
# Annual Report 2020

IGTP
Institut de Recerca Germans Trias i Pujol


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## Annual Report 2020


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# Introduction

2020 will be known as the year when the SARS-CoV-2 virus caused a global pandemic for which the full effects on health, healthcare and research are still to be seen in the years to come. At the IGTP it was also a year of transition, with Dr Manel Puig stepping down as Director after seven years to concentrate on his research and medical work and Dr Jordi Barretina taking up the position in September. The complexity of running a very diverse biomedical research centre during a global pandemic meant that, for part of the year, the two directors were working closely together, along with the Scientific Director Julia García-Prado, to guarantee the smooth running of new consortia, approve project proposals for new COVID-19 calls and provide support to the hospital, especially with PCR testing, while continually updating the protocols to guarantee the staff safety. At the start of the second quarter of the year, the institute had rapidly transformed to accommodate online working from home and the location of the campus meant that many staff needed special permits to travel outside their municipality to work during the period of emergency.

Despite the disruption to laboratories and research groups, the IGTP still managed to increase its scientific output and also followed the general trend of open data access to get research data on SARS-CoV-2 out to the rest of the scientific community. Almost exactly the same number of projects were applied for as in 2019 and the same number were obtained. Meanwhile the number of evaluated, granted and ongoing clinical trials all increased, with IGTP researchers leading and participating in many COVID-19 trials.

Finally, it should be noted that two important strategic projects of IGTP showed their value and ability to adapt immediately to a new challenge. A new infrastructure, the Centre for Comparative Medicine and Bioimaging (IGTP-CMCiB), was essential for validating prototype ventilators, needed for overloaded hospital intensive care units, and also to advance preclinical research of novel vaccine prototypes for COVID-19. Additionally, the computational modelling group based at the IGTP-CMCiB, switched to mapping the spread of the pandemic and coordinated with the Director General for Digital Excellence and Science Infrastructure of the European Commission. At the same time, the GCAT|Genomes for Life Cohort joined national and international efforts to mine data and drill down into risk factors for contracting COVID-19 and developing severe disease, participating in important publications early in the pandemic.



# A word from the out-going Director

To say that 2020 has been an exceptional year is an understatement, it has been a year that no one will forget due to the COVID-19 pandemic caused by the SARS-CoV-2 virus. I would like to highlight the fact that our medical staff and researchers have stepped up to the challenge and carried out vital work and research, getting both internal and external recognition in the process.

The year passed in a flash, but it was intense and produces conflicting emotions. We faced many crises, the most dramatic of which was probably the “ventilator crisis”. In early April ventilators were in short supply everywhere, including at our hospital, but none of our patients went without. There were initiatives all over Spain, but in Catalonia activity was feverish; in coordination with the IDIBAPS Respiratory Physiology Laboratory, we validated a total of eight different prototypes of emergency ventilators at the CMCiB in collaboration with the ICUs of our hospital and the Hospital Clínic de Barcelona. We were able to verify efficacy and safety at the clinical level, while in parallel and in continuous communication with the AEMPS, we prepared all the necessary documentation for the regulatory agency. Additionally, the IGTP and IrsiCaixa participated intensely in research projects and clinical trials of COVID-19 therapies and vaccines, which has placed us at the forefront as a center of reference, not only in Spain, but also internationally. I can only thank all the researchers and support staff, especially those of the IGTP-CMCiB and all staff members and researchers at the IGTP and the Germans Trias i Pujol Hospital, but also the hospital staff who managed an exponential rise in diagnostic PCRs within weeks.

Manel Puig Domingo, MD, PhD
Professor and Head of Endocrinology and Nutrition service
Germans Trias i Pujol Hospital and Research Institute (IGTP)
Universitat Autònoma de Barcelona

# A Word from the In-Coming Director

2020 has been uniquely marked by the global pandemic of COVID-19. This has affected everyone profoundly, changing working patterns and bringing in new research lines and innovations to meet new needs. Our staff were affected in their personal, family and working lives, some of them developing COVID-19 before the vaccination campaign started.

The institute has great experience in infectious diseases and vaccines and a strong tradition of translational research, so the research effort continued and, in many cases, was extremely focused on the SARS-CoV-2 virus. In addition, a large number of IGTP and affiliated researchers played a key part in the effort to inform the public, both on traditional media (radio and television) as well as on social media, and participated as professional advisors to policy makers.

The rapid reaction of the European Commission and other funding bodies meant that many new IGTP projects got rapidly underway, existing projects started new lines on SARS-CoV-2 and new consortia between basic research, translational research, primary care and public health were formed. The particular nature of the IGTP and its affiliated institutions made it ideally suited to take up these challenges. Projects included re-purposing of drugs, validation of diagnostic tests, vaccine trials, mathematical modelling of infection rates, epidemiological studies and important contributions from the GCAT|Genomes for Life Project and the IGTP Centre for Comparative Medicine and Bioimage (IGTP-CMCiB).

Despite the restrictions of movement, the institute continued with other projects and activities. Just to highlight a couple of things from last quarter of the year: in October, the spin-off company Time is Brain was created to develop a medical device to improve the diagnostics and prognostics of acute ischaemic stroke. Also, after signing the Commitment Charter to Gender Equity in Research - Hypatia of Alexandria - promoted by the Catalan Agency for Health Quality and Evaluation (AQuAS) – in January, our own Equality Committee completed the diagnostic and preparation phases of the new Gender Equality Plan at the end of the year, in line with our strong policy on equality issues.
Finally, I would highlight the election of Julia García-Prado to the Scientific Advisory Board of EATRIS Spain. This is recognition of all the work the institution has been carrying out to strengthen its technological infrastructures and reinforces its presence in national and European networks.

Jordi Barretina Ginesta, PhD
General Director
Germans Trias i Pujol Research Institute (IGTP)



# A comment on 2020 from the Scientific Director

Even researchers like myself who have dedicated a lifetime career to viruses that can potentially cause epidemics were not prepared for the impact of the COVID-19 global pandemic in 2020. It affected scientists immediately and caused tremendous disruption in our everyday lives in the same way as it did for everyone, but it has also profoundly changed how we do our research and will continue to change it for some time to come.

In the words of a colleague, 2020 has been the year that epidemiology and public health came out of the closet; suddenly the public were anxious to hear the experts' opinions, and concepts like the R number, herd immunity, PCR and exponential curve became part of everyday language.

Despite the speed that the virus spread, governments and institutions in Europe were slow to react and timid in their first preventive measures. The need for European and global protocols in the face of pandemics became tragically clear. Despite this, the work carried on for years, often underfunded and certainly not championed, meant that vaccine platforms were available to be adapted to the SARS-CoV-2 virus in record time. RNA vaccines were catapulted into use, changing our concept of weapons against infectious disease forever. Other technologies that have been developed, such as mathematical modelling, showed their true value and strategic projects that have taken our institute years to bring into being were able to apply the power of technology and big data to COVID-19 research.

The virus showed the need for continued investment in public health and the health system. It also sped up the adoption of digital technology in the workplace and as well as in the health services. The need for better planning and coordination for health care professional, researchers and industry became clear to overcome the emergency situation. Many things will never be the same again.

On our campus, the IGTP showed its strength in many vital areas such as vaccine development, clinical trials, high technology infrastructure and experience in large cohorts and big data. As an institute that includes primary healthcare, basic, translational and clinical research and has strong ties with companies, many of these concepts were brought into sharp focus. It was the hardest year many of us had ever lived through but it strengthened our resolve to carry out research efficiently for the benefit of society and showed us the power of a coordinated networked research system.

Julia García-Prado, PhD
Scientific Director
Germans Trias i Pujol Research Institute (IGTP)
Group Leader IrsiCaixa, AIDS Research Institute

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# Research Areas & Groups

- CANCER
- CARDIOVASCULAR DISEASE
- COMMUNITY HEALTH
- DISEASES OF THE LIVER AND DIGESTIVE TRACT
- ENDOCRINE AND DISEASES OF THE METABOLISM, BONES AND KIDNEYS
- IMMUNOLOGY AND INFLAMATION
- INFECTIOUS DISEASES
- NEUROSCIENCE
- SCIENCE OF BEHAVIOUR AND SUBSTANCE ABUSE

**RESEARCH AREAS**
**9**

**RESEARCH GROUPS**
**36**

**Program for Predictive and Personalized Medicine of Cancer (PMPPC)**

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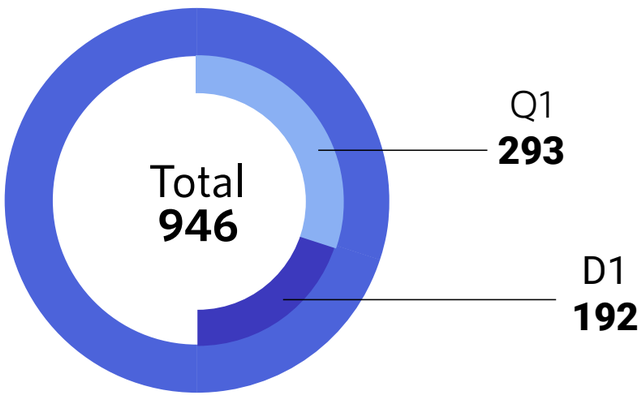
# Publications

**4865.14**
IMPACT FACTOR

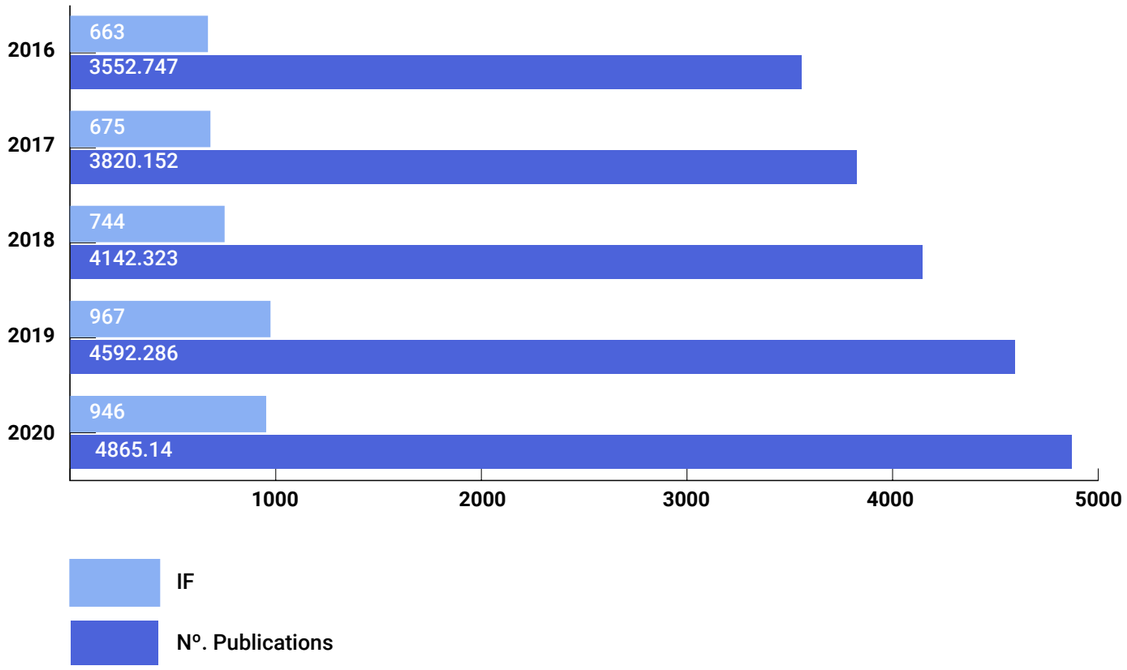
**5.14**
AVERAGE IF

**946**
PUBLICATIONS


**Publications**




**Evolution**



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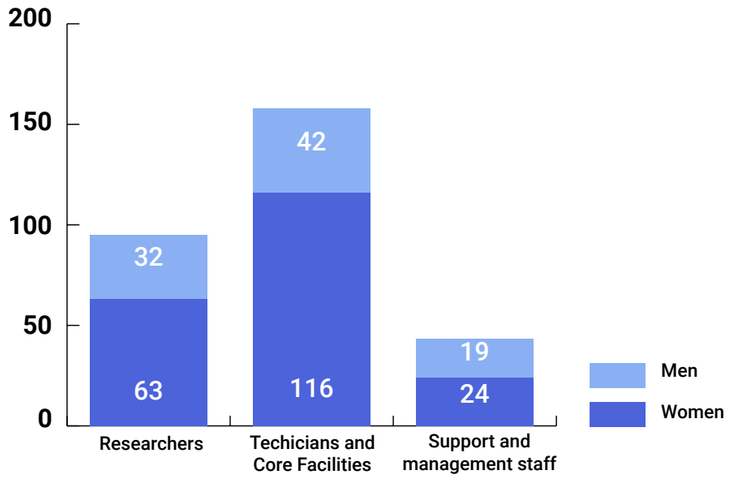
# People

## IGTP Contracted Staff

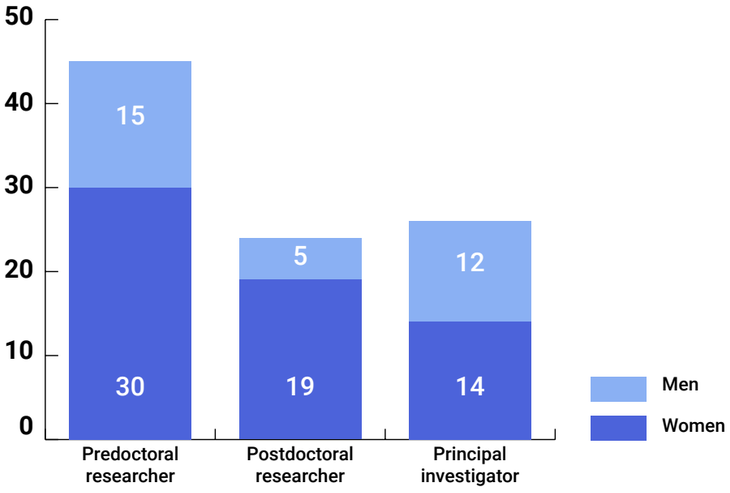
**203 Women**
**68,6%**

**93 Men**
**31,4%**

**IGTP STAFF by professional categories**

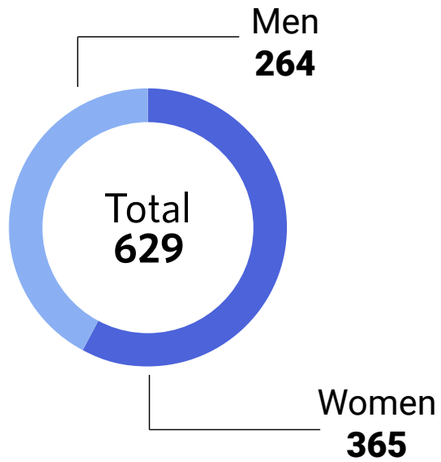



**IGTP Researchers by categories**

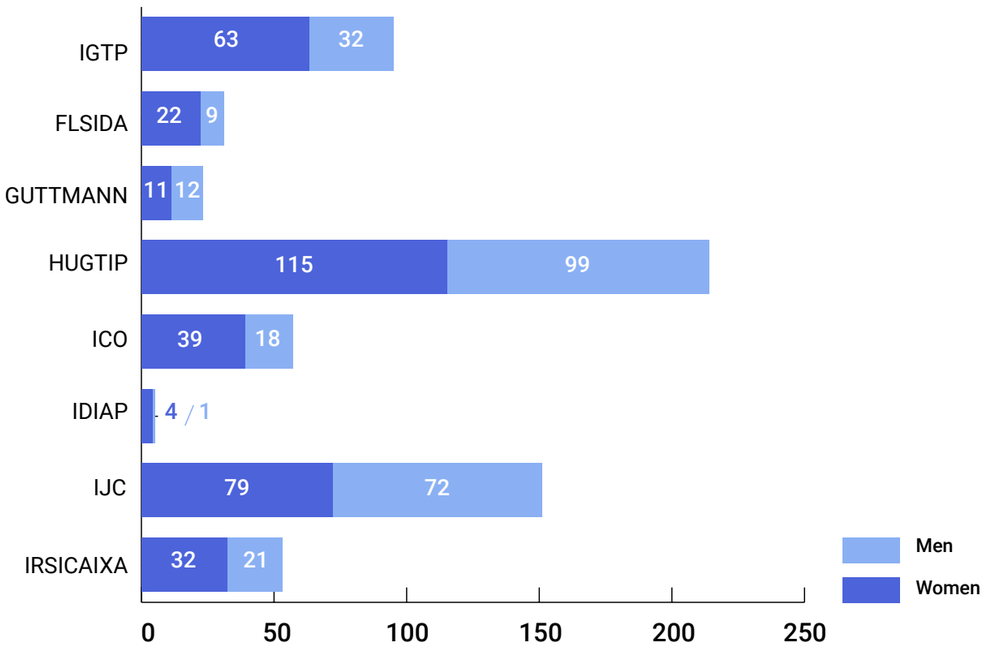



## IGTP Affiliated Researchers on the Campus

**Total researchers**




**Total researchers by institution**



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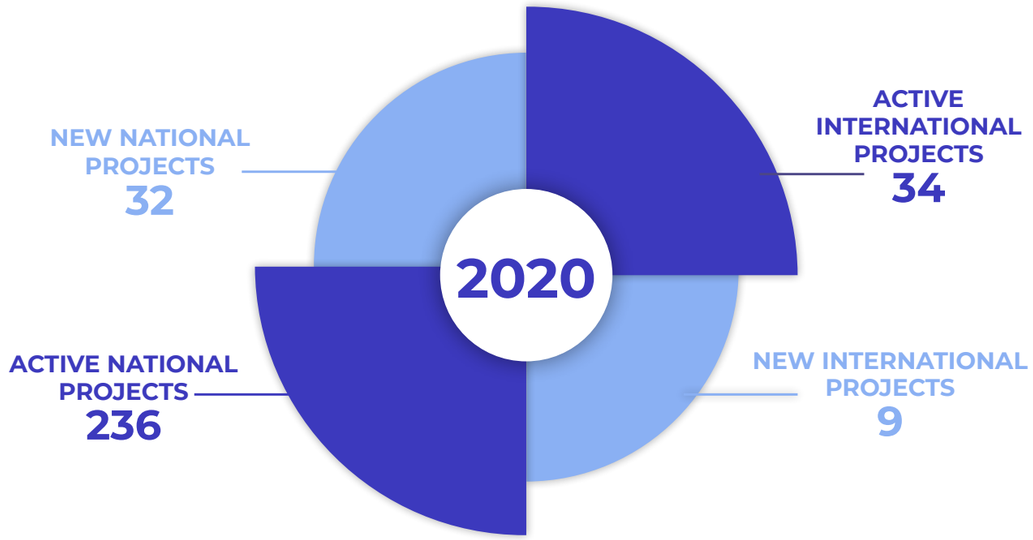
# Competitive Projects

## PROJECTS 2020




## NETWORKS

**5** Spanish Biomedical Research Network (CIBER)

**16** SGR Groups Recognized by the Government of Catalonia

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# Innovation and technology transfer


9
INNOVATION REQUESTS
34
TOTAL ACTIVE PATIENT (FAMILIES)
1
NEW SPINOFFS
9
TOTAL SPINOFFS
2
NEW LICENSES
20
TOTAL LICENSES

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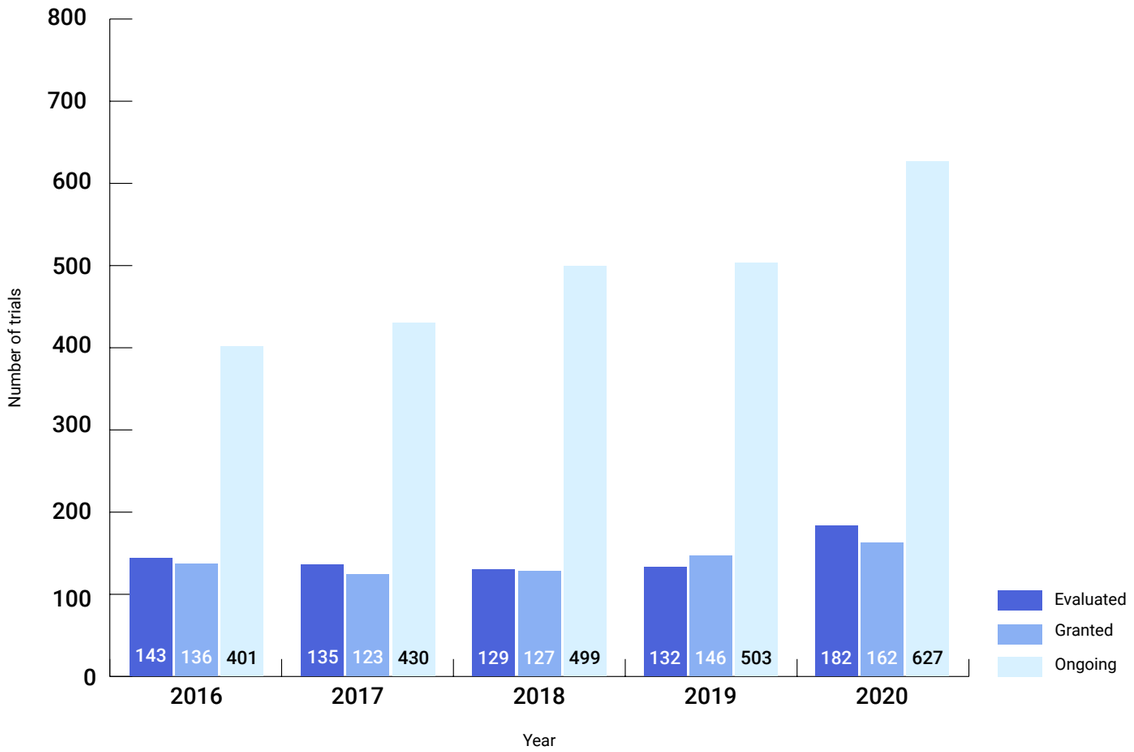
# Clinical Trials






**627**
**ONGOING CLINICAL TRIALS**

**182**
**CLINICAL TRIALS EVALUATED BY HUMAN ETHICAL COMMITTEE**

**162**
**CLINICAL TRIALS GRANTED**

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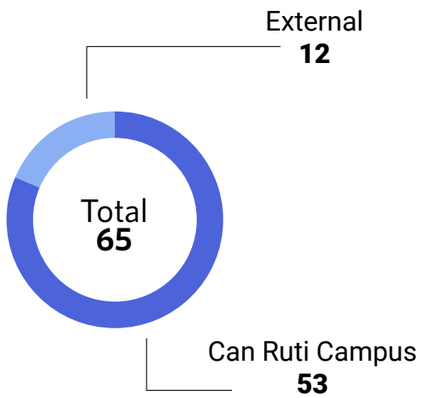
# Core Facilities

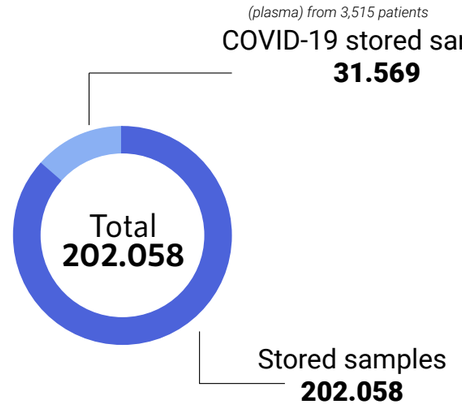
# 451
## TOTAL PROJECTS

## BIOBANK / TUMOUR BANK

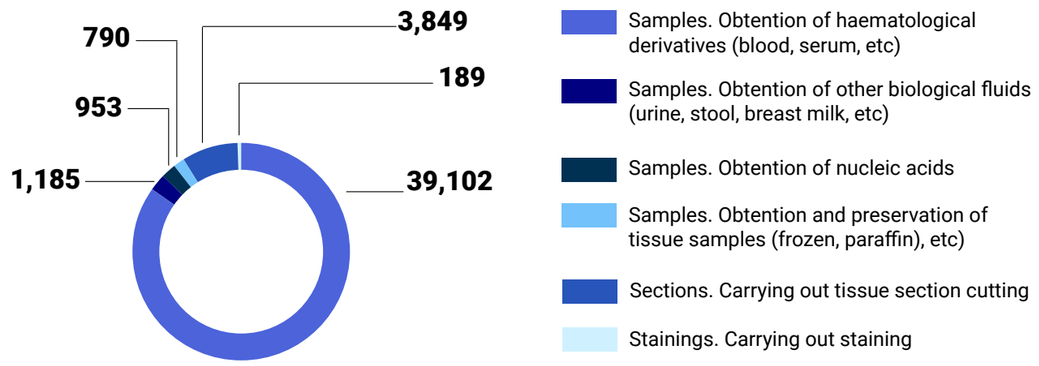
**Projects**




**Samples**



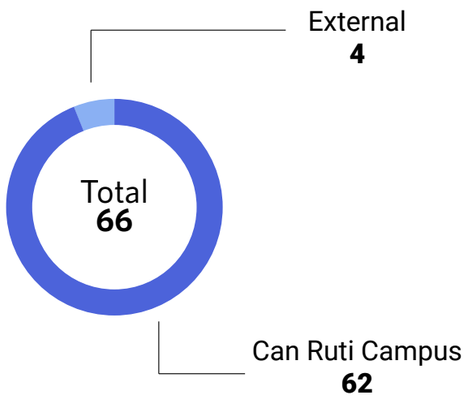

**Services**



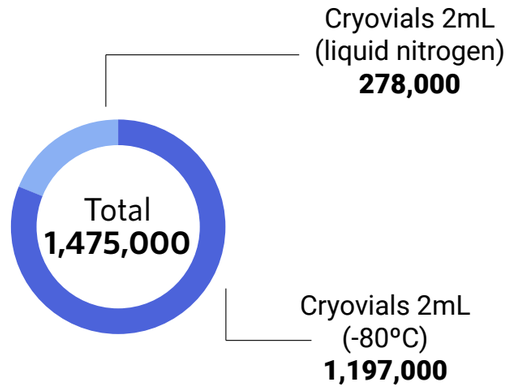



## CRYOBIOLOGY

**Projects**

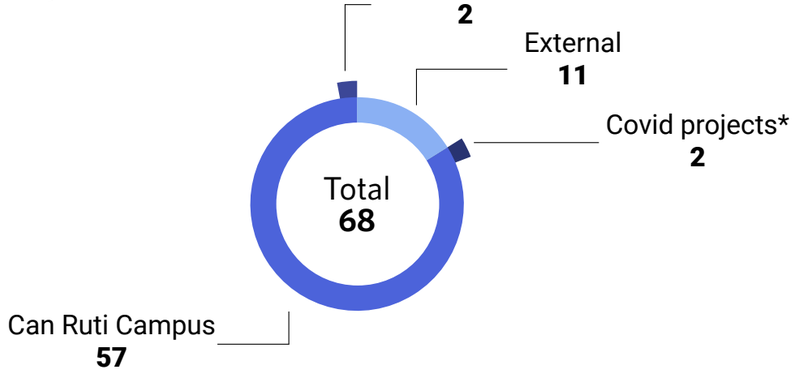



**Stored samples**

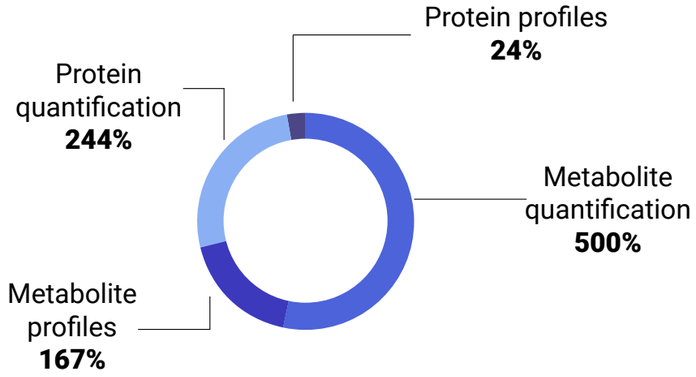



## CYTOMETRY

**Projects**

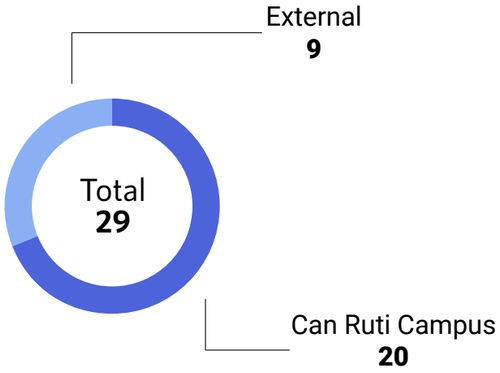



**Services by type**

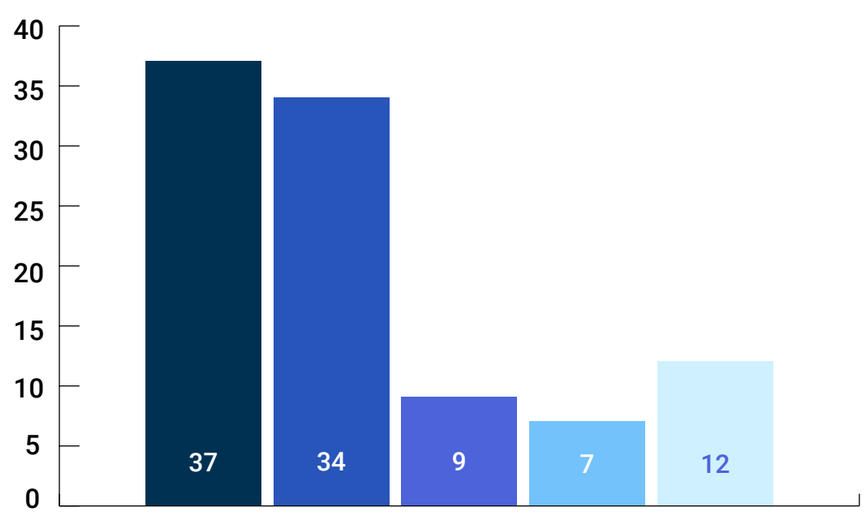


# HIGH CONTENT GENOMICS AND BIOINFORMATICS

## Projects



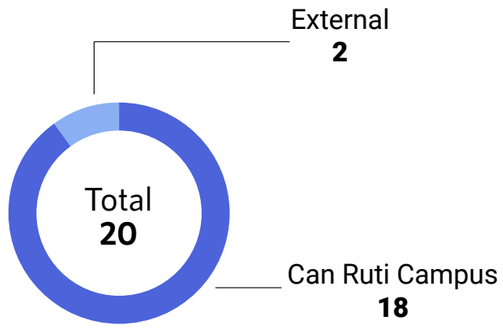

## Services by type



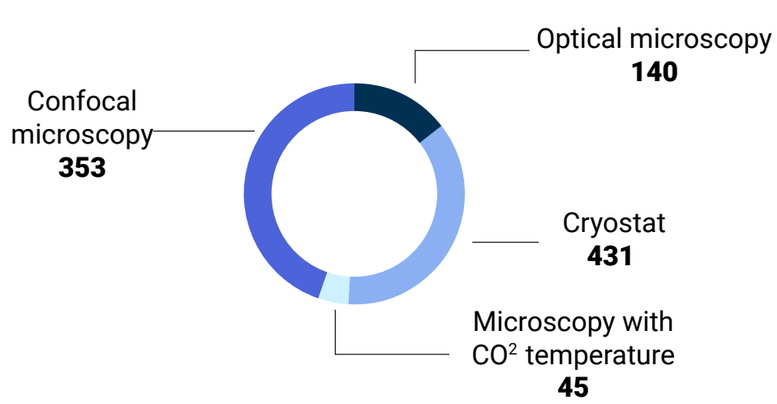



# MICROSCOPY

## Projects

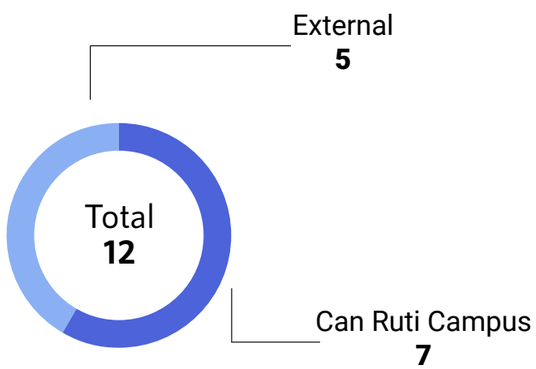



## Projects by type (hours)

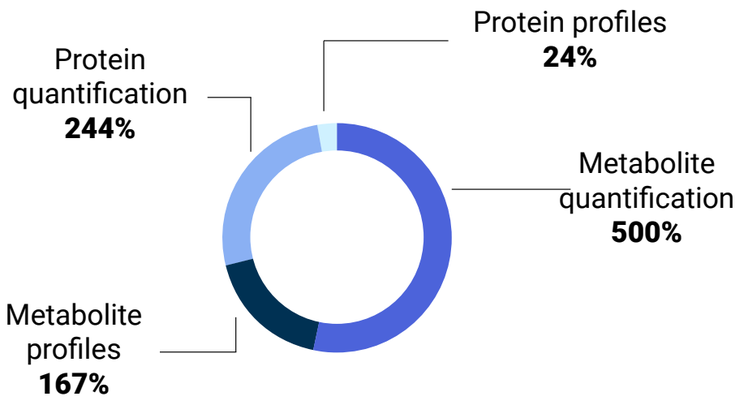



## PROTEOMICS AND METABOLISM

**Projects**



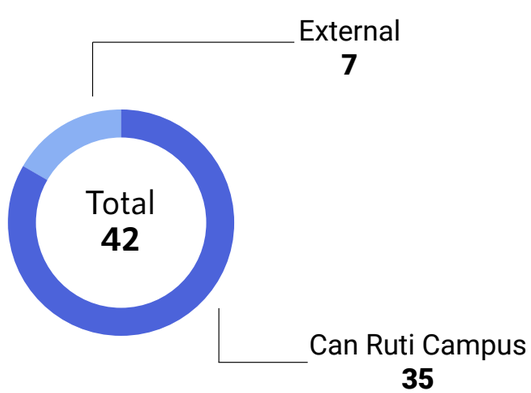

**Services by type**



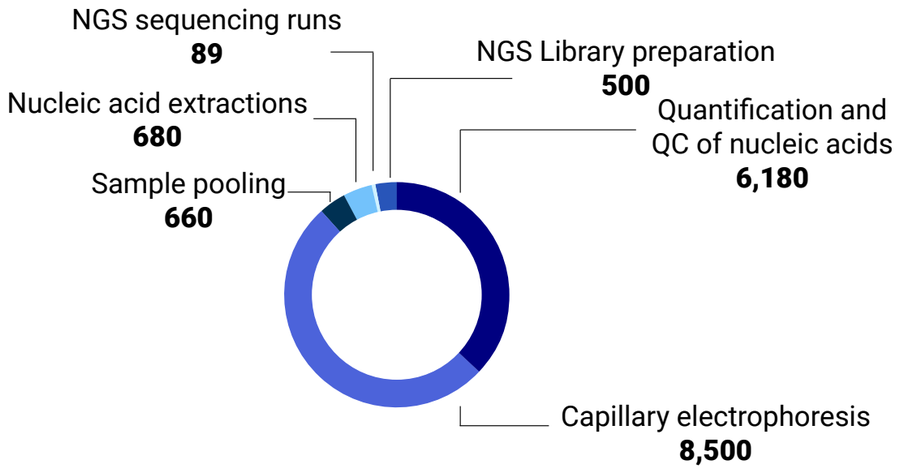



## TRANSLATIONAL GENOMICS

**Projects**

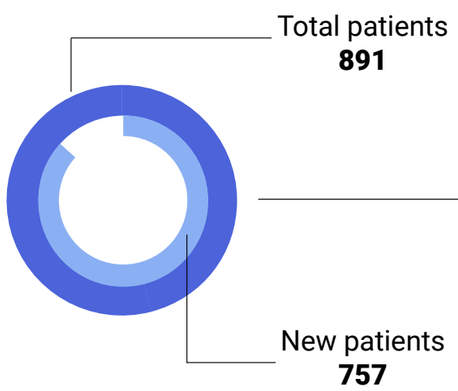



**Number of samples processed and services offered**

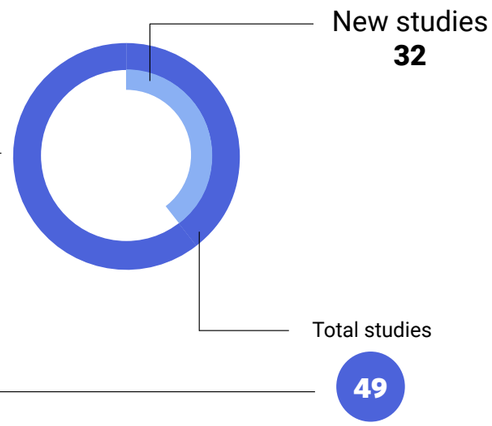


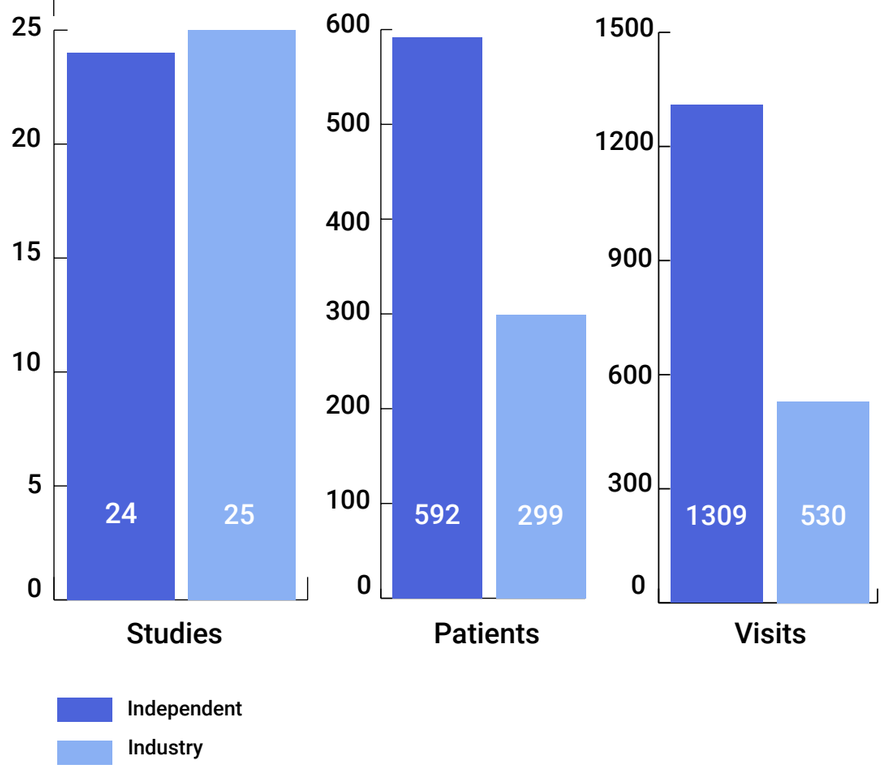
# UPIC – CLINICAL TRIALS UNIT

**No. of patients**




**No. of studies**




**SCReN projects**


# CMCiB – COMPARATIVE MEDICINE AND BIOIMAGE CENTRE OF CATALONIA

**Projects**

**31**
**AUTHORIZED BY ANIMAL ETHICS COMMITTEE**

**100**
**TOTAL ACTIVE PROJECTS**

## PROJECTS FROM 18 RESEARCH AREAS

- Immunology
- Oncology
- Endocrinology
- Digestive
- Neurogenetics
- Oncology and hematology
- Microbiology
- Pneumology
- Cardiology
- Nefrology
- Neurobiology
- Regenerative Medicine
- General and Digestive Surgery
- Laparoscopic Surgery
- Robotic Surgery
- Prosthesis
- Traumatology
- Biosensorics

**127**
**users**

**21**
**collaborations with research institutes and companies**

**55**
**research groups working in the CMCiB**

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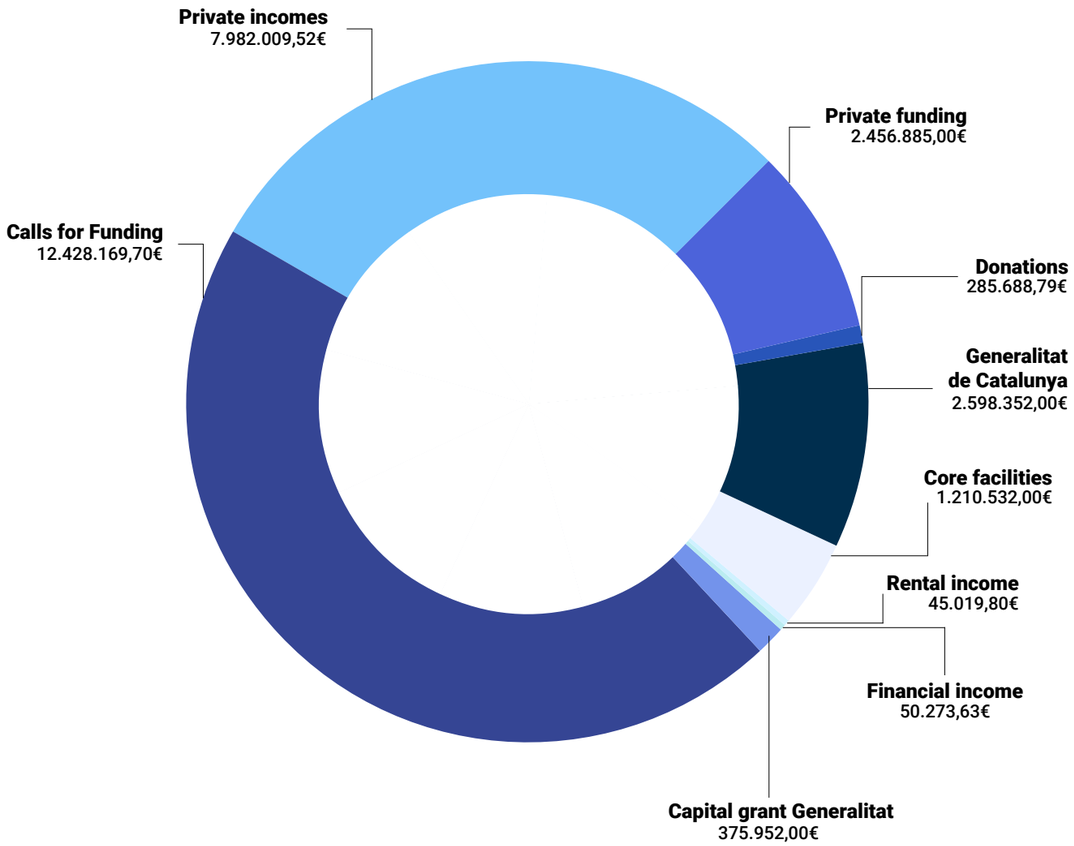
# Funding Sources


Private incomes
7.982.009,52€
Private funding
2.456.885,00€
Calls for Funding
12.428.169,70€
Donations
285.688,79€
Generalitat de Catalunya
2.598.352,00€
Core facilities
1.210.532,00€
Rental income
45.019,80€
Financial income
50.273,63€
Capital grant Generalitat
375.952,00€

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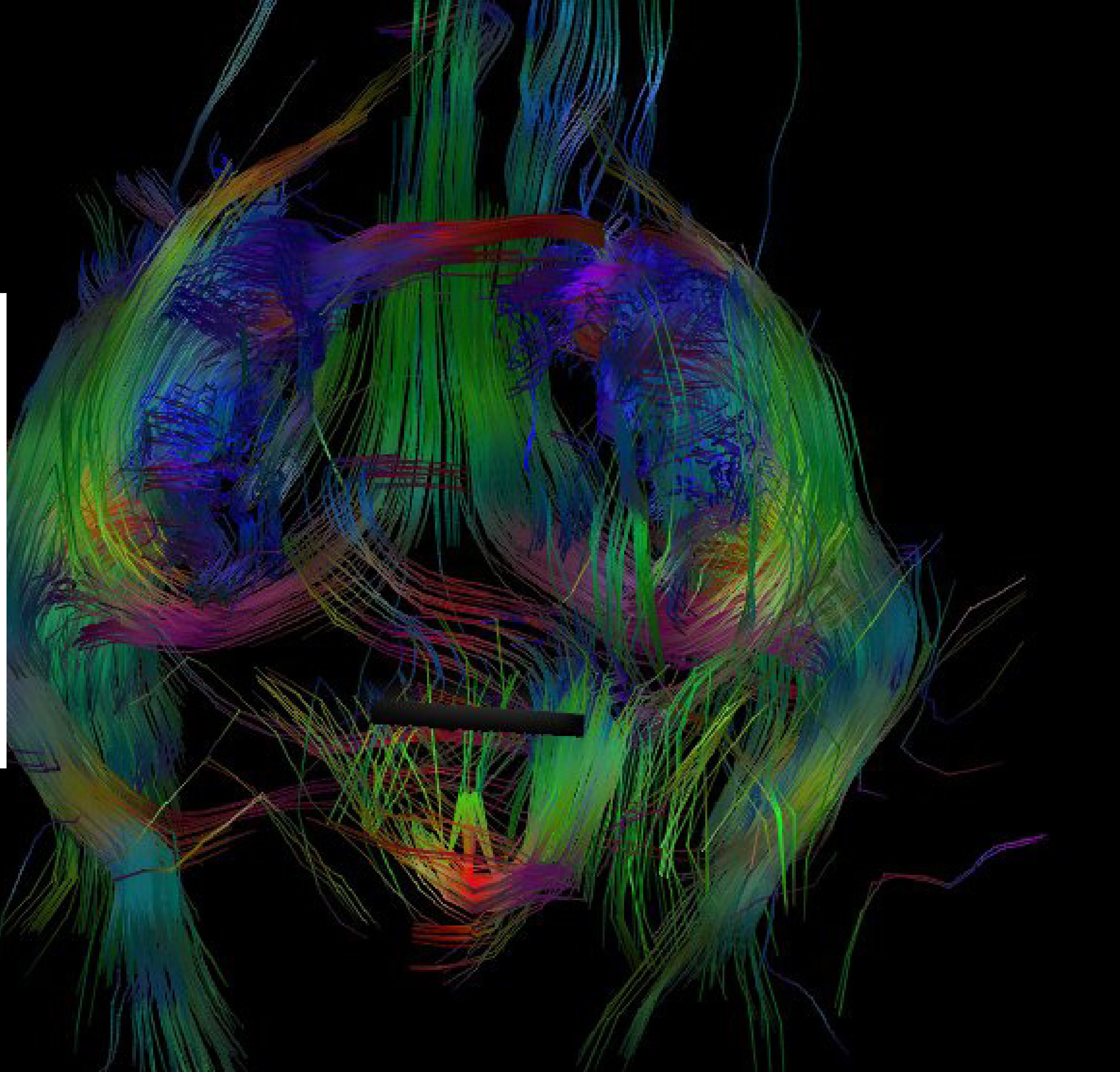
## Research Groups



# Research Groups Summary


**Area 1 - Cancer** **52**
- Badalona·Applied Research Group in Oncology (B·ARGO – ICO Badalona) 53
- Hereditary Cancer 54
- Endocrine Tumours 55
- Epigenetic Mechanisms in Cancer and Cell Differentiation 56
- Cancer Genetics and Epigenetics 57
- Resistance, chemotherapy and predictive biomarkers 58
- Childhood Liver Oncology Group (C-LOG) 59
- Molecular and Structural Pathology 60
- Clinical Genomics Research 61

**Area 2 - Cardiovascular Disease** **62**
- Heart Failure and Cardiac Regeneration Research Program 63

**Area 3 - Community Health** **64**
- CEEISCAT - Centre for Epidemiological Studies of Sexually Transmitted Disease and AIDS in Catalonia 65

**Area 4 - Diseases of the Liver and Digestive Tract** **66**
- Digestive Inflammatory and Pathology Group 67
- Innate Immunity 68
- Neurogastroenterology and Motility Research Group 69
- Translational Research on Hepatic Diseases 70

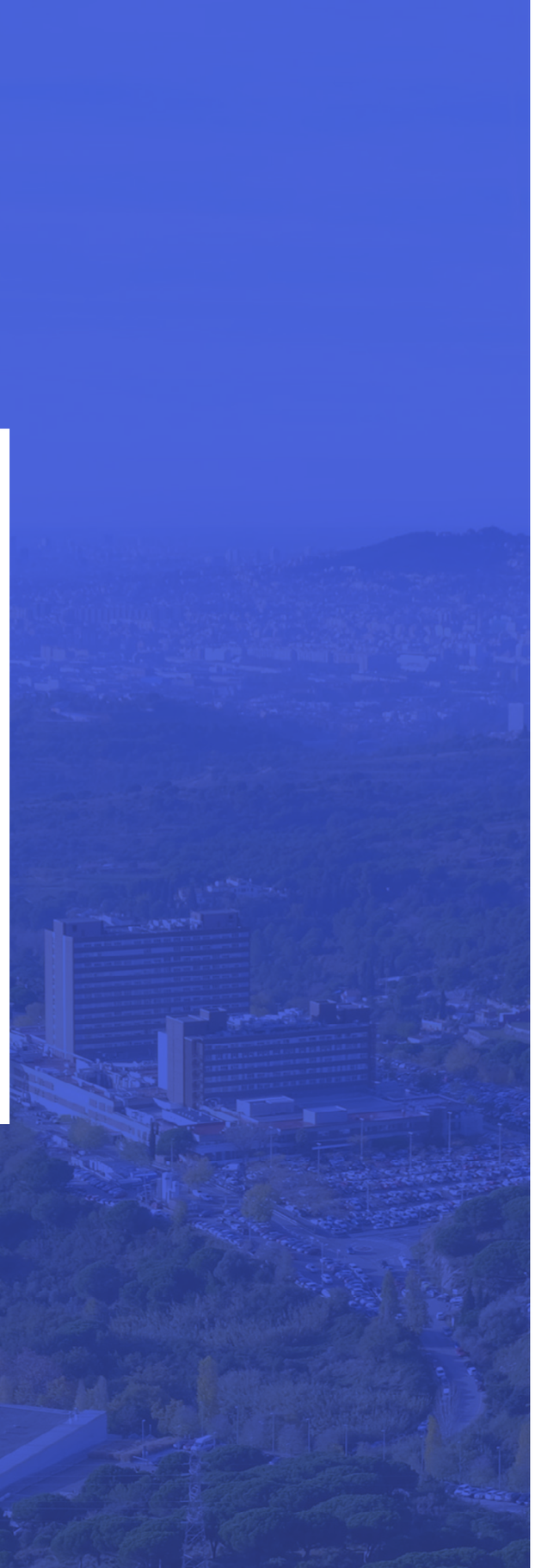
**Area 5 - Endocrine and Diseases of the Metabolism, Bones and Kidneys** **71**
- Endocrine Thyroid and Obesity 72
- Diabetes Research 73
- Obesity and Type 2 Diabetes: Adipose Tissue Biology 74
- Kidney-affecting Diseases Research Group 75
- Innovation in Vesicles & Cells for Application in Therapy (IVECAT) 76

**Area 6 - Immunology and Inflamation** **77**
- Immunology of Diabetes 78
- Immunopathology 79

**Area 7 - Infectious Diseases** **80**
- Clinical and Experimental Microbiology 81
- Experimental Tuberculosis Unit (UTE) 82
- Innovation in Respiratory Infections and Tuberculosis (One and a Half Lab) 83
- Clinical Virology and New Diagnostic Tools 84
- Clinical and Environmental Infectious Diseases Study Group (CEID) 85
- Plasmodium vivax and Exosome Research Group (PvREX) 86

**Area 8 - Neuroscience** **87**
- Vascular Pathologies of the Brain 88
- Cellular and Molecular Neurobiology Research Group (CMN Group) 89
- Neuromuscular and Neuropaediatric Research 90
- Neurogenetics 91
- Genomics and Transcriptomics of Synucleinopathies (GTS) 92
- Psychoneuroendocrinology and Stress in Psychosis (PSICPNEC) 93

**Area 9 - Science of Behaviour and Substance Abuse** **94**
- Medical Complications of Substance Use Disorder (GIAS) 95
- Clinical Pharmacology of Substance Use Disorder 96



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Research Groups
# Area 1
Cancer

## Group: Badalona·Applied Research Group in Oncology (B·ARGO – ICO Badalona)

Group Leader: Ricard Mesía Nin

Scientific Coordinator: Anna Martinez Cardús, amartinezc@igtp.cat

### Research Overview

B·ARGO is a recent transversal organization of the translational and clinical research that has been carried out for many years at the IGTP, the Germans Trias University Hospital and the Catalan Institute of Oncology Badalona located at the hospital. The group consists of senior researchers, junior researchers and fellows from the IGTP and personnel of the Medical Oncology Department of the ICO who are affiliated to the IGTP. The multidisciplinary group is made up of over 30 professionals working on the different aspects of research.
The mission of the B·ARGO is to be a translational research group of excellence that contributes to the application of personalized oncology.
The vision of the B·ARGO is to maintain an integrated cancer research and healthcare system that optimizes the management of cancer patients and improves the length and quality of their lives.

The general aims of the B·ARGO are:
- To fill the existing gap between clinical and basic cancer research
- To identify new strategies, emerging from basic research and apply them in clinical practice
- To typify new biomarkers for cancer diagnosis and prognosis
- To identify new predictive biomarkers of response to current anti-neoplastic therapies
- To determine biomarkers for tumor resistance acquisition during exposure to treatment

### Group Highlights 2020

- Human Resources: 2 Rio Hortega grants and 1 Juan Rodés grant from the Instituto de Salud Carlos III advancing the milestone of establishing a mixed research program, based on clinical healthcare, combined with translational research activity in the laboratory.
- Competitive Research Projects: 2 grants from the Sociedad Española de Oncología (SEOM) and another from ISCIII permitting planning of stable research lines
- Research: Participation in several national collaborative projects and contributions to transversal research programs at other ICO centers and the institutes

### Selected publications 2020

1. **Taxane-induced Attenuation of the CXCR2/BCL-2 Axis Sensitizes Prostate Cancer to Platinum-based Treatment.** Ruiz de Porras V, Wang XC, Palomero L, Marin-Aguilera M, Solé-Blanch C, Indacochea A, Jimenez N, Bystrup S, Bakht M, Conteduca V, Piulats JM, Buisan O, Suarez JF, Pardo JC, Castro E, Olmos D, Beltran H, Mellado B, Martinez-Balibrea E, Font A, Aytes A. European Urology. 2020 Nov 2: S0302-2838(20)30778-8

2. **RNA-Sequencing and immunohistochemistry reveal ZFN7 as a stronger marker of survival than molecular subtypes in G-CIMP-negative glioblastoma**. Esteve-Codina et al. Clin Cancer Res. 2020 Oct 26: clincanres.2141.2020.

3. **Glioblastoma TCGA mesenchymal and IGS 23 tumors are identifiable by immunohistochemistry and have an immune-phenotype indicating potential benefit from immunotherapy.** Carrato et al. Clin Cancer Res. 2020 Sep 30: clincanres.2171.2020.

4. **Pharmacological Modulation of SAMHD1 Activity by CDK4/6 Inhibitors Improves Anticancer Therapy.** Castellví M, Felip E, Ezeonwumelu IJ, Badia R, Garcia-Vidal E, Pujantell M, Gutiérrez-Chamorro L, Teruel I, Martínez-Cardús A, Clotet B, Riveira-Muñoz E, Margelí M, Ballana E. Cancers (Basel). 2020 Mar 18;12(3):713.

5. **Curcumin: a therapeutic strategy for colorectal cancer?** Ruiz de Porras V, Layos L, Martinez-Balibrea E. Seminars in Cancer Biol. 2020 Sep14; S1044-579X (20)30192-9.

# Group: Hereditary Cancer

Group Leader: Eduard Serra, eserra@igtp.cat

## Research Overview

Neurofibromatosis type 1 (NF1) is a genetic disease with an incidence at birth of 1:3000. NF1 individuals present a high predisposition to develop multiple tumors of the peripheral nervous system. These tumors are the main cause of morbidity, have a high impact on their quality of life and, in the case of malignant soft tissue sarcomas, represent the main cause of mortality. Clinical management of NF1 patients with high tumor burden is complex.

Our research is based in the generation of in vitro/in vivo cell-based model systems for these tumor types, such as the use of induced pluripotent stem cells (iPSC) in combination with editing tools and the generation of 3D model systems. We apply genomics and integrative bioinformatic analyses to both tumors and models, with a translational view. We seek a better understanding of tumor initiation, progression and cellular composition, and to understand the impact of tumor heterogeneity on treatment response. We also aim to develop better surveillance tools for monitoring tumor initiation and progression and for an accurate differential diagnosis. In addition, our research centres on the development of more effective therapeutic strategies.

## Group Highlights 2020

**New projects awarded:**

- Impacto de la heterogeneidad celular, genética y epigenética en la progresión y el tratamiento de los tumores del sistema nervioso periférico asociados a la neurofibromatosis tipo 1; Instituo de Salud Carlos III, **PIs: Bernat Gel, Eduard Serra**
- NF1-Associated Peripheral Nerve Sheath Tumors at Single-Cell Resolution: Heterogeneity, Tumor Growth, and Malignant Progression; DOD-Congressionally Directed Medical Research Programs (CDMRP), USA; **PI: Eduard Serra**

## Selected publications 2020


1. Mazuelas H, Carrió M, Serra E (2020) **Modeling tumors of the peripheral nervous system associated with Neurofibromatosis type 1: Reprogramming plexiform neurofibroma cells.** Stem Cell Res. 2020 Oct 29; 49:102068. doi: 10.1016/j.scr.2020.102068.
2. José Marcos Moreno-Cabrera, Jesús del Valle, Elisabeth Castellanos, Lidia Feliubadaló, Marta Pineda, Joan Brunet, Eduard Serra, Gabriel Capellà, Conxi Lázaro, Bernat Gel (2020) **Evaluation of CNV detection tools for NGS panel data in genetic diagnostics.** Eur J Hum Genet DOI: 10.1038/s41431-020-0675-z
3. Ernest Terribas, Marco Fernández, Helena Mazuelas, Juana Fernández-Rodríguez, Josep Biayna, Ignacio Blanco, Gabriela Bernal, Irma Ramos-Oliver, Craig Thomas, Rajiv Guha, Xiaohu Zhang, Bernat Gel, Cleofé Romagosa, Marc Ferrer, Conxi Lázaro, Eduard Serra (2020) **KIF11 and KIF15 mitotic kinesins are potential therapeutic vulnerabilities for malignant peripheral nerve sheath tumors** Neuro-Oncology Advances, vdz061, DOI:10.1093/noajnl/vdz061
4. Moreno-Cabrera JM, Del Valle J, Feliubadaló L, Pineda M, González S, Campos O, Cuesta R, Brunet J, Serra E, Capellà G, Gel B, Lázaro C (2020) **Screening of CNVs using NGS data improves mutation detection yield and decreases costs in genetic testing for hereditary cancer.** J Med Genet. jmedgenet-2020-107366. doi: 10.1136/jmedgenet-2020-107366
5. Elisabeth Castellanos, Inma Rosas, Alex Negro, Bernat Gel, Andreu Alibés, Neus Baena, Mercè Pineda, Graciela Pi, Guillem Pintos, Hector Salvador, Conxi Lázaro, Ignacio Blanco, Lluïsa Vilageliu, Hilde Brems, Daniel Grinberg, Eric Legius, Eduard Serra (2020) **Mutational spectrum by phenotype: panel-based NGS testing of patients with clinical suspicion of RASopathy and children with multiple café-au-lait macules.** Clinical Genetics 2020; 1–12 DOI: 10.1111/cge.13649






# Group: Endocrine Tumours

Group Leader: Mireia Jordà, mjorda@igtp.cat

## Research Overview

The group seeks to better understand the molecular landscape of thyroid cancer and pituitary tumours. The aim is to characterize mechanisms of progression and response/resistance to treatments to advance biomarker and drug target discovery with the final goal of helping treatment decision making and improve patient outcomes. There are 2 main research lines:

1. Thyroid cancer. The majority of patients have an excellent prognosis; however, a subset of carcinomas progress and there are no effective biomarkers available. The group is investigating the molecular basis of aggressive thyroid cancer, with special focus on epigenetics, to identify prognostic and predictive markers and potential therapeutic targets. The team is especially interested in kallikreins, a family of 15 secreted serine proteases, which they found to be deregulated in thyroid cancer. They are currently assessing their clinical utility and functional implications in the disease.
2. Pituitary adenomas. The group investigates the pathogenesis of pituitary tumours in collaboration with the Endocrinology Service at the Germans Trias i Pujol University Hospital led by Dr Manel Puig. The team combines clinical, pathological and molecular information to identify prognostic markers, predictors of response and new therapeutic strategies that allow the shift towards personalized medicine.

## Group Highlights 2020

- Joan Gil obtained his PhD from the Autonomous University of Barcelona
- Juan Carlos Pardo, was awarded a Río Hortega fellowship (CM20/00028) to work in our lab
- Lorena González joined the laboratory as a technician
- The group established and validated an epigenetic assay based on an algorithm they had previously generated to predict the development of distant metastases in thyroid cancer
- Consolidation of the research line on radioiodine refractory thyroid cancer

## Selected publications 2020


1. **Molecular profiling for acromegaly treatment: a validation study.** Puig-Domingo et al. Endocr Relat Cancer. 2020 Jun;27(6):375-389. doi: 10.1530/ERC-18-0565. PMID: 32302973
2. **Epigenetic footprint enables molecular risk stratification of hepatoblastoma with clinical implications.** Carrillo-Reixach et al. J Hepatol. 2020 Aug;73(2):328-341. doi: 10.1016/j.jhep.2020.03.025. Epub 2020 Mar 30. PMID: 32240714
3. **Tissue and cancer-specific expression of DIEXF is epigenetically mediated by an Alu repeat**. Martín B, Pappa S, Díez-Villanueva A, Mallona I, Custodio J, Barrero MJ, Peinado MA, Jordà M. Epigenetics. 2020 Jun-Jul;15(6-7):765-779. doi: 10.1080/15592294.2020.1722398. Epub 2020 Feb 11. PMID: 32041475
4. **Hsa-miR-139-5p is a prognostic thyroid cancer marker involved in HNRNPF-mediated alternative splicing.** Montero-Conde et al. Int J Cancer. 2020 Jan 15;146(2):521-530. doi: 10.1002/ijc.32622. Epub 2019 Aug 28. PMID: 31403184
5. **Laparoscopic sleeve gastrectomy induces molecular changes in peripheral white blood cells.** Beisani M, Pappa S, Moreno P, Martínez E, Tarascó J, Granada ML, Puig R, Cremades M, Puig-Domingo M, Jordà M, Pellitero S, Balibrea JM. Clin Nutr. 2020 Feb;39(2):592-598. doi: 10.1016/j.clnu.2019.03.012. Epub 2019 Mar 19. PMID: 30948220

# Group: Epigenetic Mechanisms in Cancer and Cell Differentiation

Group Leader: MA Peinado, mpeinado@igtp.cat

## Research Overview

The main focus of the group's research is the characterization of the molecular mechanisms underlying cell programs and the identification of molecular markers with clinical applications. The specific topics under development in the laboratory include:

- Chromatin architecture in cell differentiation and cancer (MA Peinado)
- The role of repeat elements in genome structure and function (MA Peinado).
- Clinically oriented research on the epigenetic changes involved in human cancer (MA Peinado)
- Genomic Medicine Technological Innovation (MA Peinado)
- Epigenetic changes in muscle pathologies (M Suelves)
- Deciphering the role of HDAC11 in skeletal muscle (M Suelves)

## Selected publications 2020

1. **DNA methylation events in transcription factors and gene expression changes in colon cancer.** Díez-Villanueva A, Sanz-Pamplona R, Carreras-Torres R, Moratalla-Navarro F, Alonso MH, Paré-Brunet L, Aussó S, Guinó E, Solé X, Cordero D, Salazar R, Berdasco M, Peinado MA, Moreno V. Epigenomics. 2020 Sep;12(18):1593-1610. doi: 10.2217/epi-2020-0029. Epub 2020 Sep 22. PMID: 32957849
2. **Loss of HDAC11 accelerates skeletal muscle regeneration in mice.** Núñez-Álvarez Y, Hurtado E, Muñoz M, García-Tuñon I, Rech GE, Pluvinet R, Sumoy L, Pendás AM, Peinado MA, Suelves M. FEBS J. doi: 10.1111/febs.15468. Epub 2020 Jul 21. PMID: 32602219
3. **HDAC11 is a novel regulator of fatty acid oxidative metabolism in skeletal muscle.** Hurtado E, Núñez-Álvarez Y, Muñoz M, Gutiérrez-Caballero C, Casas J, Pendás AM, Peinado MA, Suelves M. FEBS J. doi: 10.1111/febs.15456. Epub 2020 Jul 14. PMID: 32563202
4. **Tissue and cancer-specific expression of DIEXF is epigenetically mediated by an Alu repeat**. Martín B, Pappa S, Díez-Villanueva A, Mallona I, Custodio J, Barrero MJ, Peinado MA, Jordà M. Epigenetics. 2020 Jun-Jul;15(6-7):765-779. doi: 10.1080/15592294.2020.1722398. Epub 2020 Feb 11. PMID: 32041475





# Group: Cancer Genetics and Epigenetics

Group Leader: Sergio Alonso, salonsou@igtp.cat

## Research Overview

2020 was dramatically marked by the closure of the laboratory due to the covid-19 pandemic. The group is mainly experimental and, adding this to the small size of the group, the closure forced a complete halt to research for over three months. The abrupt interruption of three master's theses and the experiments that required finishing to complete very advanced studies meant that these were finally submitted in 2021. (now in revision in Genome Research and in Clinical Cancer Research, respectively). Despite the extremely unfavourable circumstances, the three students successfully defended their master's theses in October and November.

The group led the formation of a multi-disciplinary team of IGTP researchers to apply for funding from the Fundación Mutua Madrileña, to explore the association between alterations in genes coding for extracellular matrix remodellers and lymphocytic infiltration. This funding has been awarded.

The group has strengthened collaboration with Professor P. Zavattari's group at the University of Cagliari. The team applied for a European project and for a Mark Foundation for Cancer Research project to study epigenetic markers for early detection of biliary tract cancers.

## Group Highlights 2020

Funding from the Fundación Mutua Madrileña to study the relationship between remodelling of the extracellular matrix with lymphocytic infiltration and explore their use as predictive biomarkers, or as future therapeutic targets to improve the response to immunotherapy for colorectal cancer.

# Group: Resistance, chemotherapy and predictive biomarkers

Group Leader: Eva Martínez Balibrea, embalibrea@iconcologia.net

## Research Overview

In 2020 we kept on working on projects PI16/01800 and PIE16/00011 that are focused on the study of CXC chemokines and their role as biomarkers in colorectal cancer (CRC) and on the discovery of chromatin regulators that could be used as new biomarkers and drug targets, also in CRC, respectively. We started to implement a new technique in our lab called MDOTS and PDOTS consisting of growing tumors ex vivo and test immunotherapy (and other) treatments. The project has been funded by Merck. We have also started a new research line in collaboration with Dr. Balañà from ICO Badalona in which we will study the role of proteins UBXN7 and ZNF7 in glioblastomas. We have published a review article about curcumin as possible therapy in CRC in the journal Seminars in cancer biology. In 2020 we have been awarded with 2 research projects led by Dr. Martinez-Balibrea: PI20/01183 and a SEMILLA project from the AECC foundation. We also participate as collaborators in awarded projects from Fundación Mutua Madrileña (AP174232020) led by Sergio Alonso (IGTP) and from Fundación MERCK (INSPECTA) led by Cinta Hierro (ICO-IGTP).

## Group Highlights 2020

- Publications
  The paper Curcumin: A therapeutic strategy for colorectal cancer? (PMID: 32942023)
- Projects
  - » Funding for Eva Martínez-Balibrea as PI on an Ideas SEMILLA project from the Asociación Española contra el Cáncer (AECC)
  - » Funding as collaborators on the Fundació Mútua Madrileña project led by Sergio Alonso Utrilla
  - » Funding as part of the INSPECTA Project (Merck) led by Cinta Hierro
- Establishment of a new research line
  Research in glioblastoma: Implementation of MDOTS/PDOTS ex vivo models (in collaboration with David Barbie – Dana Farber Cancer Institute, Boston)

## Selected publications 2020

1. Ruiz de Porras V, Wang XC, Palomero L, Marin-Aguilera M, Solé-Blanch C, Indacochea A, Jimenez N, Bystrup S, Bakht M, Conteduca V, Piulats JM, Buisan O, Suarez JF, Pardo JC, Castro E, Olmos D, Beltran H, Mellado B, Martinez-Balibrea E, Font A, Aytes A. **Taxane-induced Attenuation of the CXCR2/BCL-2 Axis Sensitizes Prostate Cancer to Platinum-based Treatment.** Eur Urol. 2020 Nov 2:S0302-2838(20)30778-8. doi: 10.1016/j.eururo.2020.10.001. Article. PMID: 33153817
2. Ruiz de Porras V, Layos L, Martínez-Balibrea E. **Curcumin: A therapeutic strategy for colorectal cancer?** Semin Cancer Biol. 2020 Sep 14: S1044-579X(20)30192-9. doi: 10.1016/j.semcancer.2020.09.004. Review. PMID: 32942023





# Group: Childhood Liver Oncology Group (C-LOG)

Group Leader: Carolina Armengol, carmengol@igtp.cat

## Research Overview

The main goals of this pioneering group focussing on translational research of paediatric liver cancer in Spain are to increase the molecular knowledge of hepatoblastoma. Although it is the main liver cancer in children, it is extremely rare and the group aims to identify biomarkers and therapeutic targets to improve quality of life and survival of patients with primary liver cancer, including hepatocellular carcinoma.

Another objective is to boost translational research into childhood liver cancer. In 2010 the group was responsible for creating the first national collection of biospecimens from patients with liver cancer (ISCIII National Biobank Registry, collection section, ref. C.0000226), called CLCN. The collection also includes samples from adult patients with liver cancer thanks to the group's participation in the international Paediatric Hepatic International Tumour Trial (PHITT). The CLCN collection is the basis of our 3 main research lines:

1. Understanding the molecular biology of childhood liver cancer using the latest high-throughput technologies and computational tools.
2. Identification and validation of diagnostic and prognostic biomarkers to improve the clinical management of childhood liver cancer using samples of the EU PHITT cohort.
3. Establishing new experimental patient-derived models of childhood liver cancer (i.e. PDXs, organoids) to test innovative therapies against tumor cells.

## Group Highlights 2020

- **Scientific milestones**
  - » Establishment of one of the largest collections of clinical and pathological annotated biological samples from childhood liver cancer patients worldwide
  - » Exhaustive omics characterization led to the discovery that RNA editing and 14q32 DLK1/DIO3 cluster of genes are dysregulated in hepatoblastoma and the definition of a first Molecular Risk Stratification of hepatoblastoma.
- **New research line established**
- **Extensive communication and popularization of science activities**
- Publication of an illustrated a children's book for children with liver cancer

## Selected publications 2020

1. **Epigenetic Footprint Enables Molecular Risk Stratification of Hepatoblastoma With Clinical Implications.** Carrillo-Reixach et al. (J Hepatol, 73: 328-341, 2020. doi: 10.1016/j.jhep.2020.03.025.) Impact Factor: 20.58
2. **A combined clinical and biological risk score predicts outcome in hepatoblastoma patients**. S Cairo, C Armengol, A de Reyniès, R Maibach, B Häberle, K Becker, M Simon-Coma, C Guettier, C Vokuhl, MA Buendia, S Branchereau, D von Schweinitz, R Kappler (European J Cancer, Eur J Cancer. 2020 Dec; 141:30-39. doi: 10.1016/j.ejca.2020.09.026.) Impact Factor: 6.7

# Group: Molecular and Structural Pathology

Group Leader: Pedro L. Fernández Ruiz, plfernandez.germanstrias@gencat.cat

## Research Overview

The group is mostly dedicated to research on biomarkers and molecular mechanisms underlying the development and progression of malignant neoplasms and aims to provide translational knowledge to advance the diagnosis, prognosis and prediction of a variety of human cancers. For this purpose, the team combines both morphological (light and ultrastructural microscopy) and advanced molecular tools including next generations sequencing (NGS), in situ hybridization and immunohistochemistry and these are integrated with bioinformatics tools such as digital pathology to provide a multidisciplinary approach to cancer research. The group also has a special interest and long and productive research tradition in non-neoplastic conditions, including dermatopathology and nephropathology amongst others.
The Molecular and Structural Pathology Group has been repeatedly recognized as a Consolidated Research Group (2017SGR639) by the Agency for Management of University and Research Grants (AGAUR) of the Government of Catalonia and has the financial support of several competitive grants, including those of Instituto Carlos III and Marató de TV3.

## Group Highlights 2020

The main highlight of 2020 was the start of implantation of digital pathology in the service in collaboration with the Universitat Politècnica de Catalunya (UPC).

## Selected publications 2020


1. Prat A, Saura C, Pascual T, Hernando C, Muñoz M, Paré L, González Farré B, Fernández PL, Galván P, Chic N, González Farré X, Oliveira M, Gil-Gil M, Arumi M, Ferrer N, Montaño A, Izarzugaza Y, Llombart-Cussac A, Bratos R, González Santiago S, Martínez E, Hoyos S, Rojas B, Virizuela JA, Ortega V, López R, Céliz P, Ciruelos E, Villagrasa P, Gavilá J**. Ribociclib plus letrozole versus chemotherapy for postmenopausal women with hormone receptor-positive, HER2-negative, luminal B breast cancer (CORALLEEN): an open-label, multicentre, randomised, phase 2 trial.** Lancet Oncol. 2020, 21:33-43. doi: 10.1016/S1470-2045(19)30786-7. Epub 2019 Dec 11

2. Cristina Carrato; Francesc Alameda; Anna Esteve-Codina; et al. **Glioblastoma TCGA Mesenchymal and IGS 23 Tumors are Identifiable by IHC and have an Immune-phenotype Indicating a Potential Benefit from Immunotherapy.** Clinical Cancer Research. 2020. 26-24, pp.6600-6609.

3. Urbizu A, Beyer K. **Epigenetics in Lewy Body Diseases: Impact on Gene Expression, Utility as a Biomarker, and Possibilities for Therapy**. Int J Mol Sci. 2020 Jul 2;21(13):4718. doi: 10.3390/ijms21134718. PMID: 32630630;

4. Fonseca KL, Maceiras AR, Matos R, Simoes-Costa L, Sousa J, Cá B, Barros L, Fernandes AI, Mereiter S, Reis R, Gomes J, Tapia G, Rodríguez-Martínez P, Martín-Céspedes M, Vashakidze S, Gogishvili S, Nikolaishvili K, Appelberg R, Gärtner F, Rodrigues PNS, Vilaplana C, Reis CA, Magalhães A, Saraiva M. **Deficiency in the glycosyltransferase Gcnt1 increases susceptibility to tuberculosis through a mechanism involving neutrophils.** Mucosal Immunol. 2020 Sep;13(5):836-848.

5. Moreira-Teixeira L, Stimpson PJ, Stavropoulos E, Hadebe S, Chakravarty P, Ioannou M, Aramburu IV, Herbert E, Priestnall SL, Suarez-Bonnet A, Sousa J, Fonseca KL, Wang Q, Vashakidze S, Rodríguez-Martínez P, Vilaplana C, Saraiva M, Papayannopoulos V, O'Garra A. **Type I IFN exacerbates disease in tuberculosis-susceptible mice by inducing neutrophil-mediated lung inflammation and NETosis**. Nat Commun. 2020 Nov 4;11(1):5566. doi: 10.1038/s41467-020-19412-6. PMID: 33149141






# Group: Clinical Genomics Research

Group Leader: Ignacio Blanco, Iblanco.germanstrias@gencat.cat
& Elisabeth Castellanos, Ecastellanosp.germanstrias@gencat.cat

## Research Overview

This group is made up of medical staff and researchers of the Germans Trias i Pujol University Hospital and the IGTP. It is dedicated to improving the diagnosis and treatment of the RASopathies.

The team has improved the custom panel developed in 2015 to genetically diagnose the RASopathies (Castellanos et al. 2020) and is working to improve problems such as the presence of overlapping clinical manifestations and the genetic heterogeneity of these diseases. It has also improved the UK score system for Spanish patients attended in the CSUR (National Reference Centre in genetic neurocutaneous syndromes (Facomatosis) at the hospital.

During the covid-19 pandemic, Ignacio Blanco has been leading the Multidisciplinary Unit for the Diagnosis of covid-19 in the Clinical Laboratory of the North Barcelona Metropolitan Area (LCMN). Together with the LCMN, the group has participated in the search and development of different diagnostic methods for covid-19. Ignacio Blanco has led the screening of health professionals for covid-19 (Barallat et al, 2020) and the team have participated in the identification of genetic susceptibility factors to SARS-CoV-2 (Zhang et al 2020, Bastard et al 2020), the study of the mechanisms of transmission through species (Segalés et al 2020) and the identification of possible treatments (Revollo et al 2020) among others.

## Group Highlights 2020

Funding was secured for 2021 (PI20-00215 (AES, Instituto de Salud Carlos III); MARATÓ DE TV3 de Malalties Minoritàries (126/C/2020) and Chromo 22), the group's research plan includes:

1. Expansion of capacities of the custom panel to analyse the genes associated to Phakomatoses also at the RNA level.
2. Development of new clinical tools to improve the clinical follow-up, genetic counselling and clinical management of patients with Neurofibromatosis type 2, as well as the evaluation of the impact of the disease on Quality of Life in order to establish an algorithm.
3. Participation in the evaluation of SARS-cov-2 variants in the Catalan population to monitor them epidemiologically together with Microbiology department of HGTP, IGTP and IRSICaixa (Hub de Seqüenciació del Campus Can Ruti)

## Selected publications 2020


1. Castellanos et al. Clin Genet. **"Mutational spectrum by phenotype: panel-based NGS testing of patients with clinical suspicion of RASopathy and children with multiple café-au-lait macules"** doi: 10.1111/cge.13649

2. Zhang et al. Science. **"Inborn errors of type I IFN immunity in patients with life-threatening COVID-19"**. doi: 10.1126/science.abd4570

3. Barallat J et al PLoS One. **"Seroprevalence of SARS-CoV-2 IgG specific antibodies among healthcare workers in the Northern Metropolitan Area of Barcelona, Spain, after the first pandemic wave"**. doi: 10.1371/journal.pone.0244348

4. Bastard et al. Science. **"Autoantibodies against type I IFNs in patients with life-threatening COVID-19"**. doi: 10.1126/science.abd4585

5. Segalés et al. PNAS. **"Detection of SARS-CoV-2 in a cat owned by a COVID-19-affected patient in Spain".** doi: 10.1073/pnas.2010817117

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Research Groups

# Area 2
# Cardiovascular Disease



## Group: Heart Failure and Cardiac Regeneration Research Program (ICREC Research Group)

Group Leader: Antoni Bayés Genís, abayes.germanstrias@gencat.cat

### Research Overview

The Program has five main coordinated research lines, it maximises synergy with the sole purpose of improving quality of life and extending life expectancy for patients.

1. Myocare Lab is focused on development and testing of innovative biotherapies using in vitro, small and large animal models.
2. ASAC, the Clinical Trials Unit, is responsible for translating validated pre-clinical results to the clinical scenario with the required approvals.
3. The Platform of Cardiovascular Precision Medicine (PMPCV) focuses on the discovery of novel cardiovascular biomarkers and expands the use of those already known
4. The Innovation Unit gives commercial outlet to new products and devices derived from ICREC research.
5. The Cardiometabolism line has recently been created to find out the underlying molecular mechanisms of cardiometabolic diseases.

In 2020 we pioneered first-in-human studies, including the PERISCOPE trial (NCT03798353), and AGTP-II trial (NCT02798276), and we have developed and tested pre-clinically a new cardiac tissue engineering product with extracellular vesicles for myocardial repair.

### Group Highlights 2020

- Development of a new advanced therapy product based on cardiac tissue engineering and multifunctional extracellular vesicles
- PeriCord: a successful collaborative research milestone in scalability and GMP manufacturing of a cardiac tissue engineering bioimplant for clinical use
- 5 competitive national projects from ISCIII, MICIIN, CaixaImpulse, the Generalitat de Catalunya and Societat Catalana de Cardiologia
- ICREC Program has signed a partnership with Boehringer-Ingelheim giving rise the new Creation of the Cardiometabolism Platform to address the molecular mechanisms responsible for cardiometabolic disorders
- Award for the best study at the Societat Catalana de Cardiologia Congress 2020

### Selected publications 2020


1. Prat-Vidal et al. A. **First- in-human PeriCord cardiac bioimplant: Scalability and GMP manufacturing of an allogeneic engineered tissue graft.** EBioMedicine. 2020 Apr; 54:102729
2. Iborra-Egea O, Rueda F, García-García C, Borràs E, Sabidó E, Bayes-Genis A. **Molecular signature of cardiogenic shock.** Eur Heart J. 2020 Oct 14;41(39):3839-3848
3. Elena Revuelta-López, Julio Núñez, Paloma Gastelurrutia, Germán Cediel, James L. Januzzi, Nasrien E. Ibrahim, Michele Emdin, Roland VanKimmenade, Domingo Pascual-Figal, Eduardo Núñez, Frank Gommans, Josep Lupón, Antoni Bayés-Genís. **Neprilysin inhibition, endorphin dynamics, and early symptomatic improvement in heart failure: a pilot study ESC Heart Fail.** 2020 Apr; 7(2): 559-566
4. Lázaro I, Rueda F, Cediel G, Ortega E, García-García C, Sala-Vila A, Bayés-Genís A. **Circulating Omega-3 Fatty Acids and Incident Adverse Events in Patients With Acute Myocardial Infarction.** J Am Coll Cardiol. 2020 Nov 3;76(18):2089-2097
5. Asensio Lopez MDC, Lax A, Hernandez Vicente A, Saura Guillen E, Hernandez-Martinez A, Fernandez Del Palacio MJ, Bayes-Genis A, Pascual Figal DA. **Empagliflozin improves post-infarction cardiac remodeling through GTP enzyme cyclohydrolase 1 and irrespective of diabetes status.** Sci Rep. 2020 Aug 11;10(1):13553

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Research Groups
# Area 3
Community Health



## Group: CEEISCAT - Centre for Epidemiological Studies of Sexually Transmitted Disease and AIDS in Catalonia

Group Leader: Jordi Casabona jcasabona@iconcologia.net

### Research Overview

CEEISCAT is a structural service of the Catalan Institute of Oncology (ICO) and it is functionally directed by the Programme for the Prevention, Control and Care for HIV, Sexually Transmitted Diseases (STDs) and Viral Hepatitis (PCAVIHV) of the Ministry of Health of the Government of Catalonia.

Since 1995 CEEISCAT has been responsible for the epidemiological surveillance and monitoring and evaluation of HIV and STDs in Catalonia, and since 2018 has been responsible for monitoring and evaluating the Elimination Plan for Hepatitis C in Catalonia, within the PCAVIHV.

CEEISCAT carries out applied research projects in public health through funding from national and international agencies and from the private sector that has improved knowledge about the HIV epidemic in Catalonia, promoted the integration of community-based testing in the surveillance systems of information in Europe and piloted innovative testing strategies, among others.

CEEISCAT has been recognized by the Catalan Agency for Management of University and Research Grants (AGAUR) as a consolidated research group since 2006 and together with the Microbiology Service of the Germans Trias Hospital, it constitutes a Node (Group 27) in the Network of Excellence in Epidemiology and Public Health (CIBERESP).

### Group Highlights 2020

Activity during 2020 has been clearly impacted by the COVID-19 pandemic. Researchers focused on the design and implementation of epidemiological studies on the impact of COVID-19 on different populations and services such as blood doning, people living with HIV, young people or community-based testing centers, among others. In the same way, CEEISCAT researchers have analyzed the impact of COVID-19 on epidemiological surveillance data in Catalonia and have collaborated with various studies on COVID-19 that have been carried out in Catalonia and especially at the Can Ruti Campus.

### Selected publications 2020

1. Mitjà et al. BCN-PEP-CoV2 Research Group. **A Cluster-Randomized Trial of Hydroxychloroquine for Prevention of Covid-19.** N Engl J Med . 2021 Feb 4;384(5):417-427. doi: 10.1056/NEJMoa2021801. Epub 2020 Nov 24. Impact factor: 74.699 (D1)

2. Mitjà et al. BCN PEP-CoV-2 RESEARCH GROUP. **Hydroxychloroquine for Early Treatment of Adults with Mild Covid-19: A Randomized-Controlled Trial.** Clin Infect Dis. 2020 Jul 16;ciaa1009. doi: 10.1093/cid/ciaa1009. Impact factor: 8.313 (D1)

3. Fernàndez-López L, Reyes-Urueña J, Conway A, Saz J, Morales A, Quezadas J, Baroja J, Rafel A, Pazos A, Avellaneda A, Meroño M, Andreo L, Romero L, Lara A, Otón A, Rifà B, Mansilla R, Colom J, Casabona J. **The contribution of HIV point-of-care tests in early HIV diagnosis: community-based HIV testing monitoring in Catalonia**, 1995 to 2018. Euro Surveill. 2020 Oct;25(43):1900424. doi: 10.2807/1560-7917.ES.2020.25.43.1900424. Impact factor: 6.454 (D1)

4. Maté T, Hoyos J, Guerras JM, Agustí C, Chanos S, Kuske M, Fuertes R, Stefanescu R, Pulido J, Sordo L, de la Fuente L, Belza MJ; EURO HIV EDAT Group. **Potential of HIV Self-Sampling to Increase Testing Frequency Among Gay, Bisexual, and Other Men Who Have Sex With Men, and the Role of Online Result Communication: Online Cross-Sectional Study.** J Med Internet Res. 2020 Nov 30;22(11):e21268. doi: 10.2196/21268. Impact factor: 5.034 (D1)

5. Folch C, Casabona J, Majó X, Meroño M, González V, Colom J, Brugal T, Espelt A. **Mujeres que usan drogas inyectadas y violencia: necesidad de una respuesta integrada.** Adicciones. 2020 Jul 14;0(0):1322. doi: 10.20882/adicciones.1322. Impact factor: 3.167 (Q1)

**Annual Report**
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Research Groups
**Area 4**
Diseases of the Liver and Digestive Tract

# Group: Digestive Inflammatory and Pathology Group

## Group Leader: Eugeni Domènech

### Research Overview

The group is integrated into the Gastroenterology Service of the Germans Trias i Pujol University Hospital and has been well established for over 30 years. The Inflammatory Bowel Disease (IBD) Unit is a healthcare reference centre with more than 1,600 IBD patients. It has been part of the CIBEREHD Network (Centro de Investigación Biomédica en Red en Enfermedades Digestivas y Hepáticas) since 2007 and since 2017 has the Certification of Excellence as an Integral IBD Patient Care by the Ad Qualitatem Foundation.

The main lines of research of the group are: 1) characterization and treatment safety/efficacy; 2) postoperative recurrence in Crohn's disease; and 3) Response to corticosteroids in ulcerative colitis. In translational research the group has incorporated massive genomic analysis with innovative computational analyses, as well as in vitro and in vivo genetic experimental models and molecular analysis.

Additionally, the group have projects in innovation and business development, pending patent applications and collaborations with the pharmaceutical industry. Additionally, members of the group are very much involved in academic work, teaching and training.

### Group Highlights 2020

- 3 Projects financed by *Instituto de Salud Carlos III* (Government of Spain) in development during 2020: ISCIII (PI20/00420); 2021-2023; IP Josep Manyé Almero, ISCIII (PI18/00892); 2019-2022; IP Dr. Miriam Mañosa Ciria and ISCIII (PI16/01937); 2017-2021; IP Eugeni Domènech Morral.
- European patent extension (P3614EP01): microRNAs as biomarkers of cortico-refractoriness in ulcerative colitis
- Young Researcher Scholarship of the Catalan Society of Digestology 2021, Roger Suau

### Selected publications 2020


1. **Antitumor Necrosis Factor Agents to Treat Endoscopic Postoperative Recurrence of Crohn's Disease: A Nationwide Study with Propensity-Matched Score Analysis.** Cañete et al. INFLIRECU study. Clin Transl Gastroenterol 2020; 11(8):e00218.
2. **Transcriptomic identification of TMIGD1 and its relationship with the ileal epithelial cell differentiation in Crohn's disease.** Zabana Y, Lorén V, Domènech E, Aterido A, Garcia-Jaraquemada A, Julià A, Vicario M, Pedrosa E, Ferreiro M, Troya J, Lozano JJ, Sarrias MR, Cabré E, Mañosa M, Manyé J. Am J Physiol Gastrointest Liver Physiol 2020; 319(2):G109-G120.
3. **Switching to a Second Thiopurine in Adult and Elderly Patients With Inflammatory Bowel Disease: A Nationwide Study From the ENEIDA Registry**. Calafat et al. ENEIDA registry of GETECCU. J Crohns Colitis 2020; 14(9):1290-1298.
4. **Increased risk of thiopurine-related adverse events in elderly patients with IBD.** Calafat et al. ENEIDA registry of GETECCU. Aliment Pharmacol Ther 2019; 50(7):780-788.
5. **ANP32E, a Protein Involved in Steroid-Refractoriness in Ulcerative Colitis, Identified by a Systems Biology Approach.** Lorén V, Garcia-Jaraquemada A, Naves JE, Carmona X, Mañosa M, Aransay AM, Lavin JL, Sánchez I, Cabré E, Manyé J, Domènech E. J Crohns Colitis 2019 26; 13(3):351-361.

# Group: Innate Immunity

Group Leader: Maria Rosa Sarrias, mrsarrias@igtp.cat

## Research Overview

One of the main aims of the group is to define the role of Innate Immunity proteins as prognostic or diagnostic biomarkers of disease. Another objective is to generate knowledge and develop new therapies to target Innate Immune responses. Research is mostly centred on the role of macrophages in the control of immune homeostasis and inflammatory disease. The group has 3 main lines of research:

1. Understanding macrophages as central drivers of pathology (PI: MR Sarrias) Combining basic, translational and innovation approaches this line is mostly centred on understanding liver disease, within the CIBERehd consortium. We are developing a novel immunotherapy to target macrophages in cancer in collaboration with Dr Alhelí Rodriguez (UAB). Our laboratory has been working on one of the stages of this project for the last 2 years. Additionally, we have joined efforts with Dr PJ Cardona (Clinical Experimental Microbiology) to understand trained immunity in the context of the covid-19 pandemic.
2. Generation of novel in vitro diagnostic tests (PI: MR Sarrias) Based on the group's findings in biomarker studies, research continues in collaboration with a diagnostics company (Lionex, Germany), and within the context of an international consortium led by Dr Vilaplana, (UTE, SMA-TB, IGTP).
3. Novel stratification strategies that complement the current clinical criteria of cirrhosis (PI: Helena Masnou). This new line of research started in 2020 thanks to the award of a collaborative FIS project with Dr Masnou of the Department of Gastroenterology, HUGTiP.

## Group Highlights 2020

In the context of the covid-19 pandemic, we have joined forces with Dr PJ Cardona (UTE) to analyse trained immunity in the context of the SARS-CoV-2 virus.
Additional funding has allowed us to incorporate 2 new post-doctoral researchers and two new pre-doctoral students into our team in addition to our technician and UAB collaborator.
An important addition in 2020 was the opening of a new line of research in hepatology, made possible by the funding of a FIS project, in collaboration with Dr H Masnou (HUGTiP).

## Selected publications 2020


1. **Role of the Scavenger Receptor CD36 in Accelerated Diabetic Atherosclerosis.** Navas-Madroñal M, Castelblanco E, Camacho M, Consegal M, Ramirez-Morros A, Sarrias MR, Perez P, Alonso N, Galán M, Mauricio D. Int J Mol Sci. 2020 Oct 5;21(19):7360. doi: 10.3390/ijms21197360.
2. **Transcriptomic identification of TMIGD1 and its relationship with the ileal epithelial cell differentiation in Crohn's disease.** Zabana Y, Lorén V, Domènech E, Aterido A, Garcia-Jaraquemada A, Julià A, Vicario M, Pedrosa E, Ferreiro M, Troya J, Lozano JJ, Sarrias MR, Cabré E, Mañosa M, Manye J. Am J Physiol Gastrointest Liver Physiol. 2020 Jun 8. doi: 10.1152/ajpgi.00027.2020. Online ahead of print. PMID: 32508154
3. **The Circulating Fatty Acid Transporter Soluble CD36 Is Not Associated with Carotid Atherosclerosis in Subjects with Type 1 and Type 2 Diabetes Mellitus.** Castelblanco E, Sanjurjo L, Barranco-Altirriba M, Falguera M, Hernández M, Soldevila B, Sarrias MR, Franch-Nadal J, Arroyo JA, Fernandez-Real JM, Alonso N, Mauricio D.J Clin Med. 2020 Jun 2;9(6): E1700. doi: 10.3390/jcm9061700. PMID: 32498389
4. **Epigenetic footprint enables molecular risk stratification of hepatoblastoma with clinical implications.** Carrillo-Reixach et al. J Hepatol. 2020 Mar 30:S0168-8278(20)30187-2. doi: 10.1016/j.jhep.2020.03.025.






# Group: Neurogastroenterology and Motility Research

Group Leader: Pere Clavé, pere.clave@ciberehd.org

## Research Overview

This group is part of the Maresme Health Consortium (CdSM) based in the Mataró Hospital. It is made up of medical staff and researchers working in primary care and is recognized as a consolidated group by the Government of Catalonia (2017 SGR772) AGAUR, and forms part of the National CIBERehd Network. The group has 4 lines of research:

1. **Oropharyngeal Dysphagia:** This includes compensatory strategies, rheology and texture, nutritional research and optimal-massive interventions; clinical and basic studies. Also new diagnostic and treatment strategies: screening with Artificial Intelligence algorithms, pharmacological agonists (TRP agonists), neurorehabilitation strategies. Peripheral electrical stimulation (Intrapharyngeal, Transcutaneous), non-invasive brain stimulation (NIBS, TDCs, rTMS).
2. **Upper GI tract motility. GERD in Morbid Obese patients, Achalasia, Upper Esophageal Sphincter Motility**
3. **Colorectal Motility:** This includes the study of pathophysiology, diagnosis and treatments for fecal incontinence and the development of neurorehabilitation strategies. Also, research into prevalence, pathophysiology and diagnosis of functional constipation and functional defecatory disorders.
4. **Basic Studies: In vitro gastrointestinal motility**

## Group Highlights 2020

Together with the Mataró Town Council the group received a prestigious European Regional Development Fund grant (PEC Mataró-Maresme Innovation Ecosystem for Caring Cities 2021) aimed at promoting healthy aging and improving the care, autonomy and quality of life of elderly people from Mataró through: 1) promoting healthy habits and lifestyles; 2) urbanism and housing; 3) health and social aspects; and 4) research and education. One of the specific programs of this project is dedicated to oropharyngeal dysphagia in older people.

We are in the process of founding a start-up company to exploit the patent AIMS-OD (PCT/ES2020/070723) that uses artificial intelligence algorithms to predict the risk of several prevalent pathologies.

## Selected publications 2020


1. Clavé P, Cabib C, Ortega O. **Cortical metaplasticity as a novel candidate mechanism for boosting brain swallow performance in neurogenic dysphagia.** J Physiol. 2020 Nov; 598(22):5003-5004. Perspectives article.
2. Tomsen N, Alvarez-Berdugo D, Rofes L, Ortega O, Arreola V, Nascimento W, et al. **A randomized clinical trial on the acute therapeutic effect of TRPA1 and TRPM8 agonists in patients with oropharyngeal dysphagia.** Neurogastroenterol Motil. 2020 Jun;32(6):e13821. Article.
3. Cabib C, Nascimento W, Rofes L, Arreola V, Tomsen N, Mundet L, et al. **Short-term neurophysiological effects of sensory pathway neurorehabilitation strategies on chronic poststroke oropharyngeal dysphagia**. Neurogastroenterol Motil. 2020 Sep;32(9):e13887. Article.
4. Ortega O, Bolívar-Prados M, Arreola V, Nascimento WV, Tomsen N, Gallegos C, et al. **Therapeutic Effect, Rheological Properties and α-Amylase Resistance of a New Mixed Starch and Xanthan Gum Thickener on Four Different Phenotypes of Patients with Oropharyngeal Dysphagia.** Nutrients. 2020 Jun 23;12(6):1873. Article.
5. Cabib C, Nascimento W, Rofes L, Arreola V, Tomsen N, Mundet L, et al. **Neurophysiological and Biomechanical Evaluation of the Mechanisms Which Impair Safety of Swallow in Chronic Post-stroke Patients.** Transl Stroke Res. 2020 Feb;11(1):16-28. Article.

# Group: Translational Research on Hepatic Diseases

Group Leader: Rosa Mª Morillas rmorillas.germanstrias@gencat.cat

## Research Overview

This is a multidisciplinary group led on the clinical side by Dr Rosa Mª Morillas, Head of the Hepatology Department at the Germans Trias i Pujol University Hospital and at the IGTP Dr Ramon Bartolí, Principal Investigator for Basic and Translational Research and CIBER researcher.
The group focuses on clinical and translational research on chronic hepatitis, non-alcoholic fatty liver disease, cirrhosis and complications of portal hypertension (ascites, haemorrhage due to portal hypertension, hepatic encephalopathy, spontaneous bacterial peritonitis, infections) and hepatocellular carcinoma. They are also experienced in the development of different experimental models of liver disease: cirrhotic rat model with ascites -carbon tetrachloride-; hepatic encephalopathy model -cirrhosis + portal vein ligation-; secondary biliary cirrhosis model due to ligation of the common bile duct and steatohepatitis model with different degrees of fibrosis (metabolic model + carbon tetrachloride). They have developed an endoscopic platform able to release drugs and active agents in colonic tract and are studying its applicability in different liver diseases. The group is also highly networked with other groups or lead collaborative projects within organizations such as: the Societat Catalana de Digestología (ACD); the Asociación Española para el Estudio del Higado (AEEH); the European Association for the Study of the Liver (EASL); the National network CIBERehd (the Center for Biomedical Research in Networks in Hepatic Diseases and Digestive 2006 / Area 1: Portal hypertension and mechanisms of transition to cirrhosis) and member of the working group Prevention and treatment of the complications of chronic liver disease (GTiPUH), which which is part of the National Network of Research in Hepatology and Gastroenterology (RNIHG)

## Group Highlights 2020

In May the group signed the license agreement for two patents (WO2016135219A1, WO2018019881A1), which have been developed by members of the group to the start-up Inmedical Therapeutics.

A new basic-translational research line was established on the use of the platform developed by the group (COVERGEL) for the modification of the intestinal microbiota in the treatment of fatty liver with fibrosis.

## Selected publications 2020


1. **Significant fibrosis predicts new-onset diabetes mellitus and arterial hypertension in patients with NASH.** Ampuero J et al. J Hepatol 2020 Jul; 73 (1): 17-25. PMID: 3214736.
2. **Deep-sequencing reveals broad subtype-specific HCV resistance mutations associated with treatment failure**. Chen Q et al. Antiviral Res 2020 Feb; 174: 104694. PMID: 31857134.
3. **Effectiveness and safety of obeticholic acid in a Southern European multicenter cohort of patients with primary biliary cholangitis and suboptimal response to ursodeoxycholic acid.** Gómez E et al, and IBER-PBC leading Cooperative Group. Aliment Pharmacol Ther 2020 Dec 12. PMID: 33314220
4. **Development and Characterization of a New Endoscopic Drug-Eluting Platform With Proven Efficacy in Acute and Chronic Experimental Colitis**. Front Med (Lausanne). Bon I et al, 2020 Aug 20; 7: 415. PMID: 32974357
5. **Rebleeding and mortality risk are increased by ACLF but reduced by pre-emptive TIPS**. Trebicka J et al and International Variceal Bleeding Observational Study Group and Baveno Cooperation. J Hepatol 2020 Nov; 73 (5): 1082-1091. PMID: 32339602




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Research Groups

# Area 5
## Endocrine and diseases of the metabolism bones and kidneys

# Group: Endocrine Thyroid and Obesity

Group Leader: Manel Puig Domingo mpuigd@igtp.cat

## Research Overview

The IGTP Translational Endocrinology research group (ENDOGRUP- 2017 SGR 1262) is coordinated by Manel Puig Domingo, currently Head of the Endocrinology and Nutrition Service at the Germans Trias i Pujol Hospital (HUGTiP) and Professor of Endocrinology at the UAB Department of Medicine. The group has 3 areas of research:

1. **Thyroid pathology**
   The group has been working for many years on (i) the evaluation of thyroid function in relation to iodine nutrition and its consequences during pregnancy, (ii) autoimmune thyroid diseases, and (iii) thyroid cancer; specifically, we are characterizing the phenotypic and molecular (-omic) data of thyroid tumors to discover molecular pathways likely to generate new therapeutic targets and also to identify diagnostic and prognostic marker profiles with potential applicability to clinical practice.
2. **Pituitary tumors**
   The group studies the molecular phenotyping of pituitary tumors and also researches the use of bioimaging markers for applications in personalized medicine as predictive markers of therapeutic response and biological evolution.
3. **Obesity**
   Since 2010, different lines of research have been initiated to study the complications of obesity and its possible reversal after therapeutic bariatric surgery. We have also done studies focused on brown adipose tissue.

## Group Highlights 2020

Despite the situation caused by the pandemic, we have validated markers of therapeutic response of pituitary adenomas by studying more than 12 different markers, establishing the importance of E-cadherin and RORC and initiated studies using artificial intelligence procedures, specifically radiomics and data mining. We are concluding the ACROFAST I clinical trial, the first study worldwide on precision medicine in acromegaly, coordinated by Can Ruti. In thyroid cancer, we continued to study kalikreins. Finally, in the field of obesity, we are concluding a study on microbiota and starting another study on the value of succinate as a predictor of response to two types of bariatric surgery. Regarding the pandemic, we have been actively involved in clinical research and guidelines.

## Selected publications 2020


1. Marazuela M, Giustina A, Puig-Domingo M. **Endocrine and metabolic aspects of the COVID-19 pandemic.** Rev Endocr Metab Disord. 2020 Dec;21(4):495-507. doi: 10.1007/s11154-020-09569-2. Erratum in: Rev Endocr Metab Disord. 2021 Mar;22(1):145. PMID: 32643004; PMCID: PMC7343578.
2. Puig-Domingo M, Gil J, Sampedro-Nuñez M, Jordà M, Webb SM, Serra G, Pons L, Salinas I, Blanco A, Marques-Pamies M, Valassi E, Picó A, García-Martínez A, Carrato C, Buj R, Del Pozo C, Obiols G, Villabona C, Cámara R, Fajardo-Montañana C, Alvarez CV, Bernabéu I, Marazuela M. **Molecular profiling for acromegaly treatment: a validation study.** Endocr Relat Cancer. 2020 Jun;27(6):375-389. doi: 10.1530/ERC-18-0565. PMID: 32302973.
3. Piquer-Garcia I, Campderros L, Taxerås SD, Gavaldà-Navarro A, Pardo R, Vila M, Pellitero S, Martínez E, Tarascó J, Moreno P, Villarroya J, Cereijo R, González L, Reyes M, Rodriguez-Fernández S, Vives-Pi M, Lerin C, Elks CM, Stephens JM, Puig-Domingo M, Villarroya F, Villena JA, Sánchez-Infantes D. **A Role for Oncostatin M in the Impairment of Glucose Homeostasis in Obesity.** J Clin Endocrinol Metab. 2020 Mar 1;105(3):e337–48. doi: 10.1210/clinem/dgz090. PMID: 31606738; PMCID: PMC7112982.
4. Giustina et al. **A Consensus on the Diagnosis and Treatment of Acromegaly Comorbidities: An Update.** J Clin Endocrinol Metab. 2020 Apr 1;105(4):dgz096. doi: 10.1210/clinem/dgz096. PMID: 31606735.
5. Montero-Conde et al. **Hsa-miR-139-5p is a prognostic thyroid cancer marker involved in HNRNPF-mediated alternative splicing.** Int J Cancer. 2020 Jan 15;146(2):521-530. doi: 10.1002/ijc.32622. Epub 2019 Aug 28. PMID: 31403184.






# Group: Diabetes Research

Group Leader: Núria Alonso nalonso@igtp.cat

## Research Overview

The fundamental clinical issue addressed in this area is the detection and characterization (phenotypic and molecular) of preclinical atheromatous cardiovascular disease in patients with diabetes (types 1 and 2). Dr N Alonso (NA) leads this line of research (PI14 / 01772; PI17 / 01362; PI 21/00817), which since 2016 has been part of CIBERDEM as a recognized group. The group is also working on the characterization of myocardial microvascular disease and metabolic toxicity associated with hyperglycemia in diabetic cardiomyopathy (DCM) (TV3 Marathon Project 201602-03, IP: NA) and on the relationship between diabetic retinopathy (DR) and cognitive dysfunction (European project RECOGNIZED). Relevant findings published in recent years are: an increase in subclinical atherosclerosis in patients with DR in the absence of kidney disease; the description of cerebral microvascular disease associated with diabetes; the existence of microangiopathy in the carotid wall in patients with diabetes, and its association with DR; the differential utility of markers of heart failure in diabetes. Recently, a new line of research related to non-alcoholic fatty liver disease (NAFLD) has been initiated in patients with diabetes in collaboration with two leading national and international groups in NAFLD.

## Group Highlights 2020

The most relevant published results of the group are: 1) Description of the advanced lipoprotein profile in subjects with varying degrees of impaired glucose metabolism, 2) the HDL lipoprotein as a prognostic factor for CV death in patients with chronic heart failure (CHF), 3) description of the prevalence of liver fibrosis and relationship with lipid parameters in general population and in diabetes, 4) the trajectory of the cardiac ejection fraction is different in patients with CHF in the presence of diabetes.

## Selected publications 2020


1. Julián MT, Alonso N, Lupón J, Gavidia-Bovadilla G, Ferrer E, de Antonio M, López-Ayerbe J, Domingo M, Santiago-Vacas E, Zamora E, Codina P, Moliner P, Núñez J, Santesmases J, Puig-Domingo M, Bayes-Genis A. **Long-term LVEF trajectories in patients with type 2 diabetes and heart failure: diabetic cardiomyopathy may underlie functional decline.** Cardiovasc Diabetol. 2020 Mar 23;19(1):38. doi: 10.1186/s12933-020-01011-w.
2. Puig-Jové C, Castelblanco E, Falguera M, Hernández M, Soldevila B, Julián MT, Teis A, Julve J, Barranco-Altirriba M, Franch-Nadal J, Puig-Domingo M, Ortega E, Amigó N, Alonso N, Mauricio D. **Advanced lipoprotein profile in individuals with normal and impaired glucose metabolism.** Rev Esp Cardiol (Engl Ed). 2021 Mar 27:S1885-5857(21)00073-6. English, Spanish. doi: 10.1016/j.rec.2021.02.006
3. Julián MT, Pera G, Soldevila B, Caballería L, Julve J, Puig-Jové C, Morillas R, Torán P, Expósito C, Puig-Domingo M, Castelblanco E, Franch-Nadal J, Cusi K, Mauricio D, Alonso N. **Atherogenic dyslipidemia, but not hyperglycemia, is an independent factor associated with liver fibrosis in subjects with type 2 diabetes and NAFLD: a population-based study.** Eur J Endocrinol. 2021 Apr;184(4):587-596. doi: 10.1530/EJE-20-1240.
4. Teis A, Cediel G, Amigó N, Julve J, Aranyó J, Andrés-Cordón J, Puig-Jové C,Castelblanco E, Gual-Capllonch F, Ferrer-Sistach E, Vallejo N, Juncà G, López-Ayerbe J, De Antonio M, Domingo M, Santiago-Vacas E, Codina P, Mauricio D, Lupón J, Alonso N, Bayes-Genis A. **Particle size and cholesterol content of circulating HDL correlate with cardiovascular death in chronic heart failure.** Sci Rep. 2021 Feb 4;11(1):3141.
5. Palanca A, Castelblanco E, Betriu À, Perpiñán H, Soldevila B, Valdivielso JM,Bermúdez-Lopez M, Puig-Jové C, Puig-Domingo M, Groop PH, Fernández E, Alonso N,Mauricio D. **Subclinical atherosclerosis burden predicts cardiovascular events inindividuals with diabetes and chronic kidney disease.** Cardiovasc Diabetol. 2019Jul 19;18(1):93. doi: 10.1186/s12933-019-0897-y.

# Group: Obesity and Type 2 Diabetes: Adipose Tissue Biology

Group Leader: David Sanchez-Infantes, dsanchez@igtp.cat

## Research Overview

This research team focusses on the study of obesity and type 2 diabetes. They search for molecules secreted by white and brown adipose tissue involved in the inflammatory state that occurs during the obesity. They also evaluate the capability of these molecules to inhibit/activate the brown adipose tissue and to modulate the properties of subcutaneous white adipose tissue, which is replaced by thermogenic beige adipose tissue (browning) in obesity. The goal of this group is to decipher why the excess of fat is inhibiting the normal activation and function of brown adipose tissue and browning, and to search for novel pharmacological approaches to treat obesity and related diseases.

## Selected publications 2020

1. Laura Campderrós; David Sánchez-Infantes; Joan Villarroya; Lexa Nescolarde; Antoni Bayès-Genis; Rubén Cereijo; Emma Roca; Francesc Villarroya. **GDF15 and FGF21 as biomarkers of the biological response to strenuous exercise: a study in Marathon runners. Frontiers in Physiology.** *Co-first author. In press Impact factor: 3.367 (Q2), 11/2020. DOI: 10.3389/fphys.2020.550102

2. Ruben Cereijo; Tania Quesada-López; Aleix Gavaldà-Navarro; Jordi Tarasco; Silvia Pellitero; Marjorie Reyes; Manel Puig-Domingo; Marta Giralt; David Sanchez-Infantes; Francesc Villarroya. **The chemokine CXCL14 is negatively associated with obesity and concomitant type 2 diabetes in humans.** International Journal of Obesity. In press Impact factor: 4.36 (Q1) *Corresponding author, 11/2020. DOI: 10.1038/s41366-020-00732-y

3. Irene Piquer-Garcia; Rubén Cereijo; Juan Corral-Pérez; Silvia Pellitero; Eva Martínez; Siri D. Taxerås; Jordi Tarascó; Pau Moreno; José Balibrea; Manel Puig-Domingo; Dolors Serra; Laura Herrero; David Jiménez-Pavón; Carles Lerin; Francesc Villarroya; David Sánchez-Infantes. **Use of infrared thermography to estimate brown fat activation after a cooling protocol in patients with severe obesity that underwent bariatric surgery**. Obes Surg. doi:10.1007/s11695-7, Last author and Corresponding author IF: 3.603 (Q1), 2020. DOI: 10.1007/s11695-020-04502-7

4. Silvia Ribo; David Sanchez-Infantes; Laura Martinez-Guino; Izaskun García-Mantrana; Marta Ramon-Krauel; Mireia Tondo; Erland Arning; Miquel Nofrarías; Óscar Osorio-Conles; Antonio Fernández-Pérez; Pedro González-Torres; Judith Cebrià; Aleix Gavaldà-Navarro; Empar Chenoll; Elvira Isganaitis; Francesc Villarroya; Mario Vallejo; Joaquim Segalés; Josep C. Jiménez-Chillarón; Teodoro Bottiglieri; Ellen W. Demerath; María Carmen Collado; David A. Fields; Carles Lerin. **Increasing breast milk betaine content modulates offspring Akkermansia abundance during early life and improves long-term metabolic health.** Sci Transl Med. Co-first author - In press, IF: 16.3 (D1), 2020.

5. Minéia Weber; Paula Mera; Josefina Casas; Javier Salvador; Amaia Rodríguez; Sergio Alonso; David Sebastián; M Carmen Soler-Vázquez; Carla Montironi; Sandra Recalde; Raquel Fucho; María Calderón-Domínguez; Joan Francesc Mir; Ramon Bartrons; Joan Carles Escola-Gil; David Sánchez-Infantes; Antonio Zorzano; Vicenta Llorente-Cortes; Núria Casals; Víctor Valentí; Gema Frühbeck; Laura Herrero; Dolors Serra. **Liver CPT1A gene therapy reduces diet-induced hepatic steatosis in mice and highlights potential lipid biomarkers for human NAFLD.** FASEB J. IF: 5.39 (D1), 2020. DOI: 10.1096/fj.202000678R





# Group: Kidney-affecting Diseases Research Group

Group Leader: Jordi Bonal, jbonal.germanstrias@gencat.cat

Coordinator: Francesc E. Borràs, feborras@igtp.cat

## Research Overview

The REMAR group (REcerca en Malalties d'Afectació Renal) or Kidney Related Diseases Research Group is a multidisciplinary group of medical professionals from the Germans Trias University Hospital (HUGTP) and researchers from the Germans Trias i Pujol Research Institute (IGTP). The group was recognized as an emerging group (2014SGR804) and as a Pre-consolidated group (2017SGR301) by the Catalan Government.

The team aims to carry out basic, clinical and translational research in the field of kidney diseases and disorders associated with kidney failure. Our research lines are focused in identifying non-invasive biomarkers and developing innovative therapies for kidney-related diseases.

## Selected publications 2020

1. **Local administration of porcine immunomodulatory, chemotactic and angiogenic extracellular vesicles using engineered cardiac scaffolds for myocardial infarction.** Monguió-Tortajada M, Prat-Vidal C, Moron-Font M, Clos-Sansalvador M, Calle A, Gastelurrutia P, Cserkoova A, Morancho A, Ramírez MÁ, Rosell A, Bayes-Genis A, Gálvez-Montón C, Borràs FE, Roura S. Bioact Mater. 2021 Mar 15;6(10):3314-3327. doi: 10.1016/j.bioactmat.2021.02.026. PMID: 33778207

2. **Urinary vitronectin identifies patients with high levels of fibrosis in kidney grafts.** Carreras-Planella L, Cucchiari D, Cañas L, Juega J, Franquesa M, Bonet J, Revuelta I, Diekmann F, Taco O, Lauzurica R, Borràs FE. J Nephrol. 2020 Dec 4. doi: 10.1007/s40620-020-00886-y. PMID: 33275196

3. **Proteomic Characterization of Urinary Extracellular Vesicles from Kidney-Transplanted Patients Treated with Calcineurin Inhibitors.** Carreras-Planella L, Juega J, Taco O, Cañas L, Franquesa M, Lauzurica R, Borràs FE. Int J Mol Sci. 2020 Oct 14;21(20):7569. doi: 10.3390/ijms21207569. PMID: 33066346

4. **Proteomic Research in Peritoneal Dialysis.** Bonomini M, Borras FE, Troya-Saborido M, Carreras-Planella L, Di Liberato L, Arduini A. Int J Mol Sci. 2020 Jul 31;21(15):5489. doi: 10.3390/ijms21155489. PMID: 32752018. Review.

5. **Recommendations on management of the SARS-CoV-2 coronavirus pandemic (Covid-19) in kidney transplant patients.** López V, Vázquez T, Alonso-Titos J, Cabello M, Alonso A, Beneyto I, Crespo M, Díaz-Corte C, Franco A, González-Roncero F, Gutiérrez E, Guirado L, Jiménez C, Jironda C, Lauzurica R, Llorente S, Mazuecos A, Paul J, Rodríguez-Benot A, Ruiz JC, Sánchez-Fructuoso A, Sola E, Torregrosa V, Zárraga S, Hernández D; Grupo de Estudio GREAT (Grupo Español de Actualizaciones en Trasplante). Nefrologia. 2020 May-Jun;40(3):265-271. doi: 10.1016/j.nefro.2020.03.002. Epub 2020 Apr 3. PMID: 32278616

# Group: Innovation in Vesicles & Cells for Application in Therapy (IVECAT)

Group Leader: Francesc E. Borràs, feborras@igtp.cat

## Research Overview

The IVECAT group is dedicated to the study of different aspects of extracellular vesicles such as exosomes and microvesicles and also of different cells types including mesenchymal stem cells. The aim is always to move basic research through the pipeline to clinical application.

The group's research interests are mainly the discovery of new biomarkers for better diagnostic and prognostic of patients and the study of novel biotherapies for immunomodulation and regeneration of affected tissues.

Although we focus on transplantation and renal related diseases, we also study EVs in cardiac repair, in neuro-degenerative diseases, and pathologies affecting other systems.

## Selected publications 2020


1. **Local administration of porcine immunomodulatory, chemotactic and angiogenic extracellular vesicles using engineered cardiac scaffolds for myocardial infarction**. Monguió-Tortajada M, Prat-Vidal C, Moron-Font M, Clos-Sansalvador M, Calle A, Gastelurrutia P, Cserkoova A, Morancho A, Ramírez MÁ, Rosell A, Bayes-Genis A, Gálvez-Montón C, Borràs FE, Roura S. Bioact Mater. 2021 Mar 15;6(10):3314-3327. doi: 0.1016/j.bioactmat.2021.02.026. PMID: 33778207
2. **In Vitro Characterization of Human CD24 hi CD38 hi Regulatory B Cells Shows CD9 Is Not a Stable Breg Cell Marker.** Fatin N Mohd Jaya, Sergio G Garcia, Francesc E Borras, Dolores Guerrero, Godfrey C F Chan, Marcella Franquesa Int J Mol Sci. 2021 Apr 27;22(9):4583. doi: 10.3390/ijms22094583. PMID: 33925530
3. **Urinary vitronectin identifies patients with high levels of fibrosis in kidney grafts.** Carreras-Planella L, Cucchiari D, Cañas L, Juega J, Franquesa M, Bonet J, Revuelta I, Diekmann F, Taco O, Lauzurica R, Borràs FE. J Nephrol. 2020 Dec 4. doi: 10.1007/s40620-020-00886-y. PMID: 33275196
4. **Proteomic Characterization of Urinary Extracellular Vesicles from Kidney-Transplanted Patients Treated with Calcineurin Inhibitors**. Carreras-Planella L, Juega J, Taco O, Cañas L, Franquesa M, Lauzurica R, Borràs FE. Int J Mol Sci. 2020 Oct 14;21(20):7569. doi: 10.3390/ijms21207569. PMID: 33066346
5. **Proteomic Research in Peritoneal Dialysis**. Bonomini M, Borras FE, Troya-Saborido M, Carreras-Planella L, Di Liberato L, Arduini A. Int J Mol Sci. 2020 Jul 31;21(15):5489. doi: 10.3390/ijms21155489. PMID: 32752018. Review.




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Research Groups
**Area 6**
Immunology and Inflamation

# Group: Immunology of Diabetes

Group Leader: Marta Vives-Pi, mvives@igtp.cat

## Research Overview

The multidisciplinary Immunology of Diabetes Group at the IGTP is part of the Immunology Section of the Germans Trias i Pujol University Hospital (HUGTiP). It is made up of researchers, endocrinologists, paediatricians and technicians; the group works to understand more about the causes of type 1 diabetes. The research of the group is focused on translational research: Immunotherapies for the prevention and treatment of Type 1 diabetes, pathogenic mechanisms of autoimmunity and paediatric type 1 diabetes: tolerance, spontaneous remission and biomarkers. Our goal is to contribute to therapeutic intervention in type 1 diabetes and other autoimmune diseases.

The principal investigator, **Marta Vives-Pi**, has been working in the field of autoimmune diseases since 1988. Since 1996 she has been leading a variety of research projects with special emphasis on the development of immunotherapies. In 2000 she started the specific pathogen free Unit (SPF) at the IGTP, designed for the study of experimental models of type 1 diabetes. M. Vives-Pi is also the co-founder and Scientific Officer of Ahead Therapeutics SL a spin-off company set up to transfer the immunotherapy technology generated by the group to the clinical arena and convert know-how into treatments for autoimmune diseases.

## Group Highlights 2020

**News** (Communication and popularization of science)
During 2020, despite the challenges of the pandemic, the Immunology of Diabetes Group continued its research and in parallel, extended its science for the citizen activities.

- 13 May Adrián Villalba on the 24 News service in Catalonia
- 29 October Marta Vives-Pi interviewed on the Hub de Salud con Rosa Quintana, a health news and information website run by the ell-known national television presenter
- 30 November, Marta Vives-Pi interviewed by the Catalan Immunology Society

## Selected publications 2020


1. Villalba A, Rodriguez-Fernandez S, Ampudia RM, Cano-Sarabia M, Perna-Barrull D, Bertran-Cobo C, Ehrenberg C, Maspoch D, Vives-Pi M. **Preclinical evaluation of antigen-specific nanotherapy based on phosphatidylserine-liposomes for type 1 diabetes.** Artif Cell Nanomed Biotech. 48 (1):77-83, 2020

2. Villalba A, Rodriguez-Fernandez S, Perna-Barrull D, Ampudia RM, Gomez-Muñoz L, Pujol-Autonell I, Aguilera E, Coma M, Cano-Sarabia M, Vazquez F, Verdaguer J, Vives-Pi M. **Repurposed analogue of GLP-1 ameliorates hyperglycaemia in diabetic mice through pancreatic cell reprogramming.** Frontiers in Endocrinology, May 2020, 11:258, 2020

3. Villalba A, Rodriguez-Fernandez S, Perna-Barrull D, Ampudia RM, Gomez-Muñoz L, Pujol-Autonell I, Aguilera E, Risueño RM, Cano-Sarabia M, Maspoch D, Vazquez F, Vives-Pi M. **Antigen-specific immunotherapy combined with a regenerative drug in the treatment of experimental type diabetes.** Sci Rep 10:18927, 2020.

4. Perna-Barrull D, Gieras A, Rodriguez-Fernandez S, Tolosa E, Vives-Pi M. **Immune system remodelling by prenatal betamethasone: effects on -cells and type 1 diabetes.** Frontiers in Endocrinology. 11:540, 2020. Review

5. Piquer-Garcia I, Campderros L, Taxerås SD, Gavaldá-Navarro A, Pardo R, Vila M, Pellitero S, Martínez E, Tarascó J, Moreno P, Villarroya J, González L, Rodriguez-Fernandez S, Vives-Pi M, Lerin C, Elks C, Stephens JM, Puig-Domingo M, Villarroya F, Villena JA, Sánchez-Infantes D. **A role for Oncostatin M in the impairment of glucose homeostasis in obesity.** J Clin Endocrinol Metab 105 (3):1-12, 2020. Article






# Group: Immunopathology

Group Leader: Eva Mª Martínez Cáceres, emartinezc@igtp.cat

## Research Overview

The Immunopathology group of the Germans Trias i Pujol Research Institute, Can Ruti Campus is a multidisciplinary team of immunologists, pharmacists, biologists, biochemists and biotechnologists working in various aspects of immunopathology, in particular on the study of immunological tolerance mechanisms and how their failure causes disease. The research team is led by Dr Eva Martínez Cáceres, Head of the Immunology Division and Associate professor of Immunology at the Universitat Autònoma de Barcelona. The team members carry out their research in the Immunology Department, Germans Trias Hospital, and the Germans Trias i Pujol Research Institute (IGTP). The team has numerous national and international collaborations and is one of the European Centres of Excellence recognized by the International Federation of Clinical Immunological Societies (FOCIS).
The eminently translational team has extensive experience of more than 20 years in the study of tolerance mechanisms, immunotherapy and immune monitoring. The group has an important line of research based on the analysis of disease biomarkers of response to immunomodulatory treatments, mainly in multiple sclerosis, reflected in numerous publications.
The research lines currently active in the Immunopathology group are:

- Cell-based tolerance-inducing therapies
- Clinical immunology/ Clinical Epidemiology Research
- Biomarkers Innovation and Diagnostic Immunology
- SARS-CoV2 immune response
- Inflammation and sepsis
- Immune monitoring of treatment response in immune-mediated diseases

## Selected publications 2020


1. **Seroprevalence of SARS-CoV-2 IgG specific antibodies among healthcare workers in the Northern Metropolitan Area of Barcelona, Spain, after the first pandemic wave.** Barallat J, Fernández-Rivas G, Quirant-Sánchez B, González V, Doladé M, Martinez-Caceres E, Piña M, Matllo J, Estrada O, Blanco I. PLoS One. 2020 Dec 28;15(12):e0244348.

2. **COVID-19: age, Interleukin-6, C-reactive protein, and lymphocytes as key clues from a multicentre retrospective study.** Jurado A, Martín MC, Abad-Molina C, Orduña A, Martínez A, Ocaña E, Yarce O, Navas AM, Trujillo A, Fernández L, Vergara E, Rodríguez B, Quirant B, Martínez-Cáceres E, Hernández M, Perurena-Prieto J, Gil J, Cantenys S, González-Martínez G, Martínez-Saavedra MT, Rojo R, Marco FM, Mora S, Ontañón J, López-Hoyos M, Ocejo-Vinyals G, Melero J, Aguilar M, Almeida D, Medina S, Vegas MC, Jiménez Y, Prada Á, Monzón D, Boix F, Cunill V, Molina J. Immun Ageing. 2020 Aug 14;17:22.

3. **Comprehensive flow cytometric reference intervals of leukocyte subsets from six study centers across Europe**. Oras A, Quirant-Sanchez B, Popadic D, Thunberg S, Winqvist O, Heck S, Cwikowski M, Riemann D, Seliger B, Martinez Caceres E, Uibo R, Giese T. Clin Exp Immunol. 2020 Dec;202(3):363-378.

4. **Analytical techniques for multiplex analysis of protein biomarkers.** Van Gool A, Corrales F, Čolović M, Krstić D, Oliver-Martos B, Martínez-Cáceres E, Jakasa I, Gajski G, Brun V, Kyriacou K, Burzynska-Pedziwiatr I, Wozniak LA, Nierkens S, Pascual García C, Katrlik J, Bojic-Trbojevic Z, Vacek J, Llorente A, Antohe F, Suica V, Suarez G, t'Kindt R, Martin P, Penque D, Martins IL, Bodoki E, Iacob BC, Aydindogan E, Timur S, Allinson J, Sutton C, Luider T, Wittfooth S, Sammar M. Expert Rev Proteomics. 2020 Apr;17(4):257-273.

5. **Immunological Pattern in IgA Nephropathy.** Esteve Cols C, Graterol Torres FA, Quirant Sánchez B, Marco Rusiñol H, Navarro Díaz MI, Ara Del Rey J, Martínez Cáceres EM. Int J Mol Sci. 2020 Feb 18;21(4):1389

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Research Groups

**Area 7**
Infectious Diseases



# Group: Clinical and Experimental Microbiology

Group Leader: Pere Joan Cardona Iglesias, pcardonai.germanstrias@gencat.cat

## Research Overview

This is a consolidated multidisciplinary research group accredited by the Catalan Government. Several group members belong to CibeRes (Centro de Investigación Biomédica en Red en Enfermedades Respiratorias), while some others belong to CiberEsp (Centro de Investigación Biomédica en Red en Epidemiología y Salud Pública).
The research group focuses its activity on the development, standardization and clinical evaluation of microbiological, immunological and molecular techniques susceptible for use in the diagnosis of infectious diseases and the development of "in vivo" experimental models including the Drosophila model, the study of the molecular mechanisms underlying antimicrobial resistance, the assessment of the antimicrobial activity of new antiseptic and disinfectants, and the fight against nosocomial infection through classic and molecular epidemiology tools. Molecular epidemiology through whole genome sequencing has also been applied to pathogens of public health interest, such as Mycobacterium tuberculosis (as reference centre in Catalonia) or SARS-CoV-2, for surveillance purposes and especially for the characterization of outbreaks.
Due to its daily clinical services in the hospital the group aims to be the reference for the "pathogen view" on the campus. It has a strong history of collaborations connecting the essential triangle of healthcare, research and education. The objective is to be a reference group for innovation and tech-transfer activities.

## Group Highlights 2020

2020 has been an exceptional year for the entire research community and infectious disease research in particular. Research and healthcare has seen an unprecedented readjustment of activity to focus on diagnostics, treatment and prevention during the SARS-CoV-2 epidemic.

## Selected publications 2020

1. **Impact of adjuvant therapeutic surgery on the health-related quality of life of pulmonary tuberculosis patients**. Benito P., Vashakidze S., Gogishvili S., Nikolaishvili K., Despuig A., Tukvadze N., Shubladze N., Avaliani Z., Vilaplana C. European Respiratory Journal Open Research. 2020 Aug 31; 6(3): 00083-2020. IF: 12,339

2. **Type I IFN exacerbates disease in tuberculosis-susceptible mice by inducing neutrophil-mediated lung inflammation and NETosis.** Moreira-Teixeira L., Stimpson PJ., Stavropoulos E., Hadebe S., Chakravarty P., Ioannou M., Aramburu IV., Herbert E., Priestnall SL., Suarez-Bonnet A., Sousa J., Fonseca KL., Wang Q., Vashakidze S., Rodríguez-Martínez P., Vilaplana C., Saraiva M., Papayannopoulos V., O'Garra A. Nature Communications. 2020 Nov 4;11(1): 5566. IF: 12,121

3. **Macrophage mitochondrial MFN2 (mitofusin 2) links immune stress and immune response through reactive oxygen species (ROS) production.** Lloberas J., Muñoz JP., Hernández-Álvarez MI., Cardona PJ., Zorzano A., Celada A. Autophagy. 2020 Dec;16(12): 2307-2309. IF: 9,77

4. **Detection of SARS-CoV-2 in a cat owned by a COVID-19-affected patient in Spain.** Segalés J., Puig M., Rodon J., Avila-Nieto C., Carrillo J., Cantero G., Terrón MT., Cruz S., Parera M., Noguera-Julián M., Izquierdo-Useros N., Guallar V., Vidal E., Valencia A., Blanco I., Blanco J., Clotet B., Vergara-Alert J. Proceedings of the National Academy of Sciences of the United States of America. 2020; 117(40): 24790-24793. IF: 9,412

5. **Mitofusin 2 in macrophages links mitochondrial ros production, cytokine release, phagocytosis, autophagy, and bactericidal activity.** Tur J., Pereira-Lopes S., Vico T., Marín EA., Muñoz JP., Hernández-Alvarez M., Cardona PJ., Zorzano A., Lloberas J., Celada A. Cell Reports. 2020 Aug 25; 32(8): 108079. IF: 8,109

# Group: Experimental Tuberculosis Unit (UTE)

Group Leader: Dra. Cristina Vilaplana Massaguer, cvilaplana@igtp.cat

## Research Overview

The Experimental Tuberculosis Unit (UTE) is a research group at the IGTP also affiliated with the Department of Microbiology at the Germans Trias i Pujol University Hospital (HUGTIP) and the Departments of Genetics and Microbiology at the Universitat Autònoma de Barcelona. The group was founded in 1997 by Dr Pere-Joan Cardona to study tuberculosis (TB) and is now led by Dr Cris Vilaplana. In recent years the unit has specialized in the field of design and evaluation of new prophylactic and therapeutic strategies against TB and tools to monitor its course, as well as the study of the disease from a multidisciplinary point of view from bench to bedside. With its 20-years' experience the group are recognized internationally as experts in the field of infectious diseases.

The UTE has 3 main research lines:

1. Study of biomarkers of TB disease course and prognosis
2. Evaluation of new prophylactic and therapeutic strategies against TB in:

   - experimental models of infection

   - clinical studies and trials
3. Study of Health dimensions and quality of life in the context of infectious diseases

## Group Highlights 2020

- Start of the SMA-TB, a multicentric project funded by the EC through the H2020 program and coordinated by UTE
- Participation in several projects to tackle the covid-19 pandemic, including an international one funded by the 2020-EC
- 12 scientific manuscripts published in international journals

## Selected publications 2020


1. Benito P, Vashakidze S, Gogishvili S, Nikolaishvili K, Despuig A, Tukvadze N, Shubladze N, Avaliani Z, Vilaplana C. **Impact of adjuvant therapeutic surgery on the health-related quality of life of pulmonary tuberculosis patients.** ERJ Open Res. DOI: 10.1183/23120541.00083-2020. 2020 August. Article.
2. Moreira-Teixeira L, Stimpson PJ, Stavropoulos E, Hadebe S, Chakravarty P, Ioannou M, Aramburu IV, Herbert E, Priestnall SL, Suarez-Bonnet A, Sousa J, Fonseca KL, Wang Q, Vashakidze S, Rodríguez-Martínez P, Vilaplana C, Saraiva M, Papayannopoulos V, O'Garra A. **Type I IFN exacerbates disease in tuberculosis-susceptible mice by inducing neutrophil-mediated lung inflammation and NETosis.** Nat Commun. DOI: 10.1038/s41467-020-19412-6. 2. 2020 November. Article.
3. Fonseca KL, Maceiras AR, Matos R, Simoes-Costa L, Sousa J, Cá B, Barros L, Fernandes AI, Mereiter S, Reis R, Gomes J, Tapia G, Rodríguez-Martínez P, Martín-Céspedes M, Vashakidze S, Gogishvili S, Nikolaishvili K, Appelberg R, Gärtner F, Rodrigues PNS, Vilaplana C, Reis CA, Magalhães A, Saraiva M. **Deficiency in the glycosyltransferase Gcnt1 increases susceptibility to tuberculosis through a mechanism involving neutrophils**. Mucosal Immunol. DOI: 10.1038/s41385-020-0277-7. 2020 September. Article.
4. Arias L, Cardona P, Català M, Campo-Pérez V, Prats C, Vilaplana C Julián E, Cardona P-J. **Cording Mycobacterium tuberculosis bacilli have a key role in the progression towards active tuberculosis, which is stopped by previous immune response. Microorganisms**. DOI: 10.3390/microorganisms8020228. 2020 February. Article.
5. Cardona P-J; Català M; Prats C. **Origin of tuberculosis in the Paleolithic predicts unprecedented population growth and female resistance.** Scientific Reports. DOI: 10.1038/s41598-019-56769-1 2020 January. Article.






# Group: Innovation in Respiratory Infections and Tuberculosis (One and a Half Lab)

Group Leader: José Domínguez, jadominguez@igtp.cat

## Research Overview

The research team is a multidisciplinary group that includes basic and clinical researchers, who have been working together uninterruptedly in recent years on research activities related to the management of respiratory infections and tuberculosis. The group is recognized by the AGAUR (Agència de Gestió I Ajuts Universitaris i de Recerca, number 2017 SGR 494).

The research activity is carried out in collaboration and in close coordination with the Departments of Microbiology, Paediatrics, Pneumology, Intensive Care, Emergency and the Prevention and Preventive Medicine Departments at the Germans Trias i Pujol University Hospital. The group also collaborates with national and international groups and, belongs to the national network CIBER Enfermedades Respiratorias (CIBERes) group (CB06/0031), in the research programs for "Infectious respiratory diseases Respiratory tract infections", particularly in the areas of "Tuberculosis" and "Host-pathogen interactions".

The group has received funding from national and international public and private agencies. The research lines of the group are the following: Host-pathogen interaction, Immune response, Intracellular persistence model, Diagnostic technology innovation, and Novel therapeutic approaches

## Group Highlights 2020

The group hightlights 5 areas for 2020

1. **Publications** - 12 publications, 8 of them in Q1. Publication in Nature Medicine. D1 (1/148), Impact factor: 36.130
2. **Projects** - PLASTICHEAL. H2020 project granted
3. **Clinical Trials** - Actively involved in 3 clinical trials, 2 of them of for COVID-19
4. **Human Resources** - Irene Latorre obtained a Miguel Servet Contract, and Sergio Díaz obtained a PFIS predoctoral contract from ISCIII
5. **Tech-Transfer** Patent licence agreement with a German Company. Co-development in progress

## Selected publications 2020


1. Coppola M, et al. **Cell mediated immune responses to in vivo expressed and stage specific Mycobacterium tuberculosis antigens in latent and active tuberculosis across different age groups.** Frontiers in immunology 2020
2. Lacoma A, et al. **Novel intracellular antibiotic delivery system against Staphylococcus aureus: cloxacillin-loaded PLGA nanoparticles.** Nanomedicine 2020
3. Gupta RK, et al. **Discovery and validation of a personalised risk predictor for incident tuberculosis in settings aiming towards pre-elimination (PERISKOPE-TB).** Nature Medicine 2020
4. Molina-Moya B, et al. **Molecular detection of Mycobacterium tuberculosis in oral mucosa from patients with presumptive tuberculosis.** Journal of Clinical Medicine 2020
5. Lee SO, et al. **Dysfunctional accessory gene regulator (agr) as a prognostic factor in invasive Staphylococcus aureus infection: a systematic review and meta-analysis.** Scientific Reports. 2020

# Group: Clinical Virology and New Diagnostic Tools

Group Leader: Elisa Martró, emartro@igtp.cat

## Research Overview

The group promotes multidisciplinary translational research to improve the diagnostics, prognostics and management of infections caused by viruses and other pathogens with impacts on clinical applications and public health. Based in the Microbiology Service and the Clinical Laboratory North Metropolitan Area (LCMN) of the Germans Trias i Pujol University Hospital. It is part of a consolidated SGR AGAUR group and belongs to Group 27 within the Epidemiology and Public Health). It has three main research lines.

1. **Viral hepatitis.** Characterization of the molecular epidemiology of HCV (dynamics in key populations, such as people who inject drugs and people in prisons). 2) Improvement of the diagnosis of active HCV and HBV infection among vulnerable populations. 3) Assessment of HBV prevalence and vaccination needs in vulnerable populations.
2. **SARS-CoV-2.** Within the SeqCOVID-SPAIN consortium, in mid-2020 the group implemented the whole genome sequencing of SARS-CoV-2 virus for surveillance of viral lineages and variants. They identified the first case with the variant of B.1.1.7 in Catalonia in late December 2020 and monitored its spread. Additional surveillance of patients and healthcare workers continues.
3. **Molecular epidemiology of other infectious diseases.** The group applies its considerable experience to other clinically relevant infectious diseases, such as tuberculosis or antibiotic resistant bacteria in collaboration with the personnel at the Microbiology Department.

## Group Highlights 2020

- New collaboration with the Surveillance Evaluation and Research Program at Kirby Institute, Australia
- Participation in the pilot hepatitis C micro-elimination strategy in Pakistani migrants run by a consortium including ASPCAT and based on technology developed by the group.
- New diagnostic techniques included in the new "Guía de cribado de la infección por el VHC" from the published in July 2020 by the "Ministerio de Sanidad", Spanish government.
- A new research line on SARS-CoV-2 genomic epidemiology was initiated in 2020 with special focus on characterization of outbreaks

## Selected publications 2020

1. **The hepatitis C care cascade among people who inject drugs accessing harm reduction services in Catalonia: Major gaps for migrants**. Folch C, Saludes V, Reyes-Ureña J, Antuori A, Ibáñez N, Majó X, Colom J, Matas L, Casabona J, Martró E; HepCdetect II Study Group.Int J Drug Policy. 2021 Apr;90:103057. doi: 10.1016/j.drugpo.2020.103057. Epub 2020 Dec 11.
2. **Evaluation of the Xpert HCV VL Fingerstick point-of-care assay and dried blood spot HCV-RNA testing as simplified diagnostic strategies among people who inject drugs in Catalonia, Spain.** Saludes V, Antuori A, Lazarus JV, Folch C, González-Gómez S, González N, Ibáñez N, Colom J, Matas L, Casabona J, Martró E.Int J Drug Policy. 2020 Jun;80:102734. doi: 10.1016/j.drugpo.2020.102734.
3. **The impact of the COVID-19 pandemic on harm reduction services in Spain.** Picchio CA, Valencia J, Doran J, Swan T, Pastor M, Martró E, Colom J, Lazarus JV.Harm Reduct J. 2020 Nov 4;17(1):87. doi: 10.1186/s12954-020-00432-w.
4. **Deep-sequencing reveals broad subtype-specific HCV resistance mutations associated with treatment failure.** Chen Q et al .Antiviral Res. 2020 Feb;174:104694. doi: 10.1016/j.antiviral.2019.104694.





# Group: Clinical and environmental Infectious Diseases Study Group (CEID)

Group Leader: Maria Lluisa Pedro-Botet, mlpbotet.germanstrias@gencat.cat

## Research Overview

The CEID is a multidisciplinary group of medical staff at the Germans Trias i Pujol University Hospital and researchers based at the Germans Trias i Pujol Research Institute. Their work covers a range of strategies to prevent and combat infectious diseases. The group is a member of the the CIBEres Network (*Centro de Investigación Biomédica en Red en Enfermedades Respiratorias*). Research is divided into six research lines.

1. **Infectious endocarditis:** Prospective database of diagnosis and follow-up of patients with infectious endocarditis admitted to the Hospital. EnteroColonus GAMES Project and collaboration in the validation of the Poët study.
2. **Primary immunodeficiencies:** Monitoring and/or treatment of more than 150 patients diagnosed with primary immunodeficiency and 30% are receiving replacement treatment. Research into diagnostic and prognostic markers and reducing time to diagnosis.
3. **One Health:** Research dedicated to multidrug-resistant microorganisms involved in animal-human-animal transmission and with special dedication to methicillin-resistant Staphylococcus aureus (MRSA) CC398.
4. **Legionella:** Long-established research line; the hospital is a Reference Laboratory of the General Directorate of Public Health of Catalonia for the Study of Legionellosis Outbreaks. We have a patent developed for the rapid detection of Legionella in environmental waters and the study of biocides.
5. **Nosocomial infections:** Control and prevention of nosocomial infection (CD, surgical infection) and in particular nosocomial pneumonia. Nosocomial pneumonia outside intensive care units involves research into the risk factors for nosocomial pneumonia.
6. **Emerging infectious diseases:** Research into diseases becoming more relevant in Spain such as Chagas disease and Schistosomiasis.

## Selected publications 2020

1. Fernández-Cruz et al. **Etiology and prognosis of pneumonia in patients with solid tumors: a prospective cohort of hospitalized cases.** Oncologist. 2020 May;25(5):e861-e869. doi: 10.1634/theoncologist.2019-0031. Epub 2020 Feb 11.
2. Mireia Mensa-Vendrell, Maria Tasias-Pitarch, Miguel Salavert, Eva Calabuig, Laura Morata, Genís Castells-Lao, Ester López-Suñé, Jose Mensa, Maria Rosa Oltra-Sempere, M.Luisa Pedro-Botet, Valentina Isernia, Esteban Reynaga Sosa, Leonor Moreno-Nuñez, Juan Pasquau Liaño, Sergio Sequera-Arquelladas, Jose Yuste, and Alex Soriano. **Safety and tolerability of more than 6 days of tedizolid treatment.** Antimicrob Agents Chemother 2020 Jun 23;64(7):e00356-20.
3. Reynaga E, Carrillo J, Santos JR, Roure S, Mateu L, Paredes R, Clotet B, Izquierdo-Useros N, Pedro-Botet ML. **Outcome of hospitalized patients with COVID-19 pneumonia treated with high-dose immunoglobulin therapy in a prospective case series.** Clin Microbiol Infect. 2020 doi: 10.1016/j.cmi.2020.10.010. Epub ahead of print. PMID: 33065237; PMCID: PMC7550893.
4. Alcántara A, Soldevila L, Valerio L, Roure S, Pérez-Quílez O, Martinez-Cuevas O, Villanova X. Cutaneous larva migrans or the wandering invader. **Description of 16 cases in the Northern Metropolitan area of Barcelona.** Travel Med Infect Dis. 2020 Jul-Aug;36:101545. doi: 10.1016/j.tmaid.2019.101545. Epub 2019 Dec 10. PMID: 31830596
5. S Quero, N Párraga-Niño, M Garcia-Núñez, M L Pedro-Botet, L Gavaldà, L Mateu, M Sabrià, J M Mòdol. **The impact of pipeline changes and temperature increase in a hospital historically colonised with Legionella**. Sci Rep. 2021 Jan 21;11(1):1916. doi: 10.1038/s41598-021-81625-6.

# Group: Plasmodium vivax and Exosome Research Group (PvREX)

Group Leaders: Carmen Fernandez-Becerra, Carmen.fernandez@isglobal.org and Hernando A del Portillo (ICREA Research Professor), hdelportillo@igtp.cat

## Research Overview

**Cryptic infections and exosomes.** Asymptomatic carriers of malaria parasites are a major challenge for malaria elimination. We are presently entertaining the hypothesis that exosomes in P. vivax infections act as intercellular communicators between the bone marrow and the spleen, signalling mechanisms that will unveil the molecular basis of cryptic infections in this species.

**Reticulocyte-derived exosomes (Rex) vaccines against P. vivax.** Preclinical studies in rodent models have demonstrated that exosomes from infections can be explored as a new vaccination approach. Presently, we are pursuing efforts to "tailor" human Rex with P. vivax antigens and to determine their antigen presenting capacities as a new vaccine and delivery platform against P. vivax.

**Extracellular Vesicles and Biomarker discovery.** In the last decade, research on the biology, function and potential applications of extracellular vesicles (EVs) has grown exponentially. One of the most important biomedical applications of this research area is the potential of using EVs as non-invasive biomarkers of clinical diseases. The aim of this research line is to use EVs to identify novel biomarkers in chronic Chagas disease, specifically in the context of therapeutic response and disease prognosis during the chronic infection, as well as the discovery of biomarkers of asymptomatic infections in P. vivax malaria.

This group is jointly affiliated with the IGTP and ISGlobal, through a formal agreement between the institutions.

## Group Highlights 2020

Despite the difficulties and curtailment of travel in 2020 the group continued to advance and publish their research into P. vivax including a paper in Nature Communications.

## Selected publications 2020

1. Toda et al. **Plasma-derived extracellular vesicles from Plasmodium vivax patients signal spleen fibroblasts via NF-kB facilitating parasite cytoadherence**. Nat Commun. 2020;11(1):2761. Published 2020 Jun 2. doi:10.1038/s41467-020-16337-y Carmen Fernandez-Becerra*, Maria Bernabeu, Angélica Castellanos, Bruna R. Correa, Thomas Obadia, Miriam Ramirez, Edmilson Rui, Franziska Hentzschel, Maria López-Montañés, Alberto Ayllon-Hermida, Lorena Martin-Jaular, Aleix Elizalde-Torrent, Peter Siba, Ricardo Vencio, Myriam Arevalo-Herrera, Sócrates Herrera, Pedro L. Alonso, Ivo Mueller and Hernando A. del Portillo*. (*equal correspondence). **Plasmodium vivax spleen-dependent genes encode antigens associated with cytoadhesion and clinical protection.** Proc Natl Acad Sci U S A. 2020;117(23):13056-13065. doi:10.1073/pnas.1920596117

2. Marcelo A.M. Brito, Bàrbara Baro, Tainá C. Raiol, Alberto Ayllon-Hermida, Izabella P. Safe, Katrien Deroost, Erick F. G. Figueiredo, Allyson G. Costa, Maria del P. Armengol, Lauro Sumoy, Anne C.G. Almeida, Bidossessi W. Hounkpe, Erich V. De Paula, Cármen Fernandez-Becerra, Wuelton M. Monteiro, Hernando A. del Portillo* and Marcus V.G. Lacerda* (*equal correspondence). **Morphological and Transcriptional Changes in Human Bone Marrow During Natural Plasmodium vivax Malaria Infections** [published online ahead of print, 2020 Jun 18]. J Infect Dis. 2020;jiaa177. doi:10.1093/infdis/jiaa177

3. Monteiro W, Brito-Sousa JD, Elizalde-Torrent A, Bôtto-Menezes C, Melo GC, Fernandez-Becerra C, Lacerda M, Del Portillo HA. **Cryptic Plasmodium chronic infections: was Maurizio Ascoli right?** Malar J. 2020 Nov 30;19(1):440. doi: 10.1186/s12936-020-03516-x. PMID: 33256745; PMCID: PMC7708240.

4. Cortes-Serra N, Mendes MT, Mazagatos C, Segui-Barber J, Ellis CC, Ballart C, Garcia-Alvarez A, Gállego M, Gascon J, Almeida IC, Pinazo MJ, Fernandez-Becerra C. **Plasma-Derived Extracellular Vesicles as Potential Biomarkers in Heart Transplant Patient with Chronic Chagas Disease.** Emerg Infect Dis. 2020 Aug;26(8):1846-1851. doi: 10.3201/eid2608.191042. PMID: 32687028; PMCID: PMC7392439.



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Research Groups
**Area 8**
Neuroscience

# Group: Vascular Pathologies of the Brain

Group Leader: Antoni Dávalos, adavalos.germanstrias@gencat.cat

## Research Overview

The research area of cerebral vascular pathology at the Germans Trias Institute was set up in 2005 and is led by Antoni Dávalos, Director of the Germans Trias i Pujol University Hospital and Clinical Director of the Department of Neuroscience . It is recognized and financed by the Agency for Management of University and Research Grants of the Goernment of Catalonia (AGAUR) as an accredited emerging group and it forms part of the themed network RETICS-INVICTUS financed by the Instituto de Salud Carlos III.

## Research lines

- Endovascular treatment of acute ictus: clinical trials REVASCAT, DAWN
- Reperfusion endovenous therapies and neuroprotection: clinical trials DIAS-3/4, WAKE-UP, TANDEM
- New treatments for secondary prevention of ictus: clinical trials SOCRATES, NAVIGATE-ESUS
- Futile Rechanneling in Ischemic Acute Stroke (FURIAS): Study of new RM imaging markers for predicting future recanalization in patients undergoing vascular therapy en the acute phase of ictus. FIS P14/01955
- Use of the RACE pre-hospital clinical scale to determine the level of specialization offered to patients with acute ictus in function of its severity and to organize new referral circuits for patients (FIS P113/02041)
- Asymptomatic cerebral atherosclerosis (AsIA Study): population study of prevalence of asymptomatic intracraneal estenosis and its relation to vascular risk, cardiovascular risk and risk of dementia.
- Study of intracranial plaques (PROYECTO CRYPTICAS): Study using new HRMR sequences of intracraneal atherosclerotic plaques in atherothrombic ictus and cryptogenic ictus (FIS P113/02544).
- Neuroplasticity, cognitive function and neuroimaging in ischemic cerebral ictus: study of cognitive prognostics, structural changes in white matter, functional RM and cognitive alternations in acute ictus.
- Neurotoxicity of iron in cerebral ischemia
- STR01-STROKECHIP: Validation of a panel of biomarkers for precocious diagnostic of ictus and differentiation from analogous conditions and from ischemic ictus and haemorrhagic ictus.
- Influence of grades of physical activity previous to ictus on functional prognostic, haemorrhagic transformation and arterial rechanneling in acute occlusion of the median cerebral artery.





# Group: Cellular and Molecular Neurobiology Research Group (CMN Group)

Group Leader: Teresa Gasull, tgasull@igtp.cat

## Research lines

The group works on 5 lines of research:

1. **Novel glutamate-related targets for neuroprotection.** NMDA-glutamate receptor signalling to death, mechanisms driving excitotoxic death and targets for neuroprotection.
2. **Ferroptosis in neuronal death and antiferroptotic neuroprotective compounds**. Understand ferroptosis in neuronal death in stroke and other brain diseases: finding new targets of intervention and new treatments.
3. **Experimental modeling of stroke in rodents and the gyrencephalic, human-like, swine brain.** Models of stroke damage in gyrencephalic brains, with a special focus on damage of the white matter and brain areas connectivity.
4. **Discovery of new biomarkers to improve stroke treatment**. Discovery of new biochemical and bioimaging biomarkers useful to address point of care stroke type identification, stroke patient stratification, patient selection for treatment allocation and/or outcome prediction.
5. **Computational biology and machine/deep learning neurobehavioural assessment for the prediction of brain damage and neurological outcome in in vivo stroke models.** Development of in silico machine/deep learning methods for the neurological analysis of behaviour in stroke models, with predictive value of brain damage and outcome.

## Group Highlights 2020

- Experimental modeling of stroke in adult rodent and gyroencephlic human-like brains: focus on damage of the white matter and brain areas connectivity
- New partnership with Professor Piotr Walczak (University of Maryland, US) the team at the Ti-Com (Poland)
- New partnership with Dr. Clara Prats for the computational machine/deep learning assessment and prediction of brain damage and neurological outcome in preclinical stroke models
- Topic Editors of the journals Cells (TG) and Int. J. Mol. Sci. (OM-S).
- Our 2019 review (Deciphering the Iron Side of Stroke: Neurodegeneration at the Crossroads Between Iron Dyshomeostasis, Excitotoxicity, and Ferroptosis. DeGregorio-Rocasolano N, Martí-Sistac O, Gasull T. Front Neurosci. 2019;13:85. doi: 10.3389/fnins.2019.00085), achieved a remarkable international impact (top 2% downloads out of more than 178,000 articles published by the editorial Frontiers, top 15% views worldwide and top 12% most cited).

## Selected publications 2020

1. **Comparative Proteomics Unveils LRRFIP1 as a New Player in the DAPK1 Interactome of Neurons Exposed to Oxygen and Glucose Deprivation**. DeGregorio-Rocasolano N, Guirao V, Ponce J, Melià-Sorolla M, Aliena-Valero A, García-Serran A, Salom JB, Dávalos A, Martí-Sistac O, Gasull T. Antioxidants (Basel). 2020 Nov 30;9(12):1202. doi: 10.3390/antiox9121202. PMID: 33265962
2. **Relevance of Porcine Stroke Models to Bridge the Gap from Pre-Clinical Findings to Clinical Implementation.** Melià-Sorolla M, Castaño C, DeGregorio-Rocasolano N, Rodríguez-Esparragoza L, Dávalos A, Martí-Sistac O, Gasull T. Int J Mol Sci. 2020 Sep 8;21(18):6568. doi: 10.3390/ijms21186568. PMID: 32911769
3. **Blood biomarkers predictive of epilepsy after an acute stroke event.** Abrairaet al. 2020 Oct;61(10):2244-2253. doi: 10.1111/epi.16648. Epub 2020 Aug 28. PMID: 32857458
4. **Correlation of blood biomarkers with early-onset seizures after an acute stroke event.** Abraira et al. J. Epilepsy Behav. 2020 Mar;104(Pt B):106549. doi: 10.1016/j.yebeh.2019.106549. Epub 2019 Oct 31. PMID: 31677998

# Group: Neuromuscular and Neuropaediatric Research

Group Leader: Gisela Nogales Gadea, gnogales@igtp.cat

## Research Overview

The main focus of the multidisciplinary team is finding treatments for neuromuscular and neuropediatric diseases that currently have no cure. The laboratory is focussing on the following specific topics at the moment:

- DIMINUTES, Childhood and adult myotonic dystrophy: evaluation of new treatments and pathogenicity through genetic, epigenetic and molecular imaging analysis (G. Nogales)
- Application of more sensitive genetic diagnostic techniques, study of phenotype modulation and prognostics in patients with myotonic dystrophies (G. Nogales)
- Muscle single-cell analysis in patients with myotonic dystrophy type I (G. Nogales)
- Antisense oligonucleotides therapy in patient-derived cell models of Steinert disease (G. Nogales)
- Establishment of predictive markers of functional recovery prior to acute ischemic stroke (A. Martínez-Piñeiro)
- Improved diagnosis and testing of treatments for myotonic dystrophy type I (A.Ramos)

## Group Highlights 2020

In 2020 Alicia Martínez Piñeiro founded a spin-off company together with Dr Antoni Dávalos, Dr Jaume Coll-Cantí. Time is Brain will develop a medical device to improve the diagnostics and prognostics of acute ischaemic stroke The company also received the Seal of Excellence from the European Commission and is preparing for its seed-funding round.

## Selected publications 2020


1. **A DM1 family with interruptions associated with atypical symptoms and late onset but not with a milder phenotype.** Ballester-Lopez A, Koehorst E, Almendrote M, Martínez-Piñeiro A, Lucente G, Linares-Pardo I, Núñez-Manchón J, Guanyabens N, Cano A, Lucia A, Overend G, Cumming SA, Monckton DG, Casadevall T, Isern I, Sánchez-Ojanguren J, Planas A, Rodríguez-Palmero A, Monlleó-Neila L, Pintos-Morell G, Ramos-Fransi A, Coll-Cantí J, Nogales-Gadea G. Hum Mutat. 2020 Feb;41(2):420-431. doi: 10.1002/humu.23932. Epub 2019 Nov 4. PMID: 31608518
2. **Sex Differences and the Influence of an Active Lifestyle on Adiposity in Patients with McArdle Disease.** Rodríguez-Gómez I, Santalla A, Diez-Bermejo J, Munguía-Izquierdo D, Alegre LM, Nogales-Gadea G, Arenas J, Martín MA, Lucia A, Ara I. Int J Environ Res Public Health. 2020 Jun 17;17(12):4334. doi: 10.3390/ijerph17124334.PMID: 32560448
3. **Preliminary Findings on CTG Expansion Determination in Different Tissues from Patients with Myotonic Dystrophy Type 1**. Ballester-Lopez A, Koehorst E, Linares-Pardo I, Núñez-Manchón J, Almendrote M, Lucente G, Arbex A, Puente C, Lucia A, Monckton DG, Cumming SA, Pintos-Morell G, Coll-Cantí J, Ramos-Fransi A, Martínez-Piñeiro A, Nogales-Gadea G. Genes (Basel). 2020 Nov 7;11(11):1321. doi: 10.3390/genes11111321.PMID: 33171734
4. **Three-dimensional imaging in myotonic dystrophy type 1: Linking molecular alterations with disease phenotype**. Ballester-Lopez A, Núñez-Manchón J, Koehorst E, Linares-Pardo I, Almendrote M, Lucente G, Guanyabens N, Lopez-Osias M, Suárez-Mesa A, Hanick SA, Chojnacki J, Lucia A, Pintos-Morell G, Coll-Cantí J, Martínez-Piñeiro A, Ramos-Fransi A, Nogales-Gadea.
5. **The Biomarker Potential of miRNAs in Myotonic Dystrophy Type I.** Koehorst E, Ballester-Lopez A, Arechavala-Gomeza V, Martínez-Piñeiro A, Nogales-Gadea G. J Clin Med. 2020 Dec 4;9(12):3939. doi: 10.3390/jcm9123939.PMID: 33291833 (Review)






# Group: Neurogenetics

Group Leaders: Antoni Matilla Dueñas, amatilla@igtp.cat

## Research Overview

The IGTP Neurogenetics Research Group investigates the genetic and molecular mechanisms underlying neurodegenerative processes, in particular inherited ataxias. The ultimate goal of the research is to identify the genes, their products and molecular pathways involved in order to effectively provide genetic diagnosis and eventually develop selective therapeutic approaches to patients. The group uses multidisciplinary strategies to identify genes, proteins and other gene products involved in the function and dysfunction of the nervous system by using next-generation RNA and DNA sequencing, functional assays, biochemical, proteomics, and molecular neuro signalling studies. Furthermore, the team develops large-scale genomics technologies and bioinformatics tools to identify genetic causes underlying neurological diseases in many undiagnosed genetic diseases.

By combining some of these approaches, the group has recently identified 2 novel ataxia subtypes and characterised their gene products and the molecular pathways involved.

An important objective of the group is to identify and implement treatments for various neurodegenerative diseases such as ataxias and Sanfilippo Syndrome. To this aim, we have developed an AAV-gene therapy for Friedreich's ataxia that has proven safe and long-term efficient in 2 different mouse models of the disease.

## Group Highlights 2020

1. Completion of the pre-clinical trial to evaluate safety and efficiency of the AAV-gene therapy vector for the treatment of Friedreich's ataxia.
2. Identification of a new spinocerebellar ataxia subtype.

## Selected publications 2020


1. Matilla-Dueñas A, Infante J, Serrano-Munuera C, Ivánovic-Barbeito Y, Alvarez R, Sánchez I. **Novel Therapeutic Challenges in Cerebellar Diseases.** In: Manto M., Gruol D., Schmahmann J., Koibuchi N., Sillitoe R. (eds) Handbook of the Cerebellum and Cerebellar Disorders. Springer, Cham. https://doi.org/10.1007/978-3-319-97911-3_106-2 (2020). Book chapter
2. Delgado-Alvarado M, Matilla-Dueñas A, Altadill-Bermejo A, Setién S, Misiego-Peral M, Sánchez-de la Torre JR, Corral-Juan M, Riancho J. **A novel SGCE variant is associated with myoclonus-dystonia with phenotypic variability.** Neurol Sci. 41(12):3779-3781 [PMID: 32955639] (2020). Article.
3. Matalonga L, Laurie S, Papakonstantinou A, et al. **Improved Diagnosis of Rare Disease Patients through Systematic Detection of Runs of Homozygosity.** J Mol Diagn 22(9):1205-1215 [PMID: 32619640] (2020). Article.
4. Infante J, Serrano-Cárdenas KM, Corral-Juan M, Farré X, Sánchez I, Marco de Lucas E, Berciano J, MD1, Matilla-Dueñas A. **POLR3A-related spastic ataxia: new mutations and a look into the phenotype.** J Neurol, 267(2):324-330 [PMID: 31637490] (2020). Article

# Group: Genomics and Transcriptomics of Synucleinopathies (GTS)

Group Leader: Katrin Beyer, kbeyer@igtp.cat

## Research Overview

Synucleinopathies include Parkinson's disease (PD), the most frequent movement disorder, and dementia with Lewy bodies (DLB) the second most frequent cause of degenerative dementia after Alzheimer's disease (AD). In PD and DLB, intra-neuronal inclusion bodies, so-called Lewy bodies, develop after abnormal alpha-synuclein oligomerization and aggregation in vulnerable brain areas. DLB is also characterized by an important neuropathological overlap with AD resulting in overlapping clinical presentation and making a reliable diagnosis very difficult. So far, there are no peripheral DLB diagnostic markers and up to 80% of DLB patients are still misdiagnosed, mainly as having AD. These patients are treated as if they had AD and about 50% develop severe adverse reactions to the treatment administered, which irreversibly worsens their condition.

The molecular characterization of DLB is of paramount importance as it constitutes the basis for the successful identification of disease biomarkers. The GTS group focuses on the genetic characterization of DLB, which was only described as a separate disease 20 years ago. Following the workflow "from the brain to the periphery", the group aims to identify which of the disease-specific changes found in the brain may be reflected in peripheral biofluids to establish diagnostic DLB biomarkers. Some of the results have been patented as biomarkers for DLB, two for the identification of specific DLB subgroups, one to monitor the treatment with possible anti-alpha-synuclein aggregation therapies in DLB, and one for patient stratification. Currently, the latter two are being further developed to provide useful tools for application in clinical practice. Our latest findings indicate that specific blood cells may be directly involved in DLB pathogenesis. Consequently, the group started on the characterization of these cells and this new research topic has become one of their main objectives.

## Research lines

- Genetic characterization of DLB. DLB-specific genetic variations in brain; functional analyses of promoter, intronic and 3'UTR variants. Expression and alternative splicing analysis of DLB genes in brain; confirmation in peripheral sources (blood, saliva). Analysis of miRNA expression changes in brain and blood.
- Biomarker search. Identification of biomarkers for the diagnosis/differential diagnosis of DLB from peripheral sources (whole blood, plasma, platelets, saliva). Study of platelet dysfunction in DLB: identification and characterization of disease specific platelet activation pathways; study of mitochondria function, apoptosis induction pathways and platelet-immunoreceptor profile.

## Group Highlights 2020

In 2020 a new research line was created: Characterization of platelet function and dysfunction in Lewy body disorders

## Selected publications 2020

1. Urbizu A, Beyer K. **Epigenetics in Lewy Body Diseases: Impact on Gene Expression, Utility as a Biomarker, and Possibilities for Therapy.** Int J Mol Sci. 2020, 21:4718. doi: 10.3390/ijms21134718.





# Group: Psychoneuroendocrinology and Stress in Psychosis (PSICPNEC)

Group Leader: Javier Labad, jlabad@csdm.cat

## Research Overview

The Research Group in Psychoneuroendocrinology and Stress in Psychosis (PSICPNEC) is composed of researchers from the Mental Health Departments at the Consorci Sanitari del Maresme (Hospital de Mataró) and Parc Taulí Hospital, affiliated to the IGTP.
The main scientific interest of the group is the study of the relationship between hormones and behaviour (Psychoneuroendocrinology) in patients with a psychotic disorder or at risk of developing a psychotic disorder (at-risk mental states). Research lines include the study of the neurobiological mechanisms of stress (hypothalamic-pituitary-adrenal axis) in the pathogenesis and outcome of psychotic disorders. One of the aims of the group is to study the role of hormones in the risk of transition to psychosis in vulnerable populations and the association with a more severe phenotype (eg cognitive impairment) in established psychoses. Other research lines are focus on the study of the role of gender and hormones in the therapeutic response to pharmacological, psychotherapeutic, and cognitive rehabilitation interventions in psychotic disorders. Recent research includes the study of stress-related biomarkers in animal models in collaboration with researchers of the Neuroscience Translational Unit UAB-Parc Taulí.

## Research lines

1. Stress-related biomarkers in early psychosis and in people at risk of developing a psychotic disorder.
2. Impact of hormones on the clinical expression of psychotic disorders.
3. Psychopathological and biological consequences of abuse in adolescents and young adults

## Group Highlights 2020

Coordination of a multi-centre European project dealing with the study of stress-related biomarkers in people with psychosis and animal models (ERA-NET NEURON project of 3 centres).

## Selected publications 2020

1. Labad J, Montalvo I, González-Rodríguez A, García-Rizo C, Crespo-Facorro B, Monreal JA, Palao D. **Pharmacological treatment strategies for lowering prolactin in people with a psychotic disorder and hyperprolactinaemia: A systematic review and meta-analysis.** Schizophr Res. 2020 Aug;222:88-96. doi: 10.1016/j.schres.2020.04.031.
2. Armario A, Labad J, Nadal R. **Focusing attention on biological markers of acute stressor intensity: Empirical evidence and limitations.** Neurosci Biobehav Rev. 2020 Apr;111:95-103. doi: 10.1016/j.neubiorev.2020.01.013.
3. Giné Servén E, Boix Quintana E, Martínez Ramírez M, Guanyabens Buscà N, Muriana Batiste D, Guasp M, Torres Rivas C, Davi Loscos E, Casado Ruiz V. **Cycloid psychosis as a psychiatric expression of anti-NMDAR encephalitis. A systematic review of case reports accomplished with the authors' cooperation.** Brain Behav. 2021 Feb;11(2):e01980. doi: 10.1002/brb3.1980.
4. Bioque M, González-Rodríguez A, Garcia-Rizo C, Cobo J, Monreal JA, Usall J, Soria V; PNECAT Group, Labad J. **Targeting the microbiome-gut-brain axis for improving cognition in schizophrenia and major mood disorders: A narrative review.** Prog Neuropsychopharmacol Biol Psychiatry. 2021 Mar 8;105:110130. doi: 10.1016/j.pnpbp.2020.110130.
5. Labad J, Ortega L, Cabezas Á, Montalvo I, Arranz S, Algora MJ, Solé M, Martorell L, Vilella E, Sánchez-Gistau V. **Hypothalamic-pituitary-adrenal axis function and exposure to stress factors and cannabis use in recent-onset psychosis**. World J Biol Psychiatry. 2020 Sep;21(7):564-571. doi:10.1080/15622975.2019.1628301

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Research Groups

# Area 9
Science of behaviour and substance abuse

## Group: Medical complications of substance use disorder (GIAS)

Group Leader: Robert Muga rmuga.germanstrias@gencat.cat

### Research Overview

The group researches the medical consequences of Substance Use Disorder, although group members have increased their clinical duties because of the COVID-19 pandemic. It is a consolidate group recognized by the AGAUR of the Government of Catalonia.

The main areas of research include cardiometabolic complications, liver damage and systemic inflammation of alcohol use disorder and the impact of drug-related diseases on patient morbidity and mortality. The team focuses especially on the complications of opiates, cocaine, THC and poly-drug use.

The group collaborates with researchers from the European Union, United States and Switzerland and is currently a member of the Spanish Network on Addictive Disorders (Red de Trastornos Adictivos/RTA-RETICS, ISCIII). Members mentor PhD candidates and serve as Scientific advisors for GALEA, a start-up company devoted to the development of new drugs for the treatment of alcohol-related liver disease. Dr Muga also serves as expert consultant for research at the Public Health Agency of Catalonia, Program on Prevention, Control and Care for HIV, STIs and Viral Hepatitis -PCAVI-VH.

### Group Highlights 2020

The group has secured new research funds three competitive research projects from the Instituto de Salud Carlos III [ISCIII] and Plan Nacional Sobre Drogas/PNSD-Ministry of Health) and from two career development awards for Young researchers: the Juan Rodés Program (Paola Zuluaga) and the Sara Borrell Program (Núria Garcia-Marchena), both funded by the ISCIII.

In 2020, the research group published 15 papers in peer-reviewed scientific journals and 2 book chapters. The group has also been working on manuscripts that will be published in 2021.

### Selected publications 2020


1. P. Zuluaga, A. Sanvisens, A. Teniente-Serra, O. El Ars, D. Fuster, B. Quirant-Sánchez, E. Martínez-Cáceres, R. Muga. **Loss of naive T lymphocytes is associated with advanced liver fibrosis in alcohol use disorder.** Drug Alcohol Depend. 2020; 213:108046. doi: 10.1016/j.drugalcdep.2020.108046.
2. Hernández-Rubio A, Sanvisens A, Bolao F, Pérez-Mañá C, García-Marchena N, Fernández-Prendes C, Muñoz A, Muga R. **Association of hyperuricemia and gamma glutamyl transferase as a marker of metabolic risk in alcohol use disorder.** Sci Rep. 2020;10(1):20060. doi: 10.1038/s41598-020-77013-1.
3. D. Fuster, X. García-Calvo, F. Bolao, P. Zuluaga, G. Rocamora, A. Hernández, A. Sanvisens, J. Tor, R. Muga. **Cannabis use is associated with monocyte activation (sCD163) in patients admitted for alcohol use disorder treatment.** Drug and Alcohol Dependence. 2020; 216:108231.
4. X. García-Calvo, F. Bolao, A. Sanvisens, P. Zuluaga, J. Tor, R. Muga, D. Fuster. **Significance of markers of monocyte activation (CD163 and sCD14), and inflammation (IL-6) in patients admitted for alcohol use disorder treatment**. Alcohol Clin Exp Res. 2020; 44:152-158.
5. Serrano-Villar et al. **Effects of first-line antiretroviral therapy on the CD4/CD8 ratio and CD8 cell counts in CoRIS: a prospective multicentre cohort study.** Lancet HIV. 2020; 7: e565-e573. doi: 10.1016/S2352-3018(20)30202-2.

# Group: Clinical pharmacology of substance use disorders

Group Leader: Magí Farré, mfarre.germanstrias@gencat.cat

## Research Overview

The objectives of the group are to study the acute and chronic pharmacological and toxic effects caused by substance abuse in humans. Most of the members of the group are physicians at the Germans Trias i Pujol Hospital responsible for daily patient care.
The three main active research lines are:

- Evaluation of the acute effects of new psychoactive substances like synthetic cathinones (such as mephedrone, methylone and alpha-PVP, MDPV), and synthetic cannabinoids.
- Evaluation of the acute and chronic effects of binge alcohol consumption in young people and its combination with energy drinks.
- Evaluation of the effects of cannabis and its components, including its possible therapeutic use (medicinal cannabis)

  In all three lines of research this evaluation includes pharmacodynamics, pharmacokinetics and metabolic aspects and biomarkers associated with consumption.

## Group Highlights 2020

The group has been awarded competitive funding (projects starting 2021) from the ISCIII; one for the clinical trials platform and two research projects.

## Selected publications 2020

1. Papaseit E, Pérez-Mañá C, de Sousa Fernandes Perna EB, Olesti E, Mateus J, Kuypers KPC, Theunissen EL, Fonseca F, Torrens M, Ramaekers JG, de la Torre R and Farré M. **Mephedrone and Alcohol Interactions in Humans.** Front. Pharmacol. 2020;10:1588. doi: 10.3389/fphar.2019.01588.
2. Papaseit E, Olesti E, Pérez-Mañá C, Torrens M, Grifell M, Ventura M, Pozo OJ, de Sousa Fernandes Perna EB, Ramaekers JG, de la Torre R, Farré M. Acute Effects of 2C-E in Humans: **An Observational Study. Front. Pharmacol.** 2020; 11:233. doi: 10.3389/fphar.2020.00233
3. La Maida N, Pellegrini M, Papaseit E, Pérez-Mañá C, Poyatos L, Ventura M, Galindo L, Busardò FP, Pichini S, Farré M, Marchei E. **Determination of the Synthetic Cannabinoids JWH-122, JWH-210, UR-144 in Oral Fluid of Consumers by GC-MS and Quantification of Parent Compounds and Metabolites by UHPLC-MS/MS.** Int J Mol Sci. 2020 Dec 10;21(24): E9414. doi: 10.3390/ijms21249414.
4. Pichini S, Mannocchi G, Gottardi M, Pérez-Acevedo AP, Poyatos L, Papaseit E, Pérez-Mañá C, Farré M, Pacifici R, Busardò FP. **Fast and sensitive UHPLC-MS/MS analysis of cannabinoids and their acid precursors in pharmaceutical preparations of medical cannabis and their metabolites in conventional and non-conventional biological matrices of treated individual.** Talanta. 2020 Mar 1; 209:120537. doi: 10.1016/j.talanta.2019.120537. Epub 2019 Nov 15. PubMed
5. Papaseit E, Pérez-Mañá C, Torrens M, Farré A, Poyatos L, Hladun O, Sanvisens A, Muga R, Farré M. **MDMA interactions with pharmaceuticals and drugs of abuse.** Expert Opin Drug Metab Toxicol. 2020 Apr 12:1-13. doi:10.1080/17425255.2020.1749262



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