

Annual Scientific Report 2022 ALTER A COMPANY AND A COMPANY







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26



Introduction



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

2022 marked a period of significant activity and transformation for IGTP. Throughout the year, our institution demonstrated unwavering commitment and performed leading-edge research, with a deep-seated dedication to advancing both healthcare and our scientific understanding of diseases. The combined efforts of our research community, our devoted staff, and our invaluable partners not only cemented IGTP's standing as a prominent biomedical research institute but also propelled our mission towards shaping a healthier and more equitable global landscape. This report, which I trust you will find insightful, highlights the accomplishments of our research groups and their advancements in a variety of biomedical research fields such as oncology, infectious diseases, cardiovascular diseases, neuroscience and genetics. The noteworthy achievements of our researchers have garnered international recognition and brought about tangible benefits for patients and communities on a global scale. Collaborations with esteemed institutions and industry partners have further amplified the impact of our findings, bridging the gap between scientific insights and novel medical solutions.

Furthermore, IGTP remains dedicated to fostering the development of the next generation of scientific leaders. Our robust training and mentorship initiatives have provided emerging researchers with the resources and support needed to develop their careers. Consequently, we continue to witness the emergence of talented individuals poised to drive biomedical innovation in the years ahead.

While we celebrate our successes, we are acutely aware of the forthcoming challenges. As we navigate the complexities of the global healthcare landscape, we are resolute in our commitment to address health disparities, champion diversity and inclusion, and strengthen our institutional resilience.

In conclusion, I would like to express my heartfelt gratitude to everyone who played a part in IGTP's achievements in 2022. Your steadfast dedication, passion, and collaborative approach have propelled our organization to new heights. Looking ahead, I am confident that together we will continue to improve how we do our research to surpass boundaries and accomplish noteworthy milestones in the pursuit of scientific excellence and societal impact.

The IGTP in numbers

1

The IGTP in numbers

Research areas and groups

<u>41</u>

GROUPS WITH PI contracted directly by the IGTP, Germans Trias i Pujol University Hospital or affiliated groups from the Institut Català d'Oncologia (ICO) or ISGlobal.

8

AFFILIATED INSTITUTIONS

- IGTP, Institut Català d'Oncologia (ICO) and ISGlobal
- Consorci Sanitari del Maresme (CSdM)
- Fight Infections Foundation
- Foundation University Institute for Primary Health Care Research Jordi Gol i Gurina (IDIAPJGol)
- Fundació Institut Guttmann
- IrsiCaixa AIDS Research Institute
- Josep Carreras Leukaemia Research Institute (IJC)

Networks

18

SGR Groups accredited by the Government of Catalonia

5

Centros de Investigación Biomédica en Red (CIBER)

5

Redes Temáticas de Investigación Cooperativa en Salud (RETICS)

5

Redes de Investigación Cooperativas Orientadas a Resultados en Salud (RICORS)

2

Others (SCREN/Biobancs and Biomodels)

1

European Commission ERIC (EATRIS)

Publications in 2022

10,169.67

TOTAL IMPACT FACTOR

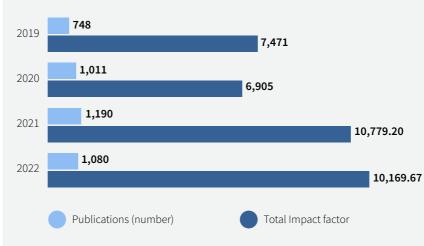
1,080

TOTAL PUBLICATIONS

9.89

AVERAGE IMPACT FACTOR

EVOLUTION (2019-2022)



235 D1 1,080 TOTAL 541 Q1

4,028

TOTAL PUBLICATIONS

36,595

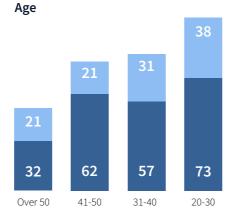
TOTAL IMPACT FACTOR

9.09

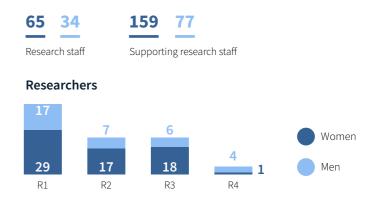
AVERAGE IMPACT FACTOR

People: IGTP contracted and affiliated staff

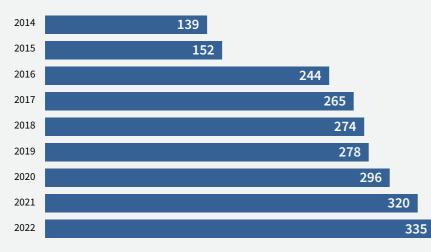




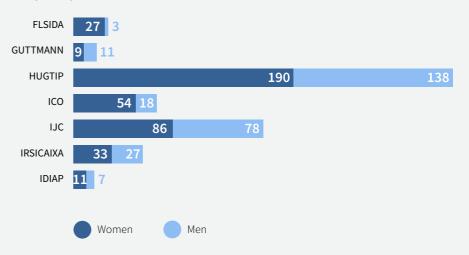
Professional categories



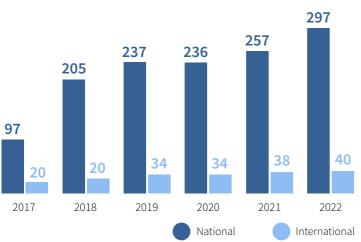
STAFF EVOLUTION



ATTACHED STAFF

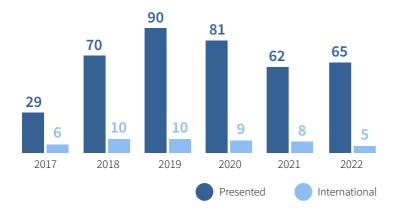


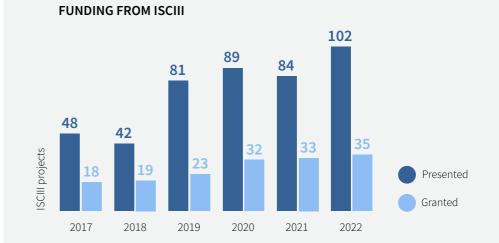
Competitive projects



TOTAL ACTIVE PROJECTS 2017-2022

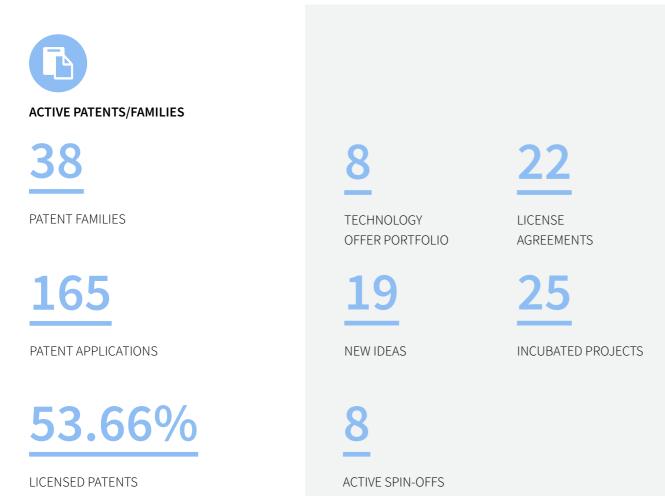








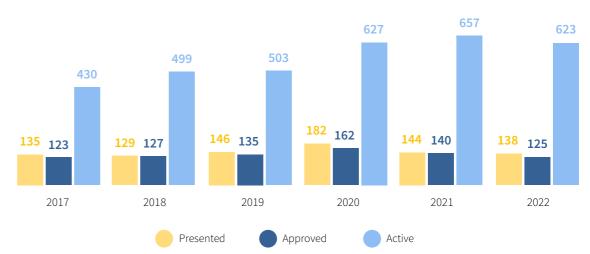
Innovation and technology transfer







Clinical trials



In 2022

138 Presented

clinical trials

125

Approved clinical trials

<u>623</u>

Active clinical trials

Strategic projects

GCAT GENOMES FOR LIFE PROJECT

GCAT USERS



Starting new collaborations

tarting n

Starting national and international competitive projects



Active collaborations 20

Scientific institutions



Cohort-design follow-up

GCAT PUBLICATIONS AND COMMUNICATIONS

16

Publications

Communications

GCAT CITATIONS

1,269

Citing articles 2022 WoS (90 average)



COMPARATIVE MEDICINE & BIOIMAGE CENTRE OF CATALONIA (CMCiB)

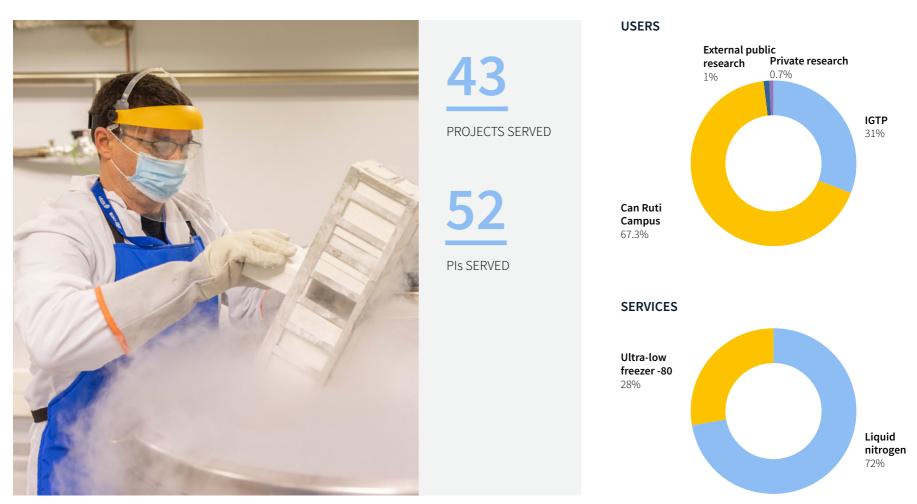


Core facilities

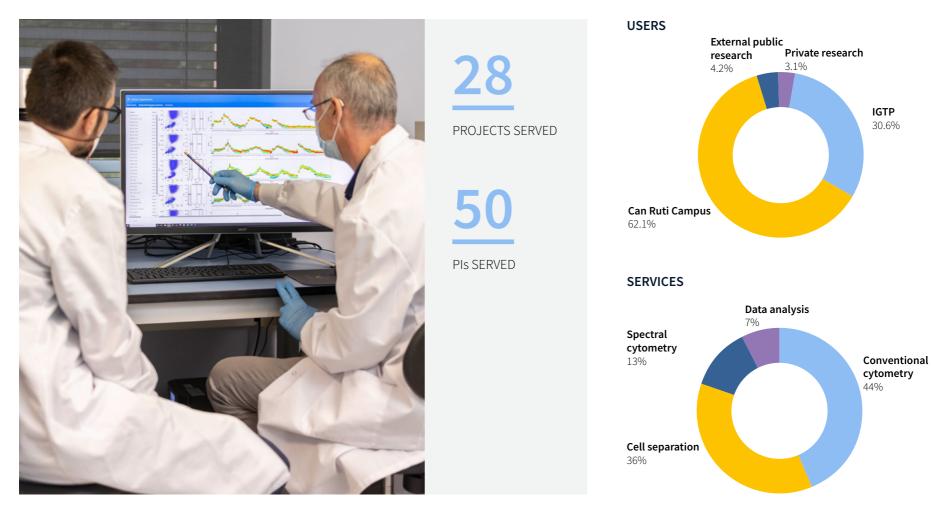
BIOBANK



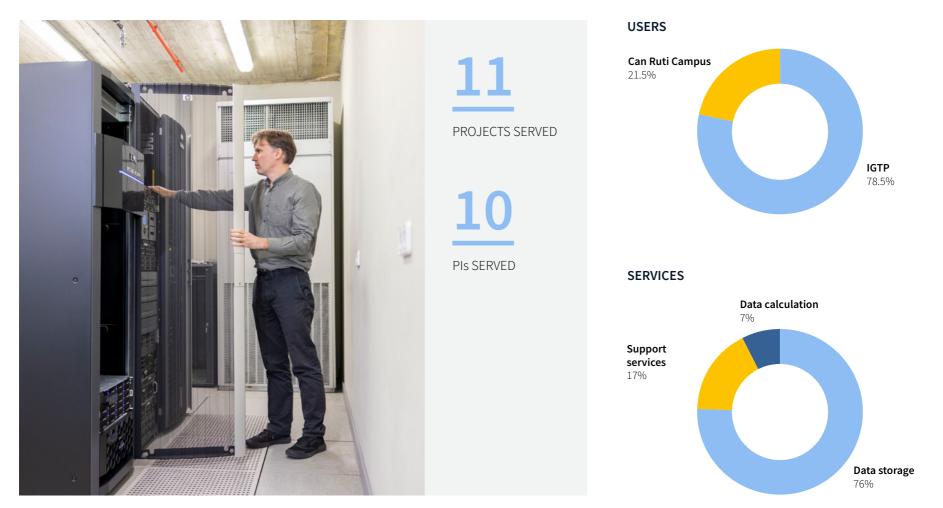
CRYOBIOLOGY



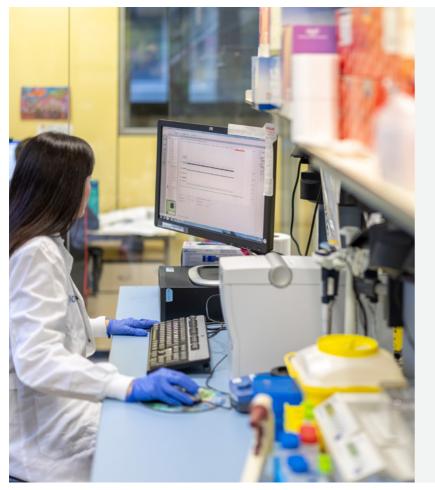
<u>CYTOMETRY</u>



HIGH PERFORMANCE COMPUTING

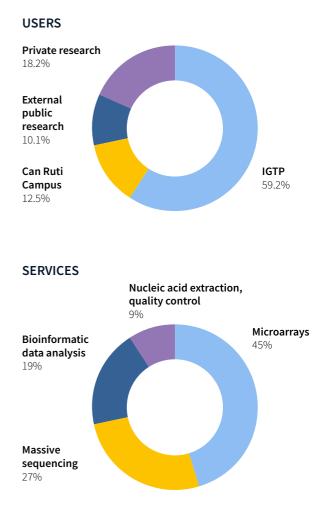


HIGH CONTENT GENOMICS AND BIOINFORMATICS



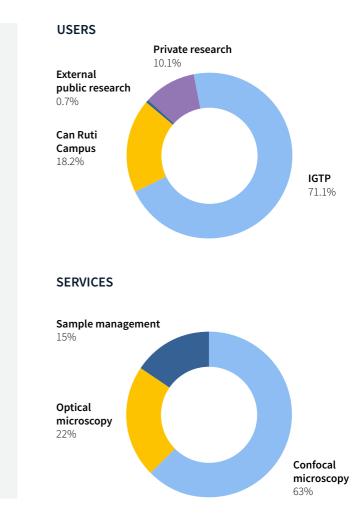






MICROSCOPY





PROJECTS SERVED

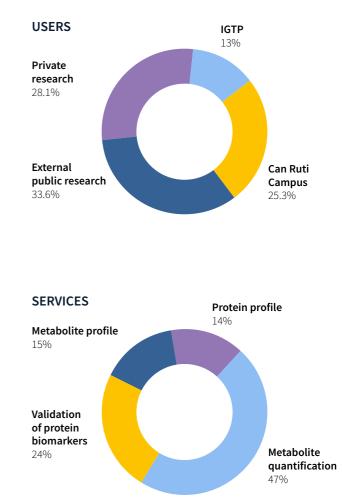
PROTEOMICS AND METABOLOMICS





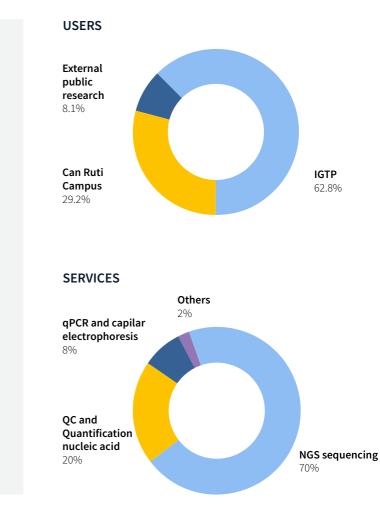
PROJECTS SERVED

11



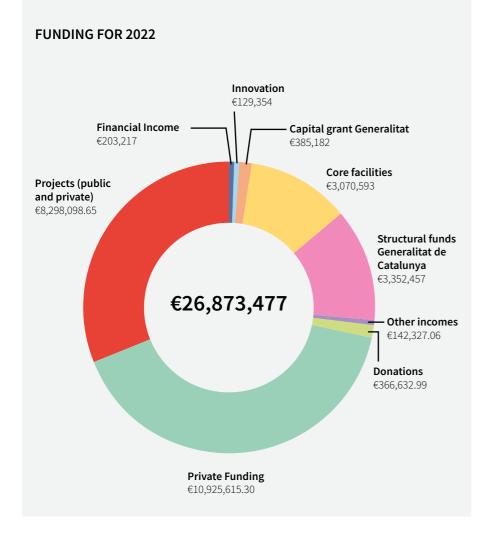
TRANSLATIONAL GENOMICS





PROJECTS SERVED

Sources of funding



Activities



Coffee talks PhD training

1

36

Kickoff to the CARE Translational Program in Cancer Research

1

EATRIS meeting

IGTP platform

seminars

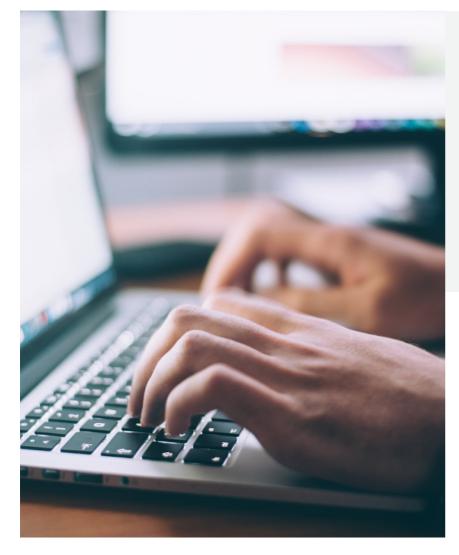
Symposium GCAT

WiS 4th Can Ruti Women in Science Symposium

Symposium and 3

seminars PhD Day

Communications



GROWING ON SOCIAL MEDIA



DAILY NEWS CLIPPING (STARTED IN MAY)

IGTP NEWSLETTERS AND ACTIVITIES THIS WEEK

10 MOST RELEVANT IGTP NEWS



JANUARY

The Catalan Minister Gemma Geis visits the Centre for Comparative Medicine and Bioimage



SEPTEMBER

Largest genetic study on stroke to date improves risk prediction



FEBRUARY

The GCAT|Panel is the first complete genetic map of the Iberian population that helps identifying possible genetic causes of common diseases.

MARCH

NIMBLE Diagnostics is founded to monitor stents using microwave technology





JULY

The IGTP coordinating two out of nine COST Actions coming to Spain and participating in a third





AUGUST

Study identifies 11 new genetic regions linked with the susceptibility and severity of COVID-19



NOVEMBER

Breaz Medical, a new spin-off of IGTP for the timely diagnosis of COPD

NOVEMBER

A project that develops a new immunotherapy based on a monoclonal antibody to treat cancer is one of the three initiatives chosen by CaixaResearch Consolidate

NOVEMBER

A study of more than 750 healthcare professionals confirms that antibodies persist 17 months after having suffered from CO-VID-19

DECEMBER

About thirty healthcare and research professionals from institutions belonging to the Can Ruti Campus, among the world's most renowned scientists

Fundraising

AMICS DE CAN RUTI

434

Amics i Amigues de Can Ruti

€305,563.09

In donations received in 2022

FOLLOW US ON INSTAGRAM



2022 HIGHLIGHTED ACTIONS







Sant Jordi Fair in Badalona

Concert for the victims of the COVID-19 pandemic

3rd charity golf tournament for research in paediatric obesity

Race and charity gala for rare diseases

Padel charity tournaments for persistent COVID and pediatric liver cancer

4th Face to Face fundraising campaign

Donations for grants

Visits to IGTP laboratories for Amics de Can Ruti members

Science talks in schools, libraries and companies

Scientific 1

24

Scientific activity in 2022

Projects

Total submitted projects 2022







22



65

25







21 (SGR



Projects Highlights 2022

THE IGTP COORDINATING TWO OUT OF NINE COST ACTIONS COMING TO SPAIN AND PARTICIPATING IN A THIRD



The <u>COST Programme</u> (European Cooperation in Science and Technology) has approved 70 new actions and Spain is coordinating nine of them, making it second in the ranking of countries leading COST Actions after Italy (coordinating 10 COSTs) and France (coordinating eight) is in third place. Three of the Spanish projects are from the IGTP. COST Actions run for four years.

The three IGTP COST Actions in the European Research Network:

IMMUNO-Model

Modeling immunotherapy response and toxicity in cancer Leader: Eva Martínez-Balibrea of the IGTP-ICO (Main Proposer) with the su-

Scientific activity in 2022 / Projects

pport of Laura Belver of the IJC-ICO (secondary proposer). Both are members of the ProCURE programme

ADVANCE-TB

TowArDs an improVement in diAgNostiCs and trEatment strategies for TB control

Leader: Alicia Lacoma (Main Proposer) of the Innovation in Respiratory Infections and Tuberculosis Diagnosis group

IMPROVE

3Rs concepts to improve the quality of biomedical science Project granted to the Bioimage Comparative Medicine and Bioimage Centre of Catalonia (IGTP-CMCiB)

END-VOC KICKS OFF WITH THE AIM OF SUPPORTING THE GLOBAL RESPON-SE TO COVID-19 AND FUTURE PANDEMICS

The European Commission-funded <u>END-VOC project</u> kicked off with the aim of elucidating the circulation and impact of current and emerging SARS-CoV-2 variants of concern (VOC) through the study of well-established cohorts across the world. The kick-off meeting organised by University College London (UCL), the coordinator of the project, was held virtually from May 16 to May 18 with the participation of all the partners including IGTP, who is leading the GCAT project and collaborating in several of the project's work packages.

RESEARCH IMPULSE INTO HEPATOBLASTOMA, THE MAIN CHILDHOOD LIVER CANCER

A collaborative CIBER project will boost hepatoblastoma (HB) research to identify new therapeutic targets that will allow strategies to be developed to improve the prognosis of those children who currently do not survive the disease. The project coordinated by Dr Carolina Armengol, principal CIBEREHD researcher at the IGTP is a collaboration between 5 CIBER groups belonging to the Hepatic and Digestive Diseases area (CIBEREHD) and the Cancer area (CIBERONC).





A PROJECT THAT DEVELOPS A NEW IMMUNOTHERAPY BASED ON A MONO-CLONAL ANTIBODY TO TREAT CANCER IS ONE OF THE THREE INITIATIVES CHOSEN BY CAIXARESEARCH CONSOLIDATE

A project that develops a new immunotherapy based on a monoclonal antibody for cancer treatment, led by the Innate Immunity group at the IGTP, is one of the three selected projects in the CaixaResearch Consolidate grants of "la Caixa" Foundation to cutting-edge biomedical innovation projects.

The project: A monoclonal antibody to treat càncer
Principal investigator: Maria Rosa Sarrias, Germans Trias i Pujol Research
Institute
Funding: €300,000



TWO IGTP PROJECTS, FINANCED WITH 1.6 MILLION EUROS BY THE EURO-PEAN COMMISSION

At the beginning of December, the results of the evaluations of the projects presented within the <u>Horizon Europe Framework Programme (HORIZON</u>) of the European Commission were made public. The Germans Trias i Pujol Research Institute (IGTP) has obtained funding for two projects in the preclinical development of immuno-therapies, with a total amount of 1,670,346 euros.

The projects that have passed the two phases and have been selected are:

IMMUTOL

Principal investigator: Eva Martínez Cáceres (Immunopathology) Funding: €1,061,971

• YTHEMIC

Principal investigator: Pere Joan Cardona (Experimental Tuberculosis Unit) Funding: € 608,375



Events



RECORD ATTENDANCE FOR THE 4TH CAN RUTI WOMEN IN SCIENCE SYMPOSIUM

Their fourth symposium was held by the Can Ruti Women in Science Working Group on 10 February to celebrate the International Day of Women and Girls in Science (11 February) and once again the focus was put on data that illustrates inequalities. This edition, on Gender Dimension: advances and resistance, was held at the IGTP and attended by 147 people from institutions on and off the campus.



CELEBRATING THE GCAT COMMUNITY SYMPOSIUM TO HIGHLIGHT THE VALUE OF PROSPECTIVE COHORTS FOR PRECISION MEDICINE IN SPAIN

On 20 June, the IGTP celebrated the GCAT|Genomes for Life Community Sympo[1]sium at the Badalona International Business Center (BCIN). GCAT is a strategic project of the IGTP and the meeting, this year by invitation-only format, included national experts in the fields of genomics and precision medicine to discuss the status of prospective cohorts in Spain in general and to showcase the current research being generated by the GCAT cohort in particular.



BADALONA WAS TRANSFORMED INTO AN ART AND SCIENCE LABORA-TORY TO EXPLORE THE FUTURE OF SOCIETY

On 28 June, the Épica Foundation of La Fura dels Baus initiated the project 'Survival vs Resilience', which turned Badalona into a laboratory of art and science. The project aimed to anticipate the future of society. The collaboration between Badalona City Council, the Fundación Épica La Fura dels Baus, the IGTP, and the Barcelona Institute of Science and Technology was presented in the context of this new project. The activity took place from 11 to 24 July and focused on addressing scientific challenges proposed by research groups through the medium of performing arts. A stimulating project that fused art, science, and technology, exploring the role of graphene in the future challenges of society.



EATRIS SPAIN WORKSHOP, A MEETING POINT FOR ADVANCES IN TRANSLATIONAL RESEARCH

The workshop "Advances in Translational Research through EATRIS", organized by the IGTP took place on 25 October and provided a space for researchers to discuss the role of EATRIS as a European infrastructure of translational research.

The workshop demonstrated the capacities of EATRIS Europe, the Spanish node of EATRIS (EATRIS-ES) and the different platforms it includes. The meeting included the scientific directors of EATRIS-ES and EATRIS-EU and some of the members of the scientific advisory board and chairs of platforms.



VI INTERHOSPITAL CONFERENCE ON GENETICS IN CATALONIA

The VI Interhospital Conference on Genetics in Catalonia was held on 7 November, organized by the Germans Trias i Pujol Hospital (HUGTiP) and Research Institute (IGTP). This annual event has been a meeting point for geneticists from a variety of Catalonia's hospitals and research centres since 2017. The main problems, advances and challenges of genetics future are shared and discussed. Other events organized by the IGTP in 2022 included the Core Facility seminars, a new initiative to provide training in methodologies available in the IGTP Core Facilities, and the continuation online of the Coffee Talks training series. These seminars were aimed at hosting and delivering seminars in English for Early Career Researchers on the Campus. The IGTP also provided support for the Can Ruti PhD Students Committee, which organized three seminars and their annual symposium.

Strategic projects

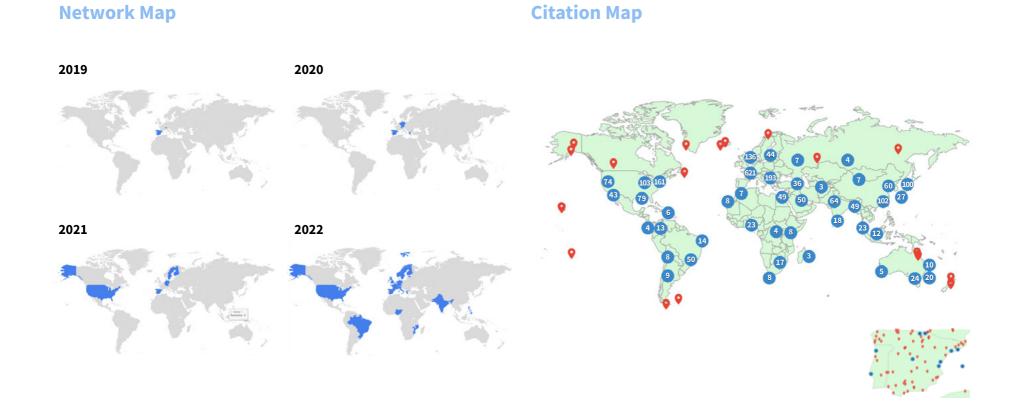
GCAT: THE POWER OF DATA TO BENEFIT PATIENTS, CLINICIANS, AND RESEARCHERS

GCAT|Genomes for Life, is a population-based multi-purpose cohort to identify genomic, epigenomic and environmental factors in the development of multi-factorial chronic diseases.

With the setting up of GCAT in 2013, IGTP opted for a stake in genomics medicine. After completing the recruitment phase, the cohort profile was published in the <u>British Medical Journal Open</u> in 2018 and GCAT published the first results of a range of projects. Two years after, the cohort showed its adaptability by quickly joining international consortia working on COVID-19, contributing to major publications on the genomic etiology of the pandemic and its social consequences.

Currently, the research team of the cohort is collaborating on projects spanning diverse health areas such as cardiology, inflammatory diseases, respiratory diseases, diabetes, neuromuscular diseases or response to infectious disease (including Covid-19), joining a diverse interconnected network of Spanish and European consortia on Diabetes, Stroke, LongCovid, Urban exposome impact and Work exposures.





Comprehensive Scientific Network

From 2022, GCAT has extended its scientific network, being present in several domains and many organisations in Europe to generate and analyse data to inform on a wide range of factors impacting health in an interdisciplinary manner, from sociodemographic, educational, clinical, lifestyle, diet, environmental exposure or genomic profiling.

4 Genetic Heredity	3 Public Environmental Occupational Health	1 Cardiac Cardiovascular Systems	1 Environmental Sciences	1 Hospitality Leisure Sport Tourism
4 Multidisciplinary Sciences	2 Biochemistry Molecular Biology	1 Medicine General Internal 1 Medicine Legal		1 Psychiatry

Being aware of the potential of data, and the power of genomic information. In 2022, GCAT gained a project to generate a detailed map of the genetic risk based on polygenic scores, allowing at first sight a risk stratification of the GCAT population for all available diseases or conditions. In the coming year, after complete genotyping, several tools for exploring disease association and risk in the cohort will be developed based on genetically informed data.

GCAT Projects and Highlights 2022

TECHNICAL HIGHLIGHTS

Valls-Margarit J et al. GCAT|Panel, a comprehensive structural variant haplotype map of the Iberian population from high-coverage whole-genome sequencing. *Nucleic Acids Res.* 2022 Mar 21;50(5):2464-2479. DOI: <u>10.1093/nar/gkac076.</u>

The combined analysis of haplotype panels with phenotype clinical cohorts is a common approach to explore the genetic architecture of human diseases. By integrating multiple variant identification methods and logistic regression models, GCAT presents a catalogue of 35,431,441 variants, including 89,178 SVs, 30,325,064 SNVs and 5,017,199 indels, across 785 Illumina high coverage (30x) whole-genomes from the Iberian GCAT cohort. This study represents the first deep characterisation of genetic variation within the Iberian population and the first operational haplotype panel to systematically include the SVs into genome-wide genetic studies.

COVID-19 RESEARCH HIGHLIGHTS

- Degenhardt F et al. Detailed stratified GWAS analysis for severe COVID-19 in four European populations. *Hum Mol Genet.* 2022 Nov 28;31(23):3945-3966. DOI: 10.1093/hmg/ddac158.
- COVID-19 Host Genetics Initiative. A first update on mapping the human genetic architecture of COVID-19. *Nature*. 2022 Aug;608(7921):E1-E10. DOI: <u>10.1038/</u> <u>s41586-022-04826-7.</u>
- Kousathanas A et al. Whole-genome sequencing reveals host factors underlying critical COVID-19. Nature. 2022 Jul;607(7917):97-103. DOI: <u>10.1038/s41586-022-04576-6.</u>
- Karachaliou M et al. SARS-CoV-2 infection, vaccination, and antibody response trajectories in adults: a cohort study in Catalonia. *BMC Med.* 2022 Sep 16;20(1):347. DOI: <u>10.1186/s12916-022-02547-2.</u>
- Goldberg X et al. Mental health and COVID-19 in a general population cohort in Spain (COVICAT study). *Soc Psychiatry Psychiatr Epidemiol*. 2022 Dec;57(12):2457-2468. DOI: 10.1007/s00127-022-02303-0.

PARTNERSHIP HIGHLIGHTS

- Mishra A, et al. Stroke genetics informs drug discovery and risk prediction across ancestries. *Nature.* 2022 Nov;611(7934):115-123. DOI: <u>10.1038/s41586-022-05165-3</u>.
- Cárcel-Márquez J et al. A Polygenic Risk Score Based on a Cardioembolic Stroke Multitrait Analysis Improves a Clinical Prediction Model for This Stroke Subtype. Front Cardiovasc Med. 2022 Jul 8;9:940696. DOI: <u>10.3389/</u> fcvm.2022.940696.
- García-Fernández C et al. **Y-chromosome target enrichment reveals rapid expansion of haplogroup R1b-DF27 in Iberia during the Bronze Age transition.** *Sci Rep.* 2022 Dec 1;12(1):20708. DOI: <u>10.1038/s41598-022-25200-7</u>.

CMCIB, A REFERENCE IN COMPARATIVE MEDICINE, BIOIMAGING, AND COMPUTATIONAL MODELS

The Comparative Medicine & Bioimage Centre of Catalonia (CMCiB) is the translational medicine centre of the Germans Trias i Pujol Research Institute (IGTP), affiliated with the Germans Trias University Hospital on the Can Ruti Campus in Badalona. The centre has been designed and equipped to accommodate and support a wide range of biomedical research and technological development projects while maintaining strict sustainability and research standards within the 3R policy.

CMCiB is a state-of-the-art high-tech biomedical research centre uniquely designed to support preclinical translational research, from the earliest stages of research to product development, across all fields of biomedicine. It serves a diverse clientele, ranging from Catalan research groups and centres to international private companies, and has multiple strategic partners. It offers opportunities for advanced biomedical research, innovation in surgery, and technological development, with expert consulting services and cutting-edge training programmes for healthcare professionals and researchers worldwide. CMCiB is one of the few centres in southern Europe that is part of the European 3R network, and since 2021, it has been accredited for Good Laboratory Practices (GLP). This accreditation has allowed CMCiB to participate in the validation of various medical devices and products currently in clinical validation or in the process of obtaining CE marking.

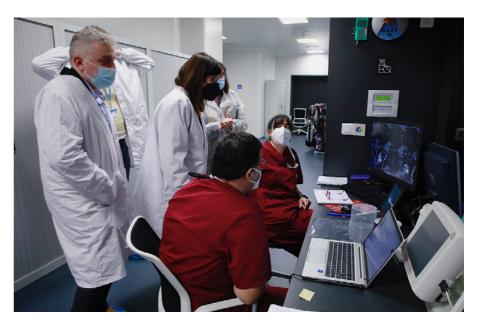


CMCiB Highlights 2022

CMCiB ACTIVITIES

- Increase of activity with humanized and GMO mice models and *in-vitro* and *in-vivo* research in infectious diseases
- Increase of Advanced Surgical Trainings
 - KOL's from > 30 countries and > 80 hospitals
 - > 20 customers worldwide
 - World class Robotic Surgery training centre
- Animal trial support in several EU consortia and International/national research projects in multiple therapeutic areas (regenerative medicine, neurology, infectious diseases, oncology, respiratory, etc.) with diferent animal models or alternative methods (Organoids, Alternative Tissue models, Computer Simulator, *Drosophila Melanogaster*, rodents, porcine and ovine models)
- Vaccine efficacy tests
- GLP validation of medical devices for industrial customers like surgical devices or intravascular catheters.
- Appointment of the Head of Bioimaging at CMCiB, expert in neuroimaging and neuroscience consultancy
- New Human MRI research projects (COVID, Friedrich's ataxia and acromegaly)
- Establishment of a full-body protocol (3T MRI)





The Catalan Minister Gemma Geis visits the CMCiB

• ~50 visits



3R PROGRAM

- CMCiB participates in the "3Rs concepts to improve the quality of biomedical science" (IMPROVE) COST Action (2022-2026)
- CMCiB takes part in the 2022 European Congress on Alternatives to Animal Testing held in September in Austria.
- 3R Seminars and specific trainings: 280 Trained researchers on animal care
- 80% reduction of mice used for immune response studies
- 5 prizes for COVID-19 modelization inSilico
- Establishment of Alternative Tissue Models (ATM) for Advanced Surgical activities

Neuhaus W, Reininger-Gutmann B, Rinner B, Plasenzotti R, Wilflingseder D, De Kock J, Vanhaecke T, Rogiers V, Jírová D, Kejlová K, Knudsen LE, Nielsen RN, Kleuser B, Kral V, Thöne-Reineke C, Hartung T, Pallocca G, Leist M, Hippenstiel S, Lang A, Retter I, Krämer S, Jedlicka P, Ameli K, Fritsche E, Tigges J, Buettner M, Bleich A, Baumgart N, Baumgart J, Meinhardt MW, Spanagel R, Chourbaji S, Kränzlin B, Seeger B, von Köckritz-Blickwede M, Sánchez-Morgado JM, Galligioni V, Ruiz-Pérez D, Movia D, Prina-Mello A, Ahluwalia A, Chiono V, Gutleb AC, Schmit M, van Golen B, van Weereld L, Kienhuis A, van Oort E, van der Valk J, Smith A, Roszak J, Stępnik M, Sobańska Z, Olsson IAS, Franco NH, Sevastre B, Kandarova H, Capdevila S, Johansson J, Cederroth CR, Sandström J, Ragan I, Bubalo N, Spielmann H. **The Rise of Three Rs Centres and Platforms in Europe**. *Altern Lab Anim*. 2022 Mar;50(2):90-120. DOI: 10.1177/02611929221099165. Neuhaus W, Reininger-Gutmann B, Rinner B, Plasenzotti R, Wilflingseder D, De Kock J, Vanhaecke T, Rogiers V, Jírová D, Kejlová K, Knudsen LE, Nielsen RN, Kleuser B, Kral V, Thöne-Reineke C, Hartung T, Pallocca G, Rovida C, Leist M, Hippenstiel S, Lang A, Retter I, Krämer S, Jedlicka P, Ameli K, Fritsche E, Tigges J, Kuchovská E, Buettner M, Bleich A, Baumgart N, Baumgart J, Meinhardt MW, Spanagel R, Chourbaji S, Kränzlin B, Seeger B, von Köckritz-Blickwede M, Sánchez-Morgado JM, Galligioni V, Ruiz-Pérez D, Movia D, Prina-Mello A, Ahluwalia A, Chiono V, Gutleb AC, Schmit M, van Golen B, van Weereld L, Kienhuis A, van Oort E, van der Valk J, Smith A, Roszak J, Stępnik M, Sobańska Z, Reszka E, Olsson IAS, Franco NH, Sevastre B, Kandarova H, Capdevila S, Johansson J, Svensk E, Cederroth CR, Sandström J, Ragan I, Bubalo N, Kurreck J, Spielmann H. **The Current Status and Work of Three Rs Centres and Platforms in Europe**. *Altern Lab Anim*. 2022 Nov;50(6):381-413. DOI: <u>10.1177/02611929221140909</u>.

ACCREDITATIONS AND PARTNERING

- CMCiB receives the certificate for Good Laboratory Practice (GLP) for preclinical research, awarded by the Government of Catalonia
- A framework agreement with the IGTP allows researchers from the Clínic-IDIABAPS to access the Centre for Comparative Medicine and Bioimage of Catalonia (CMCiB)



Innovation and technology transfer

IGTP's Innovation Unit experienced significant growth in its scope in 2022, which had an impact on the demand for services. In that sense, the unit offered new services to researchers in support of innovation management and knowledge transfer.

Innovation Unit Highlights

- Creation of a new spin-off, Breaz Medical S.L., led by Dr. Antoni Rosell.
- New regulation on the use of institute spaces by spin-offs.
- New junior project manager.
- Participation in several activities and events, including the "Implementation of an R+D+i Management System. UNE 166002" course organized by AENOR, the capsule "El Venture Capital in the Fundraising Process" by ITEMAS, and the practical workshop on "Pattern Search and Technology Surveillance to Protect Innovation" by ACCIÓ.

These achievements have prompted the unit to outline their objectives for 2023. Among these goals are joining the ITEMAS community, securing the Call for ISCI-II-ITEMAS platforms to support R+D+I in biomedicine and health sciences, focusing on communication, to expand the unit's service portfolio, and evaluating new health technologies to offer new services to IGTP's researchers.

Spin-off Companies of the IGTP



Research areas, groups and programmes at the IGTP

The Institute is associated with one of the major university hospitals in the Barcelona area, the <u>Germans</u> <u>Trias i Pujol Hospital</u>, and is part of the Can Ruti biomedical campus. IGTP is a <u>CERCA centre</u> and is also accredited as a centre of excellence by the Instituto de Salud Carlos III (ISCIII) and is in charge of coordinating the management and scientific strategy of the campus, working in close collaboration with the other centres.

The Germans Trias i Pujol Research Institute carries out research within 9 areas:

There is one transversal programme:

Cancer

Badalona Applied Research Group in Oncology (B·ARGO) Ricard Mesia Nin Anna Martínez Cardús

Cancer Genetics and Epigenetics Sergio Alonso Utrilla

Cancer Mechanisms and Pathways *Miguel Ángel Peinado*

Clinical Genomics Research *Ignacio Blanco Guillermo Elisabeth Castellanos Pérez*

Childhood Liver Oncology (C-LOG) Carolina Armengol Niell **Endocrine Tumours** *Mireia Jordà Ramos*

Hereditary Cancer Eduard Serra Arenas

Molecular and Translational Pathology Pedro Luis Fernández Ruiz

Oncology Translational Research (OTR) Jordi Barretina Ginesta

Resistance, Chemotherapy and Predictive Biomarkers Eva Martínez Balibrea

Badalona Applied Research Group in Oncology (B·ARGO)



Group leaders: Ricard Mesía Nin, Anna Martínez Cardús

Research lines

- Classical therapy: Chemotherapy
- Immunotherapy
- Targeted therapy

Selected scientific publications

Felip E, Pradenas E, Romeo M, Marfil S, Trinité B, Urrea V, Hernández A, Ballana E, Cucurull M, Mateu L, Massanella M, Clotet B, Morán T, Blanco J. Impact of chemotherapy and/or immunotherapy on neutralizing antibody response to SARS-CoV-2 mRNA-1237 vaccine in patients with solid tumors. *Mol Oncol.* 2022 Dec 10;17(4):686-694. DOI: 10.1002/1878-0261.13359.

Felip E, Gutiérrez-Chamorro L, Gómez M, Garcia-Vidal E, Romeo M, Morán T, Layos L,

Pérez-Roca L, Riveira-Muñoz E, Clotet B, Fernandez PL, Mesía R, Martínez-Cardús A, Ballana E, Margelí M. **Modulation of DNA Damage Response by SAM and HD Domain Containing Deoxynucleoside Triphosphate Triphosphohydrolase (SAMHD1) Determines Prognosis and Treatment Efficacy in Different Solid Tumor Types.** *Cancers (Basel).* 2022 Jan 27;14(3):641. DOI: <u>10.3390/cancers14030641</u>.

Pinato DJ, Aguilar-Company J, Ferrante D, Hanbury G, Bower M, Salazar R, Mirallas O, Sureda A, Plaja A, Cucurull M, Mesia R, Townsend S, Jackson A, Dalla Pria A, Newsom-Davis T, Handford J, Sita-Lumsden A, Apthorp E, Vincenzi B, Bertuzzi A, Brunet J, Lambertini M, Maluquer C, Pedrazzoli P, Biello F, Sinclair A, Bawany S, Khalique S, Rossi S, Rogers L, Murphy C, Belessiotis K, Carmona-García MC, Sharkey R, García-Illescas D, Rizzo G, Perachino M, Saoudi-Gonzalez N, Doonga K, Fox L, Roldán E, Gaidano G, Ruiz-Camps I, Bruna R, Patriarca A, Martinez-Vila C, Cantini L, Zambelli A, Giusti R, Mazzoni F, Caliman E, Santoro A, Grosso F, Parisi A, Queirolo P, Aujayeb A, Rimassa L, Prat A, Tucci M, Libertini M, Grisanti S, Mukherjee U, Diamantis N, Fusco V, Generali D, Provenzano S, Gennari A, Tabernero J, Cortellini A; OnCovid study group. **Outcomes of the SARS-CoV-2 omicron (B.1.1.529) variant outbreak among vaccinated and unvaccinated patients with cancer in Europe: results from the retrospective, multicentre, OnCovid registry study.** *Lancet Oncol.* 2022 Jul;23(7):865-875. DOI: <u>10.1016/S1470-2045(22)00273-X</u>.

Summary of activities and highlights

The group published 85 articles in indexed scientific journals, with a total impact factor of 1027.24 and an average of 12.08. B·ARGO researchers procured funding for more than 31 competitive projects, signed two non-competitive agreements and defended three doctoral theses. Additionally, two RRHH competitive national grants were conceived to the group (PFIS and Rio Hortega; IS-CIII). Its members demonstrated a great dissemination activity: 9 and 12 oral communications in national and international events respectively; 30 poster presentations in the national scope and 75 in international conferences.

Cancer Genetics and Epigenetics



Group leader: Sergio Alonso Utrilla

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Research lines

- · Epigenetic biomarkers for cancer susceptibility and metastatic spread
- DNA demethylation, predictive of the development of multiple colon cancers
- Targeting extracellular matrix remodelers to enhance lymphocytic infiltration and immunotherapy response in colorectal cancer
- Development of in vitro 3D co-culture models for cancer immunotherapy

Selected scientific publications

Loi E, Zavattari C, Tommasi A, Moi L, Canale M, Po A, Sabato C, Vega-Benedetti AF, Ziranu P, Puzzoni M, Lai E, Faloppi L, Rullán M, Carrascosa J, Amat I, Urman JM, Arechederra M, Berasain C, Ferretti E, Casadei-Gardini A, Avila MA, Alonso S, Scartozzi M, Zavattari P. **HOXD8 hypermethylation as a fully sensitive and specific biomarker** for biliary tract cancer detectable in tissue and bile samples. *Br J Cancer.* 2022 Jun;126(12):1783-1794. DOI: <u>10.1038/s41416-022-01738-1</u>.

Poppova L, Pavlova S, Gonzalez B, Kotaskova J, Plevova K, Dumbovic G, Janovska P, Bystry V, Panovska A, Bezdekova L, Maslejova S, Brychtova Y, Doubek M, Krzyzankova M, Borsky M, Mayer J, Bryja V, Alonso S, Pospisilova S. **Memory B-cell like chronic lymphocytic leukaemia is associated with specific methylation profile of WN-T5A promoter and undetectable expression of WNT5A gene.** *Epigenetics.* 2022 Dec;17(12):1628-1635. DOI: <u>10.1080/15592294.2022.2050004.</u>

Summary of activities and highlights

Group leader Sergio Alonso was a member of the <u>TransCOLONCAN</u> COST action, which concluded with a final achievement report in December. The project aimed at using innovative translational research to identify colorectal cancer biomarkers for personalised medicine. It aimed to improve screening, early detection and disease follow-up, and attain better tumour profiling, state-of-theart functional characterisation of genetic variants and new therapy approaches.

Cancer Mechanisms and Pathways



Group leader: Miguel Ángel Peinado

Research lines

- Epigenetic landmarks for cancer patient stratification
- Drivers of genome reprogramming in cancer
- New targets and tools for early diagnosis and treatment
- The role of dark DNA in genome regulation

Selected scientific publications

Matas J, Kohrn B, Fredrickson J, Carter K, Yu M, Wang T, Gui X, Soussi T, Moreno V, Grady WM, Peinado MA, Risques RA. **Colorectal Cancer Is Associated with the Presence of Cancer Driver Mutations in Normal Colon.** *Cancer Res.* 2022 Apr 15;82(8):1492-1502. DOI: <u>10.1158/0008-5472.CAN-21-3607.</u>

Clinical Genomics Research



Group leaders: Ignacio Blanco Guillermo, Elisabeth Castellanos Pérez

Catasús N, Garcia B, Galván-Femenía I, Plana A, Negro A, Rosas I, Ros A, Amilibia E, Becerra JL, Hostalot C, Rocaribas F, Bielsa I, Lazaro Garcia C, de Cid R, Serra E, Blanco I, Castellanos E; NF2 Spanish National Reference Centre HUGTP-ICO-IGTP. **Revisiting the UK Genetic Severity Score for NF2: a proposal for the addition of a functional genetic component. J** *Med Genet.* 2022 Jul;59(7):678-686. DOI: <u>10.1136/jmedge-net-2020-107548.</u>

Catasús N, Rosas I, Bonache S, Negro A, Torres-Martin M, Plana-Pla A, Salvador H, Serra E, Blanco I, Castellanos E; NF2-related SWN Spanish National Reference Centre HUGTP-ICO-IGTP. **Antisense oligonucleotides targeting exon 11 are able to partia-Ily rescue the NF2-related schwannomatosis phenotype in vitro.** *Mol Ther Nucleic Acids.* 2022 Nov 4;30:493-505. DOI: <u>10.1016/j.omtn.2022.10.026</u>.

Research lines

- Management of phakomatoses patients
- Development and implementation of new genomic techniques for genetic diagnosis of hereditary diseases
- · Personalised medicine for neurofibromatosis
- Genetic susceptibility to illness

Selected scientific publications

International Consensus Group on Neurofibromatosis Diagnostic Criteria (I-NF-DC); Huson SM, Wolkenstein P, Evans DG. **Updated diagnostic criteria and nomenclature for neurofibromatosis type 2 and schwannomatosis: An international consensus recommendation.** *Genet Med.* 2022 Sep;24(9):1967-1977. DOI: 10.1016/j.gim.2022.05.007.

Summary of activities and highlights

Elisabeth Castellanos was invited to serve as a session co-chair at the 2022 NF Conference to update on the advances of the Neurofibromatoses and Schwannomatosis Variant Curation Expert Panel. Moreover, Ignacio Blanco and Elisabeth Castellanos co-organised the "VI Jornada Interhospitalària de Genètica a Catalunya" (BCIN, Badalona; 7 November).

The group, in collaboration with other members of the CSUR of Phakomatoses, was recognised as an Established Research Group by the Generalitat de Catalunya (SGR-Cat-2021).

Childhood Liver Oncology (C-LOG)



Group leader: Carolina Armengol Niell

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Research lines

- Understanding the molecular biology of childhood liver cancer
- Identification and validation of diagnostic and prognostic biomarkers to improve the clinical management of childhood liver cancer
- Establishing new experimental models of childhood liver cancer

Selected scientific publications

Mosca N, Khoubai FZ, Fedou S, Carrillo-Reixach J, Caruso S, Del Rio-Alvarez A, Dubois E, Avignon C, Dugot-Senant N, Guettier C, Mussini C, Zucman-Rossi J, Armengol C, Thiébaud P, Veschambre P, Grosset CF. LIM Homeobox-2 Suppresses Hallmarks of Adult and Pediatric Liver Cancers by Inactivating MAPK/ERK and Wnt/Beta-Catenin Pathways. *Liver Cancer.* 2022 Apr;11(2):126-140. DOI: 10.1159/000521595. Corujo D, Malinverni R, Carrillo-Reixach J, Meers O, Garcia-Jaraquemada A, Le Pannérer MM, Valero V, Pérez A, Del Río-Álvarez Á, Royo L, Pérez-González B, Raurell H, Acemel RD, Santos-Pereira JM, Garrido-Pontnou M, Gómez-Skarmeta JL, Pasquali L, Manyé J, Armengol C, Buschbeck M. **MacroH2As regulate enhancer-promoter contacts affecting enhancer activity and sensitivity to inflammatory cytokines.** *Cell* Rep. 2022 Jun 21;39(12):110988. DOI: <u>10.1016/j.celrep.2022.110988</u>.

Li Q, Demir S, Del Río-Álvarez Á, Maxwell R, Wagner A, Carrillo-Reixach J, Armengol C, Vokuhl C, Häberle B, von Schweinitz D, Schmid I, Cairo S, Kappler R. **Targeting the Unwindosome by Mebendazole Is a Vulnerability of Chemoresistant Hepatoblastoma.** *Cancers (Basel).* 2022 Aug 30;14(17):4196. DOI: <u>10.3390/cancers14174196.</u>

Summary of activities and highlights

C-LOG obtained funding for three novel projects coordinated by thze group: CIBERehd intramural project "Identificación de dianas moleculares para terapias innovadoras del hepatoblastoma" (partners IDIBAPS, FIMA, CICBIO-GUNE, USAL; €200,000), AECC-coordinated project "Precision medicine for hepatoblastoma: identification of novel therapies and predictive biomarkers using a unique EU biorepository" (partners IDIBAPS, FIMA, CICBIOGUNE, USAL; €1,200,000) and Fight Kids Cancer project "Identification of predictive Biomarkers and novel biology-driven Therapies for Childhood Liver Cancer patients using a unique EU biorepository" (partners LMU, PMC, UoN, IRP; €500,000). In addition, its researchers participated in two consortium groups: Grup de Recerca translacional en patologia hepàtica i immunitat innata and HUB d'Innovació Pediàtrica - I4KIDS. Carolina Armengol was invited to give a talk about "Present and future of precision oncology in hepatoblastoma" (Boston; 5-8 May) in the Special Conference on Advances in the Pathogenesis and Molecular Therapies of Liver Cancer, organised by the American Association for Cancer Research. C-LOG also contributed to organising the meetings "4th Course of Translational Hepatology of the Spanish Association for the Study of the Liver (AEEH)" (Santiago de Compostela; 16-17 December) and the "1st International Biology/Pathology meeting" (Barcelona; 30 September).

Scientific activity in 2022 / Research areas, groups and programmes at the IGTP

Endocrine Tumours



Group leader: Mireia Jordà Ramos

Research lines

- · Molecular pathogenesis of aggressive thyroid cancer
- · Kallikreins, new players in thyroid cancer: regulation, function and clinical use
- Molecular pathogenesis of pituitary adenomas
- Development of molecular assays for clinical settings

Selected scientific publications

Montero-Conde C, Leandro-García LJ, Martínez-Montes ÁM, Martínez P, Moya FJ, Letón R, Gil E, Martínez-Puente N, Guadalix S, Currás-Freixes M, García-Tobar L, Zafon C, Jordà M, Riesco-Eizaguirre G, González-García P, Monteagudo M, Torres-Pérez R, Mancikova V, Ruiz-Llorente S, Pérez-Martínez M, Pita G, Galofré JC, Gonzalez-Neira A, Cascón A, Rodríguez-Antona C, Megías D, Blasco MA, Caleiras E, Rodríguez-Perales S, Robledo M. **Comprehensive molecular analysis of immortalization hall**- marks in thyroid cancer reveals new prognostic markers. *Clin Transl Med.* 2022 Aug;12(8):e1001. DOI: <u>10.1002/ctm2.1001</u>.

Gil J, Marques-Pamies M, Sampedro M, Webb SM, Serra G, Salinas I, Blanco A, Valassi E, Carrato C, Picó A, García-Martínez A, Martel-Duguech L, Sardon T, Simó-Servat A, Biagetti B, Villabona C, Cámara R, Fajardo-Montañana C, Álvarez-Escolá C, Lamas C, Alvarez CV, Bernabéu I, Marazuela M, Jordà M, Puig-Domingo M. **Data mining analyses for precision medicine in acromegaly: a proof of concept**. *Sci Rep.* 2022 May 28;12(1):8979. DOI: 10.1038/s41598-022-12955-2.

Pardo JC, Ruiz de Porras V, Gil J, Font A, Puig-Domingo M, Jordà M. Lipid Metabolism and Epigenetics Crosstalk in Prostate Cancer. *Nutrients.* 2022 Feb 18;14(4):851. DOI: <u>10.3390/nu14040851</u>.

Summary of activities and highlights

The group was awarded three new projects: "Research group recognised by the Generalitat de Catalunya" (SGR-Cat 2021), "ACROMICS: next-generation precision medicine in the diagnosis and treatment of acromegaly" (ISCIII - PMP22/00021), "Validation of the diagnostic value of a global DNA methylation index in thyroid nodules with undetermined cytology" (FSEEN). The team also received two awards for the best oral communication at the "63rd Congress of the Spanish Society of Endocrinology and Nutrition (SEEN)" and Helena Rodríguez-Lloveras was awarded with a PFIS predoctoral contract from Carlos III Health Institute (ISCIII).

Global DNA hypomethylation of Alu elements (PUMA) was incorporated into the 2022 WHO Classification of Thyroid Neoplasms as an adverse marker of thyroid cancer (ZW Baloch et al., Endocr Pathol 2022), following the results of the Endocrine Tumours research group in 2018 (Klein Hesselink et al., JCEM 2018).

Hereditary Cancer



Group leader: Eduard Serra Arenas

Research lines

- Cancer genomics and integrative biology of tumours of the peripheral nervous system, other neural crest-derived tumours and sarcomas
- · Primary and iPSC-based models for cancer and regeneration
- Molecular pathogenesis of neurofibromatosis type 1
- Applied cancer genomics for translation into the clinics

Selected scientific publications

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. Screening of CNVs using NGS data improves mutation detection yield and decreases costs in genetic testing for hereditary cancer. *J Med Genet*. 2022 Jan;59(1):75-78. DOI: <u>10.1136/</u>jmedgenet-2020-107366.

Mazuelas H, Magallón-Lorenz M, Fernández-Rodríguez J, Uriarte-Arrazola I, Richaud-Patin Y, Terribas E, Villanueva A, Castellanos E, Blanco I, Raya Á, Chojnacki J, Heyn H, Romagosa C, Lázaro C, Gel B, Carrió M, Serra E. **Modeling iPSC-derived human neurofibroma-like tumors in mice uncovers the heterogeneity of Schwann cells within plexiform neurofibromas.** *Cell Rep.* 2022 Feb 15;38(7):110385. DOI: 10.1016/j.celrep.2022.110385.

Fernández-Rodríguez J, Creus-Bachiller E, Zhang X, Martínez-Iniesta M, Ortega-Bertran S, Guha R, Thomas CJ, Wallace MR, Romagosa C, Salazar-Huayna L, Reilly KM, Blakely JO, Serra-Musach J, Pujana MA, Serra E, Villanueva A, Ferrer M, Lázaro C. **A High-Throughput Screening Platform Identifies Novel Combination Treatments for Malignant Peripheral Nerve Sheath Tumors.** *Mol Cancer Ther*. 2022 Jul 5;21(7):1246-1258. DOI: <u>10.1158/1535-7163.MCT-21-0947</u>.

Summary of activities and highlights

The group published in Cell Reports the development of an *in vitro/in vivo* iPSC-derived 3D neurofibromasphere model and first plexiform neurofibroma single-cell genomic data. Additionally, the Hereditary Cancer group received an international grant from the Neurofibromatosis Therapeutic Acceleration Program (NTAP)-Johns Hopkins University for a project starting in 2023. Its researchers will also collaborate with La Nineta dels Ulls, an association to develop a liquid biopsy-based assay for monitoring the development of secondary neoplasia in patients with hereditary retinoblastoma. Finally, Eduard Serra was awarded with the Theodor Schwann Award, the unique European distinction on Neurofibromatosis research, awarded by the European NF Group.

Molecular and Translational Pathology



Group leader: Pedro Luis Fernández Ruiz

Research lines

- Breast and genitourinary neoplasms
- Lymphoid and mesenchymal neoplasms
- Respiratory tract, and head & neck neoplasms
- Digestive and hepatobiliary tract neoplasms
- · Nervous and endocrine systems neoplasms, and neurodegenerative disorders
- Skin neoplasms
- Nefropathology and fetal pathology
- Molecular pathology
- Paleopathology

Selected scientific publications

Felip E, Gutiérrez-Chamorro L, Gómez M, Garcia-Vidal E, Romeo M, Morán T, Layos L, Pérez-Roca L, Riveira-Muñoz E, Clotet B, Fernandez PL, Mesía R, Martínez-Cardús A, Ballana E, Margelí M. **Modulation of DNA Damage Response by SAM and HD Domain Containing Deoxynucleoside Triphosphate Triphosphohydrolase (SAMHD1) Determines Prognosis and Treatment Efficacy in Different Solid Tumor Types.** *Cancers (Basel)*. 2022 Jan 27;14(3):641. DOI: <u>10.3390/cancers14030641</u>.

Fernández PL, Rodriguez P, Margeli M, Sanz C, Muñoz AM, Urbizu A, Quiroga V, Castillo A, Cirauqui B, Teruel I, Castella E, Felip E, Perello C, Pons L, Leon LH. **Characterization of Residual TN and HER2 Breast Carcinomas after Neoadjuvant Therapy.** Modern Pathology. 2022 Mar 1.

Pons L, Hernández-León L, Altaleb A, Ussene E, Iglesias R, Castillo A, Rodríguez-Martínez P, Castella E, Quiroga V, Felip E, Cirauqui B, Margelí M, Fernández PL. **Conventional and digital Ki67 evaluation and their correlation with molecular prognosis and morphological parameters in luminal breast cancer.** *Sci Rep.* 2022 May 17;12(1):8176. DOI: <u>10.1038/s41598-022-11411-5</u>.

Summary of activities and highlights

The group implemented a lung liquid biopsy technique and started to perform the genetic determinations. This achievement paved the way for the procurement of funding for a project on breast liquid biopsies, starting in 2023. In addition, digital pathology technology (DigiPatics project) was implemented for diagnosis and histopathology research.

The "1st Meeting of the UDMGMP" (Molecular Diagnosis, Genetics and Precision Medicine Unit) was held on 17 February to show what is discussed in the weekly meetings of this unit regarding the North Metropolitan area. The unit includes several groups of the Germans Trias i Pujol University Hospital, including the Molecular and Translational Pathology group, and meets weekly to discuss the NGS results obtained for every patient.

This research group is developing artificial intelligence tools in collaboration with Universitat Politècnica de Catalunya (UPC) for application to histopathology. It also collaborates with centres such as the Institute of Photonic Sciences (ICFO) and researchers Jordi Barretina, Bonaventura Clotet, Mireia Jordà, Anna Martínez Cardús, Julia Garcia, Hernando A. del Portillo, among others.

Cristina Carrato started a FIS project called "Validation of genomic alterations in glioblastoma: finding weaknesses for therapeutic intervention (VAL-GLIO-THE-RINT)". The FIS and La Marató de TV3-funded projects led by Pedro Luis Fernández continued for a third year.

Oncology Translational Research (OTR)



Group leader: Jordi Barretina Ginesta

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Research lines

- Understanding treatment response in ovarian cancer with new omics techniques
- Organoid-based treatment screening to optimize colorectal cancer management

Selected scientific publications

Mustafa Sibai, Sergi Cervilla, Daniela Grases, Eva Musulen, Arola Fortian, Margarita Romeo, Adrià Bernat, Collin Tokheim, Manel Esteller, Jordi Barretina, Li Ding, Matthew Bailey, Eduard Porta-Pardo. **Charting the Spatial Landscape of Cancer Hallmarks.** *bioRxiv* 2022.06.18.496114; DOI: <u>10.1101/2022.06.18.496114</u>.

Resistance, Chemotherapy and Predictive Biomarkers



Group leader: Eva Martínez Balibrea

Research lines

- · Deciphering mechanisms of resistance to treatment in colorectal cancer
- Finding predictive biomarkers for treatment selection
- Development and implementation of in vitro and ex vivo models of acquired resistance to different anti-cancer therapies

Selected scientific publications

Bernat-Peguera A, Trigueros M, Ferrando-Díez A, Ibáñez C, Bystrup S, Martínez-Cardús A, Margelí M, Martínez-Balibrea E. **Efficacy of CT-P6 (trastuzumab biosimilar)** versus reference trastuzumab in combination with pertuzumab in HER2-positive early-stage breast cancer: Preclinical and real-life clinical data. *Breast.* 2022 Apr;62:1-9. DOI: <u>10.1016/j.breast.2022.01.007.</u> Layos L, Martínez-Balibrea E, Ruiz de Porras V. Curcumin: A Novel Way to Improve Quality of Life for Colorectal Cancer Patients? *Int J Mol Sci.* 2022 Nov 14;23(22):14058. DOI: <u>10.3390/ijms232214058</u>.

Cucurull M, Notario L, Sanchez-Cespedes M, Hierro C, Estival A, Carcereny E, Saigí M. **Targeting KRAS in Lung Cancer Beyond KRAS G12C Inhibitors: The Immune Regulatory Role of KRAS and Novel Therapeutic Strategies.** *Front Oncol.* 2022 Jan 13;11:793121. DOI: <u>10.3389/fonc.2021.793121</u>.

Summary of activities and highlights

The research group was awarded with an INVESTIGO contract and its leader, Eva Martínez-Balibrea, was nominated as new secretary of the EORTC cross-disciplinary group on Pathobiology.

Eva Martínez and Laura Belver (Josep Carreras Research Institute, IJC), hosted the Spring meeting of the ProCURE programme from the Institut Català d'Oncologia (ICO) (IJC, Badalona; 14 July). Both researchers also started a COST Action by the name of <u>IMMUNO-Model</u>, which aims to promote research and innovation in preclinical oncology models with the objective of advancing the treatment of cancer patients for better results and a better quality of life. In the context of this project, the "Modelling Immuno-oncology Workshop" (30 March) was held online, with more than 160 participants. International experts in the field of pre-clinical models in immuno-oncology took part in the event.

The "XX edition of the Conference on Translational Research and Digestive Neoplasms" (BCIN, Badalona; 6 October) had a very positive reception from the fifty attendees and the organization. It was organized jointly by the IGTP and the ICO and directed by José Luis Manzano (ICO), Eva Martinez-Balibrea (ICO-IGTP) and Albert Abad (Mi Tres Torres).

Cardiovascular and respiratory diseases

Heart Disease Antoni Bayés Genís

Lung Immunity Translational Research Group Raquel Guillamat Prats

Heart Disease



Group leader: Antoni Bayés Genís

Research lines

- Advanced Therapies
- Translational animal models (mouse, rat and pig)
- Cardiometabolism
- Heart Precision Medicine Platform (PMP-Heart)
- Clinical Trials Support Area / Clinical Trials Unit ASAC
- Innovation and Technology Transfer

Selected scientific publications

Bayes-Genis A, Coats AJS. **'Peptide for Life' in primary care: work in progress.** *Eur Heart J.* 2022 Mar 1;43(9):892-894. DOI: <u>10.1093/eurheartj/ehab829.</u>

Lee KK et al.; CoDE-HF investigators. **Development and validation of a decision support tool for the diagnosis of acute heart failure: systematic review, me-ta-analysis, and modelling study.** *BMJ.* 2022 Jun 13;377:e068424. DOI: <u>10.1136/</u><u>bmj-2021-068424</u>.

Bayés-Genís A, Díez J. **Transition to heart failure in hypertension: going to the heart of the matter.** *Eur Heart J.* 2022 Sep 14;43(35):3332-3334. DOI: 10.1093/eur-heartj/ehab651.

Summary of activities and highlights

The Heart Institute made significant progress in multiple areas of study, including biotherapies, heart failure, cardiac imaging, and cardiac biomarkers, among others. Its efforts were directed towards various research projects and clinical trials aimed at exploring new treatment options and enhancing patient management.

Overall, the research group published 281 articles with a total impact factor of 2,115.82 (average of 7.52) and presented more than 50 oral and poster presentations at national and international conferences. One notable accomplishment was the improvement of extracellular vesicles (EVs) production in collaboration with Banc de Sang i Teixits (BST) and conducting initial studies in mice. This research focused on harnessing the therapeutic potential of EVs for cardiac regeneration and immune regulation. The group also studied the use of cardiac organoids in pigs to model cardiac diseases and assess potential treatments. Furthermore, its researchers conducted experiments to examine the effects of Empagliflozin and Sacubitril Valsartan in pigs, which could have implications for improving patient health after suffering a myocardial infarction. Additionally, the Vascraft project, which centres on vascular tissue engineering, was started. The goal is to develop a new decellularized and re-endothelialized human vascular graft for use in arterial bypass procedures in collaboration with BST and IQS Barcelona.

Regarding clinical trials, new patients were enrolled in the AGTPII and PERIS-COPE trials. These trials aimed to evaluate the effectiveness of a novel surgical procedure and a new treatment for non-revascularizable myocardial infarction and infarcted myocardial tissue, respectively. The research group also actively engaged in clinical studies, promoted by both private industry and academia, with a particular focus on heart failure (UIC), interventional cardiology, and cardiac hospitalization units.

The group established a new Corelab of Cardiac Imaging and welcomed new fellows who would participate in internships at the Germans Trias i Pujol University Hospital (HUGTiP). The research line on heart arrhythmia increased their studies in pigs and offered several specialised training courses at the Comparative Medicine & Bioimage Centre of Catalonia (CMCiB).

Furthermore, the group collaborated with the Universitat Politècnica de Catalunya (UPC) and the University of Barcelona (UB) to establish a new spin-off, NIMBLE Diagnostics, a company with the aim of becoming the standard of care for the monitoring of implanted stents.

Lung Immunity Translational Research Group



Group leader: Raquel Guillamat Prats

Research lines

- Role of cannabinoid system in pulmonary fibrosis
- G-protein couple receptor 55 (GPR55) in neutrophil activation during acute lung injury
- The pivotal role of macrophages in lung cancer and pulmonary fibrosis
- Role of diet as master of regulating of immune system and its impact in respiratory diseases

Selected scientific publications

Guillamat-Prats R. **Role of Mesenchymal Stem/Stromal Cells in Coagulation.** *Int J Mol Sci.* 2022 Sep 8;23(18):10393. DOI: <u>10.3390/ijms231810393</u>.

Guillamat-Prats R, Hering D, Derle A, Rami M, Härdtner C, Santovito D, Rinne P, Bindila L, Hristov M, Pagano S, Vuilleumier N, Schmid S, Janjic A, Enard W, Weber C, Maegdefessel L, Faussner A, Hilgendorf I, Steffens S. **GPR55 in B cells limits atherosclerosis development and regulates plasma cell maturation.** *Nat Cardiovasc Res.* 2022 Nov;1:1056-1071. DOI: <u>10.1038/s44161-022-00155-0</u>.

Summary of activities and highlights

This emergent group incorporated Paula Goncalves Romeu, Biotechnology graduate and master's in Advanced Immunology, with an INVESTIGO contract. Paula is pursuing her PhD, studying the role of the cannabinoid system in respiratory diseases.

The group trained two master's students: Marina Pastor, who explored the "Role of the cannabinoid receptors in pulmonary fibrosis", and Meiling Ma, who examined the "GPR55 receptor in neutrophil response during acute lung injury".

The team organized and participated in several outreach activities, such as an open-day for 13 to 14-year-old students from the Col·legi Cultural Badalona. The principal investigator of the group, Raquel Guillamat, participated in various international project evaluation panels such as at the American Heart Association (USA) and the National Science Centre of Poland (Narodowe Centrum Nauki, Poland). She was also part of the Editorial Board of *Frontiers in Cardiovascular Medicine Journal* and was a reviewer for the *European Journal of Pharmacology, Frontiers in Medicine, Biomolecules, International Journal of Molecular Sciences, Journal of Clinical Medicine, Cells, Cell Stem Cell, Therapeutic Advances in Respiratory Disease, Respiratory Research, and Annals of Intensive Care.*

Community Health

Centre for Epidemiological Studies on HIV/ AIDS and STI of Catalonia (CEEISCAT) Jordi Casabona i Barbarà

Innovation, Health Economics and Digital Transformation Research Group (INEDIT) Oriol Estrada Cuxart

Maresme Study Group on Community-Acquired Pneumonia and COPD (GEMPAC) Ramon Boixeda Viu

Centre for Epidemiological Studies on HIV/AIDS and STI of Catalonia (CEEISCAT)



Group leader: Jordi Casabona i Barbarà

Research lines

- Formal systems of epidemiological surveillance of HIV and other STIs
- Monitoring of the diagnosis and evaluation of new technologies and screening strategies for HIV and other STIs
- Antiretroviral treatment monitoring and study of the effect of comorbidities and aging in HIV positive patients
- Study and monitoring of the multilevel determinants of HIV transmission and other STIs
- Determinants of transmission and knowledge, attitudes and behaviours about the prevention of SARS-CoV-2
- Coverage and determinants of early diagnosis and healthcare linkage of hepatitis C

Selected scientific publications

Martin-Iguacel R, Reyes-Urueña J, Bruguera A, Aceitón J, Díaz Y, Moreno-Fornés S, Domingo P, Burgos-Cibrian J, Tiraboschi JM, Johansen IS, Álvarez H, Miró JM, Casabona J, Llibre JM; PISCIS study group. **Determinants of long-term survival in late HIV presenters: The prospective PISCIS cohort study.** *EClinicalMedicine.* 2022 Aug 3;52:101600. DOI: 10.1016/j.eclinm.2022.101600.

Agustí C, Cunillera O, Almeda J, Mascort J, Carrillo R, Olmos C, Montoliu A, Alberny M, Molina I, Cayuelas L, Casabona J. Efficacy of an electronic reminder for HIV screening in primary healthcare based on indicator conditions in Catalonia (Spain). *HIV Med*. 2022 Sep;23(8):868-879. DOI: <u>10.1111/hiv.13270</u>.

Ganem F, Bordas A, Folch C, Alonso L, Montoro-Fernandez M, Colom-Cadena A, Mas A, Mendioroz J, Asso L, Anton A, Pumarola T, González MV, Blanco I, Soler-Palacín P, Soriano-Arandes A, Casabona J; Sentinel School Network Study Group of Catalonia. **The COVID-19 Sentinel Schools Network of Catalonia (CSSNC) project:** Associated factors to prevalence and incidence of SARS-CoV-2 infection in educational settings during the 2020-2021 academic year. *PLoS One*. 2022 Nov 17;17(11):e0277764. DOI: <u>10.1371/journal.pone.0277764</u>.

Summary of activities and highlights

Since 2021, CEEISCAT has been recognised as a Consolidated Research Group by AGAUR (2021/SGR/00927, Generalitat de Catalunya).

In order to reinforce population-based research at IGTP, the Institute's Board of Trustees approved the creation of the "Public Health and Primary Care Program" at the end of 2022. The implementation of this programme was entrusted to both CEEISCAT and the North Metropolitan Research Support Unit (USRMN).

CEEISCAT was involved in two competitive projects. The first, "Community Led and Based HIV Services – Key to Ending the HIV Epidemic in Europe and Central Asia 'Zeroing In – Ending the HIV Epidemic'", led by Ferenc Bagyinszky, featured CEEISCAT's support of the COBATEST network. The group developed innovative online scheduling and follow-up tools aimed at enhancing community-based testing services for HIV/AIDS, viral hepatitis, and other STIs, while advocating for the rollout of self-tests in Europe and Central Asia. The second project, "Viabilidad e impacto del cribado online de VIH / ITS dirigido a hombres que tienen sexo con hombres y mujeres transgénero en España usuarios de profilaxis pre-exposición (TÉSTATE PrEP)", had the primary objective of evaluating the feasibility and impact of online HIV/STI screening aimed at users of pre-exposure prophylaxis (PrEP). In this case, men who have sex with men and transgender women in Spain.

CEEISCAT consolidated its collaborations with international networks of scientific relevance: RIGHT-PLUS Network, COBATEST, and CHIP. In the latter,

CEEISCAT coordinated the Joint Action INTEGRATE work package focused on monitoring and evaluating HIV, STI and viral hepatitis testing, led by Denmark's CHIP.

The contributions of CEEISCAT researchers, like Cristina Agustí, received recognition from the Sociedad Española de Epidemiología (Spanish Epidemiology Society). Her work "El Proyecto Serocap: Vigilancia Epidemiológica reforzada de la infección SARS-COV-2 en pacientes de atención primaria como población centinela en la región sanitaria de Barcelona", was awarded the "XI Premio SEE-EASP «Emilio Perea»" as one of the year's top four senior communications.

CEEISCAT produced more than 24 oral communications and 14 posters, nationally and internationally.

Innovation, Health Economics and Digital Transformation Research Group (INEDIT)



Group leader: Oriol Estrada Cuxart

Research lines

- Technological innovation
- Transformation and digital health
- Health economics

Summary of activities and highlights

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Established in 2022, the INEDIT Research group has been actively cultivating its presence in the Can Ruti Campus. Throughout the year, the group sought out various funding opportunities and was successful in securing two Erasmus+ grants and three EIT Health projects. This achievement enabled the recruitment of two researchers, in collaboration with the NURECARE research group. INEDIT also led IGTP's participation in XarFa and other competitive funding calls managed by AGAUR. Recently, the health economics and innovation management units at IGTP gained recognition as expert centres for EATRIS. The group continues its efforts to attract more dedicated researchers and to establish robust networks within the campus community.

Maresme Study Group on Community-Acquired Pneumonia and COPD (GEMPAC)



Group leader: Ramon Boixeda Viu

Research lines

- Population study on acute COPD
- Study of risk factors for pneumonia in respiratory patients (asthma and COPD)
- Study of infectious comorbidity in patients admitted to hospital for acute COPD
- Study of risk factors for community acquired pneumonia

Selected scientific publications

Boixeda R, Moreno MI, Bartolomé M, Juanola J; en nombre del grupo GEMPOC. Incidencia de agudizaciones en la EPOC: estudio INAMPOC. Importancia del error diagnóstico. Aten Primaria. 2022 Aug;54(8):102389. Spanish. DOI: <u>10.1016/j.</u> aprim.2022.102389.

Fernández Fernández EP, Almirall J, Pere T, Roca J, Boixeda R. **Correlation between C reactive protein in capillary blood and in venous blood in lower respiratory tract infections.** Aten Primaria. 2022 Mar;54(3):102210. DOI: <u>10.1016/j.</u> aprim.2021.102210.

Diseases of the Liver and Digestive Tract

Inflammatory Bowel Diseases (IBD) Eugeni Domènech Morral Josep Manyé Almero

Innate Immunity Maria Rosa Sarrias Fornés

Neurogastroenterology and Motility Pere Clavé Civit Omar Ortega Fernández

Translational Research in Hepatic Diseases *Rosa Maria Morillas Cunill Ramon Bartolí Solé*

Inflammatory Bowel Diseases (IBD)



Group leaders: Eugeni Domènech Morral, Josep Manyé Almero

Research lines

- Ageing and obesity in IBD
- Therapeutic efficacy and safety in IBD: Biological agents & JAK inhibitors
- Utility of fecal calprotectin in predicting IBD complications
- Epitranscriptomic biomarkers for ulcerative colitis corticorefractoriness and postoperative recurrence in Crohn's disease
- Development of cutting-edge therapies using acellular strategies targeting adipose tissue for Crohn's disease

Selected scientific publications

Cañete F, Vela E, Calafat M, Clèries M, Mañosa M, Domènech E. **Morbid obesity, a new sus**ceptibility factor for developing Inflammatory Bowel Disease. Results of a population-based study. *J Crohns Colitis.* 2022 Jan 21;16(1):56. DOI: <u>10.1093/ecco-jcc/jjab232.044</u>. Suau R, Pardina E, Domènech E, Lorén V, Manyé J. **The Complex Relationship Between Microbiota, Immune Response and Creeping Fat in Crohn's Disease.** *J Crohns Colitis.* 2022 Mar 14;16(3):472-489. DOI: <u>10.1093/ecco-jcc/jjab159.</u>

Rivière P, Bislenghi G, Vermeire S, Domènech E, Peyrin-Biroulet L, Laharie D, D'Hoore A, Ferrante M. **Postoperative Crohn's Disease Recurrence: Time to Adapt Endoscopic Recurrence Scores to the Leading Surgical Techniques.** *Clin Gastroenterol Hepatol.* 2022 Jun;20(6):1201-1204. DOI: <u>10.1016/j.cgh.2022.02.025.</u>

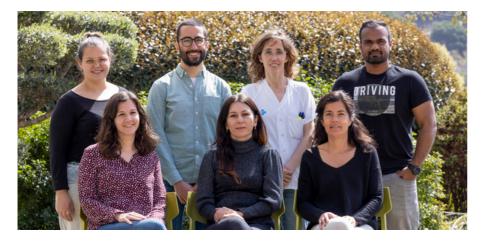
Summary of activities and highlights

Margalida Calafat received the Extraordinary Doctoral Award from the UAB for her thesis titled "Phenotype, natural history, utilization, and safety of healthcare resources in Inflammatory Bowel Disease among the elderly", successfully defended in 2020 under the direction of Miriam Mañosa.

Maria Puig was awarded the TALENT 2022 grant for the study titled "Correlation between mesenteric fat and the risk of post-operative recurrence in Crohn's disease", which was conducted with the guidance of Eugeni Domènech.

In 2023, the Miquel Angel Gassull international course on updating in IBD will reach its 30th edition. The group also promotes a course on basic-translational research in liver and digestive diseases of the Societat Catalana de Digestologia.

Innate Immunity



Selected scientific publications

Martori C, Sanchez-Moral L, Paul T, Pardo JC, Font A, Ruiz de Porras V, Sarrias MR. **Macrophages as a Therapeutic Target in Metastatic Prostate Cancer: A Way to Overcome Immunotherapy Resistance?** *Cancers (Basel)*. 2022 Jan 16;14(2):440. DOI: <u>10.3390/</u> <u>cancers14020440</u>.

Sánchez-Rodríguez MB, Téllez É, Casulleras M, Borràs FE, Arroyo V, Clària J, Sarrias MR. Reduced Plasma Extracellular Vesicle CD5L Content in Patients With Acute-On-Chronic Liver Failure: Interplay With Specialized Pro-Resolving Lipid Mediators. *Front Immunol.* 2022 Mar 7;13:842996. DOI: <u>10.3389/fimmu.2022.842996</u>.

Group leader: Maria Rosa Sarrias Fornés

Research lines

- Role of innate immunity in liver disease
- Novel cancer immunotherapy strategy targeting macrophages
- Role of macrophage protein CD5L in infection, with a focus on *Mycobacterium tuberculosis*

Neurogastroenterology and Motility



Group leaders: Pere Clavé Civit, Omar Ortega Fernández

Research lines

- Oropharyngeal dysphagia, pathophysiology, neurophysiology and new treatments
- Oropharyngeal dysphagia, complications and compensatory interventions
- TRP receptors and pharmacological treatment of oropharyngeal dysphagia
- Neurorehabilitation, rTMS, tDCS, neuroplasticity
- Gastro-oesophageal motility
- Basic studies
- Digestive and anorectal motility disorders
- Pelvic floor pathology

Selected scientific publications

Viñas P, Bolivar-Prados M, Tomsen N, Costa A, Marin S, Riera SA, Barcons N, Clavé P. **The Hydration Status of Adult Patients with Oropharyngeal Dysphagia and the Effect of Thickened Fluid Therapy on Fluid Intake and Hydration: Results of Two Parallel Systematic and Scoping Reviews.** *Nutrients.* 2022 Jun 16;14(12):2497. DOI: <u>10.3390/</u> nu14122497.

Tomsen N, Ortega O, Alvarez-Berdugo D, Rofes L, Clavé P. A Comparative Study on the Effect of Acute Pharyngeal Stimulation with TRP Agonists on the Biomechanics and Neurophysiology of Swallow Response in Patients with Oropharyngeal Dysphagia. *Int J Mol Sci.* 2022 Sep 15;23(18):10773. DOI: <u>10.3390/ijms231810773</u>.

Viñas P, Martín-Martínez A, Alarcón C, Riera SA, Miró J, Amadó C, Clavé P, Ortega O. **A Comparative Study between the Three Waves of the Pandemic on the Prevalence of Oropharyngeal Dysphagia and Malnutrition among Hospitalized Patients with COVID-19.** *Nutrients.* 2022 Sep 16;14(18):3826. DOI: <u>10.3390/nu14183826.</u>

Summary of activities and highlights

In June, the group, in collaboration with ACMCB and CIBERehd, welcomed David Julius, the Nobel Laureate in Physiology or Medicine 2021. He delivered a CI-BER webinar to 300 attendees, in which he discussed his discovery, focusing on the use of natural TRP receptor agonists for the study of the molecular mechanisms of pain, and on his advances in the study of TRPA1 receptor and its role in perception of irritant substances and neurogenic inflammation. Pere Clavé also shared insights about his experience employing TRP receptors as therapeutic targets for active sensory treatment of patients with oropharyngeal dysphagia (OD). Following this, David Julius addressed Acadèmia de Ciències Mèdiques i de la Salut de Catalunya i Balears (Academy of Medical and Health Sciences of Catalonia and the Balearic Islands, ACMCB) on the clinical applications of TRP receptors, particularly in pain management. On the subsequent day, the research group hosted a scientific meeting with David Julius at the Hospital de Mataró, discussing their research line on using TRP receptors for OD treatment.

In another major achievement, the group founded, developed and created the first startup of the Fundació Salut del Consorci Sanitari del Maresme - Artificial Intelligence Massive Screening-Medical SL (AIMS-Medical). This startup aims to develop cutting-edge technologies that empower medical professionals to improve diagnosis and manage age-related illnesses such as OD or malnutrition. The team created an expert system for the automatic screening of OD in hospitalized patients, which is operational in the Hospital de Mataró and is being extended to ten additional Catalan hospitals.

Furthermore, they designed and implemented texture-modified diets (TMD) at the Hospital de Mataró wards. These TMDs, developed in their Rheology and Texture Lab, are based on the Mediterranean diet and are tailored for patients with OD. They ensure safe and effective feeding, meeting all caloric and protein requirements, and have organoleptic adaptations to enhance intake. These diets are now offered daily to OD patients at the hospital, with high acceptance rates. This accomplishment is part of the <u>Territorial Competitive-ness Specialization Project (PECT)</u> of Mataró-Maresme.



Translational Research in Hepatic Diseases

Group leaders: Rosa Maria Morillas Cunill, Ramon Bartolí Solé

Research lines

- Chronic hepatitis
- Metabolic associated fatty liver disease (MAFLD)
- Cirrhosis and its complications

Selected scientific publications

Bartoli R, Iborra I, Barbosa S, Dolade M, Fortuny M, Masnou H, Morillas, RM. **Fecal microbiota trasplant using endoscopic-placement hydrogel reduces liver fibrosis with no changes in steatosis in a rat model of steatohepatitis with fibrosis.** *Journal of Hepatology.* 2022 Jul 1. <u>Poster</u> Sanchez R, Villanueva C, Genesca J, Garcia JC, Brujats A, Calleja JL, Aracil C, Banares R, Morillas RM, Poca M, Penas B, Augustin S, Abraldes J, Alvarado E, Torres F, Bosch J, Albillos A. **Worsening of low-grade systemic inflammation heralds decompensation in patients with compensated cirrhosis.** *Journal of Hepatology.* 2022 Jul 1. <u>Poster</u>

Ampuero J, Lucena A, Hernández-Guerra M, Moreno-Moraleda I, Arenas J, Conde I, Muñoz L, Canillas L, Fernandez E, Quiñones R, Simon MA, Gómez-Dominguez E, Gutierrez ML, Fernandez-Rodriguez C, Domper-Arnal MJ, Jorquera F, Garcia-Buey ML, Garcia-Retortillo M, Morillas R, Berenguer M, Casado M, Morales-Arraez D, Sousa JM, Molina E. **Primary biliary cholangitis and SARS-CoV-2 infection: incidence, susceptibility and outcomes.** *Gut.* 2022 Sep 7;71: 2138-2140. DOI: <u>10.1136/gutjnl-2021-325700</u>.

Summary of activities and highlights

The group established a new line of basic-translational research focusing on utilising the platform developed by its researchers, COVERGEL, for altering the intestinal microbiota in the treatment of fatty liver disease with fibrosis.

Endocrine and Diseases of the Metabolism, Bones and Kidneys

Diabetes Research Group Núria Alonso Pedrol

Endocrine, Thyroid and Obesity *Manel Puig Domingo*

Innovation in Vesicles and Cells for Application in Therapy (IVECAT) Francesc Enric Borràs Serres Marcel·la Franquesa Bartolomé

Kidney affecting diseases (REMAR) Marcel·la Franquesa Bartolomé Jordi Bover Sanjuán

Research Group on Sarcopenia, Frailty and Dependency (GRESFD) Mateu Serra Prat

Diabetes Research Group

Group leader: Núria Alonso Pedrol

Research lines

- · Study of atherosclerosis and other complications associated with diabetes
- Epidemiological studies of diabetes: studies with real-life practice databases

Selected scientific publications

Domingo MM, Teis A, Alonso N, Julian T, Bares D, Barcelo E, Revuelta-Lopez E, Gonzalez B, Codina P, Cediel G, Santiago-Vacas E, Santesmases J, Zamora E, Lupon J, Bayes-Genis A. Effect of diuretic down-titration on pulmonary congestion assessed by lung ultrasound when introducing sodium-glucose cotransporter 2 inhibitors. *European Heart Journal*. 2022 Oct. 43(2). DOI: 10.1093/eurheartj/ehac544.951

Domingo MM, Teis A, Alonso N, Julian T, Bares D, Barcelo E, Revuelta-Lopez E, Gonzalez B, Codina P, Cediel G, Santiago-Vacas E, Santesmases J, Zamora E, Lupon J, Bayes-Genis A. **No harmful effect of diuretic down-titration on pulmonary congestion when introducing sodium-glucose cotransporter 2 inhibitors**. *European Journal of Heart Failure*. 2022 Jul. 24.

Castelblanco E, Hernández M, Alonso N, Ribes-Betriu A, Real J, Granado-Casas M, Rossell J, Rojo-Lopez MI, Dusso AS, Julve J, Mauricio D. **Association of α-klotho with subclinical carotid atherosclerosis in subjects with type 1 diabetes mellitus.** *Cardiovasc Diabetol.* 2022 Oct. 21, 207. DOI: <u>10.1186/s12933-022-01640-3</u>

Endocrine, Thyroid and Obesity



Group leader: Manel Puig Domingo

Research lines

- Molecular phenotyping of pituitary tumors and its application to personalised medicine
- Thyroid pathology
- Obesity

Selected scientific publications

Soldevila B, Puig-Domingo M, Marazuela M. Basic mechanisms of SARS-CoV-2 infection. What endocrine systems could be implicated? *Rev Endocr Metab Disord*. 2022 Apr. 23(2):137-150. DOI: <u>10.1007/s11154-021-09678-6</u>

Ramos A, Joaquin C, Ros M, Martin M, Cachero M, Sospedra M, Martínez E, Sánchez Migallón JM, Sendrós MJ, Soldevila B, Puig-Domingo M. **Impact of COVID-19 on nutritional status during the first wave of the pandemic.** *Clin Nutr.* 2022 Dec. 41(12):3032-3037. DOI: <u>10.1016/j.clnu.2021.05.001</u>

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.* 2022 Jan. 75(1):22-30. DOI: <u>10.1016/j.</u> rec.2021.02.006

Innovation in Vesicles and Cells for Application in Therapy (IVECAT)



Group leaders: Francesc Enric Borràs Serres, Marcel·la Franquesa Bartolomé

Research lines

- Development of new strategies for the improvement in the objective diagnosis of diseases/pathologies (Biomarkers)
- Research in the field of preventive and therapeutic cell & "Cell-free" advanced therapies for immunomodulation and regenerative medicine (Advanced Therapies)

Selected scientific publications

Monguió-Tortajada M, Prat-Vidal C, Martínez-Falguera D, Teis A, Soler-Botija C, Courageux Y, Munizaga-Larroudé M, Moron-Font M, Bayes-Genis A, Borràs FE, Roura S, Gálvez-Montón C. Acellular cardiac scaffolds enriched with MSC-derived extracellular vesicles limit ventricular remodelling and exert local and systemic immunomodulation in a myocardial infarction porcine model. *Theranostics*. 2022 Jun 6;12(10):4656-4670. DOI: <u>10.7150/thno.72289</u>.

Sánchez-Rodríguez MB, Téllez É, Casulleras M, Borràs FE, Arroyo V, Clària J, Sarrias MR. Reduced Plasma Extracellular Vesicle CD5L Content in Patients With Acute-On-Chronic Liver Failure: Interplay With Specialized Pro-Resolving Lipid Mediators. *Front Immunol.* 2022 Mar 7;13:842996. DOI: <u>10.3389/fimmu.2022.842996</u>.

Sánchez-Rodríguez MB, Téllez É, Casulleras M, Borràs FE, Arroyo V, Clària J, Sarrias MR. **Reduced Plasma Extracellular Vesicle CD5L Content in Patients With Acute-On-Chronic Liver Failure: Interplay With Specialized Pro-Resolving Lipid Mediators**. *Journal of Hepatology*. 2022 Jul;77(1):361. DOI: <u>10.1016/S0168-8278(22)01077-7</u>.

Kidney affecting diseases (REMAR)



Group leaders: Marcel·la Franquesa Bartolomé, Jordi Bover Sanjuán

Research lines

- Non-invasive biomarkers for kidney diseases
- Morbid obesity and renal disease
- Mesenchymal stem cells in kidney transplant
- Peritoneal dialysis

Selected scientific publications

Sánchez-Rodríguez MB, Téllez É, Casulleras M, Borràs FE, Arroyo V, Clària J, Sarrias MR. **Reduced Plasma Extracellular Vesicle CD5L Content in Patients With Acute-On-Chronic Liver Failure: Interplay With Specialized Pro-Resolving Lipid Mediators**. *Journal of Hepatology*. 2022 Jul;77(1):361. DOI: <u>10.1016/S0168-8278(22)01077-7</u>.

Monguió-Tortajada M, Prat-Vidal C, Martínez-Falguera D, Teis A, Soler-Botija C, Courageux Y, Munizaga-Larroudé M, Moron-Font M, Bayes-Genis A, Borràs FE, Roura S, Gálvez-Montón C. Acellular cardiac scaffolds enriched with MSC-derived extracellular vesicles limit ventricular remodelling and exert local and systemic immunomodulation in a myocardial infarction porcine model. *Theranostics*. 2022 Jun 6;12(10):4656-4670. DOI: <u>10.7150/thno.72289</u>.

Sánchez-Rodríguez MB, Téllez É, Casulleras M, Borràs FE, Arroyo V, Clària J, Sarrias MR. **Reduced Plasma Extracellular Vesicle CD5L Content in Patients With Acute-On-Chronic Liver Failure: Interplay With Specialized Pro-Resolving Lipid Mediators.** *Front Immunol.* 2022 Mar 7;13:842996. DOI: <u>10.3389/fimmu.2022.842996.</u>

Research Group on Sarcopenia, Frailty and Dependency (GRESFD)



Group leader: Mateu Serra Prat

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Research lines

- Evaluation of the pathophysiology and risk factors of sarcopenia, frailty and functional decline in the elderly
- Evaluation of the effectiveness and safety of multimodal interventions aimed at preventing and/or reversing frailty and disability in the elderly
- Assessment of the impact of frailty on the health and quality of life and assessment of the economic impact of frailty
- Development and validation of electronic and automatic instruments for mass screening of frailty and/or disability to generate information at population level useful for health planning and management

Selected scientific publications

Oyon J, Serra-Prat M, Limon E, Ferrer M, Pastor N, Palomera E, Burdoy E. **Depressive** symptom severity is a major risk factor for frailty in community-dwelling older adults with depression. A prospective study. *Fam Pract.* 2022 Sep 24;39(5):875-882. DOI: 10.1093/fampra/cmab174.

Serra-Prat M, Lavado À, Cabré M, Burdoy E, Palomera E, Papiol M, Parera JM. *Develop-ment and validation of the electronic screening index of frailty. Age Ageing.* 2022 Jul 1;51(7):afac161. DOI: <u>10.1093/ageing/afac161</u>.

Pleguezuelos E, Del Carmen A, Moreno E, Ortega P, Robles A, Serra-Prat M, Miravitlles M, Yebenes JC, Garnacho-Castaño MV. **Impaired pulmonary and muscle function during moderate exercise in female patients recovered from SARS-CoV-2.** *Sci Rep.* 2022 Dec 4;12(1):20943. DOI: <u>10.1038/s41598-022-24941-9</u>.

Summary of activities and highlights

The GRESFD created the Frailty and Dependence Observatory with the objective of providing a comprehensive and quantitative view on the demographic, epidemiological, geographical, and socioeconomic characteristics of frailty and dependency in Catalonia. The primary aim is to generate pertinent scientific knowledge that aids in planning and decision-making processes associated with frailty and dependency. This knowledge is disseminated not only within the scientific community through scientific reports, publications, international communications, and doctoral theses, but also to the wider public through news in the media and succinct reports and publications available on the Observatory's website.

Immunology and Inflammation

Immunology of Diabetes Marta Vives Pi

Immunopathology Eva M^a Martínez Cáceres

Immunology of Diabetes



Group leader: Marta Vives Pi

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Research lines

- · Immunotherapies for the prevention and treatment of autoimmune diseases
- Pathogenic mechanisms of autoimmunity in type 1 diabetes
- Paediatric type 1 diabetes: tolerance, spontaneous remission and biomarkers

Selected scientific publications

Gomez-Muñoz L, Perna-Barrull D, Caroz-Armayones JM, Murillo M, Rodriguez-Fernandez S, Valls A, Vazquez F, Perez J, Corripio R, Castaño L, Bel J, Vives-Pi M. **Candidate Biomarkers for the Prediction and Monitoring of Partial Remission in Pediatric Type 1 Diabetes.** *Front Immunol.* 2022 Feb 23;13:825426. DOI: <u>10.3389/</u> fimmu.2022.825426.

Perna-Barrull D, Gomez-Muñoz L, Rodriguez-Fernandez S, Gieras A, Ampudia-Carrasco RM, Almenara-Fuentes L, Risueño RM, Querol S, Tolosa E, Vives-Pi M. **Impact of Betamethasone Pretreatment on Engrafment of Cord Blood-Derived Hematopoietic Stem Cells.** *Arch Immunol Ther Exp (Warsz).* 2022 Dec 18;71(1):1. DOI: <u>10.1007/</u> <u>s00005-022-00666-5.</u>

Almenara-Fuentes L, Rodriguez-Fernandez S, Rosell-Mases E, Kachler K, You A, Salvado M, Andreev D, Steffen U, Bang H, Bozec A, Schett G, Le Panse R, Verdaguer J, Dalmases M, Rodriguez-Vidal S, Barneda-Zahonero B, Vives-Pi M. **A new platform for autoimmune diseases. Inducing tolerance with liposomes encapsulating autoantigens.** *Nanomedicine.* 2022 5 Dec;48:102635. DOI: <u>10.1016/j.nano.2022.102635</u>.

Summary of activities and highlights

The Immunology of Diabetes group, based in the Immunology Department of the Germans Trias i Pujol University Hospital, was founded in 2000 with the aim to elucidate the mechanisms of autoimmunity in type 1 diabetes, and to contribute to find a cure for this and many other autoimmune diseases.

Throughout 2022, the group worked on six research projects funded by both national and international agencies. The research focused on three main lines: 1) immunotherapies for type 1 diabetes and other autoimmune diseases; 2) new biomarkers of early stages in type 1 diabetes; 3) pathogenic mechanisms of autoimmunity. The work is reflected in various original articles, scientific communications in national and international meetings and dissemination activities.

The team is part of the Consolidated Research Group 2021 SGR 00002, recognised by AGAUR – Generalitat de Catalunya, coordinated by Marta Vives-Pi. In terms of innovation, the group continued to encourage the growth of its spinoff, <u>Ahead Therapeutics SL</u>. The company, founded in 2017, has developed an innovative solution based on the use of liposomes containing autoantigens. Through a biomimetic process, these liposomes can induce antigen-specific immune tolerance, thereby interrupting the autoimmune reaction. In 2022 major progress has been made in the field of type 1 diabetes, myasthenia gravis, and rheumatoid arthritis.

Immunopathology



Group leader: Eva M^a Martínez Cáceres

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Research lines

- Innovation and diagnostic immunology
- Clinical epidemiology research
- Immune therapies inducing tolerance
- Neuroimmunology: cellular tolerance therapy in multiple sclerosis

Selected scientific publications

Zurera C, Hernandez A, Teniente A, Fuster D, Martinez EM, Muga R, Zuluaga YP. **Phenotypes of NK cells and the activation profile of T cells in the early stages of alcohol liver diseases.** *Journal of Hepatology.* 2022 Jul. 77. DOI: <u>10.1016/S0168-8278(22)00772-3</u>

Morante-Palacios O, Godoy-Tena G, Calafell-Segura J, Ciudad L, Martínez-Cáceres EM, Sardina JL, Ballestar E. **Vitamin C enhances NF-κB-driven epigenomic reprogramming and boosts the immunogenic properties of dendritic cells.** *Nucleic Acids Res.* 2022 Oct. 28;50(19). DOI: <u>10.1093/nar/gkac941</u>.

Català-Moll F, Ferreté-Bonastre AG, Godoy-Tena G, Morante-Palacios O, Ciudad L, Barberà L, Fondelli F, Martínez-Cáceres EM, Rodríguez-Ubreva J, Li T, Ballestar E. **Vitamin D receptor, STAT3, and TET2 cooperate to establish tolerogenesis.** *Cell Rep.* 2022 Jan. 18;38(3). DOI: <u>10.1016/j.celrep.2021.110244</u>

Infectious Diseases

Clinical and Environmental Infectious Diseases (CEID) Maria Luisa Pedro Botet

Clinical and Experimental Microbiology *Pere Joan Cardona Iglesias*

Experimental Tuberculosis Unit (UTE) *Cristina Vilaplana Massaguer*

Innovation in Respiratory Infections and Tuberculosis Diagnosis José Domínguez Benítez Cristina Prat Aymerich

Pathogen Diagnostics and Genomic Epidemiology Elisa Martró Català

Plasmodium vivax and Exosome Research (PvREX) Hernando A. Del Portillo Carmen Fernández Becerra

Clinical and Environmental Infectious Diseases (CEID)



Group leader: Maria Luisa Pedro Botet

Research lines

- Infectious endocarditis
- Primary immunodeficiencies
- One Health
- Legionella
- Nosocomial infections
- Emerging infectious diseases
- New antibacterial treatments

Selected scientific publications

Roure S, Pérez-Quílez O, Vallès X, Valerio L, López-Muñoz I, Soldevila L, Torrella A, Fernández-Rivas G, Chamorro A, Clotet B. **Schistosomiasis Among Female Migrants in Non-endemic Countries: Neglected Among the Neglected? A Pilot Study.** *Front Public Health.* 2022 Mar 9;10:778110. DOI: <u>10.3389/fpubh.2022.778110.</u>

Vallejo Camazón N, Teis A, Martínez Membrive MJ, Llibre C, Bayés-Genís A, Mateu L. **COVID-19 persistente y angina microvascular [Long COVID-19 and microvascular disease-related angina].** *Rev Esp Cardiol.* 2022 May;75(5):444-446. DOI: <u>10.1016/j.reccesp.2021.10.011</u>.

Ainsua-Enrich E, Pedreño-Lopez N, Bracke C, Ávila-Nieto C, Rodríguez de la Concepción ML, Pradenas E, Trinité B, Marfil S, Miranda C, González S, Toledo R, Font M, Benet S, Escribà T, Jimenez-Moyano E, Peña R, Cedeño S, Prado JG, Mothe B, Brander C, Izquierdo-Useros N, Vergara-Alert J, Segalés J, Massanella M, Benitez RM, Romero A, Molina-Morant D, Blanco J, Clotet B, Mateu L, Pedro-Botet ML, Carrillo J. **Kinetics of immune responses elicited after three mRNA COVID-19 vaccine doses in predominantly antibody-deficient individuals.** *iScience*. 2022 Nov 18;25(11):105455. DOI: 10.1016/j.isci.2022.105455.

Summary of activities and highlights

The Legionellosis Study Group, or GELeg, consolidated its position as a reference research group for the study of Legionella cases and outbreaks in Catalonia. More information.

Clinical and Experimental Microbiology



Group leader: Pere Joan Cardona Iglesias

Research lines

- Virology
- Mycobacteriology
- Sexually Transmitted Infections (STIs)
- Invasive infections
- Co-infection
- Antibiotic multi-resistance

Selected scientific publications

Fernández-Rivas G, Barallat J, Gonzalez V, Martinez S, Bordoy AE, Jimenez L, Casañ C, Blanco I. **Analytical Performance of Quantitative DiaSorin Liaison SARS-COV-2 Antigen Test for the Asymptomatic Population.** *Front Public Health.* 2022 Jan 7;9:788581. DOI: <u>10.3389/fpubh.2021.788581.</u>

Fernández-Rivas G, Barallat J, Quirant-Sánchez B, González V, Doladé M, Martinez-Caceres E, Piña M, Matllo J, Blanco I, Cardona PJ. **Follow up of the Humoral Response in Healthcare Workers after the Administration of Two Dose of the Anti SARS-CoV-2 Vaccines-Effectiveness in Delta Variant Breakthrough Infections.** *Viruses.* 2022 Jun 24;14(7):1385. DOI: <u>10.3390/v14071385</u>.

Català M, Coma E, Alonso S, Andrés C, Blanco I, Antón A, Bordoy AE, Cardona PJ, Fina F, Martró E, Medina M, Mora N, Saludes V, Prats C, Prieto-Alhambra D, Alvarez-Lacalle E. **Transmissibility, hospitalization, and intensive care admissions due to omicron compared to delta variants of SARS-CoV-2 in Catalonia: A cohort study and ecological analysis.** *Front Public Health.* 2022 Aug 12;10:961030. DOI: 10.3389/fpu-bh.2022.961030.

Experimental Tuberculosis Unit (UTE)



Group leader: Cristina Vilaplana Massaguer

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Research lines

- Study of biomarkers and tools for monitoring TB disease course and prognosis
- Evaluation of new prophylactic and therapeutic strategies against TB
- Study of health dimensions and quality of life in the context of infectious diseases

Selected scientific publications

Melkie ST, Arias L, Farroni C, Jankovic Makek M, Goletti D, Vilaplana C. **The role of antibodies in tuberculosis diagnosis, prophylaxis and therapy: a review from the ESGMYC study group.** *Eur Respir Rev.* 2022 Mar 9;31(163):210218. DOI: <u>10.1183/16000617.0218-</u> 2021. Soldevilla P, Vilaplana C, Cardona PJ. **Mouse Models for Mycobacterium tuberculosis Pathogenesis: Show and Do Not Tell**. *Pathogens*. 2022 Dec 28;12(1):49. DOI: <u>10.3390/</u> <u>pathogens12010049</u>.

Summary of activities and highlights

The year 2022 was a testament to UTE's unwavering dedication, tireless efforts, and steadfast commitment to excellence. The unit consistently invested in the upcoming generation of researchers as a cornerstone of their values. Marta Arch and Patricia Cuadras successfully defended their PhD theses, marking significant milestones in their academic journeys. The group also mentored and guided one master's student Tamta Kukhalashvili, from the University Claude Bernard Lyon.

The year also saw the welcome and hosting of three impactful secondments, fostering international collaborations and knowledge exchange. These partnerships not only enriched the research efforts but also catalysed the sharing of concepts, methodologies, and best practices. Additionally, the unit played a pivotal role in capacitating technicians from the PHRU laboratory in Soweto, South Africa, equipping them with new abilities and expertise.

Significant progress was made within the H2020-funded project <u>SMA-TB</u>. Surpassing 50% of the recruitment target for the multi-centre, multi-country clinical trial underscored the unit's capability to draw top-tier talent and reaffirmed the dedication to cutting-edge research in tandem with international partners.

Scientific activity in 2022 / Research areas, groups and programmes at the IGTP

A number of works were published, one of which was in collaboration with the European Society of Clinical Microbiology and Infectious Diseases.

The unit embarked on a groundbreaking initiative in collaboration with the Centre de Cultura Contemporània de Barcelona (CCCB) and LaSullivan. The Health Arts Science project aims to involve civil society in research and augment awareness on tuberculosis, with activities planned throughout 2023. Through this project, the unit demonstrates its commitment to community engagement and making research accessible to all.

Finally, the group received accreditation as a Consolidated Research Group by AGAUR (2021 SGR 00920). This accomplishment further solidifies the unit's position as leaders within its field.

Innovation in Respiratory Infections and Tuberculosis Diagnosis



Group leaders: José Domínguez Benítez, Cristina Prat Aymerich

Research lines

- Microbial interactions
- Immune response characterization
- Impact of external factors
- Diagnostic technology innovation
- New therapeutic approaches

Selected scientific publications

Wheatley, R.M., Caballero, J.D., van der Schalk, T.E. et al. **Gut to lung translocation and antibiotic mediated selection shape the dynamics of Pseudomonas aeruginosa in an ICU patient**. *Nat Commun 13*, 6523 (2022). DOI: <u>10.1038/s41467-022-34101-2</u>. Gomes-Fernandes M, Gomez AC, Bravo M, Huedo P, Coves X, Prat-Aymerich C, Gibert I, Lacoma A, Yero D. **Strain-specific interspecies interactions between co-isolated pairs of** *Staphylococcus aureus* **and** *Pseudomonas aeruginosa* **from patients with tracheobronchitis or bronchial colonization**. *Sci Rep*. 2022 Mar 1;12(1):3374. DOI:10.1038/s41598-022-07018-5.

Díaz-Fernández S, Villar-Hernández R, Stojanovic Z, Fernández M, Galvão MLS, Tolosa G, Sánchez-Montalva A, Abad J, Jiménez-Fuentes MÁ, Safont G, Romero I, Sabrià J, Prat C, Domínguez J, Latorre I. **Study of CD27, CD38, HLA-DR and Ki-67 immune profiles for the characterization of active tuberculosis, latent infection and end of treatment.** *Front Microbiol.* 2022 Jul 22;13:885312. DOI: <u>10.3389/fmicb.2022.885312</u>.

Summary of activities and highlights

The group published 12 papers in international peer-review journals, most of them being in collaboration with national and international partners. The AD-VANCE-TB consortium was granted with a COST Action in June, with the main objective of improving diagnostics and treatment strategies for tuberculosis (TB) control. The consortium, where Alícia Lacoma is the chairperson, is currently constituted by 120 members from 37 countries.

In the field of technology transfer, the group licensed a patent for an *in vitro* diagnostic algorithm that differentiates between latent and active TB. The patent was created in a collaboration between IGTP, UB, and Fundació Univ. Mútua de Terrassa and has been licensed to the diagnostic company UNIMA.

The group organised the annual TBnet Meeting at IGTP in September. The event had over 80 in-person attendees and more than 100 participants streaming online. TBnet is a scientific network dedicated to promoting clinically oriented TB research in Europe, an initiative of which José Dominguez is a Steering Committee member.

In another accomplishment, Alicia Lacoma was elected as the Scientific Officer of the Executive Committee of the ESCMID Study Group of Staphylococci and Staphylococcal Diseases during the last European Congress of Clinical Microbiology and Infectious Diseases held in Lisbon, Portugal.

The group also initiated a new research line led by Irene Latorre, focusing on the systemic and local immune-response to Mycobacterium tuberculosis. This research required the creation of various mouse models to replicate active and latent TB infection, undertaken in close collaboration with the Experimental Tuberculosis Unit Group and the CMCIB staff.

Finally, the group leads the EU project INNOVA4TB, which involves 16 partners from 6 countries, contributing to research and training in the tuberculosis field. During the crisis caused by Russian attacks on the Ukrainian electrical system, the group organised an international fundraising action in partnership with TBnet to provide a generator to supply power to the microbiology laboratory at the Centre for Socially Significant Diseases, an INNOVA4TB partner in Ukraine. This centre is the main regional TB/HIV managing facility and leads TB/HIV management in a region with 2 million of people and 100,000 internally-displaced people.

Pathogen Diagnostics and Genomic Epidemiology



Group leader: Elisa Martró Català

Research lines

- Viral hepatitis
- Molecular diagnostics and genomic epidemiology of other infectious diseases

Selected scientific publications

Wang-Wang JH, Bordoy AE, Martró E, Quesada MD, Pérez-Vázquez M, Guerrero-Murillo M, Tiburcio A, Navarro M, Castellà L, Sopena N, Casas I, Saludes V, Giménez M, Cardona PJ. **Evaluation of Fourier Transform Infrared Spectroscopy as a First-Line Typing Tool for the Identification of Extended-Spectrum β-Lactamase-Producing** *Klebsiella pneumoniae* **Outbreaks in the Hospital Setting.** *Front Microbiol.* 2022 Jun 9;13:897161. DOI: 10.3389/fmicb.2022.897161. Martró E, Ouaarab H, Saludes V, Buti M, Treviño B, Roade L, Egea-Cortés L, Reyes-Ureña J, Not A, Majó X, Colom J, Gómez I Prat J; HepClink Study Group. **Pilot hepatitis C micro-elimination strategy in Pakistani migrants in Catalonia through a community intervention.** *Liver Int.* 2022 Aug;42(8):1751-1761. DOI: <u>10.1111/liv.15327</u>.

Catlett B, Hajarizadeh B, Cunningham E, Wolfson-Stofko B, Wheeler A, Khandaker-Hussain B, Feld JJ, Martró E, Chevaliez S, Pawlotsky JM, Bharat C, Cunningham PH, Dore GJ, Applegate T, Grebely J. **Diagnostic Accuracy of Assays Using Point-of-Care Testing or Dried Blood Spot Samples for the Determination of Hepatitis C Virus RNA: A Systematic Review.** *J Infect Dis.* 2022 Sep 21;226(6):1005-1021. DOI: <u>10.1093/infdis/jiac049</u>.

Summary of activities and highlights

The group has been promoting hepatitis C virus (HCV) micro-elimination in vulnerable populations, by decentralizing diagnostics and facilitating access to care and treatment. We have validated new simplified diagnostic strategies (dried blood spots and point-of-care tests) in comparison with the standard of care both in the laboratory and in the field. In multidisciplinary collaborations with other groups, CEEISCAT, civil society and the Public Health Agency of Catalonia (ASPCAT), Martró has led pioneering new models of care that have also contributed to the characterization of the local HCV epidemiology in men who have sex with men, people who inject drugs (PWID), people entering prisons, and migrants from endemic countries. Acute infection, transmission networks, and the cascade of care have been characterized in PWID in Catalonia. This research line has led to a new PhD initiation (PFIS grant), a Doctoral Thesis de-

fended in 2022, and the direct involvement of Martró in the "Plan for the Prevention and Control of Hepatitis C in Catalonia" (ASPCAT).

The group specializes in genomic epidemiology and surveillance of several relevant pathogens. Firstly, we have been immersed in SARS-CoV-2 sequencing throughout the COVID-19 pandemic; sequencing data has been translated into meaningful information through directly reporting to the Hospital's Nosocomial Infection Control team and regional Epidemiological Surveillance services. This work has led to two master's theses, a new PhD student and a new bioinformatician involved in a project funded by Fundació La Marató de TV3. This has also allowed us to implement nanopore-based sequencing in the Microbiology Service for rapid diagnosis of bacterial infections by full 16S rRNA gene sequencing from clinical samples. Secondly, the group hosted a postdoctoral "Margarita Salas" researcher involved in the application of metagenomic sequencing to clinical samples for virome studies, leading to the confirmation of the first case of Mpox in Catalonia (and the first Monkeypox virus genome published in Spain). Thirdly, we have performed genomic epidemiology studies of multi-drug resistant bacteria involved in nosocomial outbreaks. Finally, E. Martró is leading a multicentre, genomic epidemiology study of Mycobacterium tuberculosis complex (MTBC) strains in Catalonia and is working towards the integration of genomic sequencing within tuberculosis control activities through an agreement of the Microbiology Department with ASPCAT.

Plasmodium vivax and Exosome Research (PvREX)



Group leaders: Hernando A. Del Portillo, Carmen Fernández Becerra

Research lines

- Exosome-mediated mechanisms of non-hypnozoite cryptic infections in P. vivax malaria
- Reticulocyte-derived exosomes (Rex) vaccines against P. vivax
- Hypnozoite biomarker discovery
- Functional analysis of subtelomeric variant genes
- Extracellular vesicles (EVs) as potential new biomarkers in parasitic infections

Selected scientific publications

Aparici-Herraiz I, Gualdrón-López M, Castro-Cavadía CJ, Carmona-Fonseca J, Yasnot MF, Fernandez-Becerra C, Del Portillo HA. **Antigen Discovery in Circulating Extrace**-

Ilular Vesicles From *Plasmodium vivax* **Patients.** *Front Cell Infect Microbiol.* 2022 Jan 24;11:811390. DOI: <u>10.3389/fcimb.2021.811390.</u>

Brito MAM, Baro B, Raiol TC, Ayllon-Hermida A, Safe IP, Deroost K, Figueiredo EFG, Costa AG, Armengol MDP, Sumoy L, Almeida ACG, Hounkpe BW, De Paula EV, Fernandez-Becerra C, Monteiro WM, Del Portillo HA, Lacerda MVG. **Morphological and Transcriptional Changes in Human Bone Marrow During Natural** *Plasmodium vivax* **Malaria Infections.** *J Infect Dis.* 2022 Apr 1;225(7):1274-1283. DOI: 10.1093/infdis/jiaa177.

Gualdrón-López M, Díaz-Varela M, Zanghi G, Aparici-Herraiz I, Steel RWJ, Schäfer C, Cuscó P, Chuenchob V, Kangwangransan N, Billman ZP, Olsen TM, González JR, Roobsoong W, Sattabongkot J, Murphy SC, Mikolajczak SA, Borràs E, Sabidó E, Fernandez-Becerra C, Flannery EL, Kappe SHI, Del Portillo HA. **Mass Spectrometry Identification of Biomarkers in Extracellular Vesicles From** *Plasmodium vivax* **Liver Hypnozoite Infections.** *Mol Cell Proteomics***. 2022 Oct;21(10):100406. DOI: <u>10.1016/j.mcpro.2022.100406</u>.**

Summary of activities and highlights

The group continued to make progress in its main Research lines.

Exosome-mediated mechanisms of non-hypnozoite cryptic infections in *P. vi-vax* malaria: Strong support of non-hypnozoite cryptic infections, mainly in the spleen and bone marrow, was publishe d. Noticeably, extracellular vesicles in the size range of exosomes obtained from human patients facilitated binding to the human spleen. The group thus hypothesizes that EVs, specifically reticulo-cyte-derived exosomes, from *P. vivax* infections mediate bone marrow defects on erythropoiesis and spleen extramedullary erythropoiesis facilitating cryptic infections likely responsible for asymptomatic transmission. As this species cannot be continuously cultured *in vitro*, proving this hypothesis represents a major technical challenge. Two different approaches implementing new human scien-

ce technological frontiers are being pursued, organs-on-a-chip and humanized mouse models of these human organs, thus facilitating to stringently test the role of exosomes as intercellular communicators in a space and velocity that will facilitate their uptake by cells in these hemopoietic tissues.

Functional analysis of subtelomeric variant genes: As infected reticulocytes with mature developmental stages of *P. vivax* are detected in the peripheral circulation, it has been amply accepted that there is no cytoadherence, hence no sequestration in this species. Against this dogma, this group identified the largest subtelomeric multigene family of human malaria parasites, the vir multigene family with expressed VIR proteins, likely involved in vivax pathology through cytoadherence of (pRetics). Proof-of-principle of vivax pRetics cytoadherence partly mediated by VIR proteins was later demonstrated in vitro using endothelial, placental and brain cells, and more recently the team demonstrated that a *P. falciparum* transgenic line expressing a VIR protein was able to cytoadhere to human spleen fibroblasts. They are performing functional binding assay of variant surface proteins using CRIS-PR/cas-9 technologies to produce new transgenic lines of *P. falciparum*.

Reticulocyte-derived exosomes (Rex) vaccines against *P. vivax*: T-cell responses were believed not to play a major role in natural immunity against blood stages of malaria as *P. falciparum*, the most virulent human malaria parasite, predominantly invades mature red blood cells which lack antigen presenting machinery. However, a PvREX study demonstrated that reticulocyte exosomes contain HLA Class I antigens actively up taken by dendritic cells and that circulating extracellular vesicles directly obtained from patients contained novel parasite antigens 4. These results support further studies of reticulocyte exosomes from vivax infections to discover new antigens for vaccination and of human reticulocyte exosomes as a potential vaccine delivery platform for eliciting cytotoxic T-cell responses against vivax malaria.

Hypnozoite biomarker discovery: The group is using human liver-chimeric FRG-KO-(huHep) mice treated with schizonticidal drugs to determine the proteome composition of plasma-derived exosomes from animals exclusively infected with *P. vivax* hypnozoites. Moreover, PvREX's previous proteome analysis showed the presence of unique human proteins that are presently being used to highly enriched exclusively for exosomes coming from human hepatocytes; thus, increasing the signal for biomarker discovery. The team will produce 3-5 unique parasite proteins and monoclonal antibodies against them to facilitate the construction of microfluidic devices with the ultimate goal of developing POC diagnostic device easily deployable in the field to contribute to the elimination of vivax malaria.

Extracellular vesicles (EVs) as potential new biomarkers in parasitic infections: The fact that EVs have been found in most biological fluids makes them an important target for the identification of new biomarkers in parasitic infections. In Chagas disease, the group is exploring EVs for identifying novel biomarkers specifically in the context of therapeutic response and disease progression during the chronic phase of the disease. In the field of Leishmaniasis, PvREX has recently started a collaborative project, planned to characterize EVs recovered from plasma in different clinical groups of human leishmaniasis (symptomatic, asymptomatic, treated). In parallel, the team also intends to evaluate the potential of extracellular vesicles as biomarkers for canine leishmaniasis. More recently, the group has started a new collaborative project to identifying EV-Biomarkers in the context of severe *P. falciparum* malaria in children.

Neuroscience

Cellular and Molecular Neurobiology (CMN) *Teresa Gasull Dalmau Octavi Martí Sistac*

Genomics and Transcriptomics of Synucleinopathies Katrin Beyer

Group of Research in Neuromuscular Diseases from Badalona (GRENBA) Gisela Nogales Gadea

Mental Health and Illness Cristanto Díez Quevedo Maria Iglesias González **Neurogenetics** Antoni Matilla Dueñas Ivelisse Sánchez Díaz

Neurovascular Research Group *Mònica Millán Torné Natalia Pérez de la Ossa Herrero*

Psychoneuroendocrinology and Stress in Psychosis (PSICPNEC) *Javier Labad Arias*

Cellular and Molecular Neurobiology (CMN)



Group leaders: Teresa Gasull Dalmau, Octavi Martí Sistac

Research lines

- · Novel glutamate-related targets for neuroprotection
- · Ferroptosis in neuronal death and antiferroptotic neuroprotective compounds
- Experimental modelling of stroke in rodents and swine
- Discovery of new biomarkers to improve stroke treatment
- Computational biology: machine/deep learning assessment of behaviour in in vivo stroke models

Selected scientific publications

Gasull T, Arboix A. Molecular Mechanisms and Pathophysiology of Acute Stroke: Emphasis on Biomarkers in the Different Stroke Subtypes. *Int J Mol Sci.* 2022 Aug 22;23(16):9476. DOI:<u>10.3390/ijms23169476</u>.

Faura J, Ramiro L, Simats A, Ma F, Penalba A, Gasull T, Rosell A, Montaner J, Bustamante A. **Evaluation and Characterization of Post-Stroke Lung Damage in a Murine Model of Cerebral Ischemia.** *Int J Mol Sci.* 2022 Jul 22;23(15):8093. DOI: <u>10.3390/ijms23158093</u>.

Summary of activities and highlights

Teresa Gasull made significant contributions to the field of neurointervention this year. She was invited to be a speaker at the "Society for Image Guided Neurointerventions' international congress, SIGN2022" (Warwick; 22-23 August). Her topic of discussion was "Neurointerventionism to Overcome Old Barriers to Model Stroke in Swine".

Additionally, Octavi Martí-Sistac received institutional recognition for good practice in higher education in 2022 by the Autonomous University of Barcelona (UAB). This recognition was related to his initiative titled 'Academic Cryptocurrency to Reinforce the Learning of Peer Assessment between Students of Their Original Projects of Scientific Innovation'. This project was supported by the Institut de Ciències de l'Educació (ICE-UAB) for the academic year 2022-2023.

Teresa Gasull also became a member of the external scientific committee for the Biobank IGTP-HUGTP in September 2021.

The group had the opportunity to collaborate with Professor Piotr Walczak from the University of Maryland, US, along with Dr. Dominika Golubczyk, Dr. Izabela Malysz-Cymborska, and Dr. Miroslaw Janowski from Ti-Com, Poland. Ti-Com is an expert in the delivery of therapeutic agents in image-guided neurointerventions for experimental research models. Together, they are developing new experimental models of stroke in adult rodents and gyrencephalic human-like brains. These models enable researchers to focus on white matter damage and brain area connectivity.

Furthermore, the team partnered with Clara Prats to utilise computational machine/deep learning for assessing and predicting brain damage and neurological outcomes in preclinical stroke models.

Members of the group also took on editorial roles for the journals *Cells* and *International Journal of Molecular Sciences*.

Lastly, the topic of "Iron and Excitotoxicity/Ferroptosis in Stroke", reviewed by the team in 2019 (DeGregorio-Rocasolano N, Martí-Sistac O, Gasull T. Front Neurosci. 2019;13:85. doi: 10.3389/fnins.2019.00085), gained significant international attention. It was among the top 2% viewed, top 1% downloaded, and top 7% most cited out of over 330,000 articles published by the Frontiers editorial. This review has been cited 75 times in the literature.

Genomics and Transcriptomics of Synucleinopathies



Group leader: Katrin Beyer

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Research lines

- Molecular characterisation of Lewy body diseases
- Identification and characterisation of diagnostic biomarkers for dementia with Lewy bodies
- Biomarker development
- Genetic testing

Selected scientific publications

Fernández-Ramos JA, De la Torre-Aguilar MJ, Quintáns B, Pérez-Navero JL, Beyer K, López-Laso E; Spanish Segawa Disease Research group. **Genetic landscape of Segawa disease in Spain. Long-term treatment outcomes**. *Parkinsonism Relat Disord.* 2022 Jan;94:67-78. DOI: <u>10.1016/j.parkreldis.2021.11.014</u>.

Summary of activities and highlights

In 2022, the team welcomed Pau Pastor, a neurologist with a specialization in dementias and movement disorders with special interest in prodromal stages of dementia with Lewy bodies. He assumed the position of co-Pl, actively participating in the exhaustive clinical characterisation of patients and the obtaining of biological samples. He is the link between patients, neurologists, and neurology societies.

Toward the end of the year, Jorge Mena also became a part of the team, supported by an AGAUR Producte proposal. He underwent intensive training to assume responsibility for entrepreneurial management, innovation development, and business strategy design, all within the context of the group's biomarker development efforts.

The group also initiated a collaboration with the assistance of the "Amics de Can Ruti". The team connected with Alejandra Morales, a plastic artist who had first-hand experience handling dementia with Lewy bodies. She put together an exhibition featuring a collection of photographs and a large-scale 3D structure representing the intrusion of Lewy bodies into the brain. Alejandra agreed to repeat her exhibit in a library in Badalona. To enhance the experience, where the group additionally organized conferences for the general public and groups of students.

Group of Research in Neuromuscular Diseases from Badalona (GRENBA)



Group leader: Gisela Nogales Gadea

Research lines

- Myotonic Dystrophy type I
- Myotonic Dystrophy type II
- McArdle Disease or Glycogenosis type V
- Duchenne Muscular Dystrophy
- Epigenetic changes in muscle pathologies
- Deciphering the role of HDAC11 in skeletal muscle homeostasis, regeneration and muscular dystrophies

Selected scientific publications

Santalla A, Valenzuela PL, Rodriguez-Lopez C, Rodríguez-Gómez I, Nogales-Gadea G, Pinós T, Arenas J, Martín MA, Santos-Lozano A, Morán M, Fiuza-Luces C, Ara I, Lucia A. Long-Term Exercise Intervention in Patients with McArdle Disease: Clinical and Aerobic Fitness Benefits. *Med Sci Sports Exerc.* 2022 Aug 1;54(8):1231-1241. DOI: <u>10.1249/</u>MSS.00000000002915.

García-Puga M, Saenz-Antoñanzas A, Gerenu G, Arrieta-Legorburu A, Fernández-Torrón R, Zulaica M, Saenz A, Elizazu J, Nogales-Gadea G, Gadalla SM, Araúzo-Bravo MJ, López de Munain A, Matheu A. **Senescence plays a role in myotonic dystrophy type 1.** *JCl Insight.* 2022 Oct 10;7(19):e159357. DOI: <u>10.1172/jci.insight.159357</u>.

Villarreal-Salazar M, Santalla A, Real-Martínez A, Nogales-Gadea G, Valenzuela PL, Fiuza-Luces C, Andreu AL, Rodríguez-Aguilera JC, Martín MA, Arenas J, Vissing J, Lucia A, Krag TO, Pinós T. Low aerobic capacity in McArdle disease: A role for mitochondrial network impairment? *Mol Metab.* 2022 Dec;66:101648. DOI: <u>10.1016/j.mol-</u> met.2022.101648.

Summary of activities and highlights

The group was recognised as a Consolidated Research Group by AGAUR – Generalitat de Catalunya, under the name "Grup de Recerca en Malalties Neuromusculars i Neuropediatriques Can Ruti". A new research line was started with the project "DM1-Heart in Myotonic Dystrophy", which aims to unveil biomarkers of early cardiac damage in these patients. Additionally, the team incorporated three new doctoral students: Pau Maestre Mora, Eva Coll Liesa, and Alexandra Mercado Amarillo.

Mental Health and Illness



Group leaders: Cristanto Díez Quevedo, Maria Iglesias González

Research lines

- Innovation in acute psychiatric hospitalization
- Catatonia & delirium
- Inflammation and affective disorders
- Neurodevelopmental disorders
- Perinatal mental health
- Health psychology

Selected scientific publications

Giné-Servén E, Serra-Mestres J, Martinez-Ramirez M, Boix-Quintana E, Davi-Loscos E, Guanyabens N, Casado V, Muriana D, Torres-Rivas C, Cuevas-Esteban J, Labad J. Anti-NMDA receptor encephalitis in older adults: A systematic review of case reports. Gen Hosp Psychiatry. 2022 Jan-Feb;74:71-77. DOI: <u>10.1016/j.genhos-ppsych.2021.11.006</u>.

Diago M, Vila-Badia R, Serra-Arumí C, Butjosa A, Del Cacho N, Esteban Sanjusto M, Colomer-Salvans A, Sánchez L, Dolz M, Muñoz-Samons D, Profep G, Usall J. **Emotio**nal abuse and perceived stress: The most relevant factors in suicide behavior in first-episode psychosis patients. *Psychiatry Res.* 2022 Sep;315:114699. DOI: <u>10.1016/j.</u> psychres.2022.114699.

Vila-Badia R, Serra-Arumí C, Butjosa A, Del Cacho N, Abella M, Colomer-Salvans A, Cuevas-Esteban J, Alcalde R, Muñoz-Samons D, Bogas JL, Usall J; G. PROFEP. **Risk and pro-tective factors for the appearance of first-episode psychosis: The role of childhood trauma and coping strategies**. *Asian J Psychiatr.* 2022 Dec;78:103284. DOI: <u>10.1016/j.ajp.2022.103284</u>.

Summary of activities and highlights

The group received an award for the best oral communication of the "XXXV Symposium on Behavioral Therapy and Behavioral Medicine in Clinical Practice" (Barcelona; April 7).

Neurogenetics



Group leaders: Antoni Matilla Dueñas, Ivelisse Sánchez Díaz

Selected scientific publications

Corral-Juan M, Casquero P, Giraldo-Restrepo N, Laurie S, Martinez-Piñeiro A, Mateo-Montero RC, Ispierto L, Vilas D, Tolosa E, Volpini V, Alvarez-Ramo R, Sánchez I, Matilla-Dueñas A. **New spinocerebellar ataxia subtype caused by SAMD9L mutation triggering mitochondrial dysregulation (SCA49).** *Brain Commun.* 2022 Feb 10;4(2):fcac030. DOI: 10.1093/braincomms/fcac030.

Research lines

- Identification of the genetic causative deficits and the molecular mechanisms underlying hereditary ataxias, spastic paraplegias and other neurodegenerative disorders
- Genetic diagnosis of more than 400 neurological diseases
- Development of a gene therapy strategy for Friedreich Ataxia and its evaluation in mouse models of the disease
- Multiomics-based identification of biomarkers of disease progression in hereditary ataxias and other neurodegenerative disorders
- Identification of signalling targets and therapeutic strategies for the neurological phenotypes in hereditary metabolic disorders and the analysis of mice models through machine learning and artificial intelligence

Summary of activities and highlights

The neurogenetics research group identified a novel spinocerebellar ataxia subtype, denoted SCA49, in nine members of a Spanish five-generation family from Menorca with affected individuals variably presenting with ataxia, nystagmus, dysarthria, polyneuropathy, pyramidal signs, cerebellar atrophy and distinctive cerebral demyelination. It affected individuals with horizontal and vertical gaze-evoked nystagmus and hyperreflexia as initial clinical signs, and had a variable age of onset ranging from 12 to 60 years. Neurophysiological studies showed moderate axonal sensory polyneuropathy with altered sympathetic skin response predominantly in the lower limbs.

Summary of activities and highlights

The group participated in several competitive projects during 2022 dealing with the study of stress-related biomarkers in psychosis. Javier Labad coordinated two competitive grants in this field.

The first project, under the ERA-NET initiative, known as GEPI-BIOPSY, focused on the exploration of 'omics' biomarkers - including genomics, epigenetics, and proteomics - in both animal models and humans, studying cognitive outcomes, social interaction, and anhedonia.

The second project, named SchizOMICS, was a randomized, open-label, multi-center clinical trial which compared two antipsychotic drugs (aripiprazole and paliperidone) for treating first episode psychosis using artificial intelligence that allowed identifying a series of 'omics' biomarkers that can predict shortand long-term treatment response and prognostic outcomes. This project involved the collaboration of 18 research groups linked to the CIBER network and spanned five CIBER areas.

The group was prolific in its scholarly output, publishing over 30 articles related to mental disorders and/or stress throughout the year. Results of the research of the group include the identification of cerebrospinal fluid biomarkers biomarkers that involve bioenergetic systems in association with prodromal symptoms and the phenotype of psychotic disorders during the early stages of the disease. In terms of individual recognitions, two researchers from the PSICPNEC group were awarded for their work. Alex Ferrer received the best PhD thesis award from the Spanish Society of Psychiatry for his research titled "Association of genetic and epigenetic factors with transdiagnostic intermediate phenotypes in mental disorders", supervised by Javier Labad and Virginia Soria. Furthermore, Eloi Giné-Servén received the IX Eduardo Zárate Prize from the Academy of Medical and Health Sciences of Catalonia (Maresme branch) for his contribution to the study of autoimmune encephalitis in patients with psychotic disorders.

Additionally, the PSICPNEC group is a part of the Stress National Research Network, which is funded by the Carlos III Health Institute and coordinated by Juan Nacher from the University of Valencia.

Neurovascular Research Group



Group leaders: Mònica Millán Torné, Natalia Pérez de la Ossa Herrero

Research lines

- Therapies in patients with acute stroke
- Territorial organization for stroke care
- Multimodal neuroimaging techniques (CT and MR in acute stroke)
- Diagnostic and prognostic clinical and biological markers of stroke and its complications
- Neurocardiology
- Brain recovery and post-stroke care

Selected scientific publications

Renú A, Millán M, San Román L, Blasco J, Martí-Fàbregas J, Terceño M, Amaro S, Serena J, Urra X, Laredo C, Barranco R, Camps-Renom P, Zarco F, Oleaga L, Cardona P, Castaño C, Macho J, Cuadrado-Godía E, Vivas E, López-Rueda A, Guimaraens L, Ramos-Pachón A, Roquer J, Muchada M, Tomasello A, Dávalos A, Torres F, Chamorro Á; CHOICE Investigators. Effect of Intra-arterial Alteplase vs Placebo Following Successful Thrombectomy on Functional Outcomes in Patients With Large Vessel Occlusion Acute Ischemic Stroke: The CHOICE Randomized Clinical Trial. *JAMA*. 2022 Mar 1;327(9):826-835. DOI: <u>10.1001/jama.2022.1645</u>.

Pérez de la Ossa N, Abilleira S, Jovin TG, García-Tornel Á, Jimenez X, Urra X, Cardona P, Cocho D, Purroy F, Serena J, San Román Manzanera L, Vivanco-Hidalgo RM, Salvat-Plana M, Chamorro A, Gallofré M, Molina CA, Cobo E, Davalos A, Ribo M; RACECAT Trial Investigators. Effect of Direct Transportation to Thrombectomy-Capable Center vs Local Stroke Center on Neurological Outcomes in Patients With Suspected Large-Vessel Occlusion Stroke in Nonurban Areas: The RACECAT Randomized Clinical Trial. *JAMA*. 2022 May 10;327(18):1782-1794. DOI: 10.1001/jama.2022.4404.

García-Tornel Á, Seró L, Urra X, Cardona P, Zaragoza J, Krupinski J, Gómez-Choco M, Sala NM, Catena E, Palomeras E, Serena J, Hernandez-Perez M, Boned S, Olivé-Gadea M, Requena M, Muchada M, Tomasello A, Molina CA, Salvat-Plana M, Escudero M, Jimenez X, Davalos A, Jovin TG, Purroy F, Abilleira S, Ribo M, de la Ossa NP; RACECAT trial investigators. **Workflow Times and Outcomes in Patients Triaged for a Suspected Severe Stroke.** *Ann Neurol.* 2022 Dec;92(6):931-942. DOI: <u>10.1002/ana.26489</u>.

The group demonstrated the pathogenic variant within the SAMD9L genes, the disease causative genetic defect with a significant log-odds score. The team also demonstrated themitochondrial location of human SAMD9L protein, and its decreased levels in patients' fibroblasts in addition to mitochondrial perturbations. Furthermore, mutant SAMD9L in zebrafish impaired mobility and vestibular/sensory functions.

In addition, the group continued developing a gene therapy based on adenoassociated virus (AAV) for the treatment of Friedreich's ataxia, a rare neurodegenerative disease characterised by ataxia caused by neurodegeneration of the dorsal root ganglia and the cerebellum. The disease is caused by a GAA repeated sequence in the gene coding for the mitochondrial protein frataxin. In 2022, the group completed the *in vivo* pre-clinical demonstration of efficacy and safety of the AAV-gene therapy in two mouse models of the disease, one chronic and one acute.

Psychoneuroendocrinology and Stress in Psychosis (PSICPNEC)



Group leader: Javier Labad Arias

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Research lines

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

Selected scientific publications

Álvarez A, Guàrdia A, González-Rodríguez A, Betriu M, Palao D, Monreal JA, Soria V, Labad J. A systematic review and meta-analysis of suicidality in psychotic disorders: Stratified analyses by psychotic subtypes, clinical setting and geographical region. *Neurosci Biobehav Rev.* 2022 Dec;143:104964. DOI: <u>10.1016/j.neubiorev.2022.104964</u>.

Guasp M, Rosa-Justicia M, Muñoz-Lopetegi A, Martínez-Hernández E, Armangué T, Sugranyes G, Stein H, Borràs R, Prades L, Ariño H, Planagumà J, De-La-Serna E, Escudero D, Llufriu S, Sánchez-Valle R, Santamaria J, Compte A, Castro-Fornieles J, Dalmau J; Spanish anti-NMDAR Encephalitis Study Group. *Clinical characterisation of patients in the post-acute stage of anti-NMDA receptor encephalitis: a prospective cohort study and comparison with patients with schizophrenia spectrum disorders. Lancet Neurol.* 2022 Oct;21(10):899-910. DOI: <u>10.1016/S1474-4422(22)00299-X</u>.

Giné-Servén E, Martinez-Ramirez M, Boix-Quintana E, Davi-Loscos E, Guanyabens N, Casado V, Muriana D, Torres-Rivas C, Crespo-Facorro B, Labad J. **Routine cerebrospinal fluid parameters as biomarkers in first-episode psychosis: A prospective observational study.** *Prog Neuropsychopharmacol Biol Psychiatry.* 2022 Jan 10;112:110424. DOI: 10.1016/j.pnpbp.2021.110424.

Summary of activities and highlights

Members of this group served on various scientific committees and safety committees for clinical trials. They were also part of scientific societies and held editorial positions in international journals, including *Frontiers in Neurology and Stroke: Vascular and Interventional Neurology*, among others.

Some of the team members lent their expertise to advisory roles for biomedical and pharmaceutical companies, such as Methinks and ApataTargets, aiding in the development of diagnostic devices and therapeutic strategies. Their contributions were not limited to advisory roles; they were actively involved in training initiatives, presentations, and advisory activities for various projects. One notable initiative they were involved in was the Angels Initiative, which acts at a global level in the establishment of health systems and training professionals for the improvement of care stroke.

Science of Behaviour and Substance Abuse

Clinical Pharmacology of Substance Use Disorder Magí Farré Albaladejo

Medical Complications of Substance Abuse Robert Muga Bustamante

Clinical Pharmacology of Substance Use Disorder



Group leader: Magí Farré Albaladejo

Research lines

- Evaluation of the acute effects of new psychoactive substances (synthetic cathinones such as methylone, pyrovalerone derivatives, and others), and classical psychostimulants (MDMA, amphetamines and cocaine)
- Evaluation of the acute effects of binge alcohol consumption in young people and its combination with other substances (cannabis, energy drinks)
- Evaluation of the effects of natural and synthetic cannabinoids, including cannabis and its components, and its therapeutic use (medicinal cannabis)
- Pharmacogenomics and substance use, including drug of abuse and medicines. Influence of genetic polymorphism in the effects and pharmacokinetics of drugs

Selected scientific publications

Alemany A, Millat-Martinez P, Corbacho-Monné M, Malchair P, Ouchi D, Ruiz-Comellas A, Ramírez-Morros A, Rodríguez Codina J, Amado Simon R, Videla S, Costes G, Capdevila-Jáuregui M, Torrano-Soler P, San José A, Bonet Papell G, Puig J, Otero A, Ruibal Suarez JC, Zarauza Pellejero A, Llopis Roca F, Rodriguez Cortez O, Garcia Garcia V, Vidal-Alaball J, Millan A, Contreras E, Grifols JR, Ancochea À, Galvan-Femenia I, Piccolo Ferreira F, Bonet M, Cantoni J, Prat N, Ara J, Forcada Arcarons A, Farré M, Pradenas E, Blanco J, Àngel Rodriguez-Arias M, Fernández Rivas G, Marks M, Bassat Q, Blanco I, Baro B, Clotet B, Mitjà O; CONV-ERT Group. **High-titre methylene blue-treated convalescent plasma as an early treatment for outpatients with COVID-19: a randomised, placebo-controlled trial.** *Lancet Respir Med.* 2022 Mar;10(3):278-288. DOI: 10.1016/s2213-2600(21)00545-2

Poyatos L, Lo Faro AF, Berardinelli D, Sprega G, Malaca S, Pichini S, Huestis MA, Papaseit E, Pérez-Mañá C, Busardò FP, Farré M. **Methylone and MDMA Pharmacokinetics Following Controlled Administration in Humans.** *Int J Mol Sci.* 2022 Nov 23;23(23):14636. DOI: <u>10.3390/ijms232314636</u>

Moltó J, Bailón L, Pérez-Mañá C, Papaseit E, Miranda C, Martín S, Mothe B, Farré M. Absence of drug-drug interactions between y-hydroxybutyric acid (GHB) and cobicistat. *J Antimicrob Chemother.* 2022 Jan 24;77(1):181-184. DOI: <u>10.1093/jac/dkab359</u>

Summary of activities and highlights

The group's activity is centred around various research studies that evaluate both acute and chronic effects. The research employs diverse study designs, including clinical trials and observational studies, as well as evidence synthesis approaches like systematic reviews and meta-analyses.

Medical Complications of Substance Abuse



Group leader: Robert Muga Bustamante

Research lines

- Medical complications of alcohol use disorder
- · Alcohol-associated morbidity and mortality
- Therapeutic interventions in alcohol use disorder
- Monitoring viral infections (HCV, HIV, HBV) in patients with SUD
- Intestinal permeability, systemic inflammation and cardiometabolic alterations
- Immune alterations associated with alcohol use disorder

Selected scientific publications

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Hernández-Rubio A, Sanvisens A, Bolao F, Cachón-Suárez I, Garcia-Martín C, Short A, Bataller R, Muga R. **Prevalence and associations of metabolic syndrome in patients with alcohol use disorder.** *Sci Rep.* 2022 Feb 16;12(1):2625. DOI: <u>10.1038/</u><u>s41598-022-06010-3.</u>

Alías-Ferri M, Pellegrini M, Marchei E, Pacifici R, Rotolo MC, Pichini S, Pérez-Mañá C, Papaseit E, Muga R, Fonseca F, Torrens M, Farré M. **New Psychoactive Substances Consumption in Opioid-Use Disorder Patients.** *Biology (Basel)*. 2022 Apr 22;11(5):645. DOI: <u>10.3390/biology11050645</u>.

Alías-Ferri M, Pellegrini M, Marchei E, Pacifici R, Rotolo MC, Pichini S, Pérez-Mañá C, Papaseit E, Muga R, Fonseca F, Farré M, Torrens M. **Synthetic cannabinoids use in a sample of opioid-use disorder patients.** *Front Psychiatry.* 2022 Aug 3;13:956120. DOI: <u>10.3389/fpsyt.2022.956120</u>.

Summary of activities and highlights

The Medical Complications of Substance Abuse group received recognitions for its work. Paola Zuluaga and Nuria García Marchena were awarded by the Instituto de Salud Carlos III (ISCIII) within the Juan Rodés and the Sara Borrell programmes respectively.

The group's researchers showed a strong commitment to disseminating their work to a broad audience. They regularly updated their research progress and insights via <u>Twitter</u>. Additionally, their work was shared through the Spanish Research Network on Substance Use Disorder (<u>RIAPAd</u>) and even published in a

Scientific activity in 2022 / Research areas, groups and programmes at the IGTP

r<u>esearch dissemination journal</u>. They were also dedicated to promoting the developments of their study CohRTA through a <u>dissemination campaign</u> on their website.

Notably, Daniel Fuster participated in various media outlets with the aim to raise awareness about the effects of alcohol and addiction:

- <u>La habilidad de Interna en pacientes adictos: coste-eficiente y "necesaria"</u> (redaccionmedica.com; 3:52-5:51).
- Día mundial sin alcohol: el consumo seguro no existe. Ellas hacen ciencia: estudiosas de las plantas (eitb.eus; up to minute 22).
- Tomar una copa de vino al día, ¿tan saludable como dicen? (marca.com)
- <u>Mitos y falsas creencias sobre el alcohol (info-veritas.com)</u>
- <u>Spotlight on... Daniel Fuster (</u>Urbanarch.org | Boston University)

Translational Program in Cancer Research (CARE)



The CARE Program (Translational Program in Cancer Research) is a multidisciplinary network of researchers who share common interests and resources in the field of cancer research. The program is housed at the Can Ruti campus and is an integral part of the core scientific structure of the IGTP, an accredited center under the Spanish National Research Council (ISCIII).

Scope and aim

The program's research focuses on various forms of cancer, with the goal of accelerating the transfer of cutting-edge knowledge and technological advancements in the diagnosis, treatment, and prevention of cancer. Through this program, the quality of cancer research will be enhanced and its impact in clinical practice will be maximized.

The CARE program has several scientific and functional aims that are designed to:

To promote the development and implementation of precision and personalized medicine



- To advance basic and translational research towards innovation and technology transfer
- To establish a collaborative and transversal network of clinical, translational and basic researchers,
- To implement an efficient working framework among researchers to increase research impact
- To enable advanced computational tools in translational research practices.

Structure of the program

Institutions

- Core members: IGTP / HGTiP / ICO
- Associate institutions: IJC, IRSICaixa, UAB

Program's Executive Committee

Directors: Mireia Margelí (Clinical research), Miguel A Peinado (Basic research)

Sections' Coordinators: Anna Martínez-Cardús (Networking), Eduard Serra (Scientific), Arola Fortian (Educational & Training).

Scientific activity in 2022 / Research areas, groups and programmes at the IGTP

Research groups

Principal Investigators

- Anna Martínez-Cardús
- Albert Font
- Carme Balañà
- Carolina Armengol
- Cecilia Cabrera
- Cinta Hierro
- Eduard Serra
- Elisabeht Castellanos / Ignacio Blanco
- Enric Carcereny
- Ester Ballana
- Eva Martinez-Balibrea
- Jordi Barretina

- Jose Luis Manzano
- Margarita Romeo
- Miguel A Peinado
- Mireia Jordà
- Mireia Margelí
- Montserrat Sanchez Cespedes
- Pedro Fernandez Ruiz
- Rafael Rosell
- Ricard Mesía
- Sergio Alonso
- Teresa Morán
- Verónica Rodilla

Summary of Activities in 2022

Internal presentations

- Spring ProCURE meeting 14/07/2022
- Program's Presentation at HUGTiP 23/9/2022
- Comité de tumors 5/10/2022
- IGTP external Scientific Advisory Board 10/10/2022
- ICO clinical sessions 23/11/2022

Organization of courses and scientific meetings

- 5th Edition Primers in Gastric Cancer, Small Cell Lung Cancer, and KRAS-Mutant Non-Small Cell Lung Cancer (R. Rosell) 25/11/2022
- VI Curs B·ARGO d'Immunoterapia: Avançant en el tractament dels pacients amb Càncer (E. Carcereny, M. Saigí, A. Martínez Cardús, R Mesía) 2-3/11/2022
- Translational Research meeting on Urological Tumors (A. Font, Vicenç Ruiz de Porras) 1-2/12/2022
- XVI Reunió Catalano-Balear de Neurooncología (C. Balañà) 4/11/2022
- XX edition of the Translational Research and Digestive Neoplasms Workshop (E. Martínez-Balibrea) 7/10/2022

B·ARGO - CARE program seminars (Vicenç Ruiz de Porras, Arola Fortian)

IGTP affiliated groups

Within the framework of IGTP's accreditation as a Centre of Excellence by the Instituto de Salud Carlos III (ISCIII), the IGTP has affiliation contracts with groups from various institutions.

Consorci Sanitari del Maresme (CSdM)

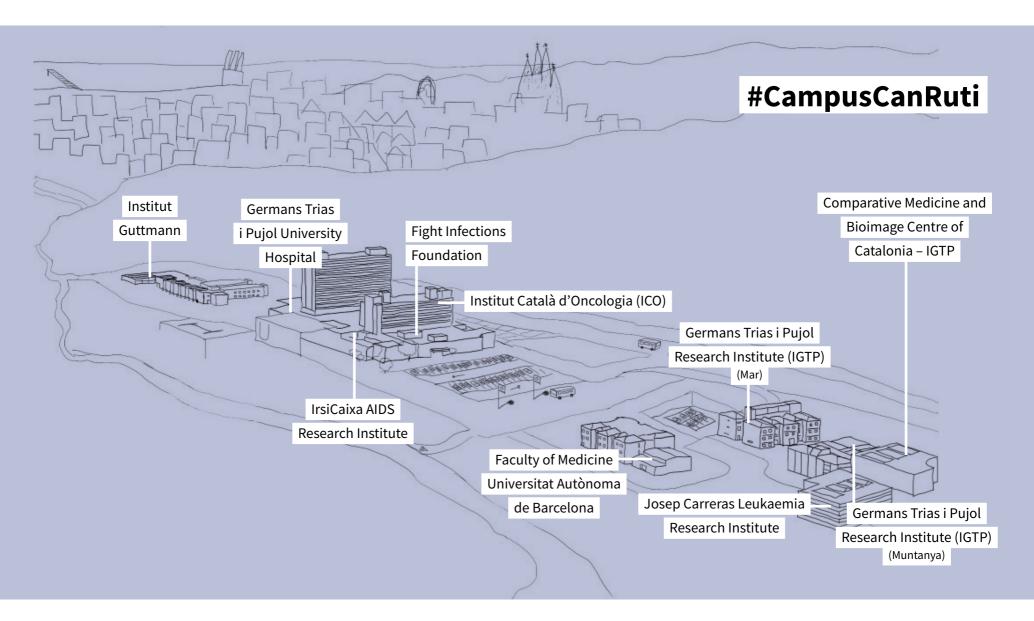
Fight Infections Foundation

Foundation University Institute for Primary Health Care Research Jordi Gol i Gurina (IDIAPJGol)

Institut Guttmann

IrsiCaixa AIDS Research Institute

Josep Carreras Leukaemia Research Institute (IJC)



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