BITRECS: Biomedicine international training research programme for excellent clinician-scientists

CALL 2: RESEARCH LINES

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RL1. Peptide-Major Histocompatibility Complex-based nanomedicines for the treatment of autoimmune disease (Dr. Pau Serra)

Key words: Nanomedicine; autoimmunity; immunoregulation; liver autoimmunity

Description of the research line: The complexity of autoimmune diseases is a barrier to the design of strategies that can blunt autoimmunity without impairing general immunity. We have shown that nanoparticles (NPs) coated with disease-relevant peptide-major histocompatibility complex (pMHC) molecules can resolve inflammation in various organ-specific autoimmune disease models (Clemente et al., *Nature* 530:434, 2016). pMHC class II-NP therapy functions by promoting the formation and expansion, in an epitope-specific manner, of cognate T-regulatory-type-1 (TR1) CD4+T-cells that are virtually identical to TR1 cells cloned from patients. These *in vivo*-expanded TR1 cells resolve autoimmune inflammation by selectively suppressing the autoantigen-loaded professional antigen-presenting cells (APCs) proximal to the affected organ. Furthermore, our data indicate that any single disease-relevant pMHC specificity will be capable, when coated onto NPs, to blunt the underlying autoimmune response, regardless of its role in the disease process.

In certain organ-specific autoimmune diseases, such as Primary Biliary Cholangitis (PBC), Primary Sclerosing Cholangitis (PSC) or Autoimmune Hepatitis (AIH) (liver autoimmune diseases with high unmet needs), the autoimmune response largely focuses on ubiquitous, non-organ-specific antigens. Although these antigens are expressed systemically, the resulting autoimmunity is liver-specific.

The goal of this translational proposal, is to validate the disease specificity of pMHC-based nanomedicine candidates for PBC, PSC, AIH and inflammatory bowel disease (frequently associated with PSC) in mouse models of these diseases as well as in mice humanized with peripheral blood mononuclear cells from patients. Our hypotheses are: (1) that the nanomedicines will trigger TR1 responses in the corresponding animal models and in humanized NSG mice; and (2) that these compounds will be liver and/or disease-specific.

Principle investigator: Pau Serra, pserra1@clinic.cat

Research group: Autoimmunity Research Group. The scientific objective of the group is to develop pMHC-based nanomedicines for the treatment of chronic autoimmune inflammation across indications, and to dissect the immunoregulatory cell networks that arise in response to treatment, both in animal models of disease and in humanized mice. The laboratory has expertise in pMHC expression and purification and employs a broad spectrum of molecular, cellular and pathological techniques as well as animal models of autoimmune inflammation to understand disease pathogenesis and mechanisms of immunoregulation. The laboratory has a very significant translational component that involves studies of peripheral blood mononuclear samples of patients with various autoimmune diseases both ex vivo as well as in in vivo, in humanized mice.

Additional information about the research group: Importance of the clinician-scientists within the group: The IDIBAPS principal investigator (P. Serra) pursued a Biology Intern Residence (BIR) in a clinical immunology lab at Hospital Son Dureta in Mallorca, before pursuing a PhD and therefore has a deep understanding of clinical immunology and autoimmunity from a laboratory diagnostic perspective. The collaborating PI as a medical degree and medical specialty in clinical immunology. The IDIBAPS research team includes Dr. Jesus Blanco, who is currently a member of the staff of the Endocrinology Department at Hospital Clinic. In addition, the research group has several active ingoing collaborations with clinician scientists of Hospital Clinic. Thus, our research efforts are highly translational and aim to bring pMHC-based nanomedicines to clinical trials. Training new clinician-scientist scholars in this highly innovative area of research is needed to increase capacity in our country, and help sustain our pioneering efforts in this promising field of research.

Interest of the group to recruit a clinician-scientist: The IDIBAPS research group has a strong translational component that includes access to patients with autoimmune diseases targeting various tissues or organs, such as liver, central nervous system, skin, eye and others. We seek to bridge basic and translational immunology by training basic immunologists in translational science, as well as clinician-scientists in basic immunology.

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RL2. Mechanisms of progression in monoclonal gammopathies (Dr. Carlos Fernández de Larrea)

Key words: Myeloma, progression, monoclonal gammopathies, amyloidosis, response

Description of the research line: Monoclonal gammopathies is a field with great advances in both biology and therapeutic tools. The discovery of the events that lead to the development of multiple myeloma after asymptomatic forms as well as the immunological mechanisms of control are crucial to understand why some patients achieve prolonged complete remission (long survivors) while others progress even with extramedullary forms (plasmacytoma). The importance of immune attack against malignant plasma cells in monoclonal gammopathies at diagnosis and at relapse and the role of immune checkpoints in this balance are being explored, as well as the potential use of CAR-T cells therapy for achieving a response in patients with progressive disease. The "evolving" pattern of progression from asymptomatic myeloma (smoldering) to symptomatic forms, already described in our institution, is analysed with new approaches, including the impact of monocytes, mesenchymal stromal cells and the cross-talk through non/coding RNA. Translational research into the biology of extramedullary progression with plasmacytomas in multiple myeloma and in the early and accurate diagnosis of systemic AL amyloidosis is also performed. The underlying mechanisms in the case of the deposition in light-chain (AL) amyloidosis in organs such as kidney and heart have also taken important steps.
The possibility of modifying early immune events in asymptomatic patients, the development of strategies that allow immune modulation throughout the natural history of symptomatic myeloma, increasing the effectiveness against plasmacytomas or elements that allow diagnosis and staging at risk of disease organism in amyloidosis by light chains would have a relevant repercussion in the clinical practice of patients with monoclonal gammopathies.

Principle investigator: Carlos Fernández de Larrea, cfernan1@clinic.cat, https://orcid.org/0000-0003-4930-9255

Research group: Mechanisms of progression in monoclonal gammopathies. Our group is focused on a comprehensive study on patients with multiple myeloma (MM) in complete remission and in those with long-lasting stable monoclonal gammopaties of undetermined significance. Translational research developed between Hospital Clinic and our lab at IDIBAPS, using many different strategies including molecular biology, immunophenotype, imaging and in vitro and in vivo models are used. Serum and bone marrow molecular and immune biomarkers of risk of progression to symptomatic myeloma in asymptomatic monoclonal gammopathies and progression/relapse after treatment are analysed.

Additional information about the research group: Importance of the clinician-scientists within the group: Our group is framed into the Amyloidosis and Myeloma Unit from the Department of Hematology. In this sense, we are composed of 4 staff clinicians, 2 physicians devoted to clinical trials, 1 data manager and one lab technician. We have incorporated two post-doctoral members in the translational research. The role of the clinician/scientists is to deal with research projects on multiple myeloma, amyloidosis and other monoclonal gammopathies, as well clinical daily meetings, weekly Amyloidosis clinical cases discussion with the multidisciplinary team as well as the opportunity to visit Day Hospital, our daily outpatient clinic devoted to monoclonal gammopathies and in-patient consultation from other departments.

Interest of the group to recruit a clinician-scientist: The candidate will be able to develop scientific projects in crucial aspects of the evolving field of myeloma and amyloidosis. The inherent translational nature of the group would allow the development of the research activity in a biological environment at IDIBAPS together with the corresponding clinical information. The Amyloidosis and Myeloma Unit is made up of a multidisciplinary team for the comprehensive approach of patients with monoclonal gammopathies. The candidate could develop research as well as improve clinical skills with the complementary training including the participation in the activities of the department of hematology.

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RL3. Digital solutions for effective intervention to prevent alcohol and tobacco use in primary health care (Dr. Antoni Gual)

Key words: screening and brief interventions; alcohol; tobacco; digital health; primary care

Description of the research line: Alcohol and tobacco, along with unhealthy diet and low levels of physical exercise, are preventable causes of the 5 non-communicable diseases (cardiovascular, cancer, diabetes, chronic respiratory, and dementia) that generate most healthcare and socioeconomic needs and costs.
Screening, Brief Intervention, and Referral to Treatment (SBIRT) is an evidence-based practice, shown to be effective to identify, reduce, and prevent problematic alcohol use, and also as an intervention for smoking cessation. In alcohol use: i. Screening quickly assesses the severity of alcohol use and identifies the appropriate level of treatment; ii. Brief Intervention focused on increasing insight and awareness regarding alcohol use and motivation toward behavioral change; iii. Referral to Treatment provides those identified as needing more extensive treatment with access to specialty care. SBIRT for tobacco use focus on enhancing users' motivation and equipping them with evidence-based resources to achieve a successful quit attempt.
Primary health care (PHC) settings provide an excellent opportunity for implementing SBIRT as an early intervention approach to effectively help individuals with nondependent substance use before they need more extensive or specialized treatment, thus to reduce the public health burden due to alcohol and tobacco.Digital health (DH) interventions using a SBIRT approach have been found both effective and cost-effective in comparison with care as usual in smoking and excessive drinking. DH tools can not only be used by individuals, but also be delivered in primary care settings as part of integrated care pathways. They are also expected to tackle inequities in access to reliable health information and affordable effective health management options, thus to provide sustainable and scalable prevention and treatment solutions. However, the vast majority of currently available DH tools tend to fail on: perceived usefulness, fit-to-needs, use of appropriate behavior change techniques, and interaction with/ integration into healthcare. In order to overcome the currently high level of failed DH interventions, we aim to explore the potential of the participatory co-creation approach and techniques and the motivational perspective in the design, deployment and evaluation of SBIRT-based DH tools for alcohol use disorders and smoking cessation specifically in primary health care settings.

Principle investigator: Antoni Gual, tgual@clinic.cat, https://orcid.org/0000-0002-7130-981X

Research group: Research Group on Addictions – Clinic. The group is part of the Red de Trastornos Adictivos (RETICS) and has been recognized by AGAUR (SGR00649). Our final goal is to promote an evidence based and high quality care for addicted patients. Our research follows three main strands: a) prevention, epidemiology, social and economic costs and morbid-mortality linked to addictions; b) New therapies (evaluation of new drugs in phases 3 and 4), mHealth interventions, screening of drugs in body fluids, group therapies, etc; c) Evaluation and management of complex patients with somatic problems and addictions (liver transplant, chronic pain, etc.)

Additional information about the research group: Importance of the clinician-scientists within the group: We believe that the process of "exploring the potential of the participatory co-creation approach and techniques and the motivational perspective in the design, deployment and evaluation of SBIRT-based DH tools for alcohol use disorders and smoking cessation specifically in primary health care settings" needs to be led and driven by a health care professionals with a clinical profile, as a person who may best understand the idiosyncrasies of the healthcare system, a person who is seen as a peer of the healthcare professionals which is expected to help overcoming barriers in communication with and accessibility to the primary care professionals. Our team includes a group of psychiatrists (6) and psychologists (4) who work in the inpatient, outpatient and consultation-liaison services of the Psychiatry Department of the Hospital Clínic of Barcelona. Other clinicians (currently 1 psychiatrist and 1 psychologist, further two employment contracts foreseen in 2018) are specifically working on research activities.

Interest of the group to recruit a clinician-scientist: The Addictions Unit has just opened a Specialised Care Centre: within the frame of this new facility, we intend to explore the potential of digital health solutions to integrate in our clinical care, in addition to our specific research line in primary care setting. Having a clinician-scientist exclusively devoted will accelerate the exploratory phase in both settings (primary care and specialised care), as the currently available clinicians are not in the position to easily take this extra task on.

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RL4. Applied research in pulmonary diseases of critically-ill patients (Dr. Antoni Torres)

Key words: community-acquired pneumonia; acute respiratory distress syndrome; hospital acquired pneumonia and ventilator-associated pneumonia; acute respiratory and distress syndrome; intensive care unit

Description of the research line: Our research focuses on patients with severe community-acquired or nosocomial pneumonia and acute respiratory distress syndrome (ARDS) who are admitted to the intensive care unit (ICU). The ICU consumes a significant portion of hospital and healthcare costs caring for the most severe patients with pulmonary diseases. In the coming years, the ICU will be a main target for attempts at cost reduction, because the number of critical care medicine beds and the costs of critically illnesses have increased exponentially. In order to investigate these conditions our facilities comprise state-of-the-art laboratories where basic research or experiments in large animals are conducted, and clinical departments, with a focus on pulmonary patients, where the results of pre-clinical research are promptly translated and applied to improve patient outcomes. Irrespective of the many advances in this field of research, mortality in patients with severe community-acquire pneumonia is still unacceptably high, up to 35-40% in the worst cases. Indeed, at present, several aspects of severe community-acquire pneumonia remain unclear. In particular, risk factors that promote progression from mild episodes of pneumonia to severe pneumonia are still elusive and in need of comprehensive experimental and clinical investigation. Our group also focuses on nosocomial pneumonia, which is a pulmonary infection developing in hospital settings. This latter condition still lacks of accurate methods to diagnose the disease or rapidly identify etiologic factors. Our goals in the next years will be to introduce novel diagnostic approaches that may improve our diagnostic precision and reduce the need for redundant empiric therapy that promotes antibiotic resistance. Additionally, mechanically ventilated patients in the ICU often present one of the most lethal pulmonary syndromes, namely ARDS. 2017 marks the 50th anniversary of the first description of ARDS. Although much progress has been made, the latest reports demonstrate an associated mortality as high as 50%. In addition, patients with ARDS present prolonged hospital stay and recovery time, which is often complicated by a cluster of physical and psychological problems in patients and family caregivers for periods of up to 5 years. One of the main reasons for the poor survival and the excessive burden associated with ARDS is that efficacious therapeutic strategies that could modify the natural course of the syndrome and facilitate swift recovery are still lacking. Our long-term goals will be to impact such unfortunate scenario and improve recovery and quality of life of ARDS patients through discoveries that could be easily translated from the bench to the bedside.

The scientific challenge facing this line of translational research is to improve the outcomes of ICU patients with severe community-acquired and nosocomial pneumonia and ARDS. In particular, we will aim at discovering new therapeutic strategies that could reduce the length of hospital stay of these patients, healthcare costs and long-term mortality. To meet these challenges our research model ranges from basic science and animal studies to interventional studies and randomized clinical trials that could provide reliable scientific evidence.

Principle investigator: Antoni Torres Martí, atorres@ub.edu, https://orcid.org/0000-0002-8643-2167

Research group: Applied research in pulmonary diseases of critically-ill patients. The group (www.idibapsrespiratoryresearch.org) develops research projects in the area of pulmonary diseases that develop in critically-ill patients. The scientific objective is to improve clinical practices and patients' quality of life. The research group, led by Prof. Antoni Torres, Chief of the Respiratory Critical Care Unit at the Hospital Clínic and full professor of Medicine at the School of Medicine at the University of Barcelona, works on the basis of three pillars for translational research: the clinical research unit, the research laboratory and the animal experimentation division. Each pillar has a highly qualified coordinator (Dr. Miquel Ferrer, Dr. Laia Fernández-Barat, Dr. Ana Motos) and a specialized team of researchers from different healthcare related disciplines (medical doctors, postdoctoral researchers, methodologists, PhD students, nurses, statisticians, physiotherapists).

Additional information about the research group: Importance of the clinician-scientists within the group: Currently, the research team predominantly comprises scientists with multi-disciplinary clinical/research experience in the areas of critical care, pulmonary medicine, and anaesthesia. Almost 70% of the research team scientists are MDs currently practising medicine in their fields of specialization. The scientists' clinical fields involve a multitude of areas including diagnosis, management and therapy of infectious respiratory

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diseases; advanced management of non-invasive and invasive mechanical ventilation; and, in the most severe cases, sophisticated methods of pulmonary support such as extracorporeal membrane oxygenation.

Interest of the group to recruit a clinician-scientist: The primary goal of the research team is to bridge the gap between research and clinical treatment. Therefore, over the years the majority of appointees have been recruited based on their clinical skills and capability to proficiently conduct translational research and improve clinical outcomes.

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RL5. Cell cancer immunotherapy: chimeric antigen receptor (Dr. Manel Juan)

Key words: cancer, immunotherapy, chimeric antigen receptor (CAR), T-cell

Description of the research line: Immune response is already one of the key elements to treat tumours. During the last 7 years, different advances have come to the clinical practice, being T-cells with chimeric antigen receptor (CART) a major proposal and one of the most promising approach to treat cancer patients, especially those with haematological diseases. CART combine gene and adoptive cell therapy to produce specific T-cells to be infused to patients. By using mainly lentivirus, gene therapy introduce this new CAR specific receptor to autologous T-cells.

Although we already has an open clinical trial with our CART19 for treating B-lymphoproliferative disorders (leukaemias and lymphomas CD19+), our main challenges are to improve this product and introduce new CARTs to treat other tumours. Technically we need to improve lentivirus proposal and a better control of the protocol to produce high quantity of transduced T-cells in central memory step of differentiation.

Monitoring immunotherapy is also a main aspect to improve indications of immunomodulatory antitumor proposal. From plasmidic and lentiviral management, diafiltration, flow cytofluorimetry or luminex, to real time PCR o antibody-based assay, several methods are available in our laboratory to be introduced in this important monitoring step. New tools should be developed by the project to better predict responders and follow up of the treatments.

Clinical aspects are also crucial: our interdisciplinary team (with immunologist, haematologist, basic biologists between others) provide a clear translational purpose of our research line.

Principle investigator: Manuel Juan, mjuan@clinic.cat, https://orcid.org/0000-0002-3064-1648

Research group: Immunogenetics of the autoinflammatory and immune response. Main scientific objective: Promotion of basic, clinical and translation research in the physiopathology of immunomediated diseases.

Facilities: Clean rooms for cell immunotherapy. General immunology equipments and protocols (from molecular and cellular studies to production of cell immune therapeutic products).

Other aspects relevant to the group: We perform clinical trials of adoptive cellular immunotherapy, including gene therapy and T-cell expansion, by using GMP compact equipments like CliniMACS Prodigy®.

Additional information about the research group: Importance of the clinician-scientists within the group: Our team, and specially the PI Manel Juan, developed a Chimeric Antigen Receptor anti-CD19 (CART19), providing this “drug” for treatment of CD19+ lymphoproliferative patients (ALL, NHL and CLL). It is expected that the group will provide treatment for more than 40 patients each year. Simultaneously Immunotherapy section develops other options of immunotherapy such as the production and administration of Dendritic Cells and also immune monitoring of several immunotherapeutic proposal.

Interest of the group to recruit a clinician-scientist: Along 2018 to 2020 we plan to develop a CART platform. A clinician-scientist could be a good option to introduce another perspective to our immunotherapy, being a key element for an interdisciplinary proposal. People with clinical experience in immunology, haematology or oncology can find a great value for a group that lead the unique Spanish clinical trial with CART.

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RL6. Antibody-mediated diseases of the central nervous system (Dr. Josep Dalmau)

Key words: Autoimmune, encephalitis, synaptic, psychosis, NMDA

Description of the research line: My research focuses in antibody-mediated diseases of the central nervous system, including the discovery of new diseases, characterization of the syndrome, identification of specific autoantibodies and their neuronal or synaptic receptor protein targets, discovery of the triggers, and determination of the underlying mechanisms of disease. The later includes models using cultured neurons and passive transfer of antibodies to mouse, as well as models of active immunization with disease-relevant synaptic or protein receptors. These models require the use of tissue, cellular and synaptic imaging, and electrophysiological studies with acute sections of rodent brain tissue. We have discovered 10 such human diseases, including the most frequent and paradigmatic antibody-mediated encephalitis (NMDAR encephalitis). Our studies have resulted in important changes in the diagnostic and treatment approach of many neurologic and psychiatric diseases previously considered idiopathic. We have reported guidelines for the diagnosis and treatment of these diseases and developed unambiguous serologic diagnostic tests that are currently used worldwide (with several licensed patents for their use). Most patients with these potentially lethal diseases are now treatable and have complete recovery.

Among the relevance of this work in clinical practice this work has received several awards and prizes among them the Jacoby award, the American Neurological Association (ANA) “Jacoby Award” which is given triennially to an investigator who “has done especially meritorious experimental work upon any neurologic or psychiatric subject”.

Principle investigator: Josep Dalmau, jdalmau@clinic.cat, https://orcid.org/0000-0001-5856-2813

Research group: Clinical and experimental neuroimmunology. Objective: comprehensive characterization of antibody-mediated diseases of the synapse, including clinical features, triggers (e.g., tumors, viruses, genetic association), disease biomarkers (e.g., antibodies and antigens), mechanisms and models of disease. Methods and techniques include tissue and cell culture, immunohistochemistry, confocal imaging, antibody and antigen purification, mice behaviour study, passive transfer of antibodies and active immunization of rodents. Electrophysiology (field recording, patch clamp), calcium imaging with mini-microscopes in free behaving mice.

Additional information about the research group: Importance of the clinician-scientists within the group: Our research is heavily based on the clinical identification of patients with diseases of unclear etiology. In addition to basic researchers, it includes 8 clinical scientists, 4 of them with regular clinics (Hospital Clinic or Sant Joan de Deu), 2 with sporadic visits, and 2 (1 from USA, and 1 from Italy) focused in 100% lab work. Clinicians from this team have led to discovery of new antibody-mediated diseases (GABAaR, IgLON5, neurexin3a, DPPX), triggers (e.g., herpes simplex encephalitis leading to autoimmune encephalitis), and coordinated 40 Spanish centers in the study of these diseases.

Interest of the group to recruit a clinician-scientist: Our research is at the intersection of neurology, immunology, and cancer. Well-trained clinical neuroscientists are crucial in our setting. Future goals are to better improve our understanding of the cellular immunology and genetic mechanisms favouring viral and autoimmune encephalitis.

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RL7. Molecular Pathology of Lymphoid Neoplasms (Dr. Elías Campo)

Key words: Lymphoid neoplasms, Molecular pathology, Next generation sequencing, Hematopathology

Description of the research line: Lymphoid neoplasms are a very heterogeneous group of diseases both biologically and clinically. This diversity is related to the complex molecular mechanisms involved in their development and progression. Recent genomic studies have provided new insights to understand their pathogenesis and clinical evolution. However, most of these studies have been performed in limited cohorts of patients or in cohorts at the moment of diagnosis. Little is known on the clinical impact of the dynamic evolution of the genomic alterations during the course of the disease under the selective pressure of different therapies. In spite of the large number of new genomic aberrations discovered it is not yet clear the potential clinical impact of all these alterations. We are interested in exploring the translation into the clinical practice of this genomic information in different types of lymphoid neoplasms, particularly chronic lymphocytic leukemia, mantle cell lymphoma and diffuse large B-cell lymphoma. The main aspects we want to investigate are: 1) Clinical impact of the genomic profile of these neoplasms evaluated in the context of specific clinical situation including homogenously treated patients and refractory and relapsed disease. 2) Influence of the complex subclonal heterogeneity in the evolution of the disease; 3) development of prognostic models that incorporate biological predictive factors to improve patient selection for new therapies, 4) Development of animal and preclinical models based on specific driver mutations to better understand the pathogenesis of these tumors and explore new target therapies, and 5) Design of methodological platform and bioinformatic pipelines to perform genomic studies in the clinical practice. The information generated will be useful to improve the characterization of these tumors, providing a better stratification of the patients for the selection of management strategies.

Principle investigator: Elías Campo, ecampo@clinic.cat, https://orcid.org/0000-0001-9850-9793

Research group: Molecular pathology of lymphoid neoplasms. We are a multidisciplinary group integrated by pathologists, molecular biologists and genetists that work in close relationship with the Hematooncologists of our Institution. Our main aim is to characterize the genetic, epigenetic, and molecular mechanisms underlying the biological diversity of lymphoid neoplasms to improve our ability to recognize these tumors, understand how these alterations influence the different evolution of the patients and identify biomarkers that can be used in the clinical practice. We extensively use next generation sequencing and other (epi) genomic technologies in primary samples of patients combined with functional studies in in vitro and animal models.

Additional information about the research group: Importance of the clinician-scientists within the group: Our research group integrates pathologists, molecular biologists and cytogenetists. Part of the members have clinical appointment and combine research activity with the clinical service in the Hematopathology Unit of the Pathology Department that include the diagnosis of around 2000 annual biopsies from the in house and consultation cases. The research projects are mainly based on the analysis of routine and frozen samples from large cohorts of patients that are associated with clinical annotations. The research and clinical groups meet weakly in different activities that include integrated diagnostic conferences and research seminars.

Interest of the group to recruit a clinician-scientist: Our group is interested in incorporating a pathologist, haematologist or oncologist with interest in the study of lymphoid neoplasms. The candidate will work in a translational project under the combine supervision of a pathologist and basic scientist and will have access to clinical activities related to the project.

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RL8. Understanding myocardial substrate for arrhythmia development (Dr. Marta Sitges)

Key words: atrial fibrillation; cardiac imaging; prevention and control; patient-specific modeling; machine learning

Description of the research line: Our research is targeted towards the understanding of pathophysiology of cardiac disorders based on the postprocessing and Integration of non-invasive cardiac imaging. This includes the study of cardiac structure and mechanics in order to detect latent cardiac dysfunction and potential abnormal myocardial substrates that can be the underlying substrate for the genesis of heart failure and arrhythmias. We have mainly been focused in the field of heart failure with preserved ejection fraction, resynchronization therapy and atrial fibrillation development. Other areas of interest of our team include the adaptation of the heart to chronic endurance training as well as valve disease. Integration of multimodality and multiparametric imaging requires more and more he collaboration with other groups with expertise in the field of computational modelling and artificial intelligence. A common clinical presentation can be observed in the presence of diferent underlying pathophysiological mechanisms or substrates; these new tools helps in understanding the diferent clinical phenotipes in order to better understand disease and to improve its treatment. During the last 10 years we have been closely collaborating with the Physense group at Universitat Pompeu Fabra in Barcelona, a bioenginnering group with expertise in this field. Our hypothesis have been always been led by a clinical observation and our research has been always directed to answer this clinical question trying to improve our treatment of disease. We aim at developing research fields that have a direct impact on clinical practice in the short and mid-term run.

Principle investigator: Marta Sitges, msitges@clinic.cat, https://orcid.org/0000-0003-1300-4732

Research group: Cardiac imaging Group. The Cardiac Imaging group has a pluridisciplinary team of people dedicated to non-invasive cardiac imaging and its application in the knowledge and research into cardiovascular pathophysiology and therapy. Their lines of research include the application of cardiac imaging in the study of cardiac mechanics and function and analysis of cardiac remodelling in order to detect latent cardiac dysfunction. Additionally, their collaboration with bioengineering groups allows for better quantification and identification of patterns of cardiac adaptations to disease and understanding of their underlying physiopathology. The research team is in close collaboration with a university hospital with high activity, creating the ideal environment for generating and testing of research hypotheses.
The center has the necessary scientific and infrastructural support to achieve excellence in research with advanced echocardiography, two magnetic resonance (1,5 and 3.0T), and a cardiac CT scanners.

Additional information about the research group: Importance of the clinician-scientists within the group: The research group envisages of a multidisciplinary approach, which includes several disciplines (cardiologists specializing in electrophysiology, cardiac imaging, radiologists, bioengineers and biologists) covering the entire spectrum of cardiovascular pathology, from basic studies to translational clinical research and therapy. Most of the members of our research group are clinically oriented and have clinical duties, combining their clinical practice with research and academic activities. Additionally, the Department of Information Technologies and Systems, supporting clinical routine and research in the Hospital. The group has a wide experience with the implementation and exploitation of state of the art clinical data and has prior experience in competitive projects as well as many clinically oriented publications.

Interest of the group to recruit a clinician-scientist: Our interest is to build our team with a new clinician devoted to improve our knowledge of pathophysiology in order to optimize the care of our patients. We look for an enthusiastic candidate with interest in translational and clinically oriented research targeted to apply the research developments into clinical practice in the short and mid-term run.

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RL9. Translational Research on Pulmonary Vascular Diseases (Dr. Isabel Blanco)

Key words: Pulmonary hypertension, training, exercise, biomarkers

Description of the research line: Pulmonary arterial hypertension (PAH), an abnormal increase of pressure in the pulmonary circulation, is a disorder with significant burden in terms of both severity and prevalence. Progression of pulmonary hypertension results in right ventricular (RV) impairment that may progress to RV failure and death. It entail a dismal prognosis, worse than that of some carcinomas (i.e. breast,colon) (Kato 2001), and affect young and middle-aged individuals, exerting substantial impact on their quality of life, daily life activities and employment (McGoon 2013).

The pathobiology of PH involves disturbances in signaling pathways of cells in the vessel wall –endothelial cells, smooth muscle cells (SMC)– and interaction with local and circulating mediators (Tuder 2013).

Recent advances in the understanding of the pathobiology of PAH have prompted the development of new drugs that have provided significant benefit, both in terms of survival and patient's well-being. Nevertheless, we are far from an optimal situation, given the fact that affected patients are relatively young and current survival in newly diagnosed cases has only raised to 65% at 3 years after diagnosis (Humbert 2010a). There is still a long way to cover before we can get a cure of the disease.
Therefore, there is a need to identify new signaling pathways in the pathogenesis of PAH, which may represent different more appropriate therapeutic targets.

In according with this statement, in the group we are now working on:
- New new drugs to reverse the proliferative remodelling phenotype: **surviving** pathway
- Biomarkers of the disease: **microparticles** and **endothelial progenitors cells**
- **Metabolomics** and **image** signaling: positron emission tomography
- Role of physical training (**rehabilitation**) as markers of endothelial function and integrity

All these objectives are being studied both in humans, in patients with PAH and also in experimental models of pulmonary hypertension with the final goal of improving the knowledge and evolution of the disease "from the bench to the bed side".

Principle investigator: Isabel Blanco, iblanco2@clinic.cat, http://orcid.org/0000-0001-9452-3432

Research group: Translational research in pulmonary vascular diseases: cell proliferation and apoptotic mechanisms, imaging, exercise and other omics in pulmonary arterial hypertension. The aim of the group is to identify new activity markers, signals and therapeutic targets for PAH, with the ultimate goal to contribute to alleviate and cure the disease through: Investigating innovative pharmacological approaches targeting new signaling pathways; Evaluating the role of circulating elements (progenitor cells, microparticles) in the pathogenesis of PAH and their potential as disease biomarkers; Identifying novel biomarkers and candidate therapeutic targets using omics sciences; Analyzing the role of new imaging techniques in the early diagnosis of pulmonary vascular remodeling; Identifying markers of endothelial dysfunction that can be modified through a physical training program and associated with a better therapeutic response.

Hospital Clínic in Barcelona is a CSUR (Centers, Services and Reference Units) of the National System of Health in Complex Pulmonary Hypertension and is the second hospital that attends greater number of patients with PAH in Spain, so that the ability to recruit patients is guaranteed. We have available basic research laboratory facilities, as well as, space and equipment to perform hemodynamic studies and a pulmonary rehabilitation program. Samples from the Pulmonary Hypertension Biobank also located at IDIBAPS-Hospital Clinic can be requested.

Additional information about the research group: Importance of the clinician-scientists within the group: Isabel Blanco has a history of research in PAH over 10 years, which includes a 2-year postdoctoral stay at Johns Hopkins University. Currently she occupies a position that combines research and clinical activity, through a shared contract with IDIBAPS and Hospital Clinic, obtained through a competition. Isabel Blanco expects to transfer and apply the scientific-technical knowledge to the improvement in the prevention, diagnosis and treatment of pulmonary vascular diseases. Additionally, she is a researcher at the Network for Biomedical Research in Respiratory Diseases (CIBERES) in which she leads the PAH work package. In addition, she is co-responsible for the CSUR of Complex Pulmonary Hypertension at Hospital Clínic, which the research line fits with the promotion of clinical research in the context of the CSUR.

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Interest of the group to recruit a clinician-scientist: We are a group with translational activity and we are very interested on recruiting someone with the profile of clinician-scientist (for example MD-PhD). The research line has a strong component in both areas: work with patients and also work in the laboratory. We are looking for someone with the ability to integrate the data coming from the two fields that may help us to understand the disease and may let us improve its prognosis.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL10. Portal hypertension and vascular liver diseases (Dr. Juan Carlos García-Pagán)

Key words: Portal hypertension, vascular liver diseases, hepatic vein catheterization, splanchnic thrombosis & endothelial dysfunction.

Description of the research line: We are dedicated to understand the physiopathology and diagnosis of portal hypertension and the search of new therapeutic targets and treatments. Our diseases of interest are liver cirrhosis and vascular liver diseases and we are a genuine translational research group composed by physicians and basic investigators. For many years we have been leading the research developed in the field of portal hypertension from a whole perspective. We have developed guidelines for the management of portal hypertension and settle the bases for its diagnosis and management. The group has more than 250 research papers published in peer-reviewed journals and directed 42 doctoral thesis.

More recently, in the two last decades the group has broaden the field of interest to vascular liver diseases. This group of disease represent a real clinical challenge due to their increasing incidence and the lack of consensus regarding their management. They affect predominantly young people impairing in a great manner their quality of live and decreasing substantially their life expectancy. Together with our European collaborators we have created VALDIG (Vascular Liver Disease Group) an independent network of researchers with the aim to foster research in this field. We are leading projects focused on the better understanding of the natural history of the disease, creation of prognosis scores and establishment of treatment protocols. Indeed recently we have coordinated the European clinical practice guidelines for the management of Vascular Liver diseases.

Principle investigator: Juan Carlos García-Pagán, jcgarcia@clinic.cat, https://orcid.org/0000-0001-9032-4954

Research group: Barcelona Hepatic Hemodynamic Laboratory. Our main objective is to advance in the global management of our diseases of interests combining clinical and basic research to get a complete overview. This is why the group has a multidisciplinary structure, which incorporates basic and clinical researchers, making possible the continuous transfer of knowledge from the bench to the bedside. The group has two transversal laboratories: the clinical one where hemodynamic studies are performed and a basic-experimental one, working simultaneously with a continuous interaction. The main techniques performed in the group are hepatic vein catheterization and a whole range of molecular biology techniques, including animal models and primary cell culture all in the framework of state of the art facilities at hospital clinic and IDIBAPS.

The Clinic Hepatic Hemodynamic Laboratory located at Hospital Clínic accommodates clinical fellows and nurses. Our state-of-the-art facility counts on a non-invasive hemodynamic testing laboratory, and two hepatic hemodynamic laboratories equipped with cutting-edge technology, digital multi-channel hemodynamic registry system and ultrasound-doppler. The Laboratory occupies a space of 140m2.
The Basic-Experimental Laboratory located at the IDIBAPS has a 120m2 (with surface areas, crop room, PCR room, cellular isolation room, cold room and animal experimentation rooms), as well as common spaces of the genomic, image, cytometry, confocal and utility microscopy of the IDIBAPS / Faculty of Medicine UB

Additional information about the research group: Importance of the clinician-scientists within the group: The hemodynamic unit is constituted by three clinical scientist fully dedicated to the diagnosis, clinical management, treatment and surveillance of patients with portal hypertension and vascular liver diseases. Moreover we perform liver interventional radiology procedures (hepatic vein catheterization, transjugular liver biopsy and TIPS). The whole team combine clinical activity with clinical and translational research and we direct a group of clinical research formed by: 1 research nurse and 4 predoctoral clinical fellows and a translational research team formed by two laboratory technicians, 3 postdoctoral and 5 predoctoral fellows. In addition we coordinate a multidisciplinary team focused on the clinical management of patients with portal hypertension and vascular liver diseases formed by hepatologists, radiologists, liver surgeons, pathologists, anaesthesiologists, haematologists, which guarantees an integral and outstanding patient's management.

Interest of the group to recruit a clinician-scientist: The main research interest is to advance in the knowledge of portal hypertension and liver vascular diseases from a clinical point improving patients care and management but also conducting translational studies aim to better understand their physiopathology and find therapeutic targets that will allow the development of new treatments.

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RL11. Brain development in youth with early psychosis: insights from resting state magnetic resonance imaging and proton magnetic resonance spectroscopy (Dr. Gisela Sugranyes)

Key words: Psychosis, magnetic resonance imaging, resting state, functional connectivity, spectroscopy, children and adolescents.

Description of the research line:

- Functional magnetic resonance imaging
- Proton magnetic resonance spectroscopy
- Imaging genetics
- Adolescent brain development
- Psychotic disorders: clinical and high risk states

Adolescence is a period of active brain maturation which is likely to hold key information relevant to the development of psychosis. However advances in identifying neuroimaging markers of risk for psychosis are limited by lack of studies in this developmental period, a predominance of cross-sectional designs, and reliance on single imaging modalities. We aim to build a predictive model of transition to psychosis during adolescence, combining different imaging modalities. We also aim to examine the additional value of incorporating genetic information into the models.

Identification of youth at risk for psychosis prior to transition to clinical illness has the potential to improve clinical outcomes. Characterisation of biological markers of risk for disease will help improve identification of individuals who are most likely to transition to clinical illness, increasing performance of current screening tools which rely on clinical/demographic criteria.

Principle investigator: Gisela Sugranyes, gernest@clinic.cat, https://orcid.org/0000-0002-2545-7862

Research group: Multimodal neuroimaging in high risk and early psychosis: our group seeks to understand the neural mechanisms underlying the development of psychotic disorders in children and adolescents. Specifically, it aims to identify neural correlates which characterize youth at high risk for psychosis and during the early phase of the disorder. It also aims to explore the relationship between imaging measures and clinical and neuropsychological phenotypes, in addition to the interaction with genotype.

Our team has access to clinical, cognitive, demographic, environmental and genetic data, as it works in coordination with clinical and basic research teams. In addition, our team collects imaging measures (resting state functional MRI, structural MRI, diffusion tensor imaging and MR spectroscopy), acquired on a 3 Tesla scanner.

Additional information about the research group: Importance of the clinician-scientists within the group: Our team consists of a combination of researchers with clinical duties at the Reference Unit for Child and Adolescent Psychology and Psychiatry – child and adolescent psychiatrists and psychologists - with researchers who are based at the Imaging Platform of IDIBAPS – biomedical engineers specialized in image analysis. We also have collaborations with basic researchers at the University of Barcelona who oversee genetic analyses.

Interest of the group to recruit a clinician-scientist: Our team is interested in recruiting a clinician-scientist with experience in imaging analysis, especially functional magnetic resonance imaging and proton magnetic spectroscopy. We will encourage them to focus on analyses of longitudinal imaging data collected from several unique cohorts of youth at risk for psychosis, and we will support them in interpreting findings with greatest translational potential.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL12. Clinical and Translational Research on Infective Endocarditis (Dr. Josep Maria Miro)

Key words: Infective endocarditis, experimental endocarditis, *in vitro* studies, cohort studies, clinical trials, antimicrobial studies.

Description of the research line: Infective endocarditis (IE) is a cardiac infection involving natural valves and intra-cardiac devices (mechanical and biological valve prosthesis, TAVI, pacemakers and defibrillators) with overall rates of cardiac surgery and mortality of 50% and 20%, respectively. Although the prevalence is relatively low (1 episode per 1,000 hospital admissions), the disorder has a significant burden in terms of both clinical management and severity, requiring a multidisciplinary approach ("an Endocarditis team") to achieve the best outcomes.
This research line undertakes both clinical and translational studies. On the clinical side, we are researching: (1) epidemiological and prognostic-factor studies on several types of endocarditis (at local, Spanish and International [International collaboration on Endocarditis [ICE], European IE Registry [Euro-ENDO] levels); (2) the association between Enterococcus faecalis endocarditis of unknown source and colonic cancer; (3) the diagnostic yield of molecular diagnosis of infective endocarditis (16S); (4) the usefulness of cardiac PET/CT scans for the diagnosis and management of device-related infections; and (5) clinical trials and cohort studies on the treatment of S. aureus, enterococci, and Candida bacteremia and endocarditis. On the translational side, we are performing in vitro and in vivo studies focused on the pathophysiology and treatment of experimental endocarditis caused by susceptible and resistant Gram-positive cocci. We have been evaluating the activity of new antibiotics or new antibiotic combinations against Staphylococcus aureus (MSSA with different vancomycin MICs, MRSA and GISA), S. epidermidis (MRSE, VRSE), Enterococcus faecalis, E. faecium and penicillin-resistant Streptococcus mitis endocarditis. The experimental endocarditis model in rabbits is an ideal model for the evaluation of antimicrobials, and most of the data from successful preclinical trials were shown to be effective in clinical trials of bacteremia and endocarditis in the human being. It is, therefore, a very good example of "from bench to bedside".

Principle investigator: Josep Maria Miro, jmmiro@ub.edu, https://orcid.org/0000-0001-8057-7755

Research group: Hospital Clinic Infective Endocarditis Research Group ("the Endocarditis Team") was created in 1986 (Dr. Miro is the Chair) and includes 20 researchers specialized in cardiovascular diseases and infections: cardiologists, cardiovascular surgeons, infectious-diseases specialists with broad experience in cardiovascular infections, electrophysiologists, microbiologists, nuclear-medicine specialists, pathologists, biologists with expertise in animal models of endocarditis, toxicologists, pharmacologists and statisticians. It is a consolidated research group that has received continuous funding from national and international agencies for more than 30 years, and has been an international research group both at clinical and translational levels. In 1979 the Hospital Clinic Infective Endocarditis Database was started, and we have collected more than 1,500 consecutive cases of infective endocarditis. Since 2014 the Hospital Clinic of Barcelona has been the referral hospital of 10 hospital centers for patients with infective endocarditis needing cardiac surgery in Catalonia, and it has created a Catalonian research network that evaluates 90–100 cases of endocarditis per year. Since 1994 it has also operated a microbiological repository of samples isolated from blood cultures or valve vegetations from patients with infective endocarditis and currently stores more than 1,200 well-characterized microbiological isolates.

Additional information about the research group: Importance of the clinician-scientists within the group: Dr. Jose M. Miro has been working on a clinical and experimental endocarditis model using human-like pharmacokinetics for over 30 years, including a six-month pre-doctoral stay at Mayo Clinic, Rochester, MN, USA. Dr. Miro currently has an 80:20 IDIBAPS Research Contract obtained through a competition for the period 2017–21. The major component of this contract is work focused on clinical and translational research, and he expects to transfer and apply scientific-technical knowledge to improving the prevention, diagnosis and treatment of infective endocarditis.

Interest of the group to recruit a clinician-scientist: We are a group with both clinical and translational activities, and we are therefore very interested in recruiting a clinician-scientist (e.g., MD-PhD). Our research line has a strong component in both areas: working both with patients and in the laboratory with an experimental endocarditis model. In particular, we are looking for someone who can integrate data coming from the two fields, which may help us to understand the disease and thereby improve its prognosis, diagnosis and antimicrobial therapy.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL13. Genetics and immunology in melanoma (Dr. Susana Puig)

Key words: Melanoma, genetics, susceptibility, prognosis, immunology.

Description of the research line: The research will be focussed on:

1. Identification of new genetic factors implicated in melanoma susceptibility
2. Identification of new genetic factors modulating melanoma outcome
3. Identification of new genetic factors able to predict treatment response or toxicities in melanoma
4. Study the role of microbiome modulating the immune system in melanoma patients under immunotherapy
5. Characterize specific immunologic profiles associated with melanoma prognosis and treatment response

Identification of population at risk to develop melanoma is essential for early diagnosis, which is the best strategy to ensure a high survival for melanoma patients. Melanoma is the tumour with the highest heritability (58%), but more than 80% of high risk genetic factors are yet unknown. The researcher will have the challenge to design strategies to identify part of the missing heritability.

Some studies have demonstrated that germline variants can modulate melanoma outcome. This information could be incorporated in prognostic and/or treatment response prediction scores to select the best treatment and follow-up strategy for each patient. The researcher will have the challenge to identify key variants to be included into those scores.

Finally immune system is an important player in the prognostic of melanoma, but we need to understand it better. One strategy in our group is focussed on the understanding of the interaction between the microbiota and our host immune system. The researcher will have the challenge to participate in studies designed to understand this interaction. Furthermore, understanding better the role of specific immune profiles in the tumour or blood can be useful to identify patients with different prognosis or to select patients that will benefit from specific therapeutic strategies. The researcher will have the challenge to give more clues on the importance of specific immunologic profiles in melanoma.

Principle investigator: Susana Puig, susipuig@gmail.com/spuig@clinic.cat; https://orcid.org/0000-0003-1337-9745

Research group: Melanoma: imaging, genetics and immunology: we are a multidisciplinary group focused on translational research with the following goals:

1. Development of non-invasive imaging techniques for the diagnosis of melanoma.
2. Study of the genetic bases implicated in susceptibility, prognosis and therapy response in melanoma.
3. Development of treatment study strategies in melanoma and skin cancer.
4. Application of artificial intelligence systems for evaluating complex data in melanoma, combining imaging, epidemiological, clinical and molecular information.

Our lab is equipped for molecular genetics, cell biology and bioinformatic studies.

Additional information about the research group: Importance of the clinician-scientists within the group: Our group is multidisciplinary including dermatologists, internists, other medical specialities, research nurses and technicians, molecular geneticists and biologists. Most of our members perform clinical activity as their main task and combines it with research. Currently we have a technician, two PhD Students and a Post-doc in the lab, mainly dedicated to research. Our studies are designed to be able to understand better each patient and offer them the best management. For this reason it is important to incorporate scientists that can be implicated directly or indirectly in patient management.

Interest of the group to recruit a clinician-scientist: We are interested in recruiting a scientist that will be mainly dedicated to research, but that can understand the clinical practice, the implication that their research will have for the patients visited in our Melanoma Unit and participate on patient management.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL14. AIDS research (Dr. Josep Mallolas)

Key words: HIV, aids, treatment, coinfections, immunopathology, vaccine.

Description of the research line: HIV Unit of Hospital Clínic Barcelona has a large cohort of Human Immunodeficiency Virus (HIV) infected subjects actively receiving antiretroviral therapy (more than 5000). From the beginning of AIDS epidemic we have been involved not only in the clinical care of the patients but also in research.
We have a 2 main research fields:
1. Clinical research: Our Unit has been involved in the main clinical trials in HIV and also in HIV-Hepatitis C Virus (HCV) infected patients for more than 30 years including new molecules, new strategies, primary HIV-infection, comorbidities, new anti-HCV therapy, pharmacokinetic studies, resistance studies, Human Papiloma Virus (HPV) and solid organ transplantation in HIV-infected patients.

2. Translational studies: We also have a very active laboratory where we perform studies in different areas like: Peripheral (blood) and central response (lymphatic tissue and cerebrospinal fluid) to different antiretroviral therapies when administered in very early evolutive stages (CD4 > 500 mm3). We have developed ultrasensitive techniques for the determination of viral load in plasma and tissues, as well as techniques for the determination of genotypic resistance and for immunophenotyping and the evaluation of CD4+ lymphocyte proliferation in response to antigens of the HIV virus. Techniques for the determination of drug levels have also been developed in collaboration with the clinical pharmacology group. The mechanism by which the virus is able to escape the cytotoxic immune response subject to study subject to study, and could correspond to the selection of quasispecies different from the reservoirs (immunological resistance). For this reason we have started a research line aimed at developing techniques for stimulating the immune system, with a view to associating them with antiretroviral therapy. Cyclic interruption of them treatment and therapeutic vaccines can induce recovery of the specific immune response to HIV antigens, associated with a spontaneous decrease in viral load, which is correlated to the degree of proliferative and specific cytotoxic response against HIV-1 in a small percentage of patients.

Principle investigator: Josep Mallolas, mallolas@clinic.cat; https://orcid.org/0000-0002-8365-141X

Research group: AIDS Research group (IDIBAPS/Hospital Clinic) is composed by 13 teams that conduct research centered on the (HIV and AIDS disease from different standpoints. This area carries out a wide range of activities, which are divided up into two parts: Clinical researches focused on primary HIV-infection, efficacy and tolerance of antiretrovirals, on resistance mechanisms and opportunistic infections and coinfections and solid organ transplantation in HIV-infected patients; Basic researches focused on retrovirology and viral immunopathology, including vaccine development and functional cure/eradication.

Additional information about the research group: Importance of the clinician-scientists within the group: This group studies the clinical, diagnostic, therapeutic and preventive aspects of HIV infection. The scientific contribution of this line of research is very competitive and is internationally renowned. This group of investigators focuses on exploration of the potential for eradicating HIV infection and on reconstruction of the immune system, including the development of preventive and therapeutic vaccines.

Interest of the group to recruit a clinician-scientist: Our main interest is to recruit a clinician-scientist to integrate with all our organization. He or she must be an enthusiastic of HIV disease in clinical and also in the basic science

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RL15. Immune profiling of human liver tumors and surrounding stroma and its evolution during systemic therapy. (Dr. Jordi Bruix)

Key words: Hepatocellular carcinoma, tumor microenvironment immunotherapy, anti-angiogenesis.

Description of the research line: Liver tumors are challenging entities since they develop in an extremely specialized organ in terms of metabolism and immunity. Liver is a highly tolerogenic organ and the fact that liver tumors usually develop on cirrhotic liver, increases their complexity and the limited treatment options at an advanced stage. Sorafenib has been key in advanced hepatocellular carcinoma (HCC) treatment as it has been the sole effective option for 10 years. Now, we have additional options for 1st and 2nd line and major hope is placed in immune modulation and its potential benefit if associated with already known effective drugs such as sorafenib or the recently approved regorafenib for 2nd line. The mechanisms of action of both drugs are not well known. Major focus is placed in its anti-angiogenic action through the Vascular Endothelial Growth Factor (VEGF) pathway, while other targets are also affected. All available data support that they also act on immune mechanisms and this may be instrumental for their efficacy. Ischemia induced by tumor proliferation and anti-angiogenic therapy impact stromal and tumour immune cell populations. These populations are unique and their phenotype and number vary significantly in comparison to their circulating counterparts. While tumour microenvironment is clearly immunosuppressive, the surrounding liver shows a pro-inflammatory pattern. Therapy may modify their status in a different manner and tumor ischemia induced by sorafenib and regorafenib may prime an immunosuppressive microenvironment that halts tumor progression for a while but later fails to do so.

In this scenario, it is expected that combining anti-angiogenic treatment with immunosuppressive molecules would be the ideal combination to improve survival benefit. However, tumors are heterogeneous both at the nodule level and at the patient level and thus, there is need to characterise the immune profile of the patients at the tumor level, at the surrounding liver and also systemically.

Principle investigator: Jordi Bruix, jbruix@clinic.cat; https://orcid.org/0000-0002-9826-0753

Research group: Hepatic Oncology/ Barcelona Clinic Liver Cancer (BCLC) group develops clinical/translational research in liver cancer. Major focus targets new treatment approaches while also aiming to molecularly stratify patients to define who benefits from established therapies, when treatment failure occurs and who benefits by novel combinations. This is done through prospective investigator initiated trials with repeated biopsies of tumour and surrounding liver during the patients' evolution. At the same time, we evaluate potential mechanisms through BCLC owned human cell lines and the exploit of a collection of human tissues and blood samples from patients under treatment.

Additional information about the research group: Importance of the clinician-scientists within the group: BCLC group is an ideal blend of clinical and lab activity that runs prospective research. This involves experts from different fields (clinical, surgery, radiology, pathology and molecular biology). J Bruix is its Director and together with M Reig and A Forner, there is a major clinical activity (250 new liver cancer patients/year). This allows to run several studies in separate aspects that include evaluation of new diagnostic tools, novel staging approaches, development of new criteria to define treatment response and ultimately, evaluation of new treatment options at all evolutionary stages (Investigator initiated trials or under contracts with industry).

Interest of the group to recruit a clinician-scientist: Since the BCLC major research aim is to characterise the relevance of immune modulation in the efficacy of treatment and the identification of the parameters that may identify the patients benefitting from immunomodulatory agents, we have given priority to the incorporation of an expert clinician with a robust background in immune-oncology.

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RL16. Translational Genomics and Targeted Therapeutics in Solid Tumors (Dr. Aleix Prat)

Key words: Solid tumors, biomarkers, gene expression, clinical trials, drug sensitivity.

Description of the research line: Use genomic or molecular data to guide clinical trial design and biomarker development and study molecular mechanisms of drug sensitivity in order to identify optimal treatment regimens for patients with solid tumors.

The main lines of research are the following:

Breast cancer and gynecological cancer

1. To evaluate the impact of the identification of the intrinsic molecular subtypes of breast cancer in the clinical setting.
2. To study the mechanisms of drug resistance and tumor progression in Luminal A and B breast cancer.
3. To identify genomic biomarkers predictive of response to anti-HER2 drugs in HER2-positive breast cancer.

Colorectal cancer

1. To evaluate intrinsic and acquired mechanisms of resistance to chemotherapy and targeted agents in metastatic colorectal cancer, in the three genotypes (KRAS/NRAS mutant, BRAF mutant and triple-WT).
2. To characterize epithelial and mesenchymal phenotypes in resectable and metastatic pancreatic carcinoma and it's correlation with drug resistance.

Urologic cancer

1. To study the molecular mechanisms of resistance to taxanes and novel hormone-therapies in preclinical models, circulating tumor cells and patients with castration resistant prostate cancer.
2. To investigate the role of the androgen receptor variants in epithelial to mesenchymal transition and progression and therapy resistance in castration resistant prostate cancer.
3. To investigate mechanisms of resistance to anti-angiogenic therapy and identification of new therapeutic targets in renal cell carcinoma.

Lung cancer

1. Validate novel molecular technologies to streamline the screening of targetable biomarkers in non-small cell lung cancer (NSCLC).
2. Identification of novel fusion gene variants in NSCLC: phenotypic characterization of targeted population and prospective clinical validation of their predictive value to targeted treatments.

Principle investigator: Aleix Prat, alprat@clinic.cat; https://orcid.org/0000-0003-2377-540X

Research group: Translational genomics and targeted therapeutics in solid tumors: Our main objective is to use genomic or molecular data to guide clinical trial design and biomarker development and study molecular mechanisms of drug sensitivity in order to identify optimal treatment regimens for patients with solid tumors. Our great potential lies in the amount of clinical data and biological samples from clinical trials that allow the development of several lines of research in solid tumors. Also, in the last few years our group has developed basic and translational research lines, thanks to the collaboration with other research groups such as: Baylor College, University of North Carolina or Institute of Cancer Research.

Additional information about the research group: Importance of the clinician-scientists within the group: As head of the Medical Oncology Department at Hospital Clínic of Barcelona, Dr. Prat created a lab team at August Pi i Sunyer Biomedical Research Institute (IDIBAPS) called "Translational Genomics and Targeted Therapeutics in Solid Tumors") that integrates medical oncologists, bioinformatics and translational biologists. On other hand, Dr Prat is the scientific coordinator of the SOLTI (http://www.gruposolti.org) and member of executive board of the Breast International Group (https://www.bigagainstbreastcancer.org/).We have established collaborations with TBCRC Group, ALLIANCE and ICR, which allows our translational research to be very focused on clinical needs.

Interest of the group to recruit a clinician-scientist: We seek a highly motivated clinician-scientist to provide expertise in establishing preclinical models of solid tumors (e.g.: breast cancer, colorectal cancer or urologic tumors) such as patient-derived xenografts and organoids to Dr Prat's translational research team. He/she will have the opportunities to learn about cutting-edge technologies including the use of the NanoString platform, to learn gene expression and clinical data analysis.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL17. Clinical, neuropsychological, neuroimaging and genetic characteristics of children and adolescent offspring of patients diagnosed with schizophrenia or bipolar disorder (Dr. Josefina Castro)

Key words: Genetics, Polygenic risk scores, neuroimaging, cognition, children and adolescents.

Description of the research line: The research line of high risk for psychotic disorders has been active in our group for the last ten years. Schizophrenia and bipolar disorder are considered neurobiological disorders with an important genetic component. Currently, our research group is exploring these disorders in high risk children and adolescents (offspring of patients diagnosed with schizophrenia or bipolar disorder). Thus, our research line studies clinical, cognitive, neuroimaging and genetic characteristics of children and adolescent offspring of patients diagnosed with schizophrenia (SZoff) or Bipolar Disorder (BDoff) in order to identify predictors and mechanisms of transition to psychosis among such individuals ascertained to be at high risk. Our group (Sanchez-Gistau et al, 2015) found higher rates of any lifetime psychopathology in both SZoff and BDoff than in community controls (CCoff). In terms of cognition, we found that child and adolescent SZoff and BDoff performed worse on visual memory than CCoff (de la Serna et al., 2017). Regarding neuroimaging, Sugranyes et al.,)2015) found that SZoff, in relation to both BDoff and CCoff, showed cross-sectional global and regional grey matter volume reductions. Gasso et al (2016) assessed, for the first time, differences in genotype frequencies of polymorphisms located in genes involved in neurodevelopment and synaptic plasticity between genetic high-risk individuals and control subjects. The results showed that two polymorphisms, CACNA1C rs10848683 and SYNE1 rs214950, were significantly associated with high risk samples.

The use of Polygenic Risk Scores derived from large datasets allow the study of the complex genetic architecture of clinical phenotypes. Interaction between risk factors and genetics can be studied using "environmental risk scores" (ERS) that can be calculated from environmental data and can be integrated with PGRS. Epigenetic mechanisms (DNA methylation) are one of the hallmarks of the modulating effects that gene-environmental interactions exert at the cellular level, which could be correlated with clinical phenotypes.

This can help increase our knowledge about markers that can indicate a higher risk for the future and anticipate some kind of intervention to prevent pathology or a least some of its consequences. It is of great importance to have prognostic variables at the clinical, neuropsychological, neuroimaging and genetic level. The use of PGRS obtained in large cohorts allows us to get good results using small samples.

Principle investigator: Josefina Castro/Amalia Lafuente, jcastro@clinic.cat/amalialafuente@ub.edu; https://orcid.org/0000-0003-0632-2687/ https://orcid.org/0000-0001-7763-9003

Research group: Child and Adolescent Psychiatry and Psychology Group: The aim is to further clinical, genetics, neuroimaging and neurobiology research in order to expand our understanding of the most prevalent psychiatric disorders in children and adolescents.
Our research group is based at the Child and Adolescent Psychiatry Department of the Neuroscience Institute of the Hospital Clinic of Barcelona. Moreover, the Pharmacogenetics Unit of the Anatomic Pathology, Pharmacology and Microbiology Department, has all the infrastructure to carry out different genetic projects.

Additional information about the research group: Importance of the clinician-scientists within the group: Dr. J. Castro Fornieles is the head of the Neuroscience Institute in the Hospital Clinic of Barcelona and she is also associate professor at the University of Barcelona. She has an extensive background and experience in child and adolescent psychiatry. Dr Amalia Lafuente is the head of the Pharmacology Department in the School of Medicine at the University of Barcelona.

Interest of the group to recruit a clinician-scientist: Genetic data can be useful to understand complex diseases. However, genetic data alone only explain a very small percentage of the overall variability. Genetic studies of clinical endophenotypes are emphasized, which require the integration of clinical and genetic knowledge. Collaboration between clinicians and basic researchers can give the whole idea of this interaction. The research line presented here is a clear reflection of this approach.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL18. Clinical and molecular research in Parkinson's disease and other movement disorders (Dr. Maria Josep Martí)

Key words: Parkinson's disease, Clinical biomarkers, Biological biomarkers, atypical parkinsonisms, Genetics.

Description of the research line:

1. Development of research projects expected to yield short term application in the diagnosis and treatment of Parkinson disease and other neurodegenerative movement disorders, including atypical parkinsonism, Huntington disease and hereditary ataxias.
2. Identification of clinical, molecular and, imaging biomarkers that characterize the early preclinical phase of Parkinson disease.
3. Elucidation of biological pathways and disease mechanisms involved in the pathophysiology of neurodegenerative movement disorders

Specific research lines

i. Creation of comprehensive biorepositories of biological samples from longitudinal cohorts PD (PD patients LRRK2 + ;prodromic PD subject and MSA patients).

ii. Biomarker Research of parkinsonisms. We aim at expanding previous findings and applicability of potential diagnostic and prognostic candidate biomarkers identified in our group (specific microRNAs, neuroimaging studies, CSF levels of tau, amyloid-beta and alpha-synuclein, cytokines, protein phosphorylation, gene expression, DNA methylation levels). Molecular imaging (FDDNP-PET as marker of amyloid pathology in PD-dementia and of tau pathology in atypical parkinsonisms).

iii. Molecular alterations in PD using cell models. We aim to clarify the biological significance of PD cells alterations, analysing in depth the epigenetic alterations in iPSC DAn, and transcriptomic changes in peripheral tissues.

iv. Genetic modifiers of dyskinesia in PD. Recently, we have described a combination of SNPs from the mTOR pathway which can modify the onset and severity of LID.

v. Clinical research in deep brain stimulation for movement disorders. Clinical investigation on the effects of deep brain stimulation on motor and cognitive aspects; investigation on new and advanced programming techniques such as steering, short pulse width and multiple frequencies

Principle investigator: Maria Josep Martí, mjmarti@clinic.cat

Research group: The group is formed by expert staff neurologists in Parkinson's disease and other movement disorders,and by biologists with experience in the field of neurodegenerative diseases research. Their investigation task is supported by neurologist fellows, psychologists, laboratory technicians, students, and administrative assistants. At IDIBAPS, the laboratory itself has all facilities to perform biorepositories from patients' tissues and specific research on molecular and genetic studies, cell culture room, and freezers for samples storage.

Additional information about the research group: Importance of the clinician-scientists within the group: Clinical research: 1) Imaging and CSF biomarkers research in PD related dementia, as well as clinic-pathological correlations in PD and other parkinsonisms; 2) Characterization of the clinical non motor prodromic stages of Parkinson's disease; 3) Characterization of non-motor symptoms in Huntington disease; 4) Clinical and technical issues in deep brain stimulation.
Clinical Researchers: Y Compta, Mj Marti, , E Muñoz, F Valldeoriola

Interest of the group to recruit a clinician-scientist: This group has a long trajectory combining clinical and genetic/molecular research. A clinical-scientist will potentiate our capabilities in the field of translational medicine, from the clinical practical in the hospital patient care and in the laboratory of neurodegenerative diseases.

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RL19. Brain networks modifications in neuroimmunological diseases (Dr. Sara Llufriu)

Key words: Connectome, brain networks, multiple sclerosis, brain plasticity, cognition.

Description of the research line: Understanding the human brain represents a grand scientific challenge in neuroscience. Recent progresses in neuroimaging enable the study of the human connectome and have made significant contributions to the knowledge of network organization and function. However, modifications and consequences of network changes in brain diseases are only partially known.

The present project aims at elucidating the changes in brain networks in patients suffering multiple sclerosis (MS), an autoimmune and neurodegenerative disease. Such disease can serve as a model to investigate the effect of focal and diffuse damage on network integrity and plasticity in the human brain.
The main objective will be to define the modifications in structural brain networks, reconstructed through advanced models of tractography in resonance imaging (MRI), along the disease and to identify the variations in disease phenotypes. Such findings could provide a "staging" of the disease evolution and characterize the consequences of network collapse on patient's disability. It will also provide valuable data on plasticity mechanisms of the network.

State of the art in MRI methods to reconstruct anatomical interactions between different brain areas and big data analyses including large cohorts and clinical information will be used to achieve such goals. This study is part of a multicenter collaborative project, coordinated by our research group, inside the European MAGNIMS research network (Magnetic Resonance Imaging in Multiple Sclerosis) that will join information from more than 1000 patients, as well as a cognitive rehabilitation trial.

Principle investigator: Sara Llufriu, sllufriu@clinic.cat; https://orcid.org/0000-0003-4273-9121

Research group: Advanced Imaging in Neuroimmunological Diseases (ImaginEM) is a multidisciplinary research team, led by Dr. Sara Llufriu, with neurologists, engineers and neuropsychologists from IDIBAPS and Hospital Clinic Barcelona. The team has also close collaboration with experts in Data Science. The main objective of the group is to understand the basis of disease evolution in MS and other neuroimmunological diseases, through the use of advanced MRI techniques. One of our major lines of research is the study of brain networks modifications and mechanisms of neural plasticity.
The project will boost the applicant's existing research competences in human neuroscience and will allow him/her to advance new research skills including neuroimaging, neurology and big data analysis. This project is designed to achieve the objective of improving the fellow research strengths, thereby obtaining a leading independent position in the future.

Additional information about the research group: Importance of the clinician-scientists within the group: The leader of the research group is a neurologist with part time clinical activity, as well as the other neurologists that compose the team. We are part of the Neuroimmunology and MS Unit, at the Neuroscience Unit and Neurology Department of Hospital Clinic of Barcelona. The MS Unit is led by Dr. Albert Saiz and follows a cohort of more than 700 patients with MS. It is considered one of the most important MS Units in Spain due to its clinical and research activity. The clinical activity is performed in the outpatient facility and at the Day Care Hospital in Hospital Clinic of Barcelona.

Interest of the group to recruit a clinician-scientist: We are interested in recruiting a clinical-scientist to be part of our team and participate in the exciting challenge of understanding the basis of brain network modifications due to the presence of MS damage, mechanisms of compensation and neural plasticity. Such findings would improve the knowledge of the human brain functioning and could help in finding better therapeutic approaches to brain dysfunction.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL20. Obesity and metabolic dysfunction (Dr. Josep Vidal)

Key words: Obesity, type 2 diabetes, adipose tissue, central nervous system, bariatric surgery.

Description of the research line: The obesity epidemic represents a major burden for health care systems because of the several comorbidities occurring in obese subjects. Thus, better understanding of the mechanisms by which obesity leads to obesity-related conditions and how those ameliorate upon weight loss is a priority.

The main area of our research deals with the effects of bariatric-metabolic surgery on the physiology underlying obesity-related metabolic complications. We are especially interested in better understanding the impact of bariatric-metabolic surgery on glucose homeostasis. We try to unravel what are the main determinants of improved glucose metabolism after bariatric surgery, with special focus on the role of gastrointestinal hormones, adipose tissue, and pancreatic beta-cell function. We are also interested in better understanding how bariatric-surgery may modify the cognitive decline associated with obesity. To do so, we take advantage of combining imaging and biological approaches. Finally, we aim at better understanding the basis for variable weight loss occurring after bariatric-metabolic surgery. There is no question bariatric-metabolic surgery is currently the best approach for weight loss in morbidly obese subjects. Nonetheless, the biological basis for weight loss variability is poorly understood. In these regards, we place special focus on gut hormones, adipose tissue, and the central nervous system.

Our research aims at rapid translation into medical practice. No question we aim at identifying potential new therapeutic targets for obesity related-conditions. However, in the short term we aim at better tailoring bariatric-metabolic surgery techniques to our obese patients.

Principle investigator: Josep Vidal, Jovidal@clinic.ub.es

Research group: Obesity: from excessive body fat to metabolic complications. Our research team is multidisciplinary. The team is led by clinicians working at the obesity clinic, and with different areas of interest in the area of our research. We work hand in hand with bioscientists with expertise in the field of adipose tissue and beta cell function. Finally, although not formally part of our research group at IDIBAPS, we have well established collaborations with experts in imaging techniques.
Our research is conducted at the facilities of IDIBAPS. From a clinical research perspective, our research facilities provide with the resources needed for metabolic characterization and body composition analysis of our research participants. Analytical determinations are performed in the Core Lab of Hospital Clínic. Basic aspects of our research are conducted at the Lab Facilities of IDIBAPS located in the 5th floor of our research building.

Additional information about the research group: Importance of the clinician-scientists within the group: Clinical scientists play a key role in our group. We strongly believe in daily medical practice as source of relevant scientific questions. Thus, staying in touch with patients at our obesity clinic faces us with the many unsolved questions in our area or research. Having said that, we acknowledge our limitations in properly addressing some of the questions that arise from our curiosity. That is why we team with experts in other areas of bioscience. As a team, we are able to better address relevant questions.

Interest of the group to recruit a clinician-scientist: Dissemination of the interest in clinical research is a must in current medical practice. Furthermore, collaboration with emerging clinical scientists in the field is an opportunity to enrich our views on the questions we are currently interested in and may help us formulate new ones.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL21. Early stages in bipolar disorders (Dr. Eduard Vieta)

Key words: bipolar disorder, prevention, staging, early intervention, personalized psychiatry.

Description of the research line: This research line focuses in early stages of bipolar disorder, ranging from at-risk subjects to first-episode patients. The staging model is based on the concept that an illness progresses following an identifiable temporal progression and that a timely diagnosis and adequate treatment in these early stages might prevent disease progression or complications like suicidal attempts. Our research involves the identification of those variables that influence illness onset, illness progression, suicidal ideation and treatment response. This includes the study of risk factors, genetics and epigenetics, molecular and neuroimaging markers, prodromal symptoms or clinical phenotypes related to a particular illness course.

The identification of those factors would help to disentangle the biological underpinnings and environmental factors involved in the triggering and progression of the bipolar disease. This would allow the development of new preventive strategies targeting molecular pathways or environmental factors that are known to increase disease vulnerability or are related to a worse prognosis. To reach this goal, it is necessary to perform studies collecting information on biographical and sociodemographic variables, family history, clinical, cognitive and neuroimaging variables, peripheral markers, genetic and epigenetic information.

To date, our group has identified several clinical patterns related to a particular illness course or prognosis, such as predominant polarity or mixed symptoms. We have extensively worked on psychoeducation programs for early stages, both on a clinical setting and through mobile devices, which have proved to reduce the time spent in any episode polarity. We have published the methodology of the psychoeducation program in a practical psychoeducation manual for clinicians. Our group has also contributed to demonstrate the progressive course of bipolar disorder by evidencing the functional and cognitive impairments that follows successive mood episodes. We have developed a therapy to improve functionality in bipolar disorder and we are currently working on cognitive enhancement treatments. Moreover, our group has experience in biomarkers research.

Principle investigator: Eduard Vieta, evieta@clinic.cat; https://orcid.org/0000-0002-0548-0053

Research group: Bipolar Disorders Program: the objective is to generate, disseminate, and apply knowledge on the causes, outcome, treatment and prevention of bipolar disorder. Neurobiology of the disease (genetics, neuromodulators, hormonal factors, neuroimaging), cognition and functional outcomes, clinical course and subtypes, comorbidity. Rating scales, pharmacological treatment, psychotherapies, family psychoeducation, and prevention of suicide. The work of the group has received more than 27 Awards of different scientific societies and universities, including the World Federation of Societies of Biological Psychiatry research prize in 2017. This award honours professionals from the field of psychiatry who outstood in the field of basic or clinical research.

Additional information about the research group: Importance of the clinician-scientists within the group: The Program has a multidisciplinary approach, involving 10 psychiatrists, 11 psychologists and 1 psychiatric nurse, with both clinical and research experience. The Bipolar Disorders Program at our institution started officially in 2001 and is devoted to research, education, and clinical care. Nowadays, it is considered a reference centre for treatment-resistant bipolar patients both nationally and internationally.

Interest of the group to recruit a clinician-scientist: Our research involves both clinical and basic research in bipolar disorder. Well-trained clinicians with experience in research are crucial in our setting. Future goals are to better understand the early stages of bipolar disorder both from a biological and a clinical perspective.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL22. Visual Pathway Lab (Dr. Elena H Martínez-Lapiscina)

Key words: Neurology; Biomarkers; Imaging, Neurophysiology; Statistics.

Description of the research line: *"We can´t improve what we can´t quantify"* Lord Kevin

Biological and economic caveats threaten drug development for neurological diseases. Non-invasive assessment of Central Nervous System (CNS) injury is limited due to anatomical barriers. Additionally, conducting phase III trials is so expensive that profit and non-profit organizations can only afford costs for few molecules.
In the last years, the technological development has fostered drug development (for instance, Magnetic Resonance Imaging- MRI- has favored development of immunomodulatory in Multiple Sclerosis- MS-). Recently, new evidence suggests that imaging and neurophysiological modalities can assist by providing markers for selecting best candidates and evaluate efficacy in phase II trials.In the visual pathway laboratory, we run retina and brain imaging and neurophysiological assessments with the aims of further knowledge of the disease and development these markers. We have already contributed to MS community with studies in Optical Coherence Tomography (OCT) and visual outcomes for neuro-axonal injury. Now we are opening scope for demyelinating markers for MS and markers for other diseases such as Parkinson Disease.

Would you join us to combat neurological diseases?

Principle investigator: Elena H Martínez-Lapiscina, hernandez@clinic.ub.es; elenahmlapiscina@gmail.com/ https://orcid.org/0000-0003-4272-0826 and Albert Saiz, asaiz@clinic.cat

Research group: Visual Pathway Lab

1. Scientific objectives:
   - Pathogenic mechanisms
   - Markers.

2. Available resources
   - Data: AON-Visualpath (n=50, over 18 months); MS-Visualpath cohorts (n=160; over 7 years); PD-VisualPath (on construction).
   - Technology: 2 Spectralis SD-OCT, 1 Optomap, 1 Daytona, 1 Humpfrey perimeters, 1 visual evoked potential, 2 multifocal VEP, 1 Electroretinogram, 1 Raman spectrophotometer, optotypes for visual function test and 1 3T MRI scan (access through image platform).
   - Team: two neurologists, two neuro-ophthalmologists, an optometrist, a clinical coordinator, an engineer.

Additional information about the research group: Importance of the clinician-scientists within the group: Visual Pathway Lab of the IDIBAPS-Hospital Clinic of Barcelona (MS and Neuroimmunology Unit) truly bridged clinical activity with research activity. The neurologist, ophthalmologist and optometrist do perform clinical activity mostly on multiple sclerosis and acute optic neuritis. We strongly believe that being close to patients inspires research focus on their needs.

Interest of the group to recruit a clinician-scientist: We are seeking a physician with experience in clinical research and strong statistical skills. Experience in markers will be desirable, even if not in neurological disorders.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL23. Personalized Immunotherapy Combinations in Liver Cancer (Dr. Josep Maria Llovet)

Key words: Hepatocellular carcinoma; Immunogenomics; Immunotherapies; Predictive biomarkers; Precision medicine.

Description of the research line: Immunotherapies have revolutionized the landscape of treatments in cancer. Hepatocellular carcinoma (HCC) is the most prevalent liver cancer with ~ 800,000 cases annually worldwide. A large phase II clinical trial testing nivolumab -a monoclonal antibody targeting the programmed cell death protein 1 (PD-1)- led to ~20% responses and promising survival outcomes. However, the mechanisms underpinning clinical responses are poorly understood and there is a lack of biomarkers that could predict responders**.** Maximizing the clinical benefit of immunotherapies in this cancer is a major need.

In this scenario, through a computational analysis of gene expression data, we have recently identified 3 distinct immune profiles (Immune, Intermediate and Exclusion) (Sia, Gastroenterology 2017). The Immune class (~30% of HCCs) shows an "inflamed" microenvironment characterized by high immune cell infiltration and expression of PD-L1 and PD-1, suggesting sensitivity to checkpoint blockade. The "non-inflamed" profiles (Intermediate and Exclusion) show low expression of T cell signatures accompanied by presence of oncogenic mechanisms associated with resistance to immunotherapy.

To explore this groundbreaking concept, the research line proposed for BITRECS Fellows will consist in:

a) decode the immunological landscape of HCC through a large-scale multi-omics integrative analysis.
b) identify candidates for immune-related blood-based biomarkers (liquid biopsy) able to capture the distinct tissue-based immune profiles for patient stratification.
c) generate of ad-hoc pre-clinical models able to faithfully reproduce the complexity of the immune microenvironment observed in human HCC tumors. These new models will be critical in testing candidate drug combinations and in streaming novel therapeutic opportunities.
d) assess whether candidate biomarkers identified during the research predict response to checkpoint inhibitors in HCC or other therapies of interest. We have access to HCC cohorts of patients treated with checkpoint inhibitors.

The BITRECS Fellow will be directly engaged in those activities. We foresee that the success of this innovative proposal will revolutionize HCC patient care by providing unprecedented survival rates resulting from accurate patient selection with a precise diagnostic tool.

Principle investigator: Josep Maria Llovet; jmllovet@clinic.cat; https://orcid.org/0000-0003-0547-2667

Research group: Liver Cancer Translational Research Laboratory: We are a multidisciplinary team dedicated to unravel the molecular classes, discovery of drivers as targets for therapies and biomarkers as predictors of outcome/ response/resistance to therapies for liver cancer. Our research pivots on high-throughput genomic data and state-of-the-art disease models. During the last 10 year we obtained funding from EU, NIH along private foundations for a total of > 15M€ in the context of around 50 grants. In terms of publications, during the last 10 years we have published 135 articles, among which 74 originals, 43 reviews and 18 editorials. The PI of the group, Prof Josep M Llovet has an h index of 102, and ~ 56,000 citations.

Additional information about the research group: Importance of the clinician-scientists within the group: IDIBAPS and Hospital Clinic are located in the same Campus. The Liver Cancer Translational Research Laboratory has a direct relationship with the Hospital Clinic, working close together with all departments involved in the management of patients with HCC (i.e Hepatology, Oncology, Surgery, Pathology, and Radiology). Dr Llovet is part of the Liver Cancer Clinical program. In parallel, he is also the Director of the Liver Cancer Program and Full Professor of Medicine at the Mount Sinai School of Medicine, New York University. This enlarges the clinician-scientist network actively participating in the projects of the group.
In our Liver Cancer Translational Group, two MDs are directly involved in the clinical activity, in the oncology and in the pathology departments respectively.

Interest of the group to recruit a clinician-scientist: The scope of our research is entirely translational. In the last decade, high throughput technologies have dramatically changed the biological understanding of liver cancer. However, the discovery of key drivers of tumor progression has not been yet followed by the approval of targeted therapies in biomarker-driven populations. In this scenario, the role of clinician-scientists, acting as leaders of translational research, is essential for the ultimate success of this continuum of research that aims to benefit our society.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL24. Fecal microbiota trasplantation to fight against antimicrobial resistance (Dr. Alex Soriano)

Key words: nosocomial infection, antimicrobial resistance, prevention, gut-microbiota, fecal microbiota transplantation.

Description of the research line: Nosocomial infections occur in 8% of patients in intensive care units. The mortality rate depends on the early administration of an adequate antibiotic treatment but the emergence of antimicrobial resistance reduces the probability of receiving it. Every year in Europe, 25000 deaths and EUR 1.5 Billion are directly attributted to antimicrobial resistance, therefore, it is necessary to address this problem. There are several approaches to control the transmision of resistant microorganisms including hand-hygiene, innert surfaces and skin desinfection, patients' isolation or reducing the consumption of broad-spectrum antibiotics but the full compliance of these measures is difficult.
The major "reservoir" of resistant microorganisms is the gut flora. In healthy people, gut-microbiota protects from the colonization by other pathogens but several interventions (e.g. broad-spectrum antibiotics, chemotherapy) significantly reduce the effectiveness of this barrier favoring the overgrowth or acquisition of resistant flora. Selective decolonization with a combination of non-absorbable antibiotics has been proposed as a potential solution but its effectiveness has been questioned by the discrepancies in the efficacy described in different trials and the potential risk for selecting pan-resistant bacteria.
Fecal microbiota trasplantation from healthy volunteers has demonstrated a high efficacy for the treatment of *Clostridium difficile* associated diarrea by inducing a rapid restoration of the gut-microbiota. Interestingly, some patients that were colonized by resistant pathogens prior to fecal microbiota transplantation were decolonized, suggesting that healthy microbiota could be able to displace resistant microorganisms avoiding the use of more antibiotics and reducing the risk for selecting pan-resistant bacteria.

The aims of our group are: 1) to develop a tablet from lyophilized feaces to simplify the administration of the fecal microbiota trasplantation, 2) to evaluate the efficacy of these tablets to eradicate resistant microorganisms from colonized patients in the intensive care unit, 3) to determine the impact on the patient's risk of developing infections by the same pathogen, and their mortality rate, and 4) to monitor the impact of this strategy in the incidence of resistant microorganisms in our hospital.

Principle investigator: Alex Soriano, asoriano@clinic.cat; https://orcid.org/0000-0002-9374-0811

Research group: Nosocomial Infections group: The scientific objective of this group is to evaluate preventive measures to control nosocomial infections in the era of multi-drug resistant microorganisms and to study the most relevant factors associated with the outcome of these infections. Infectious Diseases specialists from Hospital Clínic constitute the group. They have a long trajectory in the control and treatment of infectious diseases and they have a close contact with Microbiologists. Both departments maintain common databases on bacteremia and multi-drug resistant microorganisms since 1995. This structure is an excellent platform to perform a translational research from the Microbiology Laboratory to the patient's bed.

Additional information about the research group: Importance of the clinician-scientists within the group: The Nosocomial Infection Research group is constituted by 4 staff members of Hospital Clínic and 1 Emeritus professor and collaborates with the Microbiology Laboratory of the same hospital. Together they have been working in nosocomial infections for the last 20 years. Every year more than 2000 patients are admitted in the intensive care unit and multi-drug resistant microorganisms colonize 20% of them. This fact guarantees the number of patients needed for the study and we have all the laboratory technology to develop the project.

Interest of the group to recruit a clinician-scientist: The need of a clinical-scientist is based on the nature of the current project that combines laboratory work and clinical management of patients in the intensive care unit. Particularly, the group needs support for producing the feaces bank and the metagenomic analysis of gut-microbiota.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL25. Liver Vascular Biology (Dr. Jordi Gracia)

Key words: Liver sinusoidal endothelial cells; hepatic stellate cells; liver sinusoid; portal hypertension; hepatic microvasculature

Description of the research line: The cells of the liver microcirculation, principally sinusoidal endothelial cells, stellate cells and resident macrophages (Kupffer cells), play a key role in the development and progression of liver diseases, and therefore represent an important therapeutic target for the treatment and improvement of patients with liver damage. Our research group studies the molecular and biomechanical processes that regulate the phenotype of these sinusoidal cells, and the hepatic intercellular communication mechanisms, in health, in response to acute liver damage, in chronic liver disease (cirrhosis and fatty liver), and in ageing. Our results are the basis for the development of new therapies to improve liver microcirculation, fibrosis and function. In order to achieve our goals, we use a wide range of experimental methods that include tissues and primary cells, both from human and rodents, in vivo/in vitro models of liver disease, cell co-culture by means of liver-on-a-chip technology, and analysis of big data.

Principle investigator: Jordi Gracia, Jordi.gracia@idibaps.org; https://orcid.org/0000-0001-7736-4089

Research group: Liver Vascular Biology Research Group: The Barcelona Hepatic Hemodynamic Lab is a world leading research team focused in the study of liver vascular disorders and development of novel therapeutic approaches. Our studies have been published in numerous (>300) research articles in top-rated international scientific journals. Our team is composed of around 30 researchers including biologists, biochemists, physiologists and clinicians, and is part of the IDIBAPS Biomedical Research Institute, the Hospital Clínic, the University of Barcelona, and the Biomedical Research Networking Center on Hepatic and Digestive Disease (CIBERehd), which have international recognition in biomedical science. This location provides our MD and PhD scientists with a plural and stimulating scientific environment, cutting edge technologies, state of the art core units and high quality training programs.

Our research includes multidisciplinary basic approaches (cellular and molecular studies and in vivo studies in animal models and genetically modified murine models) and clinical links to liver pathology providing a unique combination of complementary expertises towards improving our scientific knowledge and treatment of chronic liver disease.

Additional information about the research group: Importance of the clinician-scientists within the group: We, as part of the HHLab, have several clinical scientists performing clinical and basic research activities. Our unit at the Hospital Clinic is a referent in the field of chronic liver disease and vascular liver diseases. At the same time, close collaboration between clinical scientists and research scientists allows us to develop novel and very updated research projects that combine bench research with human samples analysis.

Interest of the group to recruit a clinician-scientist: Our group is highly translational and therefore we always seek to create new projects that investigate clinically relevant problems using cutting-edge technology. To accomplish this, our group is multidisciplinary and therefore require incorporation of highly-motivated clinical researchers that will, for sure, develop excellent work and give further clinical insight.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL26. Systems biology in chronic obstructive pulmonary disease (COPD): lung development vs. lung ageing (Dr. Àlvar Agustí)

Key words: COPD, smoking, lung development, lung ageing, precision medicine, chronic inflammation, lung regeneration.

Description of the research line: Chronic Obstructive Pulmonary Disease (COPD) is a major cause of morbidity and mortality in the world. It has been traditionally explained by an enhancement of the normal lung function decline that occurs physiologically with age (lung ageing) induced by smoking in some "susceptible" individuals (Fletcher, BMJ 1977). Yet, recent studies from our group (Lange, NEJM 2015) show that this accelerated lung ageing occurs in only about 50% of adult COPD patients, whereas the other half developed COPD in adulthood because the lungs developed abnormally *in utero*, childhood and/or adolescence; further, more recently we showed that individuals with suboptimal lung development also have a higher prevalence and earlier incidence of comorbid diseases and die prematurely (Agusti, Lancet RM 2017). Collectively, these observations imply a very significant change in the traditional pathogenic model of COPD that consider both lung development and lung ageing (Faner, Lancet RM 2018). This opens new avenues for research and development of novel preventive and therapeutic strategies.

Systems biology is a novel research discipline that tries to integrate complex multi-level data (clinical, functional, imaging and molecular) using, among other tools, network analysis (Faner AJRCCM 2016). Our main working hypothesis is that multi-level network analysis of data gathered from a number of well characterized cohorts of children, adolescents, young and old individuals (already available and fully accessible to our group) will lead to the identification of distinct biological mechanisms (i.e. endotypes) and potential novel therapeutic targets/strategies. The main scientific challenge is how to translate the discovered endotypes into useful knowledge for clinical practice.

This proposal is highly relevant for clinical practice since it will allow an endotype -based stratification of COPD and a precision medicine approach to COPD (Agusti, ERJ 2016 and 2017).

Principle investigator: Àlvar Agustí; aagusti@clinic.cat; https://orcid.org/0000-0003-3271-3788 and Rosa Faner; rfaner@clinic.cat

Research group: Inflammation and repair in respiratory diseases: Our research group belongs to Area 2 of the Institute of Biomedical Research Agust Pi Sunyer in Barcelona and to the Spanish National Network of Excellence for Respiratory research (group 10; www.ciberes.es).The group has extensive experience in basic, clinical and epidemiological research and has full access to the technology needed for this project (CELLEX, plant 2, IDIBAPS; Respiratory Institute, Hospital Clinic; dbGAP and other databases). Dr. Alvar Agusti has > 400 articles (H-index >80), is the current Chairman of (GOLD; www.goldcopd.org). With Rosa Faner (co PI) he is leading the Clinical Research Collaboration CADSET sponsored by the European Respiratory Society.

Additional information about the research group: Importance of the clinician-scientists within the group: The group include basic (biologists, bioinformatisticians) and clinical (pulmonlogists) researchers with ample experience in the methods and techniques required for this project.

Interest of the group to recruit a clinician-scientist: The group is interested in recruiting a clinical scientist with interest in translating basic knowledge to clinical practice in the field of COPD in particular and airways diseases in general.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL27. Identifying predictors of response to therapy in Inflammatory Bowel Disease patients (Dr. Azucena Salas)

Key words: Inflammatory bowel disease, molecular predictors of treatment response, flow cytometry, single cell RNAseq.

Description of the research line: The research line will focus on understanding molecular and cellular predictors of response to therapy in inflammatory bowel disease. To do that we will have access to tissue samples from prospective and retrospectively collected cohorts of patients receiving different treatments and will use transcriptomics, single cell analysis, and flow phenotyping in blood and tissue samples. Potential predictors will have to be validated for their clinical application in independent cohorts.

Principle investigator: Azucena Salas, asalas1@clinic.ub.es; https://orcid.org/0000-0003-4572-2907

Research group: Cellular and molecular mechanisms of Inflammatory Bowel Disease: The main goal of our research is to understand the molecular and cellular processes that initiate and perpetuate human inflammatory bowel disease (IBD). Within this broad goal, there are several strategic objectives including the development of biomarkers to monitor disease progression and response to therapy, and the identification of new molecular and cellular therapeutically targets. We combine leading edge research technology (RNAseq, multiparameter flow cytometry and cell sorter, organoid culture, etc) and knowledge with access to patient information and samples.

Additional information about the research group: Importance of the clinician-scientists within the group: Our group is composed by 50% of IBD specialists (clinicians and research nurses) and 50 % research scientists. The IBD Unit is a multidisciplinary group integrating all medical and nursing specialities involved in IBD patient care with the purpose to provide an excellence and integral care. Clinical members of the group are involved both in the development of clinical studies and translational studies, with a focus on projects that may bring about improvements in patient care in a foreseeable future.

Interest of the group to recruit a clinician-scientist: We believe we provide an excellent atmosphere and environment for the development of a clinician with an interest in translational research as we combine an IBD referral centre of excellence with a leading research lab. Importantly the group will benefit also from a clinical scientists taking part of the lab projects and providing an additional clinical view to our research.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL28. Targeting molecular heterogeneity in lymphoma (Dr. Dolors Colomer)

Key words: Leukemia, lymphoma, microenvironment, new targether therapies.

Description of the research line: Our research focuses on the development and validation of preclinical new targeted therapies in lymphoma models and the molecular basis for their response to therapy. It draws from fundamental mechanisms of cell and tissue development, animal models of the disease, and clinical samples. Genetic studies have led to the identification of novel recurrent somatic mutations with predicted functional impact in lymphoid malignancies, offering new potential therapeutic approaches for these diseases. Often, these malignancies are comprised of multiple subclones with distinct mutational profiles. Thus, when targeting a specific alteration, the patient-specific subclonal architecture can influence the outcome of the therapeutic intervention. Furthermore, leukemic cells remain responsive to multiple stimuli originating from the microenvironment. Understanding the molecular mechanisms underlying this cross-talk may lead to the identification of new therapeutic targets. In this context, the current proposal is aimed to investigate new targeted therapies against the most recurrent mutations described in lymphomas as well as the analysis of the modulation by these new agents of the interaction between tumoral cells and the microenvironment.

Our scientific activity pursues translating research for human health, making sure that basic discoveries have practical benefits and improve the quality of patients. Our project is based on the development of preclinical new therapies of commercial value and on the in vivo validation of the experimental results in mouse models. These objectives can be achieved by an important collaboration with pharmaceutical and biotech companies in order to bring our discoveries as soon as possible to the patients. Our aim is the translation bench-to-bedside to the clinics and to make personalized therapy a reality, based on the optimization of the treatment for each patient, improving the benefits and avoiding the negative side effects.

Principle investigator: Dolors Colomer; dcolomer@clinic.cat; https://orcid.org/0000-0001-7486-8484 and Patricia Perez-Galan; pperez@clinic.cat

Research group: Experimental Therapeutics in lymphoid Malignancies: *Scientific objective*: Identification of potential points of intervention and development of new therapeutic strategies and combination approaches based on the genetic and molecular mechanisms implicated in the development and progression of lymphoid malignancies, with the idea to translate bench-to-bedside. *Facilities*: IDIBAPS and Hospital Clinic facilities. *Research methods or techniques*: 2D and 3D cultures, flow cytometry, molecular biology and cell biology techniques, ex vivo and mouse in vivo studies

Additional information about the research group: Importance of the clinician-scientists within the group: The PI of the group is the chief of the Hematopathology Section at the Hospital Clinic. This section performs the integrated diagnosis of leukemia and lymphomas and the follow up of the patients. The Section is in charge of the management of the Hematopathology collection of samples at the biobank. The research team is composed also of clinicians working at the department of Hematology. They participated actively in all the projects

Interest of the group to recruit a clinician-scientist: Our group is interested in recruiting clinician-scientists able to bridge lymphoma and leukemia research discoveries into tangible new clinical treatments.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 754550

RL29. Clinical, molecular and endoscopic characterization of high-risk conditions for colorectal cancer (Dr. Francesc Balaguer)

Key words: Colorectal cancer, Lynch syndrome, serrated polyposis, prevention, endoscopy

Description of the research line: The scientific activity of the group is aimed at deepening the knowledge of the mechanisms involved in the development and progression of premalignant and malignant gastrointestinal, with the ultimate aim of establishing new diagnostic, therapeutic and/or preventive strategies in these neoplasms. The research carried out is basic, clinical and translational, so the group has several lines of research fully interrelated. One of the main aims is the characterization and improvement in the management of the hereditary forms of colorectal cancer (CRC). A key element in this line has been the leadership of one of the most ambitious cooperative multicenter projects carried out in Spain, the EPICOLON project. The results of this project have allowed characterizing the clinical and molecular features of hereditary CRC. In addition, the group member lead a High Risk CRC Clinic in the Hospital Clinic being referral center for this conditions. As a result of collaboration with national and international groups, our group has developed a number of studies focusing on the identification and management of Lynch syndrome and serrated polyposis syndrome (JAMA 2005, Gastroenterology 2008, Clin Cancer Res 2010, Clin Cancer Res 2011, JAMA 2012, Ann Oncol 2013; J Natl Cancer Inst 2016; Gut 2016; Endoscopy 2017; Endoscopy 2018).

Many challenges lie ahead in the clinical, molecular and endoscopic characterization of high-risk conditions for colorectal cancer. Herein we describe the most relevant for our group:

- There is a lack of biomarkers for early diagnosis, prognosis and treatment in colorectal cancer in the high-risk CRC setting.
- Characterization of the clinical phenotype of high-risk conditions for CRC requires multicenter and multinational collaborations.
- A strong immunological response to Lynch syndrome tumors has been described to be a common and relevant feature in this syndrome. However, the molecular basis and the potential role of immunological intervention in Lynch syndrome tumors are still poorly understood.
- Endoscopy has experienced a very important advance in recent years and its role as the main tool for the prevention of colorectal cancer is still to be determined.

Hereditary forms of colorectal cancer are rare diseases. To improve its clinical management, it is necessary to do research in a multidisciplinary and collaborative context. Our research group has extensive experience in multicenter collaboration, has made relevant contributions in the understanding of molecular mechanisms in this context, and has a long clinical experience.

Principle investigator: Francesc Balaguer; fprunes@clinic.cat; https://orcid.org/0000-0002-0206-0539 and Maria Pellisé; mpellise@clinic.cat

Research group: Gastrointestinal and Pancreatic Oncology Research Group: The research group, consisting mainly of clinicians with basic training has extensive experience in translational research in digestive cancer, leading both clinical and molecular projects that have contributed to the characterization, diagnosis and treatment of digestive cancer. The scientific objectives are: 1) Developing biomarkers with clinical utility for early diagnosis, prognosis and treatment in high-risk conditions for CRC; 2) Characterizing the phenotype of high-risk forms of CRC in order to improve management (specially for Lynch syndrome, FAP, serrated polyposis); 3) To identify the immune response to specific neoantigens of the deficient DNA repair system in individuals with Lynch syndrome with the ultimate goal of developing a vaccine; 4) Evaluating new endoscopic techniques in high-risk conditions for CRC.

Additional information about the research group: Importance of the clinician-scientists within the group: The research group consists mainly of clinicians (board certified gastroenterologists) with basic training with extensive experience in translational research in digestive cancers. Also, the clinician-scientists have a broad experience in endoscopy, specifically in the management of hereditary forms of colorectal cancer.

Interest of the group to recruit a clinician-scientist: The interest of the group in recruiting a clinician-scientist is to be able to develop the objectives of the group by the hand of a highly motivated clinician, and to be able to offer him all the tools for his professional development. The research team is comprised of clinical experts in the management of high-risk CRC conditions. The synergy of the group with a new member will allow the successful achievement of our and her/his objectives.

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RL30. Identification of new genes involved in germline predisposition to gastric cancer (Dr. Sergi Castellví-Bel)

Key words: Gastric cancer, germline predisposition, next generation sequencing, prevention, mutation

Description of the research line: The clinical research line is part of the Gastrointestinal and Pancreatic Oncology Research Team lead by Dr. Antoni Castells. It aims at deepening the knowledge of the mechanisms involved in the development and progression of premalignant and malignant gastrointestinal and pancreatic lesions, with the ultimate aim of establishing new diagnostic, therapeutic and preventive strategies.
Gastric adenocarcinoma (GC) represents the fifth most frequent neoplasm worldwide, with a high mortality rate. Up to 10% of cases show some degree of family history for this neoplasm, which will be reflecting an underlying germline cause. Despite advances in the characterization of hereditary GC syndromes, the familial predisposition is still unknown in most cases. In the last two decades, the majority of the studies related to gastrointestinal tumors have focused on colorectal cancer, so more studies on gastric cancer are needed.
The identification of new genetic alterations associated with familial GC can be attained by selecting GC patients suggestive of a germline predisposition (GC aggregation or early-onset) and performing whole-exome sequencing in peripheral blood and tumor DNA. Germline genetic variants will be characterized and somatic profiling can be performed. By doing so, most promising candidate genetic variants can be identified by performing bioinformatics analysis. Replication of the identified candidate genes in independent GC cohorts is required in order to further confirm them. Next, state-of-the-art functional studies including gene editing with CRISPR-Cas9 are then necessary to test the role of these genes in cellular models and firmly demonstrate their implication in disease predisposition. Finally, a genotype-phenotype correlation of the newly identified GC predisposition variants could bring some light to determine specific clinical and pathological characteristics that could help identify additional GC patients with the same germline predispostion.

Principle investigator: Sergi Castellví-Bel; sbel@clinic.cat; https://orcid.org/0000-0003-1217-5097 and Leticia Moreira; lmoreira@clinic.cat

Research group: Genetic Predisposition to Gastrointestinal Cancer: Our main objective is to identify genetic variants involved in the germinal predisposition to gastrointestinal (GI) cancer through studies of genetic association and new generation sequencing, and explore the application of these variants in the clinical management of patients affected by these gastrointestinal diseases. In order to achieve it, our group has clinical and molecular expertise including hereditary gastrointestinal cancer, next generation sequencing, bioinformatics and state-of-the-art cell and molecular biology.

The research group has access to the facilities of the IDIBAPS. The group is part of the high-risk clinic for GI cancer at the Hospital Clínic and part of the Oncology group of the Spanish Association of Gastroenterology, leading to access multicenter databases for collaborative studies.

Additional information about the research group: Importance of the clinician-scientists within the group:
The research group is formed by scientists with basic training and clinicians with basic training and extensive experience in translational research in digestive cancer, leading both clinical and molecular projects that have contributed to the characterization, diagnosis and treatment of digestive cancer. The clinicians are experts in patients with high risk conditions of GI cancer, participating at different levels of their clinical care (diagnosis, treatment, prevention, surveillance).
The synergy of the clinical and scientific part of the team will facilitate the achievement of the objectives of the study and the success of its correct execution in a fast, complete and rigorous manner.

Interest of the group to recruit a clinician-scientist: The interest of the group is to involve a person with a special interest in this topic. A clinician-scientist is the perfect profile to develop this project, reinforcing the bridge between patients and laboratory. The research group will provide the clinician with the necessary tools for the successful achievement of objectives, as well as for his/her professional improvement.

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RL31. Novel approaches for fetal medicine and surgery (Dr. Eduard Gratacós)

Key words: Fetal medicine, fetal surgery, prenatal prognosis, fetal programming, fetal growth restriction

Description of the research line: Fetal medicine focuses on managing health concerns of the fetus prior to, during, and shortly after pregnancy. This period offers a critical "window of opportunity" for detecting and preventing problems that otherwise will have a profound impact later in life, when interventions may be much less effective.
The main aim of the research line is developing real solutions of diagnosis and treatment to fetal problems using a cross-disciplinary approach, and integrate these solutions to clinical practice through Maternal-Fetal and Neonatal Medicine services.

Our research is organized into 5 sub areas:

1. Prematurity. Focuses on patients at risk of preterm labor, investigating non-invasive diagnostic tools such as quantitative ultrasound textures analysis and biomarkers for intraamniotic inflammation and infection.
2. Placental Disease. Identifies suboptimal fetal growth before birth providing new diagnosis tools for the correct classification of small babies at highest perinatal risk and optimal timing to delivery
3. Fetal Brain Development. Develops quantitative imaging biomarkers for early diagnosis of neurodevelopmental disorders of prenatal origin based on ultrasound and magnetic resonance.
4. Fetal Programming. Focuses on the long-term impact of prenatal conditions such as fetal growth restriction, preeclampsia, assisted reproductive technologies, perinatal infections or congenital heart disease, providing a better phenotypic characterization and testing preventive strategies for fetal growth restriction.
5. Fetal Therapy and Surgery. Focuses on characterizing neuroprotective therapies that could mitigate the neurodevelopmental impairment related to fetal growth restriction and to develop new technological solutions for fetal surgery.

Principle investigator: Eduard Gratacós; gratacos@clinic.cat; https://orcid.org/0000-0002-7405-7224 and Fàtima Crispi; fcrispi@clinic.cat; https://orcid.org/0000-0002-7422-5240

Research group: Fetal and perinatal medicine: The main scientific objectives of the group are to develop new imaging and molecular tools for early diagnosis and monitoring prenatal diseases, to provide new clinical solutions for improving fetal growth, to develop and validate new technological solutions for fetal surgery and to consolidate animal models for better characterizing fetal programming.
We are a translational biomedical research team with more than 70 researchers, combining fetal cardiology, neurodevelopment, reproductive medicine, biology and bioengineering to develop highly competitive research on fetal medicine and surgery.

Additional information about the research group: Importance of the clinician-scientists within the group: Being a clinical research group, clinician-scientists are the main pillar of our team. In addition, our team includes other professionals such as biologists, engineers, nurses, and psychologists in order to meet the needs of the multi-disciplinary research we are developing with the final aim of finding innovative and efficient solutions and apply them to clinical setting.

Interest of the group to recruit a clinician-scientist: We are interested in incorporating an experienced clinician-scientist in fetal medicine with expertise in leading research projects and teams, who can provide new ideas for research projects and international collaborations, and complements our current team.

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RL32. Vasculitis: immunopathogenic mechanisms of vascular inflammation and remodelling (Dr. Maria Cinta Cid)

Key words: Vascular inflammation, ex-vivo models, cytokines, lymphocytes, macrophages

Description of the research line: The research line focuses on inflammatory diseases of blood vessels (systemic vasculitis) from a clinical and translational perspective. Vasculitis are serious and relapsing diseases with an overall mortality of 15-20% and with a deep impact on quality of life due to organ damage or treatment toxicity. From the clinical standpoint we are a national and international referral group for the diagnosis and treatment of systemic vasculitis, preliminarily accepted in a European Reference Network (national endorsement pending). The group has participated in the main international consensus recommendations and guidelines on the nomenclature, classification, diagnosis and treatment of systemic vasculitis funded and endorsed by the leading scientific and medical societies of Rheumatology (American College of Rheumatology [ACR] and European League Against Rheumatic Diseases [EULAR]). The group has also contributed to therapeutic innovation, with an important role in 2 recent clinical trials leading to FDA and EMA approval of new targeted treatments (*Stone JH et al N Engl J Med 2017, Weschler M et al N Engl J Med 2017*).

From the clinical research point of view,the group has assembled well characterized patient cohorts with long-term follow-up along with an approved and registered collection of serum, cells and tissue for biomarker studies, particularly on giant-cell arteritis. From the translational perspective the group investigates mechanisms involved in the persistence of vascular inflammation and in vascular remodelling with the ultimate goal of identifying clinically useful biomarkers of disease activity and vascular injury and to identify therapeutic targets. The research team has developed functional models (ex-vivo artery culture co-cultures) where relevant inflammatory and remodelling pathways are explored. Interference with relevant pathways with agents developed for therapeutic use are explored in these systems. The active participation of the group in international networks and the role of the PI as key opinion leader in the field for Pharmaceutical companies facilitates translation into clinical trials

Principle investigator: Maria Cinta Cid; mccid@clinic.cat; https://orcid.org/0000-0002-4730-0938

Research group: Vasculitis Research Unit: The research team has been recognized as consolidated excellence group by AGAUR. The group is currently exploring the role of imaging in the diagnosis and follow up of patients with large-vessel vasculitis, epigenetic and transcriptomic changes according to disease activity in specific cell populations in peripheral blood and participating in massive genotyping multi-centre studies. We are also investigating tissue and serum biomarkers of relapsing disease and abnormal vascular remodelling. We are developing ex-vivo artery cultures as well as multi-cellular co-cultures to explore mechanisms of vascular inflammation in a complex microenvironment. In these models we are currently exploring the role of various chemokines, the activation of hypoxia pathways and their role in vascular inflammation and remodeling and the impact of IL-6 receptor blockade with tocilizumab or GM-CSF receptor blockade with mavrilimumab on vascular inflammation. The group actively collaborates with other groups and provides the opportunity of short interchanges (France, Italy, Belgium, USA) leading to technological/conceptual advances. *Facilities*: Laboratoy space with core facilities (equipped tissue culture room, freezers, centrifuges, cryopreservation) and access to platforms (advanced microscopy, cytomics, genomics).

Additional information about the research group: Importance of the clinician-scientists within the group: The translational nature of our research requires trained clinical and basic researchers. The clinical scientist profile, able to interact with clinicians and basic scientists and to integrate clinical data and experimental information is essential for this type of research. The PI (MCC) is a clinican scientist trained at the Hospital Clinic of Barcelona (HCB) and at the National Institutes for Health (NIH), Bethesda, MD, USA. The group includes a full time staff clinician expert in vasculitis (JHR), trained at the HCB and at the Cleveland Clinic, Cleveland, OH, USA, a full time staff clinician (AGM) expert in emergency medicine trained at HCB, a Juan Rodés clinical scientist (GEF) expert in vasculitis and in clinical trials, trained at HCB and at the NIH, Bethesda, MD, a junior full time clinician in tenure-track trained at HCB (SPG), 2 post-doctoral basic researchers (MCB and NTG), 1 PhD student funded by FPI, SAF (RAR) , and 1 senior resident in Internal Medicine with experience in vasculitis (JMH). A new PhD student will join the lab in 2019 funded by the ITN HELICAL.

Interest of the group to recruit a clinician-scientist: The clinician scientist profile is demanding and requires intense, long and continued training. While it is essential for translational research is becoming

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difficult to motivate clinicians for this career track, due to the high dedication and commitment required. The research group has 2 members with this profile: the PI and the Juan Rodés but would be important to re-inforce this profile with a new motivated researcher.

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RL33. Translational research in new therapeutic and diagnostic strategies at the nanoscale for liver diseases (Dr. Wladimiro Jiménez)

Key words: Liver disease, nanoparticles, nanomedicine, therapy, cancer

Description of the research line: Research Field: Biofunctional materials for therapy and diagnostics in liver diseases.

The scientific challenges are to design and test functionalized biomaterials able to target, detect and treat diseased cells responsible of the pathophysiological disorders in liver disease including liver cirrhosis, non-alcoholic fatty liver disease and liver cancer.

The use of nanotechnology and biomaterials is emerging as the solution to solve technical and biomedical challenges for the diagnostic and treatment in patients with liver diseases. Our group has extensive experience using inorganic nanoparticles (antioxidant cerium oxide (CeO2) nanoparticles and functionalized carbon nanoparticles) to modulate hepatic damage in animal models of liver disease. Functional nanoparticles are novel therapeutic strategies designed to overcome the limitations of standard drug therapies by reducing the side effects due to the targeting and accumulation properties, and acting directly on diseased cells for precision therapy. It is critical for patients with advanced liver disease to develop non-toxic and selective therapies as the hepatic drug metabolism is compromised. Nanoparticles are moreover inherently accumulated in tumor mass due to their small size and the enhanced permeability effect. Therefore these biomaterials can be used as an alternative approach to target, detect and treat liver cancer (current drug therapy can only extend the lifespan for 3 months). In conclusion nanotechnologies and new biomaterials offer a wide array of possibilities to improve the clinical practice and the diagnostic and therapy of patients with liver disease.

Principle investigator: Wladimiro Jiménez; wjimenez@clinic.cat; https://orcid.org/0000-0002-9376-0214

Research group: Translational research in new therapeutic and diagnostic strategies in liver diseases: The main objective of our group is to investigate new serum biomarkers and new biomaterials to target, detect and treat diseased cells in liver disease.
Facilities, research methods and techniques: lab space fully equipped for cell and tissue culture, molecular biology techniques; access to consortium facilitites including animal facilities, microscopy, flow cytometry, Biobank of Hospital Clínic, Bioinformatics, Biostatistics and Data Management, Cytometry and Cell Sorting, Functional Genomics, and Magnetic Resonance Imaging.

Additional information about the research group: Importance of the clinician-scientists within the group: Dr. Wladimiro Jiménez is the head of the Biochemistry and Molecular Genetics (BMG) department and the Molecular biology core in the Hospital Clinic of Barcelona and lead a research group with clinicians and biomedicine researchers to find new nanomaterials for liver disease. Dr. Manuel Morales-Ruiz is specialist at BMG leading a research project focused on finding specific therapeutic targets of Akt to boost liver regeneration. Dr. Gregori Casals is specialist at the BMG leading a research project focused on the therapeutic use of cerium oxide nanoparticles for non-alcoholic fatty liver disease.

Interest of the group to recruit a clinician-scientist: Our interest is recruiting a clinician-scientist with expertise in the pathophysiology of chronic injury, regeneration and cancer and in the application of new biomaterials for therapy and diagnostics.

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RL34. Molecular pathology of uveitis and retinal inflammation (Dr. Alfredo Adán Civera)

Key words: Retinal inflammation, uveitis, cytokines, blood-retinal barrier, biological therapies

Description of the research line: The research line focuses on retinal inflammatory diseases such as uveitis, diabetic retinopathy or age-related macular degeneration from a clinical and translational perspective. Such diseases are the main cause of legal blindness worldwide with a deep impact on quality of life. From the clinical standpoint we are a national and international referral group for the diagnosis and treatment of ocular inflammation, especially in uveitis.
The group has contributed to therapeutic innovation, with important roles in recent clinical trials leading to US Food and Drug Administration and European Medicines Agency approval of new biological treatments (*Suhler et al, Bonini S et al , Ophthalmology 2018*). From the clinical research point of view, the group has assembled well characterized patient cohorts with long-term follow-up along with an approved and registered collection of serum, and aqueous humor for biomarker studies, particularly on uveitis and diabetic macular edema. From the translational perspective the group investigates mechanisms involved in the appearance and progression of ocular inflammation with the ultimate goal of identifying clinically useful biomarkers of disease activity and prognostic factors to identify therapeutic targets. The research team has developed functional in vitro co-culture models of the blood-retinal barrier where relevant inflammatory pathways are explored. Interference with relevant pathways with agents developed for therapeutic use are explored in these systems. The active participation of the group in international networks and the role of the PI as key opinion leader in the field of uveitis for Pharmaceutical companies facilitates translation into clinical trials.

Principle investigator: Alfredo Adán Civera; amadan@clinic.cat; https://orcid.org/0000-0002-5516-0891

Research group: Group of Ocular Inflammation: Clinical and Experimental Studies: The research team has been recognized as pre-consolidated group by AGAUR. Our research focuses on how the retina responds to injury, inflammation and degeneration. Our main goal is to promote the investigation on ocular inflammatory diseases such as uveitis, and scleritis with special interest in the study of pathological mechanisms, immune response, and development of new therapies. We are also interested in high prevalent ocular diseases in which inflammation plays a key role, such as diabetic retinopathy, glaucoma and age-related macular degeneration. The group actively collaborates with other groups and provides the opportunity of short interchanges (United Kingdom, USA) leading to technological/conceptual advances.

Facilities: Laboratory space fully equipped for cell and tissue culture, molecular biology (freezers, centrifuges, cryopreservation, electrophoresis, microscopy, and spectrophotometer) and access to platforms (advanced microscopy, flow cytometry, genomics, animal facility…).

Additional information about the research group: Importance of the clinician-scientists within the group: The translational nature of our research requires trained clinical and basic researchers. The clinical scientist profile, able to interact with clinicians and basic scientists and to integrate clinical data and experimental information is essential for this type of research. The PI (AAC) is a clinician trained at the Hospital Clinic of Barcelona (HCB). The group includes two full time staff clinician expert in uveitis (VLL, MSM), trained at the HCB and at the Massachusetts Eye and Ear, Boston USA, a full time staff clinician (EM) expert in glaucoma trained at HCB, two full time clinician experts in medical retina, 1 nurse expert in clinical trials, 2 optometrists, a senior basic researcher (BM), 1 PhD student (SR), and 1 Master Student).

Interest of the group to recruit a clinician-scientist: The clinician scientist profile is demanding and requires intense, long and continued training. While it is essential for translational research is becoming difficult to motivate clinicians for this career track, due to the high dedication and commitment required. We are highly interested in recruiting a clinician-scientist with expertise in the pathophysiology of ocular inflammation who can provide new ideas for research projects and international collaborations, and complements our current team.

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