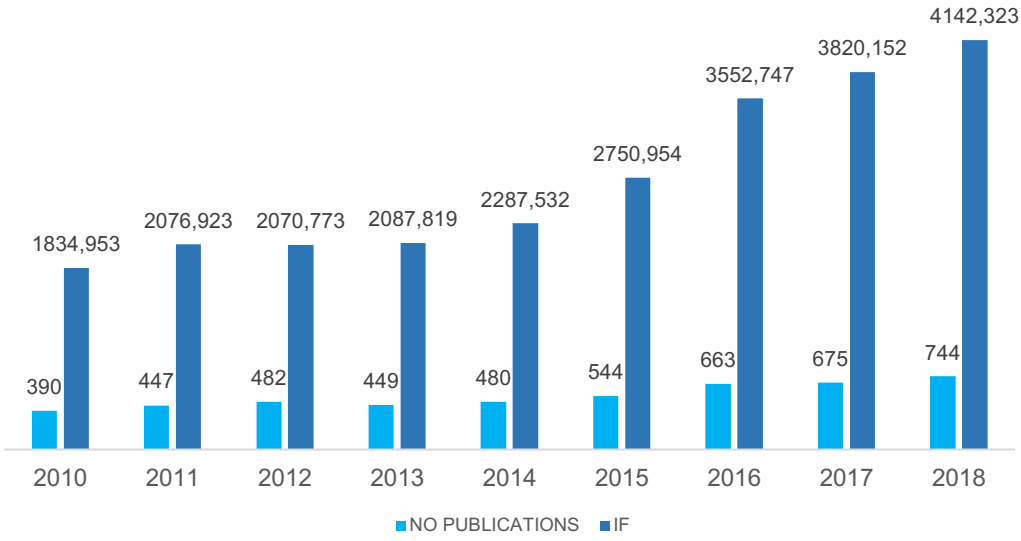
4. FACTS AND FIGURES

4.1 PUBLICATIONS

NO PUBLICATIONS	TOTAL IF	Q1	D1
744	**4,142.3**	**368** publications **49,46%**	**155** publications **20,83%**

Evolution

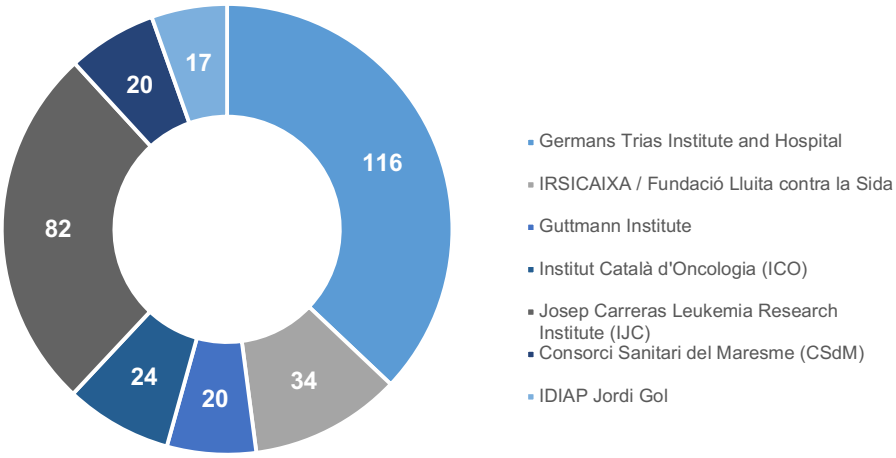
	2011	2012	2013	2014	2015	2016	2017	2018
No. publications	447	482	449	480	544	663	675	**744**
Impact Factor	2076,92	2066,5	2084,47	2287,53	2750,95	3552,75	3820,15	**4142,3**
Publications 1st decile	92	92	82	108	136	133	148	**155**
% 1st decile	20,58%	19,09%	18,26%	22,50%	25,00%	20,06%	21,93%	**20,83%**
Publications 1st Quartile	225	243	239	285	320	380	335	**368**
% 1st Quartile	50,34%	50,41%	53,23%	59,38%	58,82%	57,32%	49,63%	**49,46%**
Principal Investigators	99	98	105	110	132	163	155	**153**
Average publications/PI	4,515	4,918	4,276	4,364	4,121	4,067	4,355	**5,061**


4142,323
3820,152
3552,747
2750,954
2287,532
2087,819
2076,923
2070,773
1834,953
390
447
482
449
480
544
663
675
744
2010
2011
2012
2013
2014
2015
2016
2017
2018
NO PUBLICATIONS
IF

4.2 COMPETITIVE RESEARCH PROJECTS

ACTIVE PROJECTS	NEW NATIONAL PROJECTS	NEW INTERNATIONAL PROJECTS
313	45	10

Projects by institution



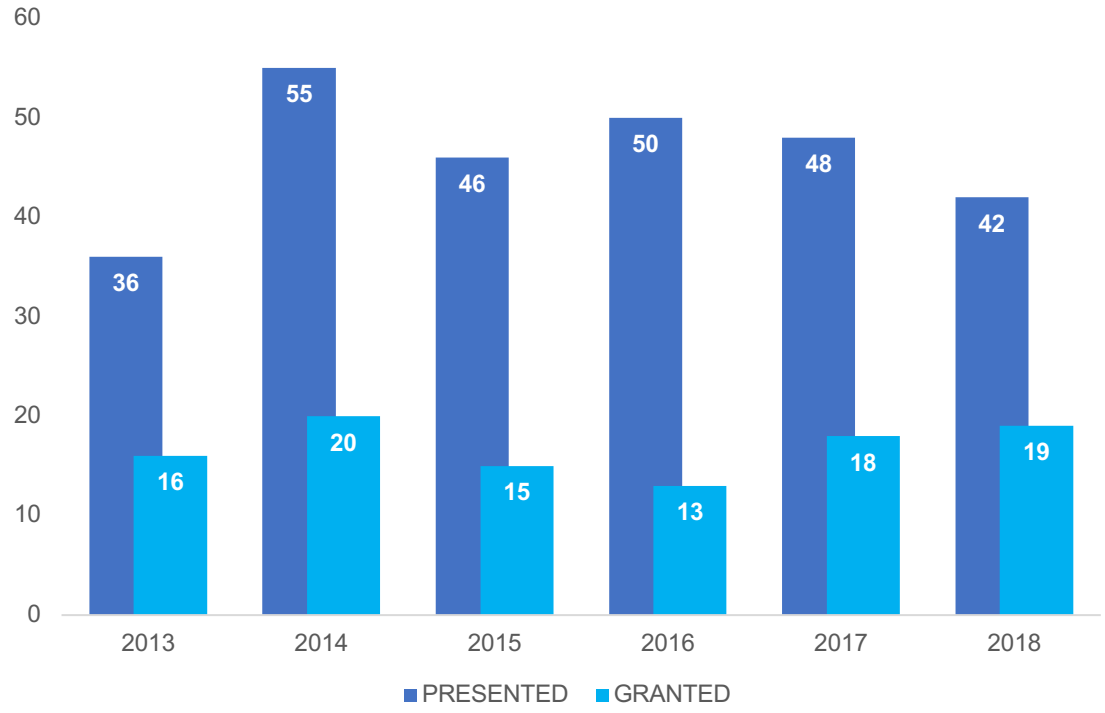
GRANTED PROJECTS

New research projects 2018		**45**
	National	35
	Internacionales	10
New human resources grants 2018		**9**
	National	7
	Autonomous Community	2

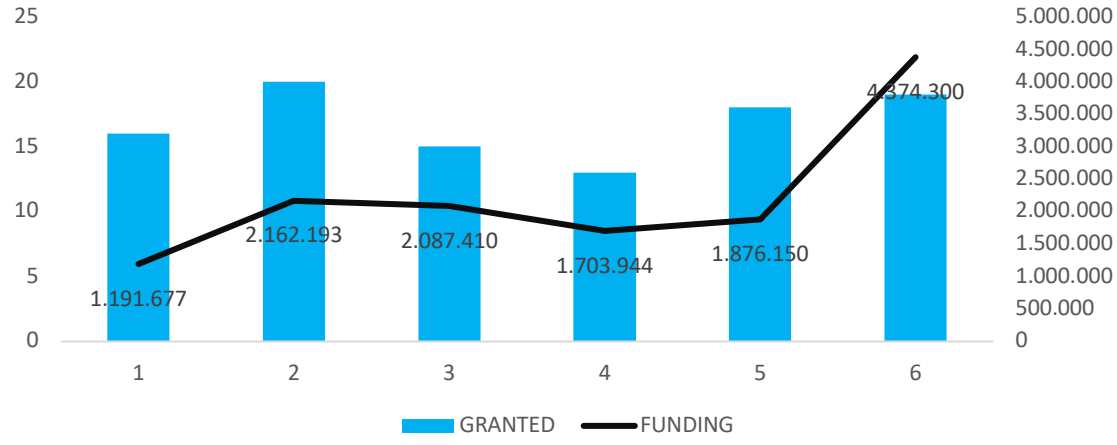
ACTIVE PROJECTS

Active projects		**119**
	National	99
	International	20
Active human resources grants		**25**
	National	18
	Autonomous Community	7

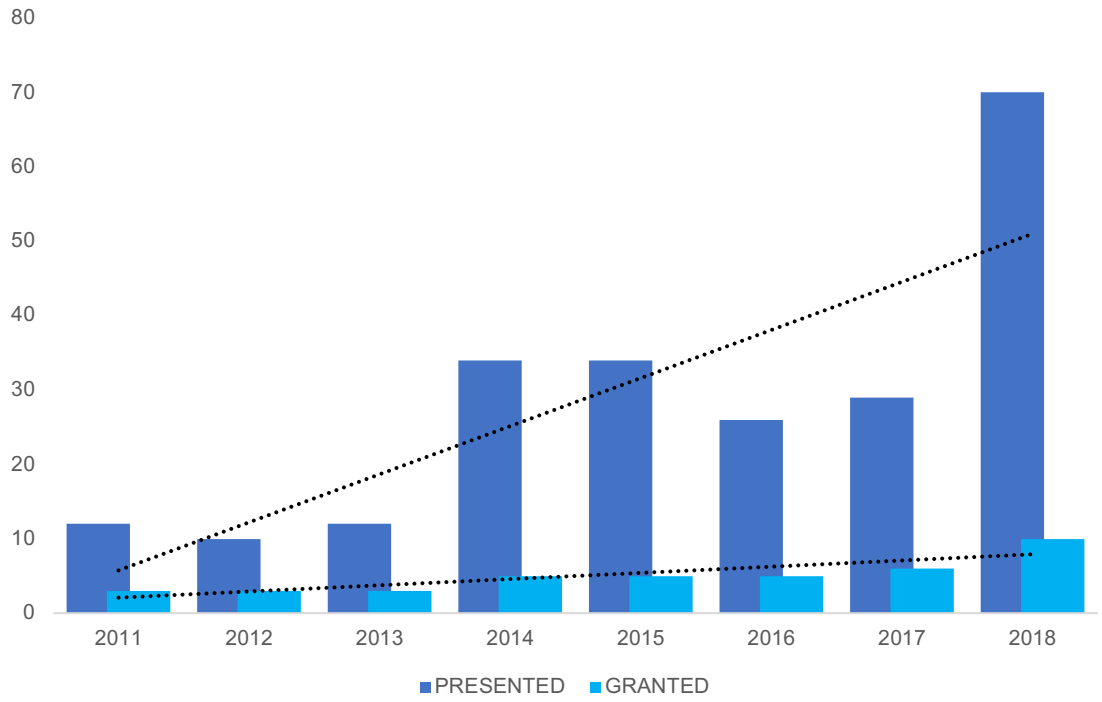
Evolution of awarded projects by ISCiii



Evolution of awarded projects and funding by ISCiii



Evolution of awarded international projects



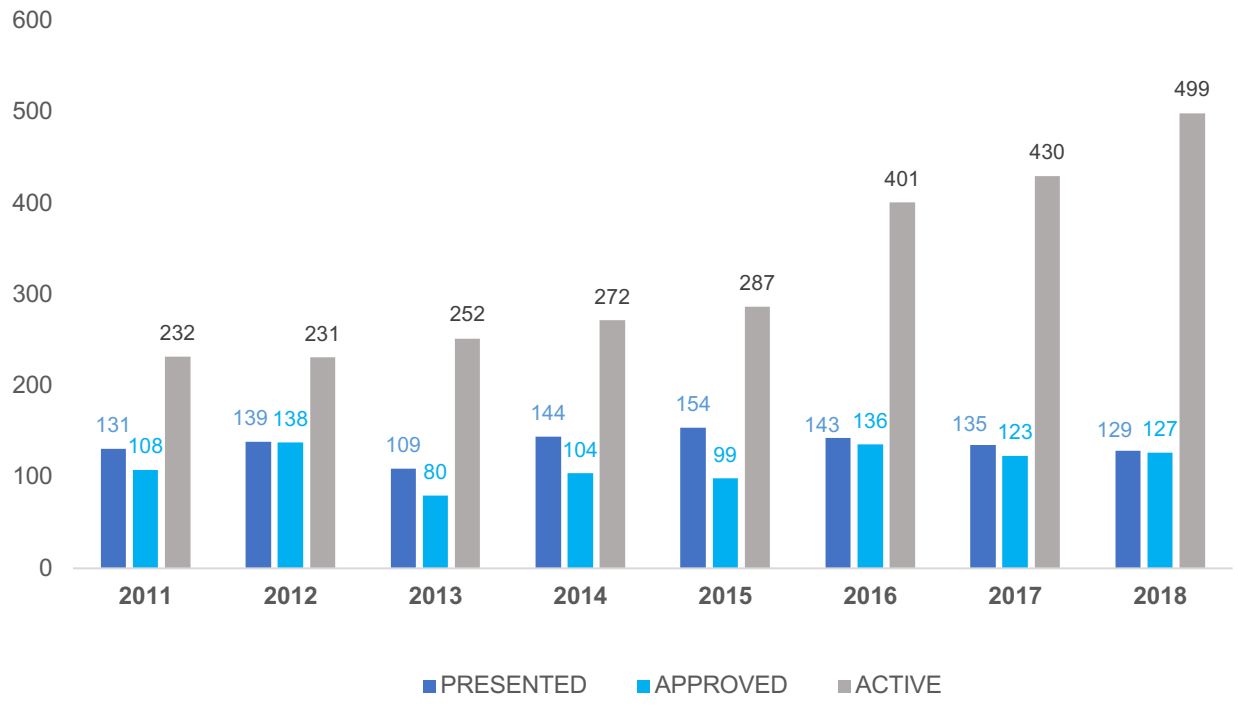
4.3 INNOVATION AND TECH TRANSFER

NEW PROJECTS	LICENSE AGREEMENTS	NEW SPIN-OFF
16	3	1

	2014	2015	2016	2017	2018
New Projects in 'idea' valorizing or development phases	25	32	50	35	**16**
Collaboration/Service… agreements signed	56	60	68	105	**58**
New priority patents filed	4	6	2	6	**5**
Licence agreements	1	2	5	2	**3**
Spin-off created	2	-	1	3	**1**
Income from licence agreements	-	-	-	34,100€	**19,372€**

4.4 CLINICAL TRIALS

PRESENTED	APPROVED	ACTIVE
129	127	499



	2011	2012	2013	2014	2015	2016	2017	2018
Presented	131	139	109	144	154	143	135	**129**
Approved	108	138	80	104	99	136	123	**127**
Active	232	231	252	272	287	401	430	**499**

4.5 HUMAN RESOURCES

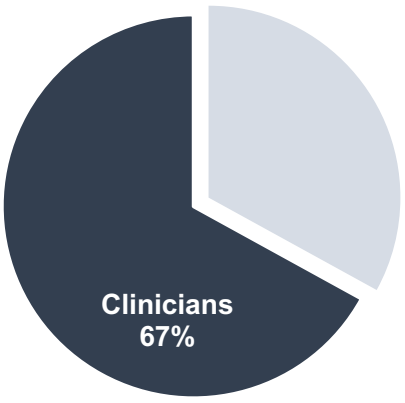
TOTAL PEOPLE INVOLVED ON RESEARCH

742

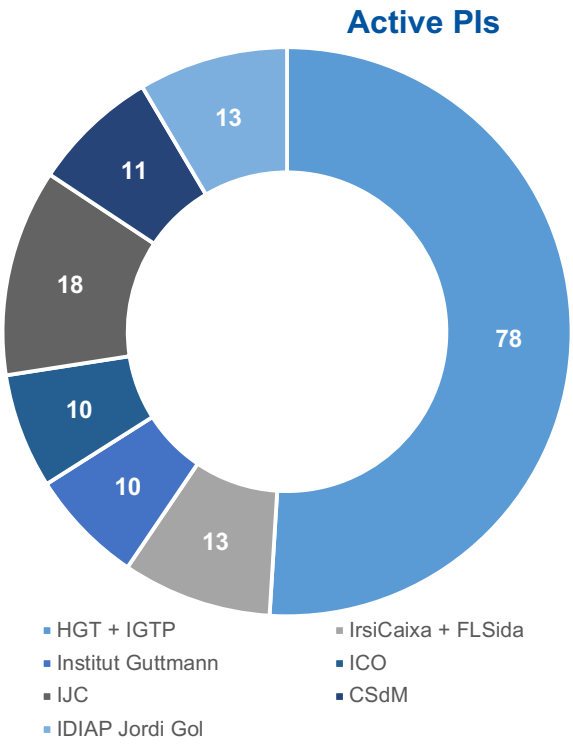
PRINCIPAL INVESTIGATORS

153

Collaborators/support staff	
Medical Doctors	**324**
Postdoctoral Fellows	**77**
Predoctoral Fellows	**122**
Research Nurses	**70**
Technicians	**84**
Administrative staff	**65**



BY GENDER
55% women
45% men



5. CORE FACILITIES

Projects

	PROJECTS 2018				TRAINING ACTIVITIES
	IGTP	Campus Can Ruti	External	Total	
Biobank	40	5	13	58	
High Performance Computing	6	9		15	
Cytometry	19	13	7	39	XX Edition Flow Cytometry Fundamentals and Applications. Flowy Cytometry Course in the Masters in Immunology UB/UAB
Cryobiology	34	8	3	45	
Translational Genomics	25	12	5	42	Flow RT-PCR Course in the Masters in Immunology UB/UAB
Genomics and Bioinformatics	16	11	8	35	
Histopathology and Electron Microscopy	15	1	2	18	
Microscopy	14	3	2	19	
Proteomics and Metabolomics	6	2	5	13	

The summary of the scientific services and consultation services can be found on our web site http://www.germanstrias.org/technology-services/technology-and-services/.

6. ECONOMIC SUMMARY

Income from contracts, agreements and clinical trials represents 38.86% of the IGTP income, it is the most important source of income in the institution.

Income from projects financed by official organizations represents 23.96% (including funds from official organizations, subsidies from official organizations and European funds).

Income from the Government of Catalonia to covr running costs represents 11.61% of total income.

Income statement

INCOME	€
Clinical trials and contracts with industry	7,540,839.32
Donations	113,362.09
Offical subsidies for contracting personnel	512,778.17
Offical subsidies for general costs	2,253,763.41
Projects financed by government agencies	3,019,052.31
Projects financed by European agencies	1,118,797.53
Projects financed by non-governmental bodies	1,433,065.43
Other income	316,685.23
Project overheads	959,159.19
Capital grants transferred to income	1,470,049.00
Work carried out for fixed assets	640,368.70
Exceptional revenues	10,120.93
Financial revenues and exchange differences	14,668.29
TOTAL	**19,402,709.60**

EXPENDITURE	€
Consumption	1,697,298.12
Work carried out by companies	1,930,536.59
Wages and salaries	7,186,330.89
Social security contributions	1,990,411,73
Depreciation for the period	1,688,965.94
Aid granted	900,308.26
Repairs and maintenance	499,855.97
Independent professional services	918,831.21
Supplies	705,657.63
Other expenditure	1,602,343.14
Taxes	57,752.19
Other costs of day-to-day running	96,809.76
Financial costs and exchange rates	369,838.04
TOTAL	**19,644,936.47**

ANNUAL RESULTS	**-242,229.87**

Balance sheet

ASSETS	
A) NON-CURRENT ASSET	**29,414,670.70**
Intangible fixed assets	11,833,543.34
Tangible fixed assets	17,563,195.92
Long-term investments in companies	2,500.00
Financial long-term investments	15,431.444
B) CURRENT ASSETS	**31,063,313.35**
Clients, sponsors and other debtors from activities	17,144,782.78
Short-term financial investments	956,781.08
Short-term accruals	57,042.46
Cash and others	12,904,707.03
TOTAL ASSETS	**60,477,984.05**

LIABILITIES	
A) NET EQUITY	**19,408,570.87**
Endowment funds	623,957.67
Surplas from previous years	6,930,872.07
Surplas from the year	-242,229.87
Grants, donations and legacies	12,095,971.03
B) NON-CURRENT ASSETS	**18,243,958.90**
Long term debts	17,475,181.70
LT debts with organizations in the group and associates	768,777.20
B) CURRENT ASSETS	**22,825,454.28**
Short term debts	12,984,550.82
ST LT debts with organizations in the group and associates	51,251.82
Creditors for business activities and others	2,390,749.99
Short term accruals	7,398,901.66
TOTAL LIABILITIES	**60,477,948.05**

7. INSTITUTIONAL AND SCIENTIFIC HIGHLIGHTS

JANUARY

Germans Trias surgeons devise Rutilight® to improve illumination during operations (+ info)

The new Spin-off Ahead Therapeutics SL, will develop new therapies for auto-immune diseases

FEBRUARY

Can Ruti ¡shows its rare' on Rare Disease Day

APRIL

20,000 healthy people from across Catalonia participate in a macro research project to better understand the risk factors for the most common diseases

JUNE

Huge turnout for the first Can Ruti PhD Day

Beatriz Mothe awarded ex aequo at the 10th Research Symposium of the ICS

JULY

The Comparative Medicine and Bioimage Centre of Catalonia (CMCiB) opens for business

SEPTEMBER

Germans Trias researchers lead an international clinical trial to halt the advance of multiple sclerosis using cell therapy

OCTOBER

Can Ruti Campus presents an international seminar series on biomedical research

Overview on recommendations on alcohol consumption for patients with liver disease

New IGTP spin-off to develop gene therapy for Friedreich's ataxia, a rare neurodegenerative disease

DECEMBER

"Covergel" recognized by the MIT Institute for Medical Engineering and Sciences

ANNEX 1
2018 Publications

Crespo Cuevas AM, Hervás Garcia JV, Abraira Del Fresno L, Grau López L.	2018 Mar;33(2):135-137. doi: 10.1016/j.nrl.2016.01.003. Epub 2016 Mar 10. English, Spanish. No abstract available.	Cranial mononeuritis multiplex as the initial manifestation of systemic lupus erythematosus: A diagnostic challenge.	0213-4853
Navarro-Artieda R, Rejas-Gutiérrez J, Pérez-Paramo M, Sicras-Mainar A.	2018 Apr;33(3):141-153. doi: 10.1016/j.nrl.2016.03.012. Epub 2016 Jun 16. English, Spanish.	Clinical and economic consequences of treating patients with peripheral neuropathic pain with brand name or generic drugs in routine clinical practice: The effects of age and sex.	0213-4853
Llibre JM, de Lazzari E, Molina JM, Gallien S, Gonzalez-García J, Imaz A, Podzamczer D, Clotet B, Domingo P, Gatell JM.	2018 Jan;36(1):16-20. doi: 10.1016/j.eimc.2016.07.006. Epub 2016 Aug 29. English, Spanish.	Cost-effectiveness of initial antiretroviral treatment administered as single vs. multiple tablet regimens with the same or different components.	0213-005X
Soriano-Arandes A, Noguera-Julian A, López-Lacort M, Soler-Palacín P, Mur A, Méndez M, Mayol L, Vallmanya T, Almeda J, Carnicer-Pont D, Casabona J, Fortuny C.	2018 Jan;36(1):9-15. doi: 10.1016/j.eimc.2016.07.011. Epub 2016 Sep 5. English, Spanish.	[Pregnancy as an opportunity to diagnose human-immunodeficiency virus immigrant women in Catalonia].	0213-005X
Hurtado-Pardos B, Casas I, Lluch-Canut T, Moreno-Arroyo C, Nebot-Bergua C, Roldán-Merino J.	2018 Jan 2;73(1):29-37. doi: 10.1080/19338244.2016.1246411. Epub 2016 Oct 20.	Psychometric Evaluation of a New Instrument in Spanish to Measure the Wellness Nursing Faculty in University.	1933-8244
Sorigue M, Maluquer C, Junca J.	2018 Mar;94(2):374-378. doi: 10.1002/cyto.b.21517. Epub 2017 Feb 21.	Phenotypic characterization of trisomy 12 monoclonal B-cell lymphocytosis.	1552-4949
Simó M, Rifà-Ros X, Vaquero L, Ripollés P, Cayuela N, Jové J, Navarro A, Cardenal F, Bruna J, Rodríguez-Fornells A.	2018 Apr;12(2):369-382. doi: 10.1007/s11682-017-9697-8.	Brain functional connectivity in lung cancer population: an exploratory study.	1931-7557
Hernández-Boluda JC, Correa JG, Alvarez-Larrán A, Ferrer-Marín F, Raya JM, Martínez-López J, Velez P, Pérez-Encinas M, Estrada N, García-Gutiérrez V, Fox ML, Luño E, Kerguelen A, Cuevas B, Durán MA, Ramírez MJ, Gómez-Casares M, Mata-Vázquez MI, Regadera A, Pereira A, Cervantes F; Grupo Español de Enfermedades Mieloproliferativas Filadelfia Negativas (GEMFIN)..	2018 May;181(3):397-400. doi: 10.1111/bjh.14601. Epub 2017 Apr 17. No abstract available.	Clinical characteristics, prognosis and treatment of myelofibrosis patients with severe thrombocytopenia.	0007-1048
Vedia Urgell C, Massot Mesquida M, Valles Fernandez R, Garcia Vicente JA, Franzi Siso A, Muñoz Ortiz L, Vilaró Jaques L, Bosch Peligero M.	2018 Jan;50(1):6-15. doi: 10.1016/j.aprim.2017.01.007. Epub 2017 Apr 14. Spanish.	[Adequacy of treatment for osteoporosis in primary prevention. Quantitative and qualitative study].	0212-6567
Signori A, Izquierdo G, Lugaresi A, Hupperts R, Grand'Maison F, Sola P, Horakova D, Havrdova E, Prat A, Girard M, Duquette P, Boz C, Grammond P, Terzi M, Singhal B, Alroughani R, Petersen T, Ramo C, Oreja-Guevara C, Spitaleri D, Shaygannejad V, Butzkueven H, et al.	2018 Apr;24(5):642-652. doi: 10.1177/1352458517703800. Epub 2017 Apr 6.	Long-term disability trajectories in primary progressive MS patients: A latent class growth analysis.	1352-4585
Puñet-Ortiz J, Hervás-García JV, Teniente-Serra A, Cano-Orgaz A, Mansilla MJ, Quirant-Sánchez B, Navarro-Barriuso J, Fernández-Sanmartín MA, Presas-Rodríguez S, Ramo-Tello C, Martínez-Cáceres EM.	2018 Mar;94(2):327-333. doi: 10.1002/cyto.b.21527. Epub 2017 Apr 17.	Monitoring CD49d receptor occupancy: A method to optimize and personalize natalizumab therapy in multiple sclerosis patients.	1552-4949

Burman M, Nikolayevskyy V, Kontsevaya I, Molina-Moya B, Rzhepishevska O, Guglielmetti L.	2018 Mar 1;40(1):210-211. doi: 10.1093/pubmed/fdx014. No abstract available.	Tackling the MDR-TB epidemic in Ukraine: every little helps . and much more needed.	1741-3842
Bernal E, Ariza-Solé A, Bayés-Genís A, Formiga F, Díez-Villanueva P, Romaguera R, González-Saldívar H, Martínez-Sellés M.	2018 Feb;27(2):219-226. doi: 10.1016/j.hlc.2017.02.033. Epub 2017 Apr 12.	Management of Nonagenarian Patients With Severe Aortic Stenosis: The Role of Comorbidity.	1443-9506
Sicras-Mainar A, Huerta A, Sánchez D, Navarro-Artieda R.	2018 Jan - Feb;44(1):13-22. doi: 10.1016/j.semerg.2017.03.005. Epub 2017 Apr 26. Spanish.	[Use of resources and costs associated with non-adherence to inhaled corticosteroid treatment in asthma].	
López-Medrano F, Fernández-Ruiz M, Silva JT, Carver PL, van Delden C, Merino E, Pérez-Saez MJ, Montero M, Coussement J, de Abreu Mazzolin M, Cervera C, Santos L, Sabé N, Scemla A, Cordero E, Cruzado-Vega L, Martín-Moreno PL, Len Ó, Rudas E, Ponce de León A, Arriola M, Lauzurica R, David MD, González-Rico C, Henríquez-Palop F, Fortún J, Nucci M, Manuel O, Paño-Pardo JR, Montejo M, Vena A, Sánchez-Sobrino B, Mazuecos A, Pascual J, Horcajada JP, Lecompte T, Moreno A, Carratalà J, Blanes M, Hernández D, Hernández-Méndez EA, Fariñas MC, Perelló-Carrascosa M, Muñoz P, Andrés A, Aguado JM; Spanish Network for Research in Infectious Diseases (REIPI); Group for the Study of Infection in Transplant Recipients (GESITRA) of the Spanish Society of Clinical Microbiology and Infectious Diseases (SEIMC); Study Group for Infections in Compromised Hosts (ESGICH) of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID); Swiss Transplant Cohort Study (STCS).	2018 Feb;24(2):192-198. doi: 10.1016/j.cmi.2017.06.016. Epub 2017 Jun 23.	Multinational retrospective case-control study of risk factors for the development of late invasive pulmonary aspergillosis following kidney transplantation.	1198-743X
Agustí C, Martín-Rabadán M, Zarco J, Aguado C, Carrillo R, Codinachs R, Carmona JM, Casabona J.	2018 Mar;50(3):159-165. doi: 10.1016/j.aprim.2017.02.008. Epub 2017 Jun 16. Spanish.	[Early diagnosis of HIV in Primary Care in Spain. Results of a pilot study based on targeted screening based on indicator conditions, behavioral criteria and region of origin].	0212-6567
Schultze A, Paredes R, Sabin C, Phillips AN, Pillay D, Mackie N, Castagna A, Chadwick D, Falconer K, Geretti AM, Post FA, Hill T, Kirk O, Pozniak A, Nelson M, Tostevin A, Dunn D, Lundgren J, Cozzi-Lepri A.	2018;23(2):105-116. doi: 10.3851/IMP3178.	The association between detected drug resistance mutations and CD4(+) T-cell decline in HIV-positive individuals maintained on a failing treatment regimen.	1359-6535
Carrascosa Carrilllo JM, Toro Montecinos M, Ballescá López F, Teniente Serra A, Martínez Cáceres E, Ferrándiz C.	2018 Mar;29(2):140-144. doi: 10.1080/09546634.2017.1341619. Epub 2017 Jul 6.	Correlation between trough serum levels of Adalimumab and absolute PASI score in a series of patients with psoriasis.	0954-6634
Cánovas López SJ, Estevez Cid F, Reyes Copa G, López Gude MJ, Melero Tejedor JM, Badía Gamarra S.	2018 Jul;71(7):587-588. doi: 10.1016/j.rec.2017.05.020. Epub 2017 Jun 7.	Miniaccess Heart Surgery. A Spanish Multicenter Registry.	0300-8932
Negredo E, Domingo P, Gutiérrez F, Galindo MJ, Knobel H, Lozano F,	2018 May;36(5):312-314. doi: 10.1016/j.eimc.2017.0	Executive summary of the consensus document on osteoporosis in HIV-infected individuals.	0213-005X

Martínez E, Masiá M, Polo R, Estrada V.	3.010. Epub 2017 May 31. English, Spanish.		
Motlló C, Ribera JM, Morgades M, Granada I, Montesinos P, Mercadal S, González-Campos J, Moreno MJ, Barba P, Cervera M, Barrios M, Novo A, Bernal T, Hernández-Rivas JM, Abella E, Amigo ML, Tormo M, Martino R, Lavilla E, Bergua J, Serrano A, García-Belmonte D, Guàrdia R, Grau J, Feliu E; PETHEMA Group, Spanish Society of Hematology.	2018 Jan;59(1):146-154. doi: 10.1080/10428194.2017.1326596. Epub 2017 May 30.	Frequency and prognostic significance of additional cytogenetic abnormalities to the Philadelphia chromosome in young and older adults with acute lymphoblastic leukemia.	1042-8194
Sorigue M, Sancho JM.	2018 Jan 23;150(2):64-66. doi: 10.1016/j.medcli.2017.04.005. Epub 2017 May 22. English, Spanish. No abstract available.	The 2016 revision of the WHO classification of lymphoid neoplasms: The clinician's view.	0025-7753
Castella M, Boronat A, Martín-Ibáñez R, Rodríguez V, Suñé G, Caballero M, Marzal B, Pérez-Amill L, Martín-Antonio B, Castaño J, Bueno C, Balagué O, González-Navarro EA, Serra-Pages C, Engel P, Vilella R, Benitez-Ribas D, Ortiz-Maldonado V, Cid J, Tabera J, Canals JM, Lozano M, Baumann T, Vilarrodona A, Trias E, Campo E, Menendez P, Urbano-Ispizua Á, Yagüe J, Pérez-Galán P, Rives S, Delgado J, Juan M.	2018 Dec 6;12:134-144. doi: 10.1016/j.omtm.2018.11.010. eCollection 2019 Mar 15.	Development of a Novel Anti-CD19 Chimeric Antigen Receptor: A Paradigm for an Affordable CAR T Cell Production at Academic Institutions.	2329-0501
Galanaud JP, Monreal M, Kahn SR.	2018 Apr;164:100-109. doi: 10.1016/j.thromres.2017.07.026. Epub 2017 Jul 24.	Epidemiology of the post-thrombotic syndrome.	0049-3848
Coll J, Videla S, Leon A, Ornelas A, García F, Fernández E, Blanco JL, Carrillo A, Bravo I, Meulbroek M, García-Cuyas F, González V, Casabona J, Leal L, Clotet B, Brander C; CHECK-EAR TEAM.. COLLABORATORS: Brander C, Clotet B, Coll J, Bravo I, Chamorro A, García-Cuyas F, Ornelas A, Piñol M, Revollo B, Sirera G, Videla S, Blanco JL, Fernández E, García F, Gatell JM, Leal L, Leon A, Carrillo A, Ditzel E, Meulbroek M, Pujol F, Saz J, Taboada H, Casabona J, Ferrer L, González V.	2018 May;24(5):540-545. doi: 10.1016/j.cmi.2017.08.012. Epub 2017 Aug 24.	Early Detection Of Hiv Infection And Of Asymptomatic Sexually Transmitted Infections Among Men Who Have Sex With Men.	1198-743X
Sorigue M, Sarrate E, Ribera JM, Sancho JM.	2018 Apr;11(4):263-264. doi: 10.1080/17474086.2017.1367659. Epub 2017 Aug 23. No abstract available.	The case for lymphoma-specific survival.	1747-4086
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