IrsiCaixa Scientific Report 2022

IrsiCaixa

Institut de Recerca de la Sida

"la Caixa" Foundation

Generalitat de Catalunya
Departament de Salut

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IrsiCaixa

The IrsiCaixa AIDS Research Institute was created in 1995 with the support of "la Caixa" Foundation and the Department of Health of the Autonomous Government of Catalonia to tackle a virus that, at the time, was wreaking havoc globally: HIV. Since then, IrsiCaixa has become an international landmark and leading centre for research into the eradication of HIV/AIDS.

Its director is Dr Bonaventura Clotet, a world-leading scientist and physician who has dedicated himself fully to fight against HIV/AIDS and to helping people suffering from infectious diseases. Dr. Clotet is also president and founder of the Fight Infections Foundation and the Catalan Health Institute (ICS) Clinical Director for Infectious Diseases for the Barcelona Northern Metropolitan Area.

The fact that both IrsiCaixa and the Fight Infections Foundation are located in the Germans Trias i Pujol University Hospital makes for a unique model of collaboration between researchers, healthcare professionals, patients and community representatives. This transfer of knowledge between key stakeholders makes for novel solutions that facilitate progress towards eradication of HIV/AIDS, as well as better treatment for emerging infectious diseases and studies of the microbiome and cancer.

The wide experience on HIV/AIDS provided a large expertise on the backbone of the human health, the immune system. This knowledge gathered during more than 25 years enables IrsiCaixa's 12 research groups and around 100 staff to face crucial challenges of human health organised in 6 different strategic lines: global infectious diseases such as HIV/AIDS and SARS-CoV-2, emerging infectious diseases, immunopathology, microbiome, cancer and the development of new therapies and vaccines.

Letter from the director

The COVID-19 pandemic has highlighted the importance of studying infectious diseases, not only from a therapeutic perspective but also from a preventive one. IrsiCaixa's vision of research has always been dedicated to tackling these diseases and the current framework has allowed it to further strengthen its work in this field. IrsiCaixa's research program during 2022, therefore, has been marked by the study of a wide range of infectious diseases with the aim of developing therapeutic and preventive measures against infectious agents. At the same time, IrsiCaixa also addresses the diseases related to these infections in order to provide a comprehensive support to all patients suffering from these pathologies.

IrsiCaixa's scientific strategy focuses on the immune system as the central axis of human health from which our strategic lines of research, redefined in 2022, emerge. I like to illustrate our research program as a solar system, in which the strategic lines surround the immune system like the planets surround the sun in the solar system. Thus, IrsiCaixa works in the following areas of research: global infectious diseases, with HIV and SARS-CoV-2 as the main points of interest; emerging infectious diseases; immunopathology; microbiome; cancer; and development of therapies and vaccines.

In 2022 the team has achieved major milestones in HIV research. One of these has been the study of the use of immunotherapy in combination with antiretroviral treatment in patients living with HIV. The results show that this immunotherapy, based on the use of an anti-HIV antibody, reduces the HIV reservoir and provides better and longer control of the virus when antiretroviral treatment is withdrawn.

With regard to SARS-CoV-2, in IrsiCaixa has continued with its studies begun during the pandemic, which include the research carried out by the CBIG consortium. Among other advances, the research team has intensified the monitoring of the variants of the virus and the protection of the population against them. At the same time, they have analysed the effectiveness of the antigen tests currently used against the different variants of COVID-19 to determine whether they are still working.

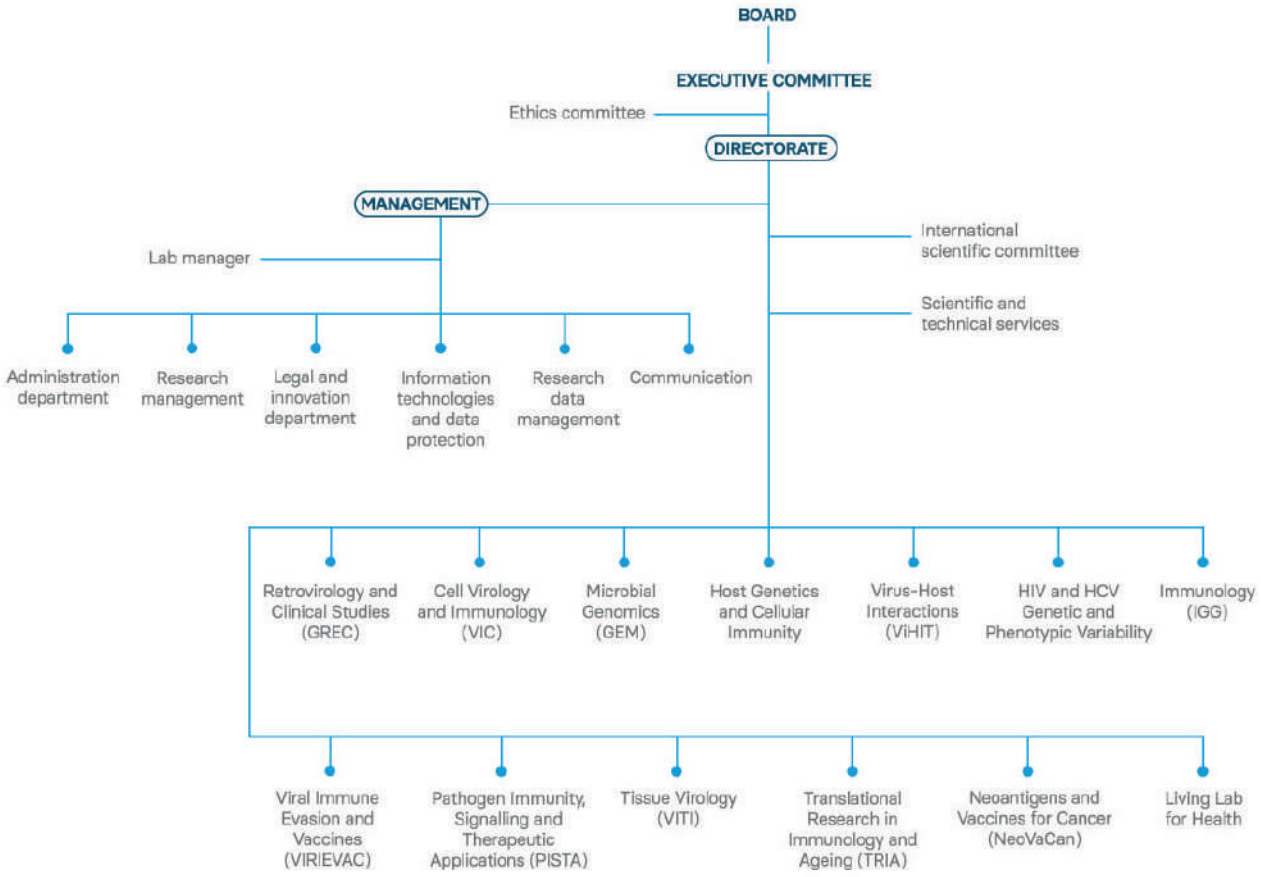
Notable progress in neuropathology line is the study of lamivudine, a common antiretroviral drug, to improve cognition in mouse model of Down syndrome. The study demonstrated the potential of using this drug to ameliorate cognitive impairment of people with Down syndrome.

These are just some of the many studies carried out in 2022 by the IrsiCaixa team, made up of more than 100 researchers who work every day to fight infectious diseases. Their hard work is reflected in the increase in the number of projects awarded to the institution and the high impact of its publications. All of this progress would not have been possible without the sustained support and continued enthusiasm of our key partners such as "la Caixa" Foundation, the Autonomous Government of Catalonia and Grifols.

Bonaventura Clotet Sala

IrsiCaixa director

Organizational structure



Board

President
Manel Balcells i Díaz
Health Minister of the Autonomous Government of Catalonia

Vice-President
Josep Vilarasau i Salat
Appointee of the Fundació Bancària Caixa d'Estalvis i Pensions de Barcelona "la Caixa" ("la Caixa" Foundation)

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Marta Casals i Virosque
Appointee of the Fundació Bancària Caixa d'Estalvis i Pensions de Barcelona "la Caixa" ("la Caixa" Foundation)

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Appointees of the Fundació Bancària Caixa d'Estalvis i Pensions de Barcelona "la Caixa" ("la Caixa" Foundation)

Montserrat Pinyol i Pina
Anna Veiga i Lluch
Appointees of the Board of the Fight AIDS Foundation

Organizational structure

Executive Committee

For "la Caixa" Foundation:

Esther Planas i Herrera
President

Marta Casals i Virosque
Secretary

Ignasi López Verdaguer

For the Department of Health of the Autonomous Government of Catalonia:

Jordi Barretina i Ginesta
Jordi Casabona i Barbarà
Aina Plaza Tesías

Director

Dr. Bonaventura Clotet Sala

Manager

Lourdes Grau Paré

Administration

Arnau Creus Orodea
Cristina Mesa Real
Penélope Riquelme Nevado

Information Technologies

Julián Eslava Campo

International Scientific Committee

Dr. Daria Hazuda
Vice-President of Infectious Disease Identification at Merck and Scientific Director of the MRL Cambridge Exploratory Science Center (Massachusetts, USA).

Dr. Danniel Kuritzkes
Professor of Medicine at Harvard Medical School, Director of AIDS Research at Brigham and Women's Hospital and Co-Director of the NIH-funded AIDS Clinical Trials Group (USA).

Dr. Douglas Richman
Professor of Pathology and Medicine at the University of California San Diego (UCSD) (USA). Director of the Research Center for AIDS and HIV Infection at the VA San Diego Healthcare System and Director of the Center for AIDS Research at the University of California San Diego (UCSD) (USA).

Dr. Gabriella Scarlatti
Head of the Viral Evolution and Transmission Group at the IRCCS Ospedale San Raffaele (Milano, Italy).

Dr. Jonathan Schapiro
Director of the HIV/AIDS Clinic at the National Hemophilia Center (Tel Aviv, Israel).

Dr. Lucy Dorrell
Senior Director of the Infectious Diseases and Clinical Development at Immunocore and professor at the Oxford University (UK).

Dr. Mario Stevenson
Head of the Infectious Diseases Division (Department of Medicine) of the University of Miami (Florida, USA).

Dr. Monique Nijhuis
Associate Researcher of Translational Virology of the Department of Medical Microbiology, University Medical Center (Utrecht, the Netherlands).


ACCESORIOS
Nikon

Key figures 2022

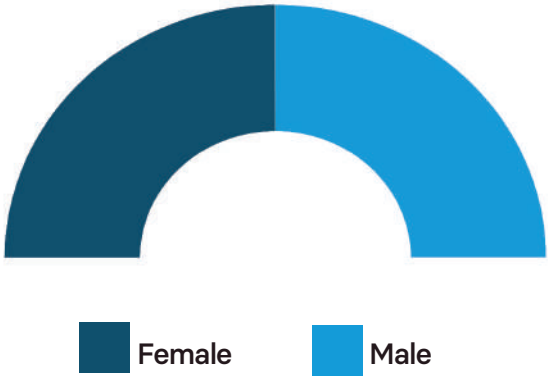
Total staff

119

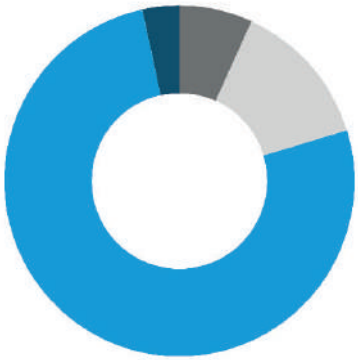
Sex

66% ♀ **34%** ♂

Principal investigators



Staff by categories



- Scientific and technical Services (6,78%)
- Administration and research support (13,56%)
- Research (76,27%)
- Living Lab for Health (3,39%)

4 Theses defended in 2022

Óscar Blanch Lombarte
Viral Immune Evasion and Vaccines (VIRIEVAC)

Ifeanyi Ezeonwumelu
Virus Host Interactions (ViHIT)

Raquel Ortiz López
Cell Virology and Immunology (VIC)

Luis Romero Martín
Host Genetics and Cellular Immunity (TIV)

Projects awarded in 2022

35

16 public

19 private

Active projects in 2022

107

68 coordinated by IrsiCaixa

Publications in 2022

116

1106 Impact Factor

Highlights 2022

January

Kick off meeting of the RBDCOV European project, with **VIRIEVAC** as a workpackage leader.

February

A team of researchers from ICFO and IrsiCaixa report on the development of a low-cost, portable, non-invasive device that uses light and saliva to test COVID-19 patients in less than 30 minutes.

March

GREC characterizes a profile of people living with HIV who have a smaller viral reservoir than is common. 47% of the latent virus in these individuals resides in short-lived cells, which may account for these lower reservoir levels.

May

IrsiCaixa studies the ability of four different brands of antigen test to detect SARS-CoV-2 alpha, beta, delta and omicron variants.

June

PISTA expands their emergent pathogen platform to isolate, produce, titrate and characterize novel viruses like Monkeypox virus and the Respiratory Syncytial virus and validation of a viral neutralization assay for clinical assessment of vaccine efficacy against SARS-CoV-2 by the EMA.

The **Living Lab for Health** co-organises the 2nd Sentinel Schools Congress, in which students present their recommendations for improving the model for promoting mental health at schools.

July

Three IrsiCaixa female researchers receive funding from Gilead to keep progressing in the field of HIV and COVID-19.

September

An IrsiCaixa project to study Long Covid, one of the 9 Catalan proposals selected by the CaixaResearch call for Health Research 2022.

October

Kick off meeting of the EPIVINF European project.

November

First publication of the ProHEpiC cohort studying the immune response to COVID-19 in more than 700 healthcare professionals.

Publication of two clinical trials which confirm the antiviral potential of oral rinses containing CPC to reduce shedding of infectious SARS-CoV-2.

December

The project FARMBANK, coordinated by Drs. Vergara Alert and Kochanowski (IRTA CReSA) and which counts with the participation of IrsiCaixa, is funded by the "Ministerio de Innovación y Ciencia" to develop alternative methods to reduce animal experiments for the study of infectious diseases.

Research groups

Viral Immune Evasion and Vaccines (VIRIEVAC)

PROJECTS AWARDED

Neurocognitive profile of Long Covid in adults living in Catalonia (ProHEpiC-19)
Funding: Department of Health, Government of Catalonia
Participating entities: IrsiCaixa, IDIAP Jordi Gol, IGTP, University of Barcelona
Starting and finishing date: 07/22-07/25
Principal investigator(s): Julia García Prado

SARS-CoV-2 post-vaccination infection: cohort study for the characterization of the immune response and development of a predictive model to establish revaccination criteria in Catalonia (BreakCOVID)
Funding: Department of Health, Government of Catalonia
Participating entities: IrsiCaixa, IDIAP Jordi Gol, IGTP
Starting and finishing date: 07/22-06/25
Principal investigator(s): Marta Massanella Luna

Immunemonitoring of T cell responses in SARS-CoV2 vaccine trials
Funding: HIPRA
Participating entities: IrsiCaixa
Starting and finishing date: 02/22-12/23
Principal investigator(s): Julia García Prado

AWARDS AND ACHIEVEMENTS

Julia García Prado, member of the CIBER network
Julia García Prado, president of the internal Scientific Advisory board of the IGTP
Julia García Prado, associate editor of Frontiers Immunology
Julia García Prado, editor of HIV&Co
Julia García Prado, elected member of the EATRIS-Spain Scientific Advisory Board
Julia García Prado, member of the Spanish AIDS Research Network (RIS)
Julia García Prado, member of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC)
Julia García Prado, member of the Equality Committee at IrsiCaixa
Julia García Prado, member of the Can Ruti Women in Science group

Presentation

The initial research interest of VIRIEVAC focused in the identification of viral and host factors associated with HIV-1 extreme disease phenotypes. These studies brought to the light limitations of antiviral CD8+ T-cell responses for the control of the disease. In the last years, these studies have shifted our research interest towards delineating the functional boundaries of viral pathogenesis and the role of antiviral CD8+ T-cell responses to control or eliminate viral infections. From a basic-translational perspective, VIRIEVAC combines tools from molecular virology, biochemistry and T-cell immunology and systems immunology focusing in the interface of host-pathogen interactions with the ultimate goal to design advance immunotherapies that restore antiviral immunity against HIV-1 and other chronic viral infections and contribute to the cure of these diseases. Moreover, during the COVID-19 pandemic VIRIEVAC move to the field of T cell immunity against CoV-2 infection to understand cellular immunity in the context of natural infection and vaccination in healthy and immune compromised individuals. VIRIEVAC research lines during 2022:

— **Pathogenesis.** Identify viral and host factors associated with disease outcomes. The studies focus on cohort studies of HIV disease phenotypes in children and adults associated with natural control of infection (elite controllers and viremic non-progressors).

— **Persistence, remission, and HIV cure.** Delineate the functional boundaries of antiviral CD8+ T-cell responses in HIV infection to control or eradicate the reservoir and to translate these findings to other persistent viral infections. This line of research aims to characterize the mechanisms of CD8+ T-cell recognition of latently infected cells and understand "T cell immune dysfunction/exhaustion" both in active and latent infection as a significant barrier to HIV remission and cure. This line is research is working to delineate the mechanisms underlying immune dysfunction/exhaustion in PLWH on ART to identify targets for advanced immunotherapeutic approaches.

— **SARS-CoV2 cellular immunity.** Characterize T-cell responses against SARS-CoV-2 elicited by infection and vaccination from immune monitoring studies to the functional characterization of peptide-specific CD4+ and CD8+ T-cell responses. Also, we are working to characterize the potential impact of cellular immunity in Neurocognitive COVID.

2022 milestones

Milestones in the past year within IrsiCaixa's strategic lines were as follows:

— **Immunopathogenesis.** Studies of virological and host factors are associated with natural infection control in viremic non-progressors (VNPs). This collaborative project between IrsiCaixa and the University of Oxford has expanded to the study of a rare small group of VNP that lost virological control over time. In collaboration with the Spanish AIDS Research Network (RIS) and the University of Oxford, this project has published one manuscript (Colomer et al., JVI 2022).

— **Prevention, eradication, and functional cure.** This research line has been successful and in continuous expansion during this year. This research line

4 **New funded research projects**

8 **Peer review publications in international scientific journals**

is funded by several competitive projects led by Dr. Prado and two newly funded projects, la Caixa Health Research program (HR20-00218) and the PI22/01120. Our ongoing work focuses on identifying long-term immune alterations in PLWH on ART combining cytofluorimetrics and bioinformatics. We identified irreversible alterations in the expression of Inhibitory receptors (IRs) on memory and effector like CD8+ T-cells characterized by the expression of TIGIT, TIGIT+TIM3. In this line, we are advancing in the preclinical development of a series of murine and human prototypes. We have completed the mode of action, binding, and affinity for them. In addition, we have been setting up relevant preclinical in vivo models of chronic infections to evaluate these molecules. These studies materialized in the pipeline for single-cell analysis, several manuscripts ongoing, and an oral presentation at the GESIDA conference. This research line has led to ongoing successful national and international collaborations (Buzon's Lab, VHIR, Barcelona, Sekalys Lab, Case Western USA).

— **SARS-CoV2 cellular immunity.** This line of research is actively working to assess cellular immune responses to SARS-CoV-2 infection and vaccination. We have been working in the immune monitoring of T cell responses in several study groups and contributing to clinical trials for CoV-2 vaccine development (RBDCoV Horizon project). Also, we continue participating in two COVID-19 consortia, the King and the Prohepic19 cohort studies that have been awarded this year with two PERIS projects to investigate further SARS-CoV-2 breakthrough infections in vaccinated individuals and the effect of infection in neurocognitive disorders. These studies materialized in an oral presentation at the GESIDA conference and five research articles.

Perspectives for the future

— **Consolidate ongoing research lines** with the following objectives: 1) to identify immunological signatures associated with dysfunctional antiviral responses, 2) to develop and validate candidate prototypes for novel HIV Cure immunoterapeutics, and 5) to characterize SARS-CoV-2 protective and long-term T-cell immunity for immune monitoring and vaccine development.

— **Increase and strength our internationalization** through new alliances and collaborations with research groups of excellence across Europe, EEUU and Africa in the search of new projects and funding opportunities.

Principal Investigator
Julia García Prado

Postdoc researchers
Raúl Pérez Caballero

Predoc researchers
Óscar Blanch Lombarte
Miguel Marín López
Laia Bernad Rosa

Research technicians
Esther Jiménez Moyano
Ruth Peña Poderós

Bioinformatician
Gabriel Felipe Rodríguez Lozano

Masters student
Eudald Vehí Piqué

Grifols project

Breaking the immune exhaustion barrier to recover antiviral immunity for a HIV-1 cure

Senior researcher: Julia García Prado

The RECOViR project aims to bring new insights to the immune regulation of chronic infections by IR, laying the basis for and proposing the proof-of-concept for novel immune therapeutics for a HIV-1 cure. RECOViR will also identify new tools for personalized treatments and potential biomarkers of responses to treatment. All these developments are expected to have far-reaching applications not only for chronic infectious diseases (HIV, HVB, TB or malaria) but also for cancer.

Microbial Genomics (GEM)

PROJECTS AWARDED

Epigenetic regulation of host immunity and neurological long-term consequences of SARS-CoV-2 infection (EPIVIRCO)
Funding: Fundació Bancària "la Caixa"
Participating entities: IrsiCaixa, CNAG-CRG, IRTA, Fight Infections Foundation
Starting and finishing date: 11/22-10/25
Principal investigator(s): Christian Brander

Assessment of changes in cell associated virus using PBMC Illumina MiSeq sequencing on samples for WISARD Study
Funding: Research Organisation (KC) LTD
Participating entities: IrsiCaixa
Starting and finishing date: 06/22-03/23
Principal investigator(s): Roger Paredes Deiros

AWARDS AND ACHIEVEMENTS

Roger Paredes Deiros, member of the CIBER network

Presentation

Our group aims to achieve a better understanding of the microbiological determinants of immune regulation in health and disease. This knowledge will enable the development of novel microbiome-based biomarkers to clinically stratify patients and of microbiome-based therapies that prevent, improve or even cure HIV and other immune-mediated diseases. Our work relies on next-generation sequencing techniques and big data analysis. Thanks to our expertise and knowledge of infectious diseases, we were able to respond to the COVID-19 health emergency and contribute to SARS-CoV-2 research.

1. Role of the gut microbiome in HIV infection prevention, pathogenesis and cure. We study: **a.** Gut microbiome influence on adequate immune reconstitution, HIV-1 replication control and HIV-associated chronic inflammation reduction in people living with HIV (PLWH). **b.** Human microbiome ability to boost the efficacy of HIV immunotherapy and cure strategies. **c.** The ability of specific mucosal microbes to protect humans from HIV infection. We identify: **a.** Human microbiome-derived biomarkers that enable stratification of HIV-infected individuals for research and clinical purposes. **b.** Novel microbiome-based concepts to improve the health of PLWH and prevent HIV-1 infection. We are developing: **a.** Cloud-based software tools to enable massively sequenced data analysis and interpretation for HIV resistance (paseq.org) and microbiome analyses. **b.** A gut-on-a-chip device to evaluate the mechanistic effects of the microbiota on the immune system, in collaboration with the National Microelectronics Centre (CNB).

2. Role of the gut microbiome in other immune-mediated diseases. a. In collaboration with the Vall d'Hebron Institute of Oncology (VHIO), research into the role of the gut microbiome in the natural history of colorectal and small gut neuroendocrine cancer. **b.** In collaboration with the ACE foundation, research into human microbiome influence on the pathogenesis of Alzheimer disease. **c.** In collaboration with the Esther Koplowitz Research Center (CEK), research into the role of the gut microbiome in the progression of skin melanoma.

3. Public health approaches to the global HIV drug resistance epidemic. a. In collaboration with the WHO ResNet group and partners in Africa, development and evaluation of strategies to contain emerging HIV drug resistance and maximize ART efficacy in resource-limited settings. **b.** In collaboration with WHO Europe, integration of HIV, TB and HCV diagnostics and care in Europe as our contribution to the European Laboratory Initiative. **c.** As members of the IAS-USA group, determination of key drug resistance mutations to be used for clinical management worldwide. **d.** Contribution to the development of global WHO ART treatment guidelines.

4. Translational research in COVID-19 therapeutics and virus sequencing. a. Roger Paredes: Spanish National Coordinator of seminal NIH/NIAID-funded randomized clinical trials to define current hospital care standards for COVID-19 and leader of clinical research into COVID-19 treatments and treatment strategies for hospitalized patients and outpatients. **b.** Marc Noguera: Coordinator for the development of SARS-CoV-2 sequencing capacities and for strategic collaboration with Germans Trias i Pujol University Hospital for epidemiological tracking of SARS-CoV-2 variants of concern.

2022 milestones and perspectives for the future

1. Microbiome. a. Description of gut microbiome signatures of HIV vaccine response from a small pilot clinicall (published as Borgognone et al, 2022, Microbiome). Relative abundance of specific bacterial classes are associated to improved immunological response to HTI-based HIV vaccines and viremia control in a small-sized clinical trial. **b.** Description of the effects of probiotic/prebiotic intake for immune recovery in immune discordant HIV patients (published as Blazquez-Bondia et al, 2022, Frontiers in Immunology). The intake of probiotics/prebiotics slightly improved inflammatory markers and immune parameters in a double-blind, randomized clinical trial, showin

subtle effects on the composition of the gut microbiome. **c.** Appointment by the Canadian Institutes of Health Research as co-PIs of an international team undertaking two projects to understand the vaginal microbiome's role in women's health, vaccine responses, antiviral metabolism and cervical cancer. **d.** Early-stage development of a gut-on-a-chip device to evaluate the mechanistic effects of the microbiota on the immune system. **e.** Organization of the Barcelona Debates on the Human microbiome, Barcelona,, 2022.

2. Global HIV. a. Roger Paredes (since 2015): member of the WHO HIV Drug Resistance Steering Group, responsible for developing a global strategy to tackle the emergence of resistant HIV-1. **b.** Advisors to the WHO European Laboratory Initiative TB, HIV and HCV Core Group, responsible for delineating the European strategy for integrated HIV, TB and HCV diagnostics and care in Europe. **c.** Participation in the drafting of the WHO ART treatment guidelines 2020, recommending dolutegravir for the first time as a first-line treatment for all infected people, including pregnant women (representing a major paradigm shift in the global fight against HIV infection). **d.** Participation in updating the WHO ART treatment guidelines.

3. COVID-19. Four manuscripts published in the New England Journal of Medicine, with Roger Paredes as co-author or corporate (ACTT-2 Study Group) co-author: **a.** Early clinical evidence that remdesivir is effective in treating COVID-19 in humans (Beigel et al., 2020: Remdesivir for the Treatment of Covid-19 – Preliminary Report). **b.** Confirmation and extension of the preliminary report on remdesivir and COVID-19 (Beigel et al., 2020: Remdesivir for the Treatment of Covid-19 – Final Report). **c.** Evidence that baricitinib plus remdesivir is more effective and safer than remdesivir alone in reducing recovery time and accelerating clinical improvement, especially among patients requiring high-flow oxygen or non-invasive mechanical ventilation (Kalil et al., 2021: Baricitinib plus remdesivir for the treatment of hospitalized adults with COVID-19). **d.** Efficacy is not demonstrated for the neutralizing monoclonal antibody LY-CoV555 administered with remdesivir in hospitalized COVID-19 patients without end-organ failure (Lundgren et al., 2021: A neutralizing monoclonal antibody for hospitalized patients with COVID-19. Preliminary report of a randomized trial by the ACTIV-3/TICO LY-CoV555 study group).

Principal Investigator
Roger Paredes Deiros

Senior research scientists
Maria Casadellà Fontdevila
Marc Noguera Julian

Postdoc researchers
Alessandra Borgognone
Aleix Elizalde Torrent

Predoc researcher
Carlos Blázquez Bondia

Data steward
Francesc Català Moll

Research technician
Mariona Parera Sallent

Grifols projects

Microbiome triggers of Alzheimer dementia (MIND)

Senior researcher: Roger Paredes Deiros

— Characterization of the composition and functional potential of the faecal microbiome in subjects with cognitive problems but not cognitively impaired, subjects with mild cognitive disability, and subjects with Alzheimer disease.
— Evaluation of longitudinal microbiome changes over one year in subjects with cognitive problems but without cognitive impairment.
— Biological evidence that the gut microbiome contains activators and/or accelerators of Alzheimer disease.

The gut microbiome in HIV infection: from microbial function to immune therapeutics (GIFT)

Senior researcher: Roger Paredes Deiros

— Characterization of species changes in the microbiome in SIV-infected Rhesus monkeys as a model to understand HIV-1 infection effects on the gut microbiome.
— Characterization of the metatranscriptomic profile of the gut during a kick-and-kill strategy for treating HIV.
— Mouse model biological evidence of the relationship between microbiota composition and T-cell vaccines.

T-cell Immunology & Vaccines (TIV)

PROJECTS AWARDED

Epigenetic regulation of host immunity and neurological long-term consequences of SARS-CoV-2 infection (EPIVIRCO)
Funding: Fundació Bancària "la Caixa"
Participating entities: IrsiCaixa, CNAG-CRG, IRTA, Fight Infections Foundation
Starting and finishing date: 11/22-10/25
Principal investigator(s): Christian Brander

Impact of Viral Tropism in HIV Reservoir Seeding and Inducibility
Funding: Gilead Sciences
Participating entities: IrsiCaixa
Starting and finishing date: 07/22-06/24
Principal investigator(s): Mª Carmen Puertas Castro

Boosted flow cytometry as a diagnostic and monitoring tool for virus/pathogen specific T-cell immune profiles in HIV, TB and COVID-19 diseases
Funding: Fundació Bancària "la Caixa"
Participating entities: IrsiCaixa
Starting and finishing date: 01/22-12/24
Principal investigator(s): Marta Ruiz Riol

ÄKTA go Liquid Chromatography System
Funding: Philanthropy
Participating entities: IrsiCaixa
Starting and finishing date: 01/22-12/24
Principal investigator(s): Christian Brander

Epigenetic regulation of host factors in viral infections (EPIVINF)
Funding: European Commission (Horizon Europe)
Participating entities: IrsiCaixa, USAAR, KI, OSR, Omniscope, IRTA
Starting and finishing date: 09/22-08/27
Principal investigator(s): Christian Brander

Identification of epigenetically regulated plasma factors associated with virus-driven neurodysfunctions
Funding: MICINN
Participating entities: IrsiCaixa
Starting and finishing date: 2022-
Principal investigator(s): Marta Ruiz Riol

AWARDS AND ACHIEVEMENTS

Christian Brander, member of the CIBER network
Christian Brander, awarded with the Foundation Dormeur annual equipment grant for IrsiCaixa
Beatriz Mothe Pujadas, invited to the HIV Persistence Conference in Miami
Luis Romero Martín, awarded Summa cum laude for his PhD thesis

Presentation

Adaptive immunity is a critical component of the host defense against viral infections and includes the development of a strong cellular immune response. Our group aims to understand the regulatory mechanisms that drive cell differentiation, immune checkpoints and epigenetic processes that regulate this cellular immunity in different patient populations. This includes people with early HIV infection, controlled and uncontrolled HIV disease, as well as people with or without HIV infection that received solid organ transplants. Furthermore, we have set out to understand the epigenetic mechanisms involved in neurological manifestations of Long-Covid19. In our investigation, we also include individuals that have been diagnosed with virus driven cancers, such as EBV lymphoma (Epstein-Barr Virus) or HPV-derived cancers (Human Papillomavirus), as well as individuals of advanced age who often show a gradual decline of immune competence. Since several of these infections are associated with the development of neurological disease, we are working to identify markers associated with neurofunctional defects related to these infections. To track virus-specific T cell responses in different compartments, including the CNS, our work also includes the analysis of the T cell receptor repertoires in the cellular immune responses against the different viruses. Through these studies, we aim to determine the molecular ontogeny of T-cell immune responses and understand the, epigenetically controlled, transcriptional program of these cells in order to guide therapeutic vaccination strategies to induce robust, effective and long-lasting antiviral immunity. Finally, we continue to work on clinical trials that test different therapeutic HIV vaccine concepts. This includes several ongoing clinical trials that use a combination of T- and B-cell immunogens and clinical and pre-clinical studies that test the role of the microbiota in the outcome of therapeutic vaccination.

2022 milestones and perspectives for the future

During 2022, we have reported (Bailon et al, Nat Med 2022) the results from the ALX-002 clinical trial that used the HTI immunogen and vector combinations developed at IrsiCaixa. This clinical trial has achieved a durable viral suppression in 40% of the vaccinated individuals that did not possess beneficial HLA genetics. These are the most significant results in the field

12 Conferences in which group members gave invited talks

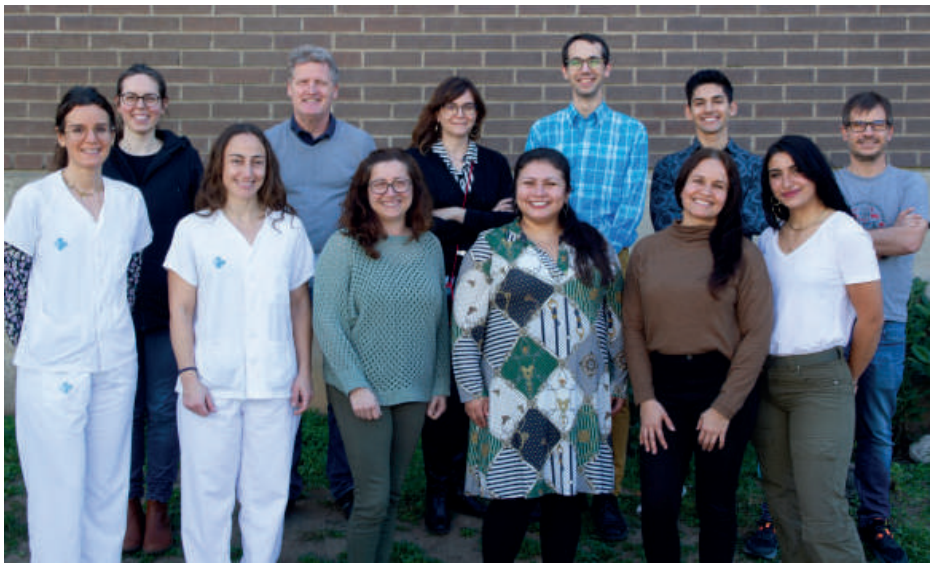
20 Publications from the group

13 Ongoing projects

of HIV therapeutic vaccination to date and we are continuing the development of these vaccines in collaboration with our spin-off AELIX Therapeutics as well as in the IrsiCaixa sponsored trial BCN-03. The BCN-03 trial is the first trial to combine potent T- and B-cell vaccines in the therapeutic use and has the potential to further strengthen the antiviral immunity in vaccinated individuals, so that more individuals can control the virus for longer and to lower levels, without taking antiretroviral treatment. This trial was successfully launched in the summer of 2022 and is fully enrolled and ongoing, with first results expected for mid 2023. In all these clinical trials, we are also exploring the role of the microbiota on the vaccine-induced immune responses and have been able to show, in the mouse model, how modulation of the microbiota prior to vaccination impacts the vaccine T cell immunity and, in humans, how the microbiota composition may predict virus control after vaccination.

In addition, in 2022 we have been awarded, as coordinators, the 7mio Euros European Horizon 2020 EPIVINF project. This project aims to gain a deeper understanding of how acute viral infections alter the epigenetic regulation of host factors that are critical for immune control and neurological health. In particular, EPIVINF will address how acute viral infections impact epigenetic control of host proteins that drive virus-associated disease and/or are involved in the antiviral immune response and how such persistent, epigenetic marks are related to long-term disease evolution. EPIVINF is focused on two major human viral infections, HIV and SARS-CoV-2, both pathogens that affect millions of people around the world and which, despite well-known differences, share some intriguing features that demand further research. We thereby aim to provide important insights into how different individuals react to different viral infections, how different infections may share similar mechanism that impact in the long term health outcomes, how these processes define the further disease course and, finally, how they could serve as targets for novel therapeutic interventions. We have also been awarded a second Caixa Health Grant, which complements the EPIVINF project and allows us to explore different ways to modulate the epigenetic dysregulation in Long Covid19. In this regard, using a customized antibody array for the determination of several hundreds of blood plasma factors, we identified Sirtuin-2 deacetylase levels to be strongly associated with HIV viral loads in plasma and the HIV pro-viral levels in peripheral blood mononuclear cells. SIRT2 levels also showed a strong correlation with different markers of neuronal damage, as well as the levels of brain-derived neurotrophic factor, the Microtubule Associated Protein Tau and the Neurofilament-linked polypeptide (NFL) in plasma as well as in the cerebrospinal fluid and in brain tissue of HIV-infected individuals. We have now been able to use described inhibitors of SIRT2 to block HIV replication in vitro models, including glial cells, and have shown that SIRT2 blockade is also reducing the reactivation of virus from the latent viral reservoir. The observation that SIRT2 levels correlate with the degree of the brain involution and reduced neuronal function, are in line with the use of SIRT2 as a therapeutic target in other brain diseases, including Alzheimer's Disease and may offer novel ways to clinically manage HIV related neurodegeneration in the future.

During 2022, and in close collaboration with experts in innate and adaptive immunity at UC Davis and structural chemist in Barcelona, we have further studied the relationship between HLA-E expression and phenotypical as well as functional characteristics of NK cells, in the context of chronic HIV infection and in an in vitro model of acute infection. Uncontrolled HIV infection was related to increased HLA-E expression and a marked modulation of the NK subpopulations, reversion of the NKG2A/NKG2C expression ratio, and a subsequent loss of positive and negative regulation of NK mediated cytotoxic activity by HLA-E. These results indicate that HLA-E molecules presenting HIV-derived epitopes may sensitize target cells for NK lysis in early HIV infection but, that such continuous exposure to elevated HLA-E levels in chronic infection may lead to NK cell dysfunction and reduced viral control.



Principal Investigator
Christian Brander

Senior research scientists
Anuska Llano Montero
Beatriz Mothe Pujadas
Àlex Olvera van der Stoep
Cristina Peligero Cruz
Marta Ruiz Riol
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Josep Coll Verd

Predoc researchers
Luis Romero Martín
Clara Duran Castells
Igor Moraes Cardoso
Marta Navarro Gutiérrez

Senior research technician
Samandhy Cedeño Briceño

Research technician
Tuixent Escribà Bel

Virus-Host Interactions (ViHIT)

PROJECTS AWARDED

Deep immunophenotyping of the Long Covid syndrome
Funding: Gilead Sciences
Participating entities: IrsiCaixa, Fight Infections Foundation
Starting and finishing date: 07/22-06/24
Principal investigator(s): Marta Massanella Luna

Modulación de la función inmune en cáncer de mama metastático hormonosensible tratado con inhibidores de CDK4/6: identificatión de factores predictivos y nuevas estrategias terapéuticas
Funding: ISCIII
Participating entities: IrsiCaixa, ICO, IGTP
Starting and finishing date: 01/22-12/24
Principal investigator(s): Ester Ballana Guix

Assessing the antiviral effect of CPC on in vitro infection cellular models of HSV-1 and HPV
Funding: Dentaid
Participating entities: IrsiCaixa
Starting and finishing date: 03/22-07/23
Principal investigator(s): Ester Ballana Guix

Nuevas oportunidades inmunoterapéuticas en cáncer de mama metastásico: los inhibidores de CDK4/6 y su impacto sobre el sistema inmune
Funding: European Comission
Participating entities: IrsiCaixa
Starting and finishing date: 12/22-05/23
Principal investigator(s): Ester Ballana Guix

Agonistas de NOD como estrategia terapéutica para la infección por SARS-CoV-2 e influenza
Funding: ISCIII
Participating entities: IrsiCaixa
Starting and finishing date: 12/22-12/26
Principal investigator(s): Roger Badia Córcoles

AWARDS AND ACHIEVEMENTS

Ester Ballana Guix, member of the CIBER network
Ifeanyi Jude Ezeonwumelu presented his PhD in September 2022
Ester Ballana, associate editor of the journal Viruses and Frontiers in Virology, section Antivirals and Vaccines.
Ester Ballana, member of Internal Scientific Advisory Board of IGTP
Roger Badia and Ester Ballana, awarded with 2 new competitive projects on respiratory infections and breast cancer immunotherapy, respectively

Presentation

Our research focus is the study and characterization of innate immune system activation mediated by nucleic acid metabolism and its role in different human diseases characterized by an imbalance in intracellular nucleic acid metabolism, such as viral infections, inflammatory diseases or cancer, with a view to developing new therapeutic strategies. Our group is currently working on two main research lines:

1. Identification and characterization of cellular factors in viral infections. We have been working in the characterization of HIV-host interactions at different stages of virus replication, focusing especially on describing innate immune pathways and modulators that impact HIV-1 replication at any stage, from viral susceptibility, antiviral targets and viral persistence. Persistence of latent HIV reservoirs is one of the main roadblocks for advancing towards an HIV-1 cure, as allows for viral rebound upon antiretroviral therapy interruption, hindering effective HIV-1 cure. Indeed, emerging evidence suggests that modulation of innate immune stimulation could impact viral latency and contribute to the clearing of HIV reservoir. Thus, we have been focusing on the latency reactivation capacity of a distinct innate immune modulators , including JAK and TBK inhibitors. Specifically, we have characterized a subclass of selective JAK2 inhibitors was characterized as a potential novel therapeutic strategy for HIV-1 cure, demonstrating significant HIV reactivation capacity through the modulation of IRF7. Overall, our data represent a promising step towards HIV eradication by demonstrating the potential of innate immune modulation for reducing the viral reservoir through a novel pathway driven by IRF7.

Since April 2020, our group has also focused on understanding SARS-CoV-2 infection and its associated pathogenesis, by developing sensitive and reproducible methods for the quantification of SARS-CoV-2 viral load in COVID-19 patients and tissues from distinct animal models has been developed. Ongoing work also includes the elucidating the role of the innate immune response in COVID-19 pathogenesis and deciphering and characterizing early events that might determine infection outcomes, with particular interest in cellular proteins that might be important for the development of broad spectrum agents that can be used as new therapeutic strategies against viral infections.

2. Immune cell function in cancer: mechanisms, biomarkers and immunotherapeutic opportunities. The mechanisms that control the interface between the metabolism of nucleic acids and their detection by the immune system determine the onset and treatment of diseases like viral infections and cancer. Our group is currently working on the development and validation of SAMHD1 as a biomarker of therapeutic response to the nucleoside analogues currently used to treat viral infections and cancer. It is also working on describing and characterizing key cellular targets that determine the antiviral and antitumoral immune response, with a particular emphasis on identifying novel immunotherapeutic strategies.

Moreover, we have also established a multidisciplinary research team whose main interest is the study and characterization of immune function in breast cancer, with the ultimate goal of providing biological basis for the development of immune-derived biomarkers of treatment response and novel therapeutic strategies that improve current anticancer immunotherapies

2022 milestones

Our group achieved the following milestones:

— **Identification of novel cell factors involved in viral infections.** Our research continued into cellular factors that affect viral infections, with special focus on the role of innate immune factors as putative therapeutic targets for acute and chronic viral infections.

— **Advances in research into the SARS-CoV-2 infection.** Our group developed a method for determining viral load in COVID-19 patients that allowed the quantification of more than 5000 samples, including patients from different study cohorts, distinct tissues from animal models and evaluation of in vitro infection on cell lines and 3D cultures, in collaboration with Dr Marta Riera from the IMIM Nephrology Department.

— **Identification and validation of prognostic and predictive biomarkers in cancer patients.** In collaboration with the ICO-Badalona B-ARGO research group, our group finalized a retrospective study in patients with different types of cancer that evaluated the predictive and prognostic value of SAMHD1. In collaboration with Dr Mireia Margelí, head of the ICO-Badalona Breast Cancer Functional Unit, our group also has started the immunophenotypic characterization of breast cancer patients treated with CDK4/6 inhibitors.

Perspectives for the future

Our goal is to develop new and more effective therapeutic strategies to fight viral infections and cancer. Studies of host-virus interactions will continue, based on the inhibition of key interactions between viral and cellular targets, so as to establish mechanisms of action, determine the role played by cellular factors in different viral replication stages and evaluate new therapeutic targets. Thanks to fruitful collaboration with B-ARGO, the identification and validation of prognostic and predictive biomarkers in patients with cancer will enter a new phase focused on in-depth study of breast cancer cohorts. Consolidation of the research group and improved competitive funding will also represent core objectives for 2023.

1 **Group of talented young researchers pursuing a common research goal**

5 **Funded competitive contracts for researchers ongoing**

4 **Invited talks in scientific meetings**

Principal Investigator
Ester Ballana Guix

Senior research scientists
Roger Badia Córcoles
Eva Riveira Muñoz

Postdoc researchers
Edurne García Vidal

Predoc researchers
Ignasi Calba Iñiguez
Ifeanyi Jude Ezeonwumelu
Eudald Felip Falgàs
Lucía Gutiérrez Chamorro

Grifols project

New Cell Targets for HIV Cure (NeCeTar)

Principal investigator: Ester Ballana Guix

Antiretroviral therapy is effective in reducing circulating viral load at undetectable levels but does not cure HIV infection. Although promising, current "shock and kill" strategies aimed at reactivation latent HIV and subsequent clearance of infected cells, have not succeed in providing a functional cure for HIV infection. Based on the need of novel agents and strategies to achieve an efficient clearance of the latent reservoir, the objectives of the project are:

— To identify new cell targets associated to HIV-1 latency establishment and reactivation. An increased understanding of the mechanisms of HIV latency, persistence and reactivation will provide novel targets for drug development.

— To identify chemical compounds that reactivate latent HIV-1 and/or limit persistence. Once identified, the mechanism of action of novel latency reversing agents will be characterized.

— To propose and validate novel therapeutic strategies for HIV cure, alone or in combination with current treatments.

Retrovirology & Clinical Studies (GREC)

PROJECTS AWARDED

Mechanisms that regulate HIV persistence
Funding: AGAUR
Participating entities: IrsiCaixa
Starting and finishing date: 04/22-03/24
Principal investigator(s): Sara Morón López

Impact of Viral Tropism in HIV Reservoir Seeding and Inducibility
Funding: Gilead Sciences
Participating entities: IrsiCaixa
Starting and finishing date: 07/22-06/24
Principal investigator(s): Mª Carmen Puertas Castro

Elimination of the latent HIV-1 reservoir using anti-CD4 chimerical antigen receptor (ANTICD4-CAR) modified T-cells
Funding: MICINN
Participating entities: IrsiCaixa
Starting and finishing date: 08/22-07/26
Principal investigator(s): Maria Salgado Bernal

AWARDS AND ACHIEVEMENTS

Javier Martínez-Picado, member of the CIBER network
Javier Martínez-Picado, elected member of the Royal Academy of Sciences and Arts of Barcelona
Sara Morón López, granted with a Sara Borrell fellowship
Maria Salgado Bernal, granted with a Miguel Servet fellowship

Presentation

The current scientific interests of our group focus on characterising the immuno-virological mechanisms of viral pathogenesis in human diseases, including HIV-1, Ebola virus, arenaviruses and, more recently, SARS-CoV-2. Our programme has a translational character with the aim of investigating potential new viral therapeutic strategies through basic and applied research. We work closely with other IrsiCaixa research groups and with national and international biomedical institutes, focusing on three priority areas in HIV research: HIV cure, viral pathogenesis mediated by dendritic cells and extreme HIV infection phenotypes.

2022 milestones

1. Understanding viral persistence to tackle HIV cure strategies. We evaluate the persistence of replication in the presence of effective antiretroviral treatment, study the location of viral reservoirs and their consequences, and work on clinical studies focused on the development of therapeutic interventions aimed at reducing these reservoirs and achieving drug-free immune control of HIV. Our group co-leads the first consortium of allogeneic stem cell transplantation in HIV patients (IciStem), a project that has resulted in the second and third case in the history of HIV remission in the absence of antiretroviral treatment, and participates in an NIH-sponsored study to reverse immune dysfunction for HIV-1 eradication. **2. Extreme phenotypes of HIV infection** (rapid progressors, exceptional natural controllers, viremic non-progressors, exposed uninfected, and pediatric populations). We evaluate the immune-viological features involved in these profiles that may contribute to the understanding of the pathogenesis of the infection and their application in new therapeutic, diagnostic and personalised patient follow-up strategies. **3. Dendritic cell-mediated HIV pathogenesis.** We base our work on our discovery of the recognition axis between viral gangliosides and their receptor CD169/Siglec-1, as well as its role in viral spread and the design of therapeutic strategies that can take advantage of this mechanism. This research has been explored in the context of HIV-1, Ebola/Marburg virus, Lassa virus and SARS-CoV-2. **4. SARS-CoV-2 and COVID-19.** We collaborate in projects that include the interaction between the virus and the host through immuno-genomic studies of cases of severe disease, the capacity of exosomes to transport viral antigens, the use of CRISPR to identify potential cellular factors relevant to virus replication, the development of lung/brain organoid models and endothelial organ-on-a-chips to study potential antiviral and anti-inflammatory therapies, and the long-term effects of the disease in paediatric patients. **4. SARS-CoV-2 and COVID-19.** We collaborate in projects that include the interaction between the virus and the host through immuno-genomic studies of cases of severe disease, the capacity of exosomes to transport viral antigens, the use of CRISPR to identify potential cellular factors relevant to virus replication, the development of lung/brain organoid models and endothelial organ-on-a-chips to study potential antiviral and anti-inflammatory therapies, and the long-term effects of the disease in paediatric patients.

Perspectives for the future

— Finding mechanisms to revert the immune dysfunction induced by HIV infection in people on stable antiretroviral therapy: a path for HIV eradication.
— Multiomics identification and validation of mechanisms triggered by immune interventions aimed at reducing the size of the replication competent reservoir.
— Deepening the characterization of the persistent HIV- 1 antigen production in people with HIV on stable antiretroviral therapy and its central role in inflammation and chronic immune activation.
— Discovery and preclinical approach to eliminate the HIV-1 latent reservoir by using novel anti-CD4 chimeric antigen receptor T cells.
— Discovery and preclinical approach of novel HIV-1 RNA biogenesis inhibitors based on disrupting the RRE-Rev ribonucleoprotein.

— Modulating viral splicing as a strategy to cure HIV
— Exploring the role of virus-host interactions in extreme HIV-1 infection phenotypes, including viremic non-progressors, whose immune system is not damaged by high levels of viremia, and HIV-exposed non-infected people.
— Dissecting CD169-mediated endocytic mechanisms in myeloid cells and their contribution to virus dissemination.
— Preclinical studies of the efficacy of humanized CD169 monoclonal antibodies with capacity to block HIV-1, Ebola virus, and SARS-CoV-2 transmission via myeloid cells.
— Designing nanocarriers that specifically target CD169 in myeloid cells as a mechanism to deliver drugs and immunogens.
— Designing nanotechnological devices based on the binding capacities of CD169 to capture enveloped viruses as well as extracellular vesicles.
— Development of a new cutting-edge mass PCR testing as a pandemic-fighting strategy: technological development, population-based implementation, epidemiological relevance and socio-economic impact.
— Investigation of the human genetic and immunological determinants of the clinical manifestations of SARS-CoV-2 infection: towards personalised medicine.
— Analytical and predictive value of brain organoids to investigate the neurodegeneration triggered by SARS-CoV-2.
— Unravelling the biological mechanisms causing long COVID in the pediatric population.

4 **Research projects have been awarded to the group**

20 **Peer-reviewed scientific publications**

1 **Master thesis has been defended**

Principal Investigator
Javier Martínez-Picado

Senior research scientists
Jakub Chojnacki
Sara Morón López
Mª Carmen Puertas Castro
Patricia Resa Infante
Maria Salgado Bernal

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Gerard Campos Gonzalez
Irene González Navarro
Cristina Gálvez Celada
Jon Izquierdo Pujol
Fernando Laguía Nueda
Xabier Muñiz Trabudua

Research statician
Víctor Urrea Gales

Bioinformatician
Lidia Garrido Sanz

Senior research technician
Itziar Erkizia Jauregi

Research technicians
Mª Carmen García Guerrero
Gisela Zamorano García

Grifols project

New techonologies mimicking virus-cell interaction to fight infectious diseases (SIGTECH)

Senior researcher: Javier Martínez-Picado
Principal investigator: Patricia Resa Infante
In collaboration with: Nuria Izquierdo Useros

— To generate a humanized version of the best murine blocking monoclonal antibody (mAb) against the Siglec-1 protein, which is able to block HIV capture and trans-infection as well as Ebola viral-like-particle capture and fusion, essential processes for infection on primary myeloid cells.

— To develop nano-vehicles using clinically approved biomaterials that allow construction of nanoparticles for therapeutic purposes. We will expand our studies to see if glycol-engineering of nanoparticles designed for clinical use can induce the reactivation of HIV-1 latency and trigger immune antiviral control.

— To develop a detection platform based on Siglec-1 receptor capacity to diagnose the presence of different enveloped viruses, and to isolate exosomes in liquid biopsies from cancer patients.

HIV and HCV Genetic and Phenotypic Variability

PROJECTS AWARDED

Evaluation of the ex vivo hepatitis C virus antiviral activity of Plitidepsin and related compounds
Funding: PharmaMar
Participating entities: IrsiCaixa
Starting and finishing date: 01/22-12/22
Principal investigator(s): Miguel Ángel Martínez de la Sierra, Sandra Franco Cirera

AWARDS AND ACHIEVEMENTS

Miguel Ángel Martínez de la Sierra, top-cited scientist in the career-long database and in the single recent year 2021 dataset (Scopus, Elsevier)
Miguel Ángel Martínez de la Sierra, associated editor of Frontiers in Immunology
Miguel Ángel Martínez de la Sierra, AIDS editorial Board member
Miguel Ángel Martínez de la Sierra, invited editor for the 2023 Viruses Special Issue: Impact of Synonymous Mutations on the Evolution, Fitness and Pathogenesis of RNA Viruses

Presentation

The research interests of our group are focused in understand the molecular mechanisms implicated in human viruses pathogenesis. In the last twenty five years, we have being studying how the genetic variability of HIV-1 and HCV has influenced virus pathogenesis, immunogenicity and response to antiviral therapy (reviewed in Martinez and Franco, Viruses 2021a; Martinez, Viruses 2021b). Recently, we have explored how synonymous codon mutations impact HIV-1 protein expression and virus replication capacity. Codon or codon pair biases and HIV-1 RNA dinucleotide frequencies (e.g. CpG/UpA) affect host innate response, virus latency and pathogenesis (reviewed in Jordan-Paiz, Franco and Martinez, Frontiers in Microbiology 2021). In relation to our work with HCV, we are quantifying the levels of plasma circulating microRNAs (miRNAs) as biomarkers of liver disease progression in HIV-1 and/or HCV infected patients (Martinez, Tural and Franco Viruses 2022). miRNAs are predicted to regulate over half of the human transcriptome. The lack of available biomarkers for diagnosing and predicting different stages of liver disease (e.g., NAFLD and NASH) is currently one of the main challenges that clinicians are facing. Lastly, we have hypothesized that an alternative antiviral agent is to target specific miRNAs associated with SARS-CoV-2 infection and subsequent manifestation of COVID-19 (Martinez Drug Discovery Today 2022; Martinez Frontiers in Microbiology 2022).

2022 milestones

1. Synonymous genome recoding of HIV-1. Synonymous replacement of CpG dinucleotides in the HIV-1 envelope (env) coding region has been correlated with evasion of the antiviral activity of the zinc-finger antiviral protein (ZAP). To explore the effect of depleting HIV-1 env CpG dinucleotides by synonymous substitution on ex vivo viral replication capacity, we eliminated 11 env CpG dinucleotides through synonymous substitutions in the CXCR4-tropic HXB2 strain. The replication kinetics in MT-4 cells and peripheral blood mononuclear cells (PBMCs) of the WT and synonymously recoded mutant viruses were indistinguishable. However, virus competition assays in MT4 cells between the WT and recoded viruses showed that the mutant with fewer CpG dinucleotides quickly overgrew the WT virus. These results demonstrate that a reduction in HIV-1 env CpG dinucleotide frequency can improve viral replication capacity in cell culture. Our results support the previous observation that the frequency of CpGs in the HIV-1 env region correlates with differences in clinical progression rates in infected individuals (Jordan-Paiz, Franco and Martinez Virus Research 2022).

2. miRNAs as disease biomarkers and antiviral targets. We recognized three plasma circulating miRNAs—miR-100-5p_iso3p:-2, miR-122-5p, and miR-192-5p—that correlate largely with liver fibrosis evolution in HIV-1/ HCV co-infected patients (Franco et al AIDS 2021). To investigated whether levels of these three circulating miRNAs can be associated to liver disease evolution in HIV-1/HCV co-infected patients which have achieved HCV sustained virologic response (SVR) 12 weeks after finishing treatment, eighty-one chronic HIV-1/HCV co-infected patients were longitudinally recruited at baseline (T0) of DAA therapy and 12 weeks (T12) after finishing therapy. At T0 most of the study patients displayed transient elastography values linked to an advanced stage of liver fibrosis. Significant reductions in the levels of circulating miR-100-5p_iso3p:-2, miR-122-5p, and miR-192-5p were detected at T12 in SVR patients, in the overall cohort and in patients with advanced liver fibrosis. Importantly, no significant

reduction in the study miRNA levels was found at T12 in patients who did not achieve SVR. Moreover, HCV-cured patients, in contrast to non-responders, significantly reduced their liver stiffness after two years of achieving SVR. Our results indicate that miRNA plasma levels may be a useful biomarker of liver damage progression in HIV-1/HCV co-infected individuals that reach DAA-induced SVR (Franco et al Scientific Reports 2022; Franco et al Heliyon 2023).

To determine whether circulating plasma miRNAs can be possible biomarkers of COVID-19 inflammation, coagulation, lung disease and other organ disease progression (Martinez Frontiers in Immunology 2021; Martinez and Franco Hepatology Communications 2021), we performed large-scale deep sequencing analysis of small RNA expression on plasma samples from SARS-CoV-2 infected patients with COVID-19. Our results indicate that there are circulating miRNA directly involved with SARS-CoV-2 infection. Furthermore, specific miRNA profiles are associated with COVID-19 prognosis in severe patients. Circulating host miRNA profiles may allow a better diagnosis of disease severity and outcome (Franco et al manuscript in preparation 2023).

Perspectives for the future

In the next future, we will continue to study the molecular basis of how HIV-1 genome synonymous variability affects virus pathogenesis. We also expect to further explore the interactions between host miRNAs and SARS-CoV-2, which are multifaceted. Specifically, we aim: 1) to study the impact of innate response, e.g. ZAP, Schlafen 11, on shaping HIV-1 nucleotide content and virus replication capacity and evolvability, 2) to characterize the mechanisms of induction of the immune response associated with the HIV-1 RNA genome nucleotide content, 3) to correlate blood levels of miRNAs and SARS-CoV-2 viral load and 4) to identify miRNAs that may directly regulate and drive a COVID-19 response.

Principal Investigator
Miguel Ángel Martínez de la Sierra

Senior research scientist
Sandra Franco Cirera

6 **Published peer-reviewed and indexed papers**

2 **Ongoing projects on HIV-1, HCV and SARS-CoV-2**

1 **Doctoral thesis supervised**

Cell Virology & Immunology (VIC)

PROJECTS AWARDED

Determination of nAb levels for AELIX-002 Clinical Trial
Funding: AELIX Therapeutics
Participating entities: IrsiCaixa
Starting and finishing date: 06/22-12/22
Principal investigator(s): Julià Blanco Arbués

Predoctoral grant
Funding: AGAUR
Participating entities: IrsiCaixa
Starting and finishing date: 05/22-04/25
Principal investigator(s): Anna Pons Grifols

Investigación de nueva vacuna para enfermedad respiratoria humana (VSRVAC)
Funding: HIPRA
Participating entities: IrsiCaixa
Starting and finishing date: 01/22-
Principal investigator(s): Julià Blanco Arbués, Nuria Izquierdo Useros

AWARDS AND ACHIEVEMENTS

Julià Blanco Arbués, member of the CIBER network

Presentation

Our group maintain the focus on the HIV envelope glycoprotein (Env) as the main target of preventative vaccines and a major target for treatments against HIV, seeking for optimal strategies to functionally cure or eradicate AIDS. Our work on HIV vaccines is based on a novel highly immunogenic VLP platform, while therapeutic approaches are based on the design of synthetic antibodies with improved antiviral activity. Both approaches have been extended to other relevant infectious diseases for human health and to cancer immunotherapies. In addition, the new SARS-CoV-2 pandemic has been a relevant additional focus of our research. In this highly dynamic research context, our group has maintained three main research lines, balancing the different objectives:

1. Translating knowledge on the HIV envelope glycoprotein (Env) and its humoral response to the development of preventative HIV vaccines.
a) We have demonstrated a link between HIV ENv function and disease prgression.
b) We have identified specific Env sequences isolated from Extreme Elite Controllers that are being tested as candidate vaccines.

2. Extending the VLP vaccine platform to other diseases
a) We have demonstrated the flexifility of our VLP technology by adapting it to other viruses.
b) In collaboration with NeoVaCan group, we have optimized the VLP platform to accomodate tumor neoantigens and develop anti tumor vaccines.

3. COVID-19 research.
a) A large effort has been made to understand the interplay between antibody responses and viral evolution. A pseudovirus neutralization assay covering different variants of the virus is already in place.
b) This assay has been transfered to Hipra and has been crucial for the success of its vaccine program.

2022 milestones

1. **A wide collaborative network to neutralize SARS-CoV-2.** We have demonstrated the different pathogenic potential of SARS-CoV-2 variants in vivo (Tarrés Freixas et al 2022).
2. **COVID vaccine research.** Relevant contribution to the development of Bimervax (Hipra) vaccine.
3. **HIV and other pathogens.** Three candidate Env vaccines selected for immunogenicity studies.

Perspectives for the future

— **COVID research.** New studies on the Bivervax (Hipra) vaccine are ongoing in the hallmark of a EU funded project.
— **New research platforms.** New collaborative projects have started (with Hipra) on RSV infection. The RNA platform is being explored in this and other vaccine fields (HIV and cancer vaccines).

15 Committed researchers to explore the One Health concept

27 Scientific articles published, mostly on SARS-CoV-2

10 New SARS-CoV-2 variants analyzed

Principal Investigator
Julià Blanco Arbués

Senior research scientists
Carmen Aguilar Gurrieri
Benjamin Trinité

Research technicians
Silvia Marfil Verchili
Carla Rovirosa Martí

Research statician
Victor Urrea Gales

Predoc researchers
Ferran Abancó i Espuga
Ana Barajas Molina
Raquel Ortiz López
Tetyana Pidkova
Anna Pons Grifols
Edwards Pradenas Saavedra
Ferran Tarrés Freixas

AlbaJuna Therapeutics SL
Ester Aparicio Prats, Amaya Blanco Perera, Francesc Cunyat Viaplana, Cristina Val Cid

Grifols projects

High Density Virus-Like Particles: a Novel Vaccine Platform Against Infectious Diseases (INDIVAC)

Senior researchers: Julià Blanco and Jorge Carrillo

Developing a preventative HIV-1 vaccine based on the generation of HIV Gag VLPs with rationally designed HIV Env-antigens. Candidate antigens have been already selected and new animal model to assess functionality of immune responses have been developed. A secondary aim is to expand the VLP technology to other pathogens (treponema in collaboration with Jorge Carrillo), FeLV (in collaboration with HIPRA) and human respiratory viruses (in collaboration with MSD).

VLPs Expressing Tumor Neoantigens as Personalized Cancer Therapeutic Vaccines (NEOVAC)

Senior researchers: Julià Blanco and Jorge Carrillo

Exploiting VLP technology as a vaccine platform (protein or DNA) to elicit cellular and humoral protective responses to tumors. The aim is to generate a platform of personalized DNA cancer vaccines. It requires the identification and selection of optimal tumoral antigens that will be included in the VLP vaccine and will activate the immune system. Animal models for melanoma and pancreatic cancer are already in place. The project is a collaboration with Dr de Mattos-Arruda at IrsiCaixa and BSC.

Tissue Virology (VITI)

PROJECTS AWARDED

Digital Twins Enabled Indoor Air Quality Management for Healthy Living
Funding: European Commission (Horizon Europe)
Participating entities: IrsiCaixa, IGTP
Starting and finishing date: 09/22-08/26
Principal investigator(s): Cecilia Cabrera Navarro

Comprehensive analysis of urine biomarkers to predict pathologic complete response in muscle invasive bladder cancer patients treated with neoadjuvant therapy
Funding: GILEAD
Participating entities: IrsiCaixa, IGTP, ICO
Starting and finishing date: 01/22-12/224
Principal investigator(s): Cecilia Cabrera Navarro

AWARDS AND ACHIEVEMENTS

Cecilia Cabrera Navarro, member of the CIBER network
Cecilia Cabrera Navarro, editor of Scientific Reports
Cecilia Cabrera Navarro, editor of Frontiers in Microbiology
Cecilia Cabrera Navarro, member of the international FEMIN (Female European Mucosa Immunity) Network

Presentation

The study of the impact of HIV on immune cells present in tissues, particularly in mucosa-associated lymphoid tissue became the hallmark of the research group. However, in recent years, the evaluation of the immune response present in tissues has emerged as a critical field in the study of several pathologies including infectious diseases and cancer. In this scenario, the research group has broadened its objectives by applying the knowledge acquired and the tools and biomodels developed, and has established a line of research focused on the characterization of tissue-specific immunopathogenesis. The group has been working in three different settings (infectious diseases, bladder cancer and lung pathologies).

— Evaluation of viral associated immunopathogenesis: HIV infection is a mucosa-associated disease, with pathogenesis in two phases: an acute phase, associated with a massive loss of CD4+ T-cells resident in the mucosa, especially in the gut-associated lymphoid tissue (GALT), and a chronic phase, responsible for the gradual destruction of CD4+ T-cells in peripheral blood and characterized by elevated immunological activation and elevated production of proinflammatory cytokines. Cellular immune response in HIV infection is not capable of controlling viral replication in most individuals, probably because the quality and place of induction may not be suitable. During this year the group has been working in the evaluation of the mechanisms of HIV associated cell death and in the characterization of new strategies to improve the antiviral response of the cells present in the tissues. In ex vivo tissue cultures we have characterized the tissue resident immune cells functionality and described a new immunomodulator capable of increase their functionality by the modulation of the innate immune response.

4 Ongoing projects

1 European research project awarded to the group

1 Group of committed people fighting human diseases

— Immunopathogenesis in bladder cancer: bladder cancer is one of the most prevalent cancers in the world. Around 70%–80% of de novo bladder cancers are diagnosed in early stages with no muscular invasion (NMIBC). These patients are often managed with transurethral resection of bladder tumor (TURBT) with or without adjuvant intravesical therapy. The standard treatment in these patients is intravesical administration of BCG (Mycobacterium bovis mycobacterium). Although the mechanism of action is not fully understood, it is thought that the immune system is activated and immune cells are attracted to the bladder wall. While BCG is effective in preventing the development of new tumours, many patients fail to respond and no alternative is as yet available. Therefore, new strategies that improve the clinical management of patients are urgently needed. Using an animal model, we have been working in the evaluation of bladder tumor immune microenvironment profile after BCG intravesical treatment. In addition, we are currently

working in the evaluation of the role of the immune system in invasive muscle bladder cancer (MIBC) and its impact on the efficacy of neoadjuvant chemotherapy (NAC).

— Development of new pre-clinical clinically relevant models for the evaluation of tissue-specific immunopathogenesis: our group is interested in the development of new 3D models for the evaluation of the pathogenesis associated with different pathologies. In this regard, we are working on the establishment of different cell culture models to study lung health and tumor tissue associated immunology.

2022 milestones

Our group achieved the following milestones:

— Mechanisms of HIV associated cell death: we have shown that autophagy is playing a key role in HIV pathogenesis, therefore, targeting the autophagic pathway could be a new therapeutic approach to be explored to treat HIV-1 infection.

— Identification of novel immunomodulator: in ex vivo tissue cultures we have characterized the tissue resident immune cells functionality and described a new immunomodulator capable of increase their functionality by the modulation of the innate immune response.

— Characterization of the bladder immune microenvironment and evaluation of new therapeutic strategies: we have demonstrated that that each mycobacterium requires specific culture conditions to induce an effective antitumor response. The cell-surface lipidomic profile could be modified and these profiles impact the triggered immune response, both local and systemic. We have also demonstrated that the bladder immune microenvironment induced by mycobacterial treatment is species specific and shaped by mycobacterial cell envelope composition. Therefore, the global bladder immune microenvironment can be remodelled, improving the quality of infiltrating immune cells, the balance between inflammatory and regulatory/ suppressive responses and increasing survival.

— Evaluation of the impact of indoor air quality in human health: we have initiated the establishment of new pulmonary study models. This has allowed us to have financing from European funds to evaluate the impact of the indoor air in the human lung (TwinAir Project).

Principal Investigator
Cecilia Cabrera Navarro

Senior research scientist
Jordi Senserrich Velasco

Research technician
Elisabet García Rodríguez

Perspectives for the future

— Our goal is to increase the knowledge that the immune system is playing in the pathogenesis of bladder cancer and to design new and more effective therapeutic strategies to fight cancer or even other diseases in which the immune system needs to be modulated, such as infectious diseases.

— Consolidation of the research group and improve competitive funding in the cancer field will be one of our main objectives for 2023.

— To establish new clinically relevant models that recapitulate the complexity of the human diseases and may be used in personalized medicine approaches.

Immunology (IGG)

AWARDS AND ACHIEVEMENTS

Jorge Carrillo Molina, member of the CIBER network

Presentation

The main interest of the IrsiCaixa's Immunology group, headed by Dr Jorge Carrillo, is the study of the immune system in infectious diseases (particularly, HIV-1, SARS-CoV-2 and syphilis). Moreover, it is also conducting research related to immuno-oncology, basic immunology and autoimmunity. The Immunology group collaborates with many researchers, both in and outside IrsiCaixa.

2022 milestones

COVID-19

— Characterization of SARS-CoV-2 immunopathogenesis and the immune response elicited after infection or vaccination in human and animal models.
— Deciphering the role of anti-SARS-CoV-2 antibodies in severe COVID-19.

HIV-1 infection

— Characterization of the humoral responses in HIV-1 infected individuals.
— Identification and characterization of novel non-neutralizing trimer specific monoclonal antibodies.
— Identification and characterization of novel HIV antibodies that block the binding of anti-CD4 neutralizing antibodies.
— Progress in HIV vaccine development.

Vaccine development

— Evaluation of the efficacy of a novel COVID-19 vaccine in geriatric K18-hACE2 mice and golden Syrian hamsters.
— Work on the development of a syphilis vaccine based on outer membrane proteins.
— Progress in the development of a HIV-vaccine based on the generation of broadly neutralizing antibodies.

Basic immunology and immuno-oncology

— Characterization of a novel anti-CD5L antibody as a novel macrophage target immunotherapy (in collaboration with Dr Maria Rosa Sarrias).
— Defining optimal linker for personalized cancer vaccines.

Perspectives for the future

We expect to further consolidate our research lines and strengthen our national and international collaborations. Our priority will be:

— to develop prophylactic HIV and syphilis vaccines.
— to characterize the role of humoral responses in severe COVID-19.
— to characterize the role of non-neutralizing antibodies in HIV infection.

13 Publications

3 Active projects

5 Invited talks

Principal Investigator
Jorge Carrillo Molina

Senior research scientist
Erola Ainsua Enrich

Postdoc researchers
Núria Pedreño López
Julieta Carabelli

Predoc researcher
Carlos Ávila Nieto

Translational Research in Immunology and Ageing (TRIA)

PROJECTS AWARDED

Deep immunophenotyping of the Long Covid syndrome
Funding: Gilead Sciences
Participating entities: IrsiCaixa, Fight Infections Foundation
Starting and finishing date: 07/22-06/24
Principal investigator(s): Marta Massanella Luna

Role of NK cells in post COVID-19 condition (LoNK-COVID)
Funding: MICINN
Participating entities: IrsiCaixa
Starting and finishing date: 07/22-06/25
Principal investigator(s): Maria Nevot Banús

SARS-CoV-2 post-vaccination infection: cohort study for the characterization of the immune response and development of a predictive model to establish revaccination criteria in Catalonia (BreakCOVID)
Funding: Department of Health, Government of Catalonia
Participating entities: IrsiCaixa, IDIAP Jordi Gol, IGTP
Starting and finishing date: 07/22-06/25
Principal investigator(s): Marta Massanella Luna

Biomarkers and underlying immunopathological mechanisms of post COVID-19 condition
Funding: ISCIII
Participating entities: IrsiCaixa, ISGlobal, ISCIII
Starting and finishing date: 08/22-07/24
Principal investigator(s): Marta Massanella Luna

Neurocognitive profile of Long Covid in adults living in Catalonia (ProHEpiC-19)
Funding: Department of Health, Government of Catalonia
Participating entities: IrsiCaixa, IDIAP Jordi Gol, IGTP, University of Barcelona
Starting and finishing date: 07/22-07/25
Principal investigator(s): Julia García Prado

AWARDS AND ACHIEVEMENTS

Marta Massanella Luna, member of the CIBER network
Marta Massanella Luna, member of the Long Covid sub-committee of Comitè Científic Assessor de la COVID-19 at the Health Department of the Generalitat de Catalunya
Marta Massanella Luna, editor from Viruses and Frontiers in Immunology
Marta Massanella Luna, topic editor from Frontiers in Tropical Diseases (Topic HIV, co-morbidities and aging)
Marta Massanella Luna, member of the Research Data Management and Training group at IrsiCaixa
Marta Massanella Luna, member of the Scientific Committee of the XIII Congreso Nacional de GeSIDA

Presentation

TRIA focuses on translational studies to investigate the remodeling of the immune system after viral infections and during the process of ageing, focusing on three main lines of research:

— Inflammageing and immunosenescence during HIV infection. Despite the great improvement brought about by ART therapy, the prevalence of age-related comorbidities is higher in HIV-infected population. We study this accentuated ageing and characterize immune dysfunction, HIV reservoir and altered metabolism in ART-treated individuals. People living with HIV have a higher prevalence of cardiovascular events than the general population, associated with persistent systemic inflammation, which has also been associated with epigenetic and metabolic changes in monocytes. In this line, and in close collaboration with Dr. David Dalmau of the Fundació de Docència i Recerca Mútua Terrassa, the TRIA group is studying the metabolic and epigenetic profile of monocytes, and their involvement in systemic inflammation and cardiovascular risk (Gilead grants, CardioMetabol).

— COVID-19 vaccine response in older adults. We are working in close collaboration with the Metropolitana Nord Primary Care Centre (DAP-MN) to evaluate the immune response generated by COVID-19 vaccines in previously infected and uninfected older adults living in long-term care facilities as well as noninstitutionalized older individuals, to adapt the SARS-CoV-2 vaccination calendar to their specific immune needs.

— Studies on Post-COVID-19 condition. In addition, our group has contributed to the establishment of the referral national clinical unit of post-COVID-19 condition at Germans Trias i Pujol Hospital, where patients who experience heterogeneous and debilitating persistent symptoms for months after SARS-CoV-2 infection are followed. In this unit, clinical care management is completely linked to longitudinal research studies to assure the well being of the patient as well to determine the origin(s) of the persistent symptomatology. In our group, we are

>1800 Participants in our clinical studies

>10 Active clinical studies of HIV and SARS-CoV-2

1st Clinical intervention in Long Covid

5 Motivated and talented young researchers

1 Ramon y Cajal contract at UVic-UCC

characterizing the immune dysfunctions behind post-COVID-19 condition, to find diagnostic markers and identify treatment interventions that could lead to the recovery of these patients. We are currently participating in a clinical intervention to treat this condition (PAX study, plasmapheresis, NCT05445674).

2022 milestones

Inflammageing and immunosenescence during HIV infection:

— Characterization of the metabolic status of T cells across ages in HIV infection and its impact in immunosenescence and in the persistence and inducibility of the HIV reservoir.

— In collaboration with Dr Negredo from Lluita contra les Infeccions (FLI), characterization of the immune system and immunosenescence (including telomere length) in subjects older than 70 years (OVER50 cohort).

— In collaboration with Dr Negredo (FLI) and Dr Martin of the Autonomous University of Barcelona (UAB), characterization of alterations in DNA repair mechanisms in HIV-infected older adults so as to associate them with accentuated immunosenescence.

— In collaboration with Dr David Dalmau (Mutua de Terrassa), characterization of the metabaolic profile of monocytes in the developement of cardiovascular diseases in PLWH

— In collaboration with Dr David Dalmau (Mutua de Terrassa), characterization of miRNA signatures as predictive hallmark of cardiovascular disease in PLWH.

COVID-19:

— Coordination of the KING cohort extension of SARS-CoV-2 infected individuals (N>1000) with different levels of severity (asymptomatic to critical), a cohort that is of use to all IrsiCaixa groups. This cohort includes also more than 600 individuals suffering from post-COVID-19 condition.

— In collaboration with Dr Lourdes Mateu (FLI), exploration of pro-inflamatory status, immune dysfunctions and viral persistence in individuals with post-COVID-19 condition, and its association with specific persistent symptomatology.

— Exploration of the specific role of NK-cells in the post-COVID-19 condition.

— In collaboration with Dr. Pere Toran (IDIAP-Jordi Gol) and Dr Julia Garcia-Prado (IrsiCaixa VIRIEVAC group), deep neurological and immune characterization of individuals with post-COVID-19 condition with persistent neurocologic complaints.

— In collaboration with Dr. Christian Brander, epigenetic studies of individuals with post-COVID-19 condition with persistent neurocologic complaints.

— In collaboration with Drs Nuria Prat (DAP-MN) and Concepció Violán (IDIAP-Jordi Gol), coordination of the CoronAVI@S and IMMERSION studies of residents of long-term care facilities or non-institutionalized older adults to evaluate the quality and duration of immune responses elicited by SARS-CoV-2 vaccine.

— In collaboration with Drs Concepció Violán (IDIAP-Jordi Gol) and Julia Garcia-Prado (IrsiCaixa VIRIEVAC group), evaluation of the SARS-CoV-2-specific immune responses in individuals susceptible to develop severe COVID-19 after breaktrough infections (BREAKCOVID).

— In collaboration with HUGTiP (Microbiology lab), Dr. José Ramon Santos (FLS) and Dr. Marc Noguera (IrsiCaixa Microbial Genomics group), evaluation of clinical characteristics and outcomes of patients with SARS-CoV-2 reinfection (RECOVID).

Principal Investigator
Marta Massanella Luna

Senior research scientist
Maria Nevot Banús

Predoc researchers
Macedonia Trigueros Peña
Franciso Manuel Muñoz López
Marina Martínez Velasco

Perspectives for the future

— **Ageing with HIV:** our group will continue to characterize accentuated immunoageing and immunosenescence in HIV-infected ART-treated individuals compared to the uninfected counterpart. The aim is to determine the origins of immune dysfunction and develop new senolytic strategies. We will also explore how the process of natural ageing in people living with HIV induces changes in the nature of the viral reservoir. We will evaluate also the role of cellular metabolism in the persistence of the HIV reservoir.

— **COVID-19:** we will continue our SARS-CoV-2 infection research, focusing especially on recovered individuals with post-COVID-19 condition. Using extensive data collected on these patients, we will implement pilot interventions aimed at reducing persistent symptomology and improving the quality of life of recovered patients.

In addition, we will further characterize the immune responses in elders living in long-term care facilities to adjust their vaccination calendar and ensure their protection against SARS-CoV-2 infection.

Pathogen Immunity, Signalling & Therapeutic Applications (PISTA)

PROJECTS AWARDED

Proteomic study of SARS-CoV-2 infected Vero E6 cells
Funding: PharmaMar S.L.
Participating entities: IrsiCaixa
Starting and finishing date: 05/22-05/23
Principal investigator(s): Nuria Izquierdo Useros

Farm-in-a-plate: developing the first biobank of farm animal organoids as an alternative to animal experiments in infectious disease research
Funding: MICINN
Participating entities: IrsiCaixa, IRTA-CReSA, BSC
Starting and finishing date: 12/22-12/25
Principal investigator(s): Nuria Izquierdo Useros

Actividad antiviral de los colutorios con CPC frente al SARS-CoV-2
Funding: Fight Infections Foundation
Participating entities: IrsiCaixa
Starting and finishing date: 01/22-12/23
Principal investigator(s): Nuria Izquierdo Useros

Actividad antiviral de extractos de plantas amazónicas frente al SARS-CoV-2 en células pulmonares
Funding: Amassence
Participating entities: IrsiCaixa
Starting and finishing date: 07/22-12/23
Principal investigator(s): Nuria Izquierdo Useros

Investigación de nueva vacuna para enfermedad respiratoria humana (VSRVAC)
Funding: HIPRA
Participating entities: IrsiCaixa
Starting and finishing date: 01/22-
Principal investigator(s): Julià Blanco Arbués, Nuria Izquierdo Useros

Pre-clinical in vitro assessment of Aplidin activity against RSV
Funding: PharmaMar
Participating entities: IrsiCaixa
Starting and finishing date: 01/22-12/23
Principal investigator(s): Nuria Izquierdo Useros

AWARDS AND ACHIEVEMENTS

Elisa Molina Molina, selected for the PhD fellowship of the project "Novel antiviral and immunomodulatory therapies against SARS-CoV-2" granted by MICINN
Jordana Muñoz Basagoiti, granted with a competitive scholarship to attend to the 29th CROI
Nuria Izquierdo Useros, member of the scientific committee of the "Virology Meeting 2022" of the Catalan Society of Biology
Nuria Izquierdo Useros, member of the organizing committee of the 4th Woman in Science Day at Can Ruti Campus
Nuria Izquierdo Useros, member of the CIBER network

Presentation

We are an emergent pathogens research group interested in finding novel therapeutic solutions while understanding the molecular basis of infectious diseases. In a constantly evolving world where climate warming and globalization trends are changing the geographical distribution of infectious diseases, our goal is to combat emerging viruses designing novel therapeutic tools. PISTA was launched in February 2020 and immediately devoted all efforts to tackle SARS-CoV-2 pandemic. Many of the techniques implemented have helped us fighting other threats, including Monkeypox or the Respiratory Syncytial Virus. The main 3 lines of our team are:

1. Identify and develop effective antivirals.
2. Find and increase efficacy of immunomodulators.
3. Provide reliable tools to test and validate novel vaccines.

2022 milestones

We continue our work to identify novel antivirals against SARS-CoV-2 while searching for innovative immunomodulatory agents that could help to avoid COVID-19 severe progression. This line of research is performed within the CBIG Consortium established by Dr. Clotet to identify new therapies, antibodies and vaccines in collaborations with IRTA-CReSA and the Barcelona Supercomputing Center, thanks to the support of Grifols. We also collaborate with different companies including PharmaMar, Hipra, Amassence and other partners to study the clinical potential of specific products against SARS-CoV-2.

As part of our commitment, we are also actively working to implement new strategies that could avoid SARS-CoV-2 transmission, and translating all the gained knowledge to tackle new viral threats.

During this year, our work has been devoted to the following activities:

1. To understand the mechanism of action of antivirals against SARS-CoV-2. In collaboration with Dr. Risco from CNB we have used electron microscopy and immunogold staining to dissect the mechanism of action of Aplidin, and also contributed to show safety in a Phase I Clinical Trial. We have also tested other new promising antivirals, and identified cyclodextrins as promising and safe agents against SARS-CoV-2 and other coronaviruses. We continue ongoing antiviral collaborations with the experimental

6 Researchers committed to fight emergent viruses

17 Accepted peer-reviewed papers

5 New viruses isolated

nephrology and transplantation unit of the Hospital Clínic, the University of Lleida and the NCI at Frederick (USA). In addition, we are helping companies such as Amassence and Palobiofarma to identify new anti-SARS-CoV-2 compounds.

2. To search for broad-spectrum antivirals in collaboration with Dr. Ballana, Dr. Martinez and other teams of IrsiCaixa and IRTA-CReSA along with Pharma Mar. We have been able to identify the mechanism of action of key compounds that display broad-spectrum antiviral activity and to precisely define their mechanism of action using deep quantitative proteomic analysis analyses in collaboration with the Proteomics unit of the IJC.

3. To integrate multiple OMIC studies to analyze relevant changes induced in key cellular targets and decipher the molecular pathways involved in SARS-CoV-2 infection, in collaboration with the Proteomics unit of the IJC.

4. To search for novel immunomodulatory agents that could decrease the cytokine storm induced by SARS-CoV-2 in critically ill COVID-19 patients. We have developed an in vitro platform to detect the cytokines released induced by SARS-CoV-2 exposure, with the aim to identify novel immunomodulatory agents. In collaboration with Drs. Vergara-Alert and Segalés from IRTA-CReSA we have continued efficacy studies in murine models testing potential compounds for further development. We also worked along the team of Dr. Thomson from CISC and advised the rational design of prospect clinical trials to the team of Dr. Mitjà from the the HUGTiP.

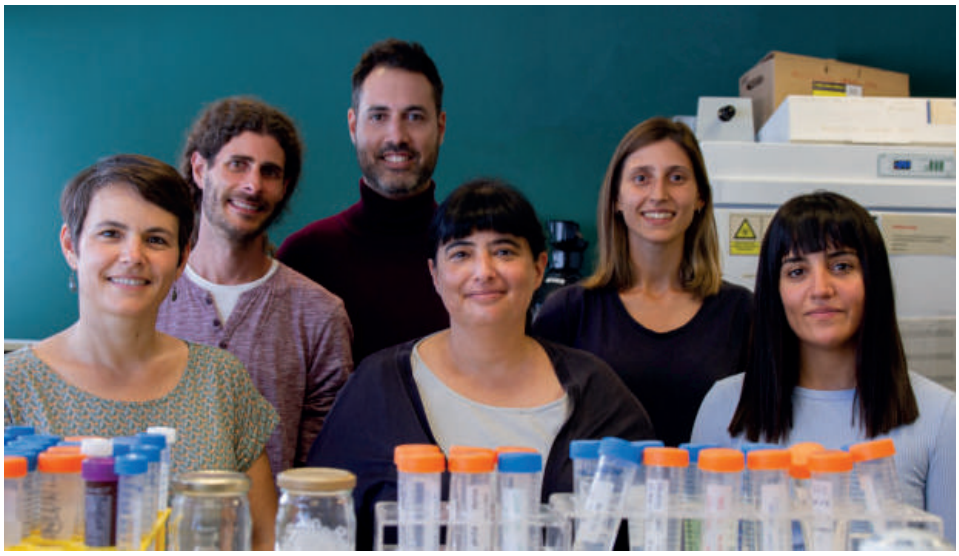
5. To identify novel strategies that could decrease SARS-CoV-2 transmission. We have finalized the evaluation of different commercial Ag-RDT against novel variants of concern including the Omicron variant along with the team of Dr. Blanco and Nesapor Europe. We have also contributed to a randomized clinical trial that confirms that CPC, a virucidal compound present in many oral mouth washes, disrupts viral particles in the saliva of SARS-CoV-2 infected individuals.

6. To perform SARS-CoV-2 viral neutralization assays for different clinical trials launched by HIPRA to test the safety and efficacy of the first SARS-CoV-2 vaccine produced in Catalonia. We assessed the levels of neutralizing antibodies in plasma from vaccinated individuals in collaboration with the team of Dr. Blanco. This year we have completed Phase I and have actively contributed to Phase 2. We have also started the analyses of a European Project to test the efficacy of this vaccine in different subsets of immunocompromised patients. This validated assay has also helped to monitor the levels of neutralizing antibodies in HIV-1 infected patients followed at Hospital Germans Trias i Pujol in the study led by Drs. Mothe and Benet.

7. To launch a collaboration to develop a novel vaccine against the respiratory syncytial virus, led by HIPRA in collaboration with Hospital Clínic, IQS and Curapath.

8. To implement the detection of different Schistosome by qPCR in clinical samples, in collaboration with Dr. Roura and the Microbiology department at HUGTIP.

9. To isolate monkeypox viruses from clinical samples to understand the epidemiological transmission of the outbreak during summer 2022 in Barcelona, in collaboration with Dr. Agustí from CEEISCAT. This study shows that self-sample collection is a viable method for diagnostic purposes and that replicative viruses are found in asymptomatic and pre-symptomatic mpox patients.



Principal Investigator
Nuria Izquierdo Useros

Senior research scientist
Dàlia Raïch Regué

Postdoc researcher
Daniel Pérez Zsolt

Predoc researcher
Elisa Molina Molina

Senior research technician
Marçal Gallemí Rovira
Jordana Muñoz Basagoiti

Perspectives for the future

We will pursue translational impacts of our research, such as:

— Validation of methodologies that can facilitate vaccine approvals.
— Description of mechanisms of action of distinct antivirals to foresee their clinical potential and anticipate side effects.
— Contribute to different clinical trials aimed at combating infections.
— Apply all the gained knowledge to combat other respiratory viruses and emergent threats.

Neoantigens and Vaccines against Cancer (NeoVaCan)

PROJECTS AWARDED

Tumor-specific neoantigens as targets for personalized vaccines
Funding: ISCIII
Participating entities: IrsiCaixa, ICO, Hospital Universitari Germans Trias i Pujol, CNAG-CRG
Starting and finishing date: 01/22-12/24
Principal investigator(s): Núria de la Iglesia Zaragoza

AWARDS AND ACHIEVEMENTS

Núria de la Iglesia Zaragoza, member of the CIBER network

Presentation

The NeoVaCan group performs immunogenomic analyses of solid tumours and liquid biopsies to study the interplay between tumor cells and the immune microenvironment. We are using multi-omics coupled to functional immune cell-based assays to get a deeper understanding of the host immune response against cancer and identify mechanisms of immune escape, ultimately taking cancer patient therapy towards personalization.

Our research has two main pillars:

1. Study of the immunobiology of specific tumor types, such as pancreatic cancer, to understand the roots of immune failure to control tumor development.
2. Identification and characterization of neoantigens to be used as targets for immunotherapies, with a special focus on neoantigen vaccines. Together with the Cell Virology and Immunology (VIC) group at IrsiCaixa, we are co-developing preventive and therapeutic neoantigen vaccines using an in-house VLP-based vaccine platform.

2022 milestones

1. Our collaboration with the EAPM group at Barcelona Supercomputing Center (IP: Dr. Guallar) has allowed us to improve a novel neoantigen prediction pipeline that has been tested to predict neoantigens in human patient samples in a personalized manner.
2. We have obtained a new grant to study "Tumor-specific neoantigens as targets for personalized vaccines" (focus on pancreatic cancer): FIS PI21/01652.
3. Dr. De la Iglesia has co-authored a paper identifying gene fusions in glioblastoma, which might constitute a source for neoantigens in this tumor type (Hernandez et al. Scientific Reports 2022; 12:1-11).
4. A manuscript describing the "Converging and evolving immuno-genomic routes leading to immune escape in breast cancer", under the leadership of Dr. Leticia de Mattos, is under revision at Nature Cancer.

Perspectives for the future

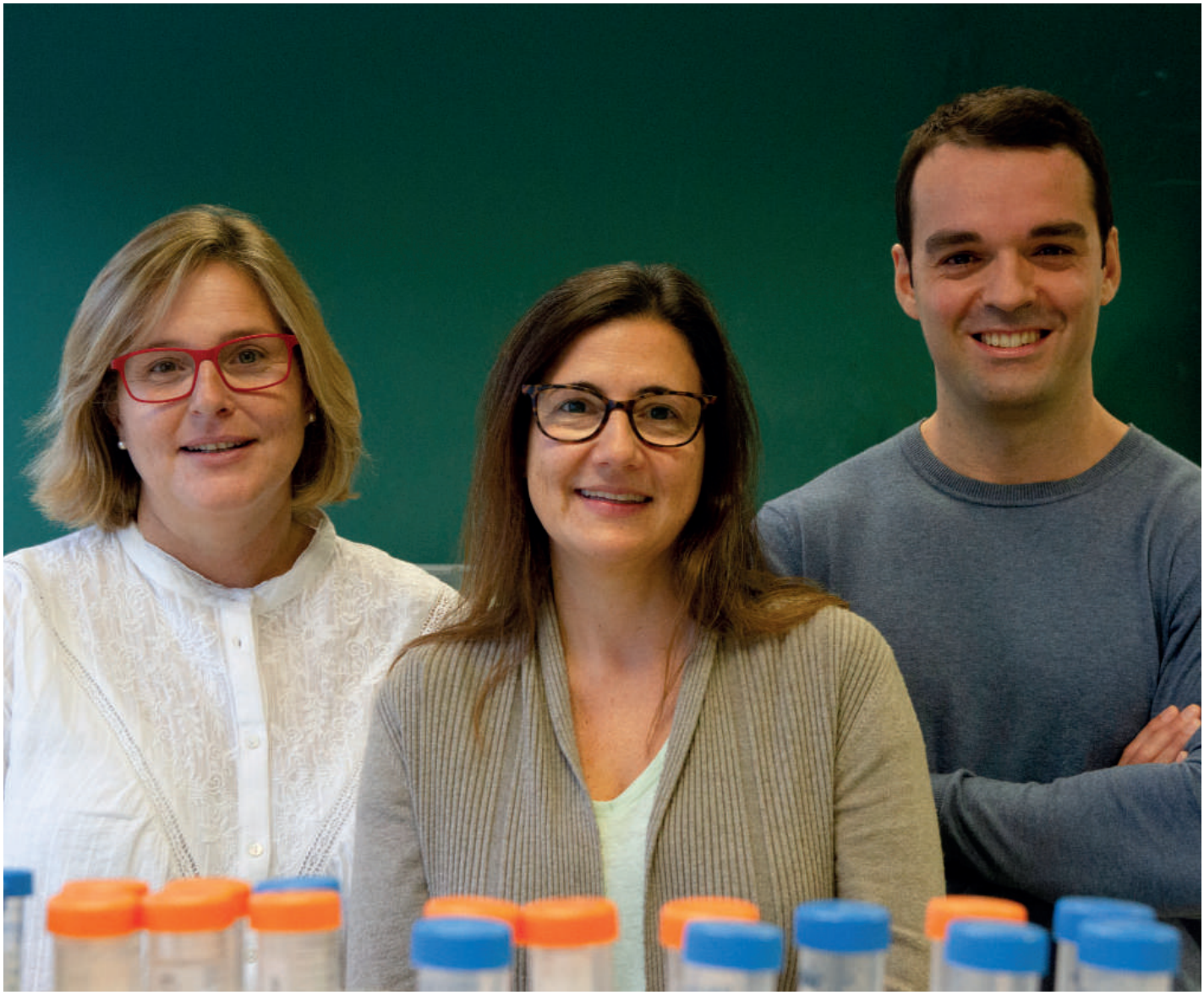
— To apply next-generation sequencing strategies, coupled with improved and novel bioinformatics pipelines and cutting-edge molecular biology procedures, to the identification and validation of immunogenic neoantigens.
— Working with immunologists and computational biologists, to lay solid foundations for the development of a therapeutic neoantigen cancer vaccine for patients with solid tumours, taking advantage of the expertise of IrsiCaixa researchers currently working on vaccines against HIV, COVID-19 and other infectious diseases.

— To expand the team, secure collaborations with external partners and incorporate state-of-the-art molecular tools and new cost-effective in-house solutions for cancer immunotherapy.

1 Published peer-reviewed paper

1 Invited talk

1 Poster presented at the EACR Annual Congress meeting 2022



Principal Investigator
Núria de la Iglesia Zaragoza

Bioinformatician
Gustavo Rodríguez Esteban

Senior research technician
Anna López Plana

Research support

Scientific and technical services

Sample conservation and processing service

IrsiCaixa, a research centre that began its activity in 1993, processes and preserves biological samples from HIV-infected patients for use in research projects.

Over the years, it has processed and conserved samples for numerous projects and clinical trials, promoted by both IrsiCaixa and external national and international sponsors. This activity has evolved into a platform that aims to further research requiring human samples.

Currently, the service routinely processes and stores samples for 44 active studies and maintains two large collections of samples (registered in the National Biobank Registry, No. C0000814 and No. C0006008) for research on HIV and other infectious diseases.

Sequencing service

Since its launch IrsiCaixa has used HIV genotyping technique to determine resistance to antiretrovirals, initially on an experimental basis for patients included in clinical trials. The technique was soon found to be very useful for optimizing antiretroviral treatments and it eventually became evident that there was a need for all HIV-infected patients to have access to this technique.

In 1999 the Sequencing Service was launched as a healthcare service to manage samples from the Germans Trias i Pujol University Hospital and other public and private centres. In addition to its healthcare role, the Sequencing Service also participates in research projects and clinical trials in collaboration with research groups and pharmaceutical companies.

In 2018, the Sequencing Service implemented next-generation sequencing (NGS) technologies. In 2019, IrsiCaixa incorporated the Sentosa® SQ HIV genotyping assay to detect HIV drug resistance.

This assay is validated in the highly automated Sentosa® NGS workflow, which enables automated RNA extraction, library construction, template preparation, sequencing, data analysis and automated reporting. The Sentosa® NGS workflow also ensures clear sample traceability, with seamless laboratory information system (LIS) integration and connectivity.

To ensure the quality of its results, the Sequencing Service undergoes regular external quality controls (QCMD ENVA HIV-1 Drug Resistance Genotyping Proficiency Programme).

Other services

Identifying SARS-CoV-2 infected individuals by means of sensitive diagnostic tools is crucial to reducing new infections and to developing strategies to control the ongoing COVID-19 pandemic at the individual and societal levels. Quantification of the humoral response elicited in SARS-CoV-2 infected individuals is a very promising line of research, as it may provide information on the immune response in those individuals. IrsiCaixa has recently introduced a specific ELISA test to detect SARS-CoV-2 antibodies.

Coordinator

Lidia Ruiz Tabuenca

Sample conservation and processing service
Eulàlia Grau Segú
Rafaela Ayen Aparicio
Lucía Gómez Espada
Mireia Martínez Gamero

Sequencing service
Teresa Puig Oliva
Cristina Ramírez Soto

Assistant
Susana Esteban Raya

27 years of sample collection

Total of samples collected

45,572 cells
77,417 plasma
11,043 serum
33,375 other

Total: **167,407 samples**

2022

Samples collected

2,926 cells
2,969 plasma
1,233 other

Total: **7,128 samples**

403 Sequenced samples

336 public centres

67 private centres

3986 Elisa tests in COVID-19 diagnosis

Grants office

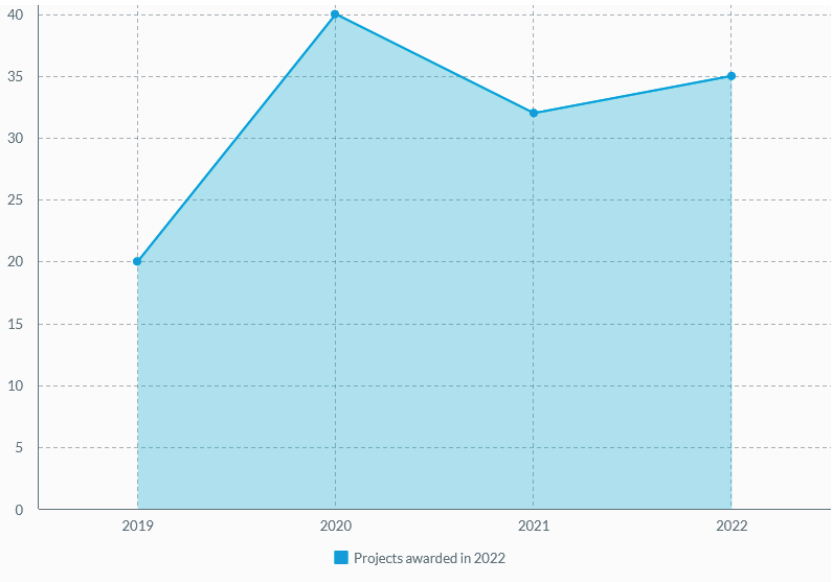
Head
Lourdes Grau Paré

Team
Sonia Bange Singh
Judith Dalmau Moreno
Elisabet Fernández Rosas
Alba Foraster Redondo
Chiara Mancuso Ponce
Natàlia Marrugat Vila
Laura Planells Ferrer

The Grants office works closely with all IrsiCaixa departments and groups to promote the development of innovative and quality research. Continuous communication with researchers ensures support at all levels, whether in detecting needs, seeking suitable funding opportunities, performing projects follow-up and justification, assisting with proposal preparation and project management, designing and following up budgets and assisting in collaboration, transfer and innovation processes. The office ensures alignment of IrsiCaixa's practices with the rules, regulations and policies of funding entities, as well as with current national and international regulations.

107 Active projects in 2022

>15 Entities that support IrsiCaixa financially



Living Lab for Health

Head
Rosina Malagrida Escala

Team
Daniela Benítez Cano
Marina Pino Cebrián
Laia Vives Adrián

Presentation

During 2022, the Living Lab for Health at IrsiCaixa has continued working to achieve its mission to facilitate multistakeholder innovation networks to increase collective impact for complex and persistent health challenges. Through participatory processes, a wide variety of stakeholders collectively explore the complexity of the challenges and co-design and implement collective and integrated Impact Strategies with system innovation approaches that lead to decentralized and collaborative solutions addressing different parts of the challenges. To define and implement the collective and integrated Impact Strategies, the Living Lab has set up a four-step methodology.

This methodology comprises the following steps: (1) Participatory research for strategic design, (2) Co-creation, (3) Implementation and (4) Reflexive monitoring in action. Simplified versions of this methodology have also been included in guidelines and education activities to empower both professionals and students in formal and non-formal education to engage in designing and implementing impact strategies.

This methodology is based on frameworks defined by the European Commission (EC) under the umbrella of Responsible Research and Innovation (RRI), Open Science, Mission Oriented Research, "partnerships" of the Horizon Europe programme, and other global initiatives such as "Community Based Participatory Research", "system thinking" and "transdisciplinary research". The methodology applied for the first step has been named as "System-Oriented Dialogue Model" and it will be disseminated through a scientific publication during 2023. The Lab has carried out its initiatives within EC funded projects, "la Caixa Foundation" programmes and within the Barcelona CaixaResearch Living Lab, also funded by "la Caixa" Foundation in collaboration with the Barcelona City Council to facilitate an intermediation structure to optimize the processes of R&I, interventions and policy development in Barcelona.

Lines of action 2022

Innovation networks

Challenge 1: Promotion of Healthy and Sustainable Diets (Alison Network)

The network, supported by the Barcelona CaixaResearch Living Lab, aims to improve the promotion of Healthy and Sustainable Diets. It started with a first pilot in the neighbourhood "La Verneda i la Pau", in Barcelona. After the co-design of a collective and integrated Impact Strategy and Action Plan, during 2022 the implementation phase started in collaboration with more than 40 professionals from 29 organisations including universities and research centres, healthcare, social and formal and non-formal educational services, food businesses and citizens. During this year, eight innovation programmes targeting the food environment have been executed. Some of these innovation programmes include implementation science projects, bringing novel tools already developed by research centres to the citizens, aiming at capacity and community building of citizens and professionals in the food environment. These initiatives have been developed and implemented for and with the neighbourhood with easy to apply methodological guidelines. In 2023 these innovation programmes are expected to scale up to other neighbourhoods in collaboration with the EC funded projects FoodCLIC and Foster and with the support of a digital exchange platform.

Challenge 2: Promotion of affective-Sexual Health for youth and adolescents (Co–ResponS(H)ibility)

Within the Barcelona CaixaResearch Living Lab during the first semester of 2022 and after various conversations with ESSIR (Estratègia de Salut Sexual i Reproductiva de Barcelona), the team arrived to the conclusion that the best way to implement the Impact Strategy and Action Plan, that had been designed during the previous year, was to incorporate its priorities in the ESSIR work plan and to invite all the stakeholders of the Co–ResponS(H)ibility Network to participate. In this case, the Living Lab has acted as a consultancy to improve the work plan of ESSIR with the identification of unmet needs and the involvement of a wider diversity of stakeholders.

Challenge 3: Prevention of SARS-CoV-2

During 2021-22 the Living Lab has facilitated the implementation of the Integrated Impact Strategy, that had been defined during the previous academic course through a participatory research process with 866 students and their families and teachers.

The Lab published educational guidelines for: washing hands, ventilation and transmissibility and mentored two research projects in collaboration with researchers specialized on infectious diseases. This challenge is being addressed in the framework of the EC funded project CONNECT and "Escoles Sentinella".

Challenge 4: Promotion of mental health

The results obtained from the research on prevention of SARS-CoV-2 showed the urgency to improve the promotion of mental health in schools. During 2021-22 the Lab coordinated a participatory research process to design an integrated Impact Strategy with and for the education community. A total of 1600 students, together with their families and teachers from 17 schools participated. During the last term of 2022, the lab co-created educational guidelines to implement the integrated intervention with participatory research methodologies, and they will be piloted and extended during the following years. This challenge is also being addressed within the projects CONNECT and "Escoles Sentinella".

Challenge 5: Healthcare and research on Long Covid

The Lab has been supporting the Long Covid Unit of the Hospital Germans Trias i Pujol, Fight Infections Foundation and IrsiCaixa to collectively design a more integrated, collaborative and decentralized model of healthcare and research for this disease in the North Metropolitan area of Barcelona.

After a co-design phase in which a strategy was built, the team has initiated the implementation of an action plan with 4 working teams.

Educational and outreach programmes

Training and consultancy on RRI, System Innovation and Open Science for students and professionals

During 2022, 614 professionals have been trained through customized trainings, webinars, conferences and workshops for undergraduate and post-graduate scientists, healthcare professionals, policymakers, experts on public engagement, educators and professionals from funding organizations, among others.

Educational programmes for youth aimed at facilitating participatory research and outreach

— **STEAMxChange programme:** developed in collaboration with EduCaixa. During 2022 the Lab has developed the educational guidelines on Mental Health, has contributed in a series of webinars to train teachers and has adapted Xplore Health content for EduCaixa (the Xplore Health website has been closed as most of its contents have already been published in EduCaixa).

— **CONNECT and Escoles Sentinella:** EC funded project to promote secondary schools to adopt a movement called Open Schooling, which promotes participatory research projects.

The Lab joined the "Escoles Sentinella" consortium, leaded by Generalitat de Catalunya, to develop guidelines and implement participatory research processes (see challenges 3 and 4 above).

— **HIV/AIDS outreach programme:** IrsiCaixa has offered dissemination sessions on HIV/AIDS, focusing on basic knowledge, current research and the importance of prevention and diagnosis, with reflection and debates.

These sessions were complemented by the LaboCosmoCaixa, an activity organized in collaboration with "la Caixa" Foundation that encourages young people to conduct research with a vaccine candidate developed by IrsiCaixa. These activities started again in February 2022 after the restrictions due to the Covid-19 pandemic.

Community Advisory Committee (CAC)

This external body facilitates communication and dialogue between the researchers and healthcare professionals at IrsiCaixa and patients, civil society representatives and policy makers.

In 2022, the Lab has contacted the members of the CAC to restart their participation after the Covid-19 pandemic, and has coordinated its function with a recently created unit in IrsiCaixa for clinical trials.

77 Participant organizations

2 Collective and integrated strategic and action plans for health challenges

11 Co-designed innovation programmes

614 Professionals trained

2 Educational guidelines developed to promote participatory research in schools

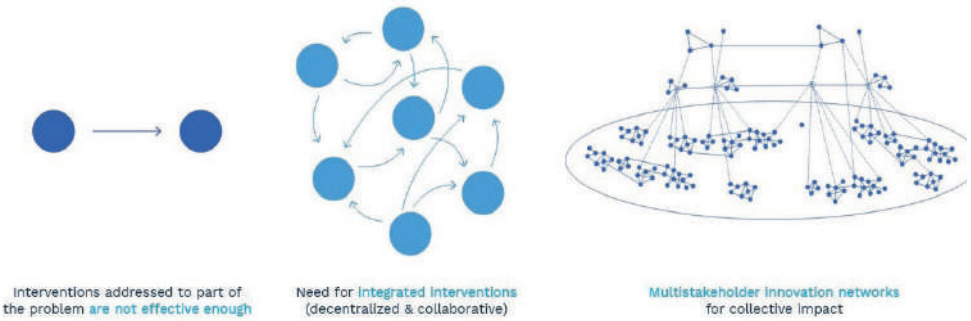
1699 Students, teachers and schools participated in the challenge of promotion of mental health in schools

1360 Students and citizens attended outreach activities

29 Mental health recommendations were communicated to policy makers

360 Social actors attended a congress on mental health

2 New EC funded projects started

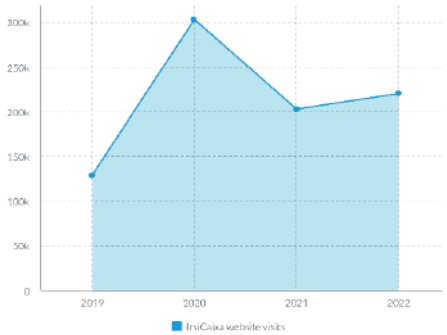


Communication

Team

Rita Casas Costa
Elena Lapaz Lorenzo

IrsiCaixa Communication Department ensures that the research conducted at the center is effectively communicated to both internal and external audiences. On the one hand, the team works with media and social networks to share IrsiCaixa's research with the general public. Our perspective is that it is important for the public to understand scientific concepts and developments, as these often impact their daily lives and helps that policy and decision-makers make informed decisions based on scientific evidence. Additionally, outreach and communication help to bridge the gap between scientists and the public, promoting greater understanding and trust between the two groups. On the other hand, the communication department pursues to be useful for IrsiCaixa employees and to foster engagement by IrsiCaixa researchers by providing internal support to them in making their work visible, as well as helping in their daily tasks through internal communication.



Media

The communications department plays a critical role in building and maintaining relationships with key stakeholders such as the media. After more than 2 years of the COVID-19 pandemic, in 2022 the activity of the scientific media has returned to normal and IrsiCaixa has adapted to its needs. From the department, we have recovered plurality in press releases, broadening the range of topics that are communicated by the institution and responding, at the same time, to the reactive requests required by current affairs. During 2022, IrsiCaixa sent 8 press releases, published 20 pieces of news and reached more than 300 media impacts (TV, radio and press hits).

>6,800
followers on Twitter

>450
followers on Instagram

>660
subscribers in the monthly newsletter

>300
press, radio and TV hits

220,568
visits to irsicaixa.es

Website and social media

The novelty in IrsiCaixa's social media in 2022 was the creation of an institutional Instagram account (@IrsiCaixa). The user was created in July and, since then, we have reached more than 33,690 accounts, published 13 reels, 8 posts and 148 stories, and ended the year with a total of 457 followers. Regarding Twitter and LinkedIn, IrsiCaixa has further consolidated its presence in these platforms. On the one hand, 208 people started following IrsiCaixa's account on Twitter in 2022, and we tweeted 277 posts that got more than 205,289 impressions. On the other hand, the sustained growth of LinkedIn followers has been maintained and the platform now counts with 2,365 followers, which is 604 more followers than the ones we got in 2021. In 2022, IrsiCaixa kept working on the social media campaigns #IrsiCaixaContesta and #IrsiCaixaAlumniNetwork, and created a new one: #WiShesInScience. As for the institutional website, traffic data endorse the high impact of the website: 123,406 users, 140,377 sessions and 220,568 visits in the website pages. During 2022, the communication department has been working on the redesign and content creation of a new IrsiCaixa website.

IrsiCaixa has resumed the IrsiCaixa Alumni Network (IAN) Talks annual meeting. The third edition of the IAN Talks was held on 17 June, a session which focused on the importance of networking. More than 50 people attended the event, held on-site and on-line.

The communication team has also designed activities for special dates, such as Christmas and Sant Jordi. At the same time, teambuilding events have been organised, such as volleyball and paddle tournaments, hiking trips, among others.

Institutional communication

In 2022, together with a graphic design company, the communication team has been developing a new institutional website and corporate identity. The team also continued working on the planning and design of corporate materials, as well as on the monitoring of the correct inclusion of the institutional image in congress materials, websites, press releases, among others.

Highlights

Institutional news

An IrsiCaixa project to study Long Covid, one of the 9 Catalan proposals selected by the CaixaResearch call for health research 2022

The 5th edition of the CaixaResearch call for Health Research 2022 will promote 33 new cutting-edge biomedical research projects in Spain and Portugal, to which it grants aid of up to one million euros. A study coordinated by ICREA researcher at IrsiCaixa Christian Brander was one of the awarded projects, whose objective is to decipher the epigenetic mechanisms involved in Long Covid.

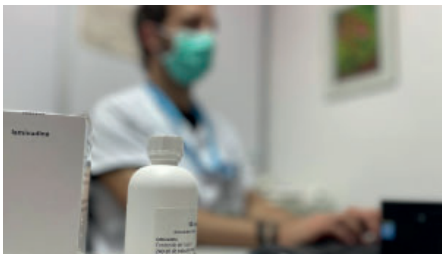
The IAN Talks are back, the meeting point of IrsiCaixa alumni

After a two-year break due to the COVID-19 pandemic, on 17 June the IrsiCaixa Alumni Network (IAN) Talks have resumed. To this end, this year not only three alumni took part, presenting their professional careers to the audience, but participatory activities were also organised with the aim of debating the importance of networking in our day-to-day lives.

Press hits

A mother living with HIV: "My child is not cured, he was born healthy"

On the occasion of World HIV Day, the IrsiCaixa research team explains the research on paediatric HIV and highlights that for the first time in 2020 no child was born with the infection. The article also features an interview with a woman living with HIV who tells her story and her experience of motherhood.



Common antiretroviral drug improves cognition in mouse model of Down syndrome

A joint new study by researchers at the Centre for Genomic Regulation (CRG) and IrsiCaixa demonstrates that lamivudine, a commonly-used antiretroviral drug for treating HIV, improves cognition in a mouse model of Down syndrome. El Periódico interviews the director of IrsiCaixa Bonaventura Clotet to comment on the study.

Giving immunotherapy at the start of antiretroviral therapy improves HIV control

The newspaper ABC interviews Javier Martínez-Picado, ICREA researcher at IrsiCaixa, to talk about an article published in the journal Nature Medicine with the participation of IrsiCaixa. "The new results tell us, for the first time, that performing the intervention right at the start of treatment could limit the persistence of HIV," he explains in the interview.

Training

IrsiCaixa has been committed, from its inception, to training young researchers and developing successful careers in biomedical research. Its training objectives are realized as follows:

— Training of pre-doctoral researchers
— Training of post-doctoral researchers
— 8 training master and undergraduates' students
— Continuing professional development for staff
— 3 visiting researcher placements (we particularly welcome trainee researchers interested in learning from IrsiCaixa research groups).

28 Predoc researchers

23 Postdoc and senior researchers

609 Training attendees

13 Research results meetings

15 Journal clubs

>50 Courses

Internal and external training

— Weekly meetings at which group members present their results. These meetings develop capacity to structure and defend experimental data before a restricted audience of experts in the field.

— Fortnightly meetings at which group members present their results. These meetings develop capacity to structure and defend experimental data before a restricted audience of experts in different fields.

— Seminars. IrsiCaixa and other Can Ruti Campus groups regularly organize open seminars with invited internationally renowned researchers.

— Greater integration and collaboration between IrsiCaixa and the Can Ruti Campus. This collaboration is translated into participation in coffee talks and scientific activities.

— Training in skills to support you in your professional career. To increase the ability of an individual in one or more areas of the professional career. Increase an individual's motivation to do their job well.
— National and international conferences. All staff are encouraged to participate in scientific encounters and to present their results at conferences.

— Specialization/perfection courses in experimental techniques.

— Journal clubs. Weekly meetings aimed at developing critical vision regarding published data in which researchers present an article of relevance to their own experimental work.

— Newsletter. Dissemination of a monthly IrsiCaixa Newsletter highlighting the most relevant scientific articles published by IrsiCaixa groups, courses and events organized by other entities and articles of general interest in matters of equality, compliance, biosafety, etc.

Chair in infectious diseases and immunity

In 2013, IrsiCaixa signed an agreement with the Fight Infections Foundation (FLI) and the University of Vic-Central University of Catalonia (UVic-UCC) to create what was then called the Chair in AIDS and Related Diseases, renamed in June 2019 as the Chair in Infectious Diseases and Immunity so as to better reflect the wide range of fields of expertise of the researchers involved in the Chair.

Headed by Dr. Bonaventura Clotet, the Chair aims to enhance collaboration between IrsiCaixa, the FLI and the UVic-UCC in fostering research into infections and related diseases and to promote the teaching and training of new researchers and healthcare professionals.

The Chair in Infectious Diseases and Immunity undertook the following activities in 2022:

Date	Type of activity	Title	Place	Conducted by
January	Lecture	Infections in Oncological-Hematological patients	Faculty of Medicine, UVic-UCC	Rosa Benítez
February	Workshop	Diabetic Foot	Faculty of Medicine, UVic-UCC	Esteban Reynaga
March	Lecture	Infections in patients with transplants (solid organs) or in treatment with immunomodulators	Faculty of Medicine, UVic-UCC (online)	Rosa Benítez
April	Seminar	Induction of protective T cell immunity in HIV vaccines	Faculty of Medicine, UVic-UCC	Christian Brander
May	Lecture	Gastroenteritis	Faculty of Medicine, UVic-UCC (online)	José Ramón Santos
May	Lecture	Parasitosis	Faculty of Medicine, UVic-UCC (online)	Silvia Roure
May	Seminar	Aging	Faculty of Medicine, UVic-UCC	Eugènia Negredo
May	Seminar	Social determinants of health: the UN sustainable development goals	Faculty of Medicine, UVic-UCC (online)	Roger Paredes
May	Seminar	Tuberculosis	Faculty of Medicine, UVic-UCC (online)	Roger Paredes
May	Continuing education course	Update on HIV infection and the pandemic of COVID-19	Althaia Hospital, Manresa	B Clotet, E Negredo, J Blanco, J Martínez-Picado, B Mothe, L Mateu, R Paredes
June	Seminar	Telemedicine: teleictus	Faculty of Medicine, UVic-UCC (online)	Cora Loste
June	Seminar	Research methodologies and clinical trials	Faculty of Medicine, UVic-UCC	Javier Martínez-Picado
June	Seminar	Virology and cinema	Faculty of Medicine, UVic-UCC	Javier Martínez-Picado
September	Inaugural lecture (biomedicine)	Biomedical research against viral pandemics	Faculty of Science, Technology and Engineering, UVic-UCC	Javier Martínez-Picado
September	Lecture	European Researchers' Night 2022. Talks on BIOMEDICAL SCIENCES (Biomedicine, disease research)	Serra de Noet Highschool, Berga	Àlex Olvera
October	Seminar	Genomic surveillance	Faculty of Medicine, UVic-UCC	Marc Noguera
November	Seminar	T Cell vaccine development for viral pandemics: from HIV to Covid-19	Faculty of Science, Technology and Engineering, UVic-UCC	Christian Brander
November	Conference	Social determinants of health: the UN sustainable development goals	Faculty of Science, Technology and Engineering, UVic-UCC	Roger Paredes
November	Lecture	TB and extrapulmonary	Faculty of Medicine, UVic-UCC	Silvia Roure
November	Lecture	Coronavirus	Faculty of Medicine, UVic-UCC	Lourdes Mateu
December	Lecture	Endocarditis	Faculty of Medicine, UVic-UCC	Lourdes Mateu
December	Lecture	Infections in traumatology	Faculty of Medicine, UVic-UCC	Esteban Reynaga

Clinical and observational studies

1. BCN003

A Phase I, Randomized, Double-Blind, Placebo-Controlled Safety, Tolerability and Immunogenicity Study of Candidate HIV-1 Vaccines ChAdOx1.HTI and MVA.HTI with Recombinant HIV-1 Envelope Protein ConM SOSIP.v7 gp140 Vaccine, Adjuvanted with MPLA Liposomes in ART-Suppressed HIV-1 Positive Individuals

Study type: interventional
Design: phase I, randomized, double-blind, placebo-controlled
Summary and objectives: BCN03 tests a novel combined regimen with T- and B-cell immunogens, and the primary endpoints of BCN03 will be safety and tolerability. BCN03 is designed as a pilot study, and the sample size has been chosen that will only allow the detection of large response differences. The BCN03 Phase I study will evaluate the safety, tolerability, immunogenicity, and efficacy of a vaccine regimen that includes a sequence of the T- and B-cell immunogens ChAdOx1.HTI and MVA.HTI and ConM SOSIP.v7 gp140 adjuvanted with MPLA liposomes in virologically-suppressed ART-treated HIV-1 positive individuals. The primary objective of this study is to assess the safety and tolerability of the vaccine components, and secondary objectives include immunogenicity and efficacy of the vaccine components
Start–end: 2021-2023
Sponsor: European Comission– EAVI2021
Principal investigators: Dr Beatriz Mothe, Dr Christian Brander
Code/reference: 2020-000292-20

2. AELIX002

A Phase I, Randomized, Double-Blind, Placebo-Controlled Safety, Tolerability and Immunogenicity Study of Candidate HIV-1 Vaccines DNA.HTI and MVA.HTI in Early Treated HIV-1 Positive Individuals

Study type: interventional
Design: phase I, randomized, double-blind, placebo-controlled
Recruitment: completed
Start-end: 2017-2021
Sponsor: AELIX Therapeutics SL
Principal investigator: Dr Beatriz Mothe
Participating centres: Germans Trias i Pujol University Hospital, AELIX Therapeutics, IrsiCaixa
Code/reference: NCT03204617

3. RV 306

Randomized, Double Blind Evaluation of Late Boost Strategies With IHV01 (FLSC in Aluminum Phosphate) and A244 With or Without ALFQ for HIV-uninfected Participants in the HIV Vaccine Trial RV306 / WRAIR 1920

Study type: interventional
Design: phase I, randomized, double-blind
Summary and objectives: the purpose of this study is to define the safety and immunogenicity of IHV01 and A244/AHFG with and without ALFQ at a full dose and at a fractional dose (one-fifth of a full dose) in a late boost setting for participants who had previously received a late boost of AIDSVAX®B/E with or without ALVAC in RV306. Safety will be assessed through the frequency of the overall and specific post-vaccination reactions. Blood, lymph nodes, sigmoid tissue, and mucosal specimens/secretions will be collected to assess humoral, cell-mediated, innate, and mucosal immune responses. Healthy, HIV-uninfected participants, at a low risk for HIV infection, available for 12 months, who were randomized to receive active vaccine in RV306 and completed all vaccinations will be enrolled. A total of 120 participants will be enrolled across four vaccination groups. In each group, 25 participants will receive IHV01 and A244/AHFG at a full or fractional dose with or without ALFQ and 5 participants will receive placebo. All injections, whether vaccine or placebo, will be a one-time intramuscular (IM) administration into the quadriceps muscle at study Day 0. Participants will be followed-up for up to 48 weeks after enrollment on days 1, 7, 14, 168 and 336. Mucosal secretion collections and endocervical cytobrush/swab procedures will be performed at Weeks 0, 2, 24, and 48 on consenting participants. Leukapheresis, sigmoid biopsy, and lymph node biopsy procedures will be performed only at Week 2 on consenting participants.
Recruitment: recruiting
Start–end: 2021-2026
Sponsor: US Army Medical Research and Development Command & Canadian Institutes for Health Research (microbiome studies)
Principal investigator: Dr Roger Paredes
Code/reference: NCT04658667

4. RUTIVAC-1

A Randomized, Double-Blind, Placebo-Controlled Phase I Trial to Evaluate the Immunomodulatory Effect of RUTI® in Individuals with High-Risk Non-Muscle-Invasive Bladder Cancer (NMIBC) Treated with Intravesical Bacillus Calmette-Guerin (BCG)

Summary and objectives: the RUTIVAC-1 study is a Phase I Clinical Trial designed to evaluate the systemic and mucosal immunological response and provide safety information after the use of RUTI® administration to individuals with NMIBC. The study will enroll individuals treated with Transurethral resection of bladder tumor (TURBT), diagnosed to have high-risk Non-muscle invasive bladder cancer (NMIBC) and suitable candidates for BCG therapy and who meet all eligibility criteria. Forty individuals will be recruited and randomized 1:1 to receive two subcutaneous shots of 25g RUTI® or placebo. After vaccination, individuals will receive the standard intravesical Bacillus Calmette–Guerin (BCG) therapy with induction course (weekly BCG for six weeks) and maintenance course (three courses of weekly BCG for three weeks at 3, 6 and 12 months after induction). After the last intravesical BCG administration (BCG15, end of Interventional Phase) immunological assays will be performed and data will be analyzed. At the end of the Interventional Phase the blind will be opened, except for the study physicians who will remain blind during all the follow-up. All the individuals will be followed up for three years since TURBT
Study type: interventional
Design: phase I, double blind, placebo-controlled, randomized
Start–end: 2016-2023
Sponsor: Archivel Farma S.L
Principal investigator: Dr Cecilia Cabrera
Participating centres: Germans Trias i Pujol University Hospital (Urology Department), Fight Infections Foundation (CRO), IrsiCaixa
Code/reference: AC-16-048-CEIM (CEIC Code)

5. DUAL TRIPLE ART

Exploratory, open-label, randomized clinical trial to assess the efficacy of first-line dual vs. triple antiretroviral therapy (ART) in HIV-1 reservoir and in peripheral compartments in HIV-infected patients (Dual_TripleART)

Design: phase III
Recruitment: completed

Clinical and observational studies

Start–end: 2019 – 2022
Sponsor: ViiV Healthcare
Principal investigators: Dr José Moltó, Dr Javier Martínez-Picado
Participating centres: Germans Trias i Pujol University Hospital (Fihgt Infections Foundation); IrsiCaixa; University of North Carolina (Chapel Hill, USA), and the Oregon Health & Sciences University (Beaverton, USA)
Code/reference: 2019-002733-10

6. KING COHORT
Prospective Comparative Observational Cohort of individuals with documented SARS-CoV-2 infection (King cohort extension)
Study type: observational
Design: prospective cohort
Recruitment: ongoing
Summary and objectives: the KING cohort extension aims to be a prospective comparative observational cohort of infected SARS-CoV-2 individuals to have a unique clinical platform og biological specimens to study the virology and immunopathogenesis of SARS-CoV-2, during acute infection and after recovery of COVID-19. An uninfected group of individuals and a vaccinated group will be included. Patients suffering from Post-COVID-19 condition are also included in this cohort.
Start–end: 2020-ongoing
Sponsor: YoMeCorono
Principal investigators: Dr Bonaventura Clotet, Dr Marta Massanella, Dr Lourdes Mateu
Participating centres: Germans Trias i Pujol University Hospital, Fight Infections Foundation, IrsiCaixa
Code/reference: HUGTiP/20-P-217

7. CoronAVI@S
Immune response to SARS-CoV-2 vaccine in institutionalized elders: the challenge for a long-term immunity
Study type: observational
Design: prospective comparative study
Recruitment: finished with 98 participants
Summary and objectives: older adults have been disproportionately affected by the COVID-19 pandemic. Among them, residents from long-term care facilities (LTCF), who live in a congregate setting (with increased risk of transmission and infection) showed higher mortality rates than the general population of the same age. Therefore, vaccination of residents from LTCF against SARS-CoV-2 has been a priority in most countries. Ageing is associated with an immunosenescent phenotype characterized by a progressive increase of a proinflammatory state and, a diminished immune response to pathogens and vaccines. Therefore, there is an urgent need to determine the quality and the duration of immune responses of the elderly population, which could be very useful for designing specific SARS-CoV-2 vaccination calendars adapted to their immune needs. The aim of the study is to evaluate the quality and the duration of immune response generated by SARS-CoV-2 Vaccine in institutionalized elders living on LTCF, comparing individuals recovered from SARS-CoV-2 infection with elders who never got infected by SARS-CoV-2 living in the same senior facilities. In addition, we will compare the immune responses generated by elders with a younger population.
Start–end: 2020-2022
Sponsor: YoMeCorono, Fundació Glòria Soler
Principal investigators: Dr Marta Massanella, Dr Núria Prat
Participating centres: ICASS long-term care facilities, IrsiCaixa
Code/reference: IDIAP/ 20/116-P

8. ReCOVID
Clinical Characteristics and Outcomes of Patients with SARS-CoV-2 Reinfection
Study type: observational
Design: retrosprospective study
Summary and objectives: cases with suspected or possible reinfection with SARS-CoV-2 have been reported worldwide since September 2020. It remains unknown the durability of immune responses to this virus, and it is a current public health problem. Whereas infections by the closely related betacoronaviruses SARS-CoV and MERS-CoV elicit long-lasting protective immunity, immune responses to common-cold coronaviruses are short-lived. Reinfections may occur after a few months from first episode, but usually with mild symptoms. The possibility of reinfection implies that individuals that have been infected once cannot be definitively considered to be immune. Although so far confirmed reinfections appear to rare events, more evidence and longer follow-up time is required to better understand duration of immunity (natural or after vaccination), transmissibility and the likelihood and implications of reinfection. Identification of predictor clinical risk factors for reinfection would be useful for implementing interventions focusing on the reduction of disease burden in populations at risk, including special vaccination efforts. The aim of this study is to evaluate the clinical characteristics and outcomes of patients with SARS-CoV-2 reinfection.
Start–end: 2021-2022
Sponsor: YoMeCorono
Principal investigators: Dr Marta Massanella, Dr José Ramón Santos
Participating centres: Germans Trias i Pujol University Hospital, Fight Infections Foundation, IrsiCaixa
Code/reference: HUGTIP/ PI-21-235

9. Aliança ProHEpiC-19 Neurocognitiu
Neurocognitive profile of Long Covid in adults living in Catalonia
Study type: observational
Design: retrosprospective/prospective observational study
Summary and objectives: clinical study dedicated to describe the neurological sequelae of people presenting with persistent neurocognitive-type COVID-19 syndrome, analyzing their relationship with the functional alterations and/or structural cerebral, with the inflammatory and immunological state, the vascular and vestibular involvement, and its impact on the activities of daily life through the experiences they have experienced in coexistence with the persistent symptomatology
Start–end: 2022-2024
Sponsor: Department of Health, Government of Catalonia
Principal investigators: Dr Julia García Prado
Code/reference: SLT021/21/000038

10. BreakCOVID
SARS-CoV-2 post-vaccination infection: cohort study for the characterization of the immune response and development of a predictive model to establish revaccination criteria in Catalonia
Study type: observational
Design: retrosprospective/prospective observational study
Summary and objectives: clinical study dedicated to describe the neurological

Clinical and observational studies

sequelae of people presenting with persistent neurocognitive-type COVID-19 syndrome, analyzing their relationship with the functional alterations and/or structural cerebral, with the inflammatory and immunological state, the vascular and vestibular involvement, and its impact on the activities of daily life through the experiences they have experienced in coexistence with the persistent symptomatology
Start–end: 2022-2024
Sponsor: Department of Health, Government of Catalonia
Principal investigators: Dr Julia García Prado
Code/reference: SLT021/21/000038

11. EPIVIRCO
Epigenetic regulation of host immunity and neurological long-term consequences of SARS-CoV-2 infection
Study type: observational
Design: retrospective/prospective observational study
Summary and objectives: the project examines if long-lasting epigenetic changes occurring after SARS-CoV-2 (COVID) infection determine the immunological and neurological long-lasting effects observed in post-COVID conditions. After epigenetic profiling of different cell types from patients with long-COVID symptoms, the proposal will validate the hypotheses in a transgenic mouse model, which will be also used to evaluate therapeutic interventions and open new treatment options.
Start–end: 2022-2025
Sponsor: Fundació Bancària "la Caixa"
Principal investigators: Dr Christian Brander, Dr Marta Ruiz-Riol
Code/reference: HR22-00681

12. VRSVAC
Investigación de nueva vacuna para enfermedad respiratoria humana
Study type: observational
Design: preclinical study
Summary and objectives: the scope of the project is the development of a vaccine for a human respiratory disease (RSV or Respiratory Syncytial Virus).
Start–end: 2022-
Sponsor: HIPRA
Principal investigators: Dr Julià Blanco Arbués, Dr Nuria Izquierdo Useros
Code/reference: MIG-20211034

13. MetabolHIV
Ageing with HIV: The role of metabolism in viral persistence and accentuated immunoageing
Study type: observational
Design: prospective observational study
Summary and objectives: this project aims to understand the metabolic mechanisms that contribute to the immunosenescent phenotype, and giving new insights on the ongoing debate of premature or accentuated ageing of the HIV population. In addition, we will determine the role of metabolism in HIV persistence, which offer novel perspectives for the development of clinical strategies for HIV eradication.
Start–end: 2021-2024
Sponsor: MICINN, Proyectos de I+D+i 2020
Principal investigator: Dr Marta Massanella
Code/reference: PID2020-114929RA-I00

14. Long-CovidCIBERINFEC
Biomarkers and underlying immunopathological mechanisms of post COVID-19 condition
Study type: observational
Design: restrospective observational study
Summary and objectives: this project aims at identifying biomarkers of PCC to improve the diagnostic of PCC and provide understanding on the mechanisms underlying this condition, with the ultimate goal of determining treatment targets and interventions to improve the management and quality of life of PCC patients. Specific objectives are: 1) To assess SARS-CoV-2 persistence in blood and feces and reactivation of other viral latent infections, which may lead to chronic immune inflammation and dysfunction; 2) To determine immune dysregulation; 3) To quantify autoantibodies and markers of autoimmunity; 4) To assess metabolic dysregulation.
Sponsor: CIBERINFEC
Principal investigator: Dr Marta Massanella
Code/reference: IM22/INF/5

15. PediaCOVID
Pediatric long-COVID: clinical, immunological, genetic and virological evaluation of a cohort of children and adolescences
Study type: observational and interventional
Design: restrospective observational study
Summary and objectives: the primary objective of the project is to evaluate the causes and consequences of long-COVID in a unique pediatric cohort. Specific aims include: 1) to describe the main clinical, epidemiological and radiological characteristics, and the physical, psychological, academic and social consequences, 2) to unveil the genetic causes that may predispose to long-COVID, 3) to evaluate the immunological and inflammatory profile, 4) to investigate viral persistence, and 5) to analyze the neuronal damage to evaluate the long-term effect of COVID-19 on cognitive impairment. The project should allow to define specific clinical guidelines and personalized treatment strategies that should directly impact in the quality of life of the affected kids and their families.
Principal investigators: Dr Sara Morón López, Dr Javier Martínez Picado
Code/reference: PediaCOVID

Innovation

Patent portfolio

GRANTED

Title: Method for monitoring HIV specific T Cell responses
Inventors: Ruiz-Riol, Marta; Brander, Christian; Ibarrondo, Javier
Reference: WO/2013/139972; PCT/EP2013/056110
Priority date: 23 Mar 2012
Publication date: 26 Sep 2013
Applicants: IrsiCaixa, ICREA
Granted: EP, Belgium, China, Germany, Spain, France, GB, Italy, The Netherlands, Sweden, Canada, Japan, US

Title: Methods for identifying HIV neutralizing antibodies
Inventors: Blanco Arbués, Julián Miguel
Reference: WO/2014/037490; PCT/EP2013/068446
Priority date: 6 Sep 2012
Publication date: 12 Mar 2014
Applicant: IrsiCaixa
Granted: US, Australia, China, Iceland, Japan, South Korea, Mexico, New Zeland, Russia, South Africa

Title: HIV antibody derivates with dual antiviral and immunomodulatory activity
Inventors: Carrillo, Jorge; Clotet Sala, Bonaventura; Blanco Arbués, Julián Miguel
Reference: WO/2017/085563; PCT/IB2016/001868
Priority date: 21 Nov 2015
Publication date: 26 May 2017
Applicant: IrsiCaixa
Licensed to: AlbaJuna Therapeutics, SL

Title: Virus-like particles with high-density coating for the production of neutralizing antibodies
Inventors: Molinos, Luis; Carrillo, Jorge; Blanco Arbués, Julián Miguel
Reference: WO/2018/020324; PCT/IB2017/001101
Priority date: 27 Jul 2016
Publication date: 01 Feb 2018
Applicants: IrsiCaixa
Granted: US
Licensed to: HIPRA

Title: Immunogens for HIV vaccination
Inventors: Brander, Christian; Mothe Pujadas, Beatriz; Llano, Anuska
Reference: WO/2013/110818; PCT/EP2013/051596
Priority date: 27 Jan 2012
Publication date: 1 Aug 2013
Applicants: IrsiCaixa, ICREA
Granted: US, AU, China, Israel, Japan, Rep. of Korea, Mexico, New Zealand, Russian Federation, South Africa
Pending: Brazil, Hong Kong
Published: Canada, India
Case inactive: EP
Licensed to: Aelix Therapeutics

Title: Human Helicase DDX3 Inhibitors as Therapeutic Agents
Inventor(s): Meyerhans, Andreas; Martínez de la Sierra, Miguel Ángel; Brai, Annalaura; Itfazi, Roberta; Tintori, Cristina; Botta, Maurizio; Araque, José-Esté; Martínez-Picado, Javier
Reference: WO/2016/128541; PCT/EP2016/052990
Priority date: 13 Feb 2015
Publication date: 18 Aug 2016
Applicants: IrsiCaixa, Azienda Ospedaliera Universitaria Senese
Granted: Japan

FILED/PUBLISHED

Title: Polypeptides for eliciting humoral and cellular immune responses against coronavirus infections
Inventors: Garcia-Prado, Julia; Brander, Christian; Olvera, Alex; Noguera, Marc; Kilpelainen, Athina; Romero Martín, Luis
Priority date: 15 Jul 20
PCT application: PCT/US21/41523
Applicants: IrsiCaixa

Title: Siglec-1 inhibitors for preventing, inhibiting the progression or treating coronavirus infections
Inventors: Izquierdo-Useros, Nuria; Martínez-Picado, Javier; Clotet Sala, Bonaventura
Priority date: 23 Feb 2021
PCT application: PCT/US22/17213
Applicant: IrsiCaixa

Title: Method for detecting and quantifying inducible HIV reservoirs
Inventors: Puertas Castro, Mari Carmen; Martínez-Picado, Javier
Priority date: 26 May 2021
PCT application: PCT/US22/30875
Applicant: IrsiCaixa

Title: PLD for use in combination in the treatment of coronavirus
Inventors: Izquierdo-Useros, Nuria; Vergara-Alert, Júlia; Avilés-Marín, Pablo
Priority date: 2 Mar 2020
Reference: WO 2021/175823
Publication date: 10 Sep 2021
Applicants: IrsiCaixa, PharmaMar

Title: Soluble TIGIT recombinant proteins
Inventors: García Prado, Julia; Marín López, Miguel Ángel; Carabelli, Julieta
Priority date: 11 Dec 2021
PCT application: PCT/ES2022/070785
Applicants: IrsiCaixa

Title: Boosted immune monitoring methods for assaying antigen-specific T cell responses
Inventors: Ruiz Riol, Marta; Olvera van der Stoep, Alexandre; Romero Martín, Luis; Brander, Christian
Priority date: 9 Mar 2022
PCT application: PCT/EP2023/055951
Applicants: IrsiCaixa

Title: Leriglitazone for treating lung inflammation and interstitial lung disease
Inventors: Martinell, Marc; Pizcueta, Maria Pilar; Vilalta Saura, Anna; Traver López, Estefanía; Maria Poli, Sonia; Izquierdo Useros, Nuria
Priority date: 30 Apr 2021
Reference: WO2021220250
Applicants: Minoryx Therapeutics

Title: Cyclodextrins for use in coronavirus infection therapy
Inventors: Risco Ortiz, Cristina; Fernández de Castro Martín, Isabel; Tenorio Vela, Raquel; Sachse, Martin; Ortega González, Paula; Fernández Oliva, Alberto; Fernández Sánchez, Sara Yolanda; Izquierdo Useros, Nuria; Pérez Zsolt, Daniel; Raïch Regué, Dàlia; Cerón Carrasco, José Pedro; Gabaldón Hernández, José Antonio; Núñez Delicado, Estrella
Priority date: 25 Mar 2022
PCT application: PCT/EP2023/057735
Applicants: IrsiCaixa, CSIC, CUD, UCAM

Title: Anti SARS-CoV-2 antibodies
Inventors: Blanco Arbués, Julián Miguel; Pradenas, Edwards; Trinité, Benjamin; Magri, Giuliana; Tejedor, Sonia; de Campos-Mata, Leire; Carolis, Carlo
Priority date: 6 Oct 2022
PCT application: EP22382940
Applicants: IrsiCaixa, CRG, IMIM

Title: Nucleoside reverse transcriptase inhibitors for use in Down syndrome and Alzheimer's disease therapy
Inventors: Clotet Sala, Bonaventura; Paredes Deiros, Roger; Elizalde Torrent, Aleix; Dierssen, Maria del Mar; Martínez de Lagrán, María
Priority date: 8 Dec 2021
PCT application: PCT/ES2022/070780
Applicants: IrsiCaixa, Fight Infections Foundation, CRG

Publications & conferences

Publications

Original publications

1. Abella E, Trigueros M, Pradenas E, Muñoz-Lopez F, Garcia-Pallarols F, Ben Azaiz Ben Lahsen R, et al. **Efficacy of SARS-CoV-2 vaccination in patients with monoclonal gammopathies: A cross sectional study.** *Life Science Alliance.* 2022;5(12).

2. Aguado-Garcia D, Olvera A, Brander C, Sanchez-Merino V, Yuste E. **Evaluation of the Thermal Stability of a Vaccine Prototype Based on Virus-like Particle Formulated HIV-1 Envelope**. *Vaccines.* 2022;10(4).

3. Ainsua-Enrich E, Pedreño-Lopez N, Bracke C, Ávila-Nieto C, Rodríguez de la Concepción ML, Pradenas E, et al. **Kinetics of immune responses elicited after three mRNA COVID-19 vaccine doses in predominantly antibody-deficient individuals**. *iScience.* 2022;105455.

4. Alemany A, Millat-Martinez P, Corbacho-Monné M, Malchair P, Ouchi D, Ruiz-Comellas A, et al. **High-titre methylene blue-treated convalescent plasma as an early treatment for outpatients with COVID-19: a randomised, placebo-controlled trial**. *The Lancet. Respiratory Medicine.* 2022.

5. Alemany A, Perez-Zsolt D, Raïch-Regué D, Muñoz-Basagoiti J, Ouchi D, Laporte-Villar C, et al. **Cetylpyridinium Chloride Mouthwash to Reduce Shedding of Infectious SARS-CoV-2: A Double-Blind Randomized Clinical Trial**. *Journal of Dental Research.* 2022:220345221102310.

6. Angel Martinez M. **Efficacy of repurposed antiviral drugs: lessons from COVID-19.** *Drug Discovery Today.* 2022.

7. Aranyó J, Bazan V, Lladós G, Dominguez MJ, Bisbal F, Massanella M, et al. **Inappropriate sinus tachycardia in post-COVID-19 syndrome**. *Scientific Reports.* 2022;12(1):298.

8. Armario-Najera V, Blanco-Perera A, Shenoy SR, Sun Y, Marfil S, Muñoz-Basagoiti J, et al. **Physicochemical characterization of the recombinant lectin scytovirin and microbicidal activity of the SD1 domain produced in rice against HIV-1**. *Plant Cell Reports.* 2022.

9. Badia R, Garcia-Vidal E, Ballana E. **Viral-Host Dependency Factors as Therapeutic Targets to Overcome Antiviral Drug-Resistance: A Focus on Innate Immune Modulation**. *Frontiers in Virology.* 2022;2.

10. Bailón L, Llano A, Cedeño S, Escribà T, Rosás-Umbert M, Parera M, et al. **Safety, immunogenicity and effect on viral rebound of HTI vaccines in early treated HIV-1 infection: a randomized, placebo-controlled phase 1 trial**. *Nature Medicine.* 2022.

11. Bastard P, Vazquez S, Liu J, Laurie MT, Wang CY, Gervais A, et al. **Vaccine breakthrough hypoxemic COVID-19 pneumonia in patients with auto-Abs neutralizing type I IFNs**. *Science Immunology.* 2022; eabp8966.

12. Batule S, Soldevila B, Figueredo C, Julián MT, Egea-Cortés L, Reyes-Ureña J, et al. **Factors associated with critical care requirements in diabetic patients treated with dexamethasone for COVID-19 infection in the first wave of the pandemia.** *Frontiers in Endocrinology.* 2022;13:1009028.

13. Beckerman R, Gori A, Jeyakumar S, Malin JJ, Paredes R, Póvoa P, et al. **Remdesivir for the treatment of patients hospitalized with COVID-19 receiving supplemental oxygen: a targeted literature review and meta-analysis**. *Scientific Reports.* 2022;12(1):9622.

14. Benet S, Ávila C, Alarcón-Soto Y, Rodriguez-Lozano GF, Miranda C, González S, et al. **Limited humoral and specific T-cell responses after SARS-CoV-2 vaccination in PLWH with poor immune reconstitution**. *The Journal of Infectious Diseases.* 2022.

15. Bengu N, Mchunu N, Mokhethi S, Fillis R, Cromhout G, Lobenstein JV, et al. **Next-generation point-of-care testing in pediatric human immunodeficiency virus infection facilitates diagnosis and monitoring of treatment.** *Medicine.* 2022;101(27):e29228.

16. Blanco I, Violán C, Suñer C, Garcia-Prieto J, Argerich MJ, Rodriguez-Illana M, et al. **Comparison between mid-nasal swabs and buccal swabs for SARS-CoV-2 detection in mild COVID-19 patients**. *The Journal of Infection.* 2022.

17. Blázquez-Bondia C, Parera M, Català-Moll F, Casadellà M, Elizalde-Torrent A, Aguiló M, et al. **Probiotic effects on immunity and microbiome in HIV-1 discordant patients**. *Frontiers in Immunology.* 2022;13:1066036.

18. Bonjoch A, Juega J, Echeverría P, Puig J, Perez-Alvarez N, Bonal J, et al. **Prevalence, progression, and management of advanced chronic kidney disease in a cohort of people living with HIV**. *HIV Medicine.* 2022.

19. Bordas A, Soriano-Arandes A, Subirana M, Malagrida R, Reyes-Urueña JM, Folch C, et al. **Study protocol for monitoring SARS-CoV-2 infection and its determinants in Catalonia (Spain): an observational and participatory research approach in a Sentinel Network of Schools.** *BMJ Open.* 2022;12(1): e055649.

20. Bordoy AE, Saludes V, Panisello Yagüe D, Clarà G, Soler L, Paris de León A, et al. **Monitoring SARS-CoV-2 variant transitions using differences in diagnostic cycle threshold values of target genes**. *Scientific Reports.* 2022;12(1):21818.

21. Borgognone A, Elizalde-Torrent A, Casadellà M, Romero L, Escribà T, Parera M, et al. **Vaccination with an HIV T-cell immunogen induces alterations in the mouse gut microbiota**. *NPJ Biofilms and Microbiomes.* 2022;8(1):104.

22. Bracke C, Miranda C, González S, Casas I, Cardona PJ, Benitez RM, et al. **Correlation between Clinical and Immunological Variables and Humoral Response to SARS-CoV-2 Vaccination in Adult Patients with Antibody Deficiency Disorders**. *Pathogens* (Basel, Switzerland). 2022;11(11).

23. Brander C, Hartigan-O'Connor D. **HIV T-cell immunogen design and delivery**. *Current Opinion in HIV and AIDS.* 2022;17(6):333-337.

24. Cabrera-Rodríguez R, Pérez-Yanes S, Montelongo R, Lorenzo-Salazar JM, Estévez-Herrera J, García-Luis J, et al. **Transactive Response DNA-Binding Protein (TARDBP/TDP-43) Regulates Cell Permissivity to HIV-1 Infection by Acting on HDAC6**. *International Journal of Molecular Sciences.* 2022;23(11).

25. Calvet J, Berenguer-Llergo A, Gay M, Massanella M, Domingo P, Llop M, et al. **Biomarker candidates for progression and clinical management of COVID-19 associated pneumonia at time of admission**. *Scientific Reports.* 2022;12(1):640.

26. Chamola V, Mohammadi R, Nair H, Goyal A, Patel A, Hassija V, et al. **COVID-19-associated mucormycosis: A review of an emergent**

Publications

epidemic fungal infection in the era of COVID-19 pandemic. *Journal of Research in Medical Sciences: the official journal of Isfahan University of Medical Sciences.* 2022;27:57.

27. Climent N, Ambrosioni J, González T, Xufré C, Casadellà M, Noguera-Julian M, et al. **Immunological and virological findings in a patient with exceptional post-treatment control: a case report**. *The Lancet HIV*. 2022.

28. Dacosta-Aguayo R, Lamonja-Vicente N, Chacón C, Carrasco-Ribelles LA, Montero-Alia P, Costa-Garrido A, et al. **Neurocognitive Profile of the Post-COVID Condition in Adults in Catalonia-A Mixed Method Prospective Cohort and Nested Case-Control Study: Study Protocol.** *Vaccines*. 2022;10(6).

29. Douin DJ, Siegel L, Grandits G, Phillips A, Aggarwal NR, Baker J, et al. **Evaluating Primary Endpoints for COVID-19 Therapeutic Trials to Assess Recovery**. *American Journal of Respiratory and Critical Care Medicine.* 2022;206(6):730-739.

30. Ezeonwumelu IJ, García-Vidal E, Felip E, Puertas MC, Oriol-Tordera B, Gutiérrez-Chamorro L, et al. **IRF7 expression correlates with HIV latency reversal upon specific blockade of immune activation**. *Frontiers in Immunology*. 2022;13:1001068.

31. Ezeonwumelu IJ, Garcia-Vidal E, Riveira-Muñoz E, Felip E, Gutiérrez-Chamorro L, Calba I, et al. **Pharmacological Inhibition of IKK to Tackle Latency and Hyperinflammation in Chronic HIV-1 Infection**. *International Journal of Molecular Sciences.* 2022;23(23).

32. Faitová T, Svanberg R, Da Cunha-Bang C, Ilett EE, Jørgensen M, Noguera-Julian M, et al. **The gut microbiome in patients with chronic lymphocytic leukemia**. *Haematologica*. 2022.

33. Felip E, Gutiérrez-Chamorro L, Gómez M, Garcia-Vidal E, Romeo M, Morán T, et al. **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*. 2022;14(3).

34. Felip E, Pradenas E, Romeo M, Marfil S, Trinité B, Urrea V, et al. **Impact of chemotherapy and/or immunotherapy on neutralizing antibody response to SARS-CoV-2 mRNA-1237 vaccine in patients with solid tumors**. *Molecular Oncology.* 2022.

35. Fernández-Bastit L, Marfil S, Pradenas E, Valle R, Roca N, Rodon J, et al. **Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Infection and Humoral Responses Against Different Variants of Concern in Domestic Pet Animals and Stray Cats from North-Eastern Spain**. *Transboundary and Emerging Diseases*. 2022.

36. Fernández-Bastit L, Roca N, Romero-Durana M, Rodon J, Cantero G, García Ó, et al. **Susceptibility of Domestic Goat (Capra aegagrus hircus) to Experimental Infection with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) B.1.351/Beta Variant**. *Viruses*. 2022;14(9).

37. Ferrando-Díez A, Felip E, Pous A, Bergamino Sirven M, Margelí M. **Targeted Therapeutic Options and Future Perspectives for HER2-Positive Breast Cancer**. *Cancers*. 2022;14(14).

38. Franco S, Pluvinet R, Sanchez-Herrero JF, Sumoy L, Martinez MA. **Rapid and accurate quantification of isomiRs by RT-qPCR**. *Scientific Reports*. 2022;12(1):17220.

39. Gálvez C, Urrea V, Garcia-Guerrero MDC, Bernal S, Benet S, Mothe B, et al. **Altered T-cell subset distribution in the viral reservoir in HIV-1-infected individuals with extremely low proviral DNA**. *Journal of Internal Medicine*. 2022.

40. Garcia-Cirera S, Calvet J, Berenguer-Llergo A, Pradenas E, Marfil S, Massanella M, et al. **Glucocorticoids' treatment impairs the medium-term immunogenic response to SARS-CoV-2 mRNA vaccines in Systemic Lupus Erythematosus patients**. *Scientific reports*. 2022;12(1):14772.

41. Gonzalez-Aumatell A, Bovo MV, Carreras-Abad C, Cuso-Perez S, Domènech Marsal È, Coll-Fernández R, et al. **Social, Academic, and Health Status Impact of Long COVID on Children and Young People: An Observational, Descriptive, and Longitudinal Cohort Study**. *Children* (Basel, Switzerland). 2022;9(11).

42. Grau-Expósito J, Perea D, Suppi M, Massana N, Vergara A, Soler MJ, et al. **Evaluation of SARS-CoV-2 entry, inflammation and new therapeutics in human lung tissue cells**. *PLoS Pathogens.* 2022;18(1):e1010171.

43. Grosso TM, Alcamí J, Arribas JR, Martín M, Sereti I, Tarr P, et al. **HIV and aging, biological mechanisms, and therapies: What do we know?**. *AIDS Reviews*. 2022;25(2):79-86.

44. Guallar-Garrido S, Campo-Pérez V, Pérez-Trujillo M, Cabrera C, Senserrich J, Sánchez-Chardi A, et al. **Mycobacterial surface characters remodeled by growth conditions drive different tumor-infiltrating cells and systemic IFN-/IL-17 release in bladder cancer treatment**. *Oncoimmunology*. 2022;11(1):2051845.

45. Gunst JD, Pahus MH, Rosás-Umbert M, Lu IN, Benfield T, Nielsen H, et al. **Early intervention with 3BNC117 and romidepsin at antiretroviral treatment initiation in people with HIV-1: a phase 1b/2a, randomized trial**. *Nature Medicine*. 2022.

46. Haeuser E, Serfes AL, Cork MA, Yang M, Abbastabar H, Abhilash ES, et al. **Mapping age- and sex-specific HIV prevalence in adults in sub-Saharan Africa, 2000-2018**.*BMC Medicine.* 2022;20(1):488.

47. Henderson M, Fidler S, Mothe B, Grinsztejn B, Haire B, Collins S, et al. **Mitigation strategies to safely conduct HIV treatment research in the context of COVID-19**. *Journal of the International AIDS Society*. 2022;25(2):e25882.

48. Hernandez A, Muñoz-Mármol AM, Esteve-Codina A, Alameda F, Carrato C, Pineda E, et al. **In silico validation of RNA-Seq results can identify gene fusions with oncogenic potential in glioblastoma**. Scientific Reports. 2022;12(1):14439.

49. Hussain R, Ongaro AE, Rodriguez de la Concepción ML, Wajs E, Riveira-Muñoz E, Ballana E, et al. **Small form factor flow virometer for SARS-CoV-2**. *Biomedical Optics Express*. 2022;13(3):1609-1619.

50. Huyveneers LEP, Bruns A, Stam A, Ellerbroek P, de Jong D, Nagy NA, et al. **Autopsy Study Defines Composition and Dynamics of the HIV-1 Reservoir after Allogeneic Hematopoietic Stem Cell Transplantation with CCR5 32/32 Donor Cells**. *Viruses*. 2022;14(9).

Publications

51. Izquierdo-Pujol J, Moron-Lopez S, Dalmau J, Gonzalez-Aumatell A, Carreras-Abad C, Mendez M, et al. **Post COVID-19 Condition in Children and Adolescents: An Emerging Problem**. *Frontiers in Pediatrics*. 2022;10:894204.

52. Izquierdo-Useros N, Marin Lopez MA, Monguió-Tortajada M, Muñoz-Moreno JA, Agusti Benito C, Morón-López S, et al. **Impact of COVID-19 lockdown in a biomedical research campus: A gender perspective analysis**. *Frontiers in Psychology*. 2022;13:906072.

53. John LN, Beiras CG, Houinei W, Medappa M, Sabok M, Kolmau R, et al. **Trial of Three Rounds of Mass Azithromycin Administration for Yaws Eradication**. *The New England Journal of Medicine*. 2022;386(1):47-56.

54. Jordan-Paiz A, Franco S, Martinez MA. **Reducing HIV-1 env gene CpG frequency increases the replication capacity of the HXB2 virus strain**. *Virus Research*. 2022;198685.

55. Jørgensen M, Nørgaard JC, Ilett EE, Marandi RZ, Noguera-Julian M, Paredes R, et al. **Metabolic Potential of the Gut Microbiome Is Significantly Impacted by Conditioning Regimen in Allogeneic Hematopoietic Stem Cell Transplantation Recipients**. *International Journal of Molecular Sciences*. 2022;23(19).

56. Karim QA, Archary D, Barré-Sinoussi F, Broliden K, Cabrera C, Chiodi F, et al. **Women for science and science for women: Gaps, challenges and opportunities towards optimizing pre-exposure prophylaxis for HIV-1 prevention**. Frontiers in immunology. 2022;13:1055042.

57. Kilpeläinen A, Jimenez-Moyano E, Blanch-Lombarte O, Ouchi D, Peña R, Quirant-Sanchez B, et al. **Skewed Cellular Distribution and Low Activation of Functional T-Cell Responses in SARS-CoV-2 Non-Seroconvertors**. *Frontiers in Immunology*. 2022;13:815041.

58. Lledó GM, Sellares J, Brotons C, Sans M, Díez Antón JM, Blanco J, et al. **Post-acute COVID-19 syndrome (PACS): a new tsunami requiring a universal case definition**. *Clinical Microbiology and Infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases*. 2022.

59. Lu MD, Telwatte S, Kumar N, Ferreira F, Martin HA, Kadiyala GN, et al. **Novel assays to investigate the mechanisms of latent infection with HIV-2**. *PLoS One*. 2022;17(4):e0267402.

60. Lundgren JD, Grund B, Barkauskas CE, Holland TL, Gottlieb RL, Sandkovsky U, et al. **Responses to a Neutralizing Monoclonal Antibody for Hospitalized Patients With COVID-19 According to Baseline Antibody and Antigen Levels: A Randomized Controlled Trial**. *Annals of Internal Medicine*. 2022;175(2):234-243.

61. Manry J, Bastard P, Gervais A, Le Voyer T, Rosain J, Philippot Q, et al. **The risk of COVID-19 death is much greater and age dependent with type I IFN autoantibodies**. *Proceedings of the National Academy of Sciences of the United States of America*. 2022;119(21):e2200413119.

62. Manry J, Bastard P, Gervais A, Le Voyer T, Rosain J, Philippot Q, et al. **The risk of COVID-19 death is much greater and age-dependent with type I IFN autoantibodies**. *Research Square*. 2022.

63. Marcelino R, Ezeonwumelu IJ, Janeiro A, Mimoso P, Matos S, Briz V, et al. **Phylogeography of hepatitis B virus: The role of Portugal in the early dissemination of HBV worldwide**. *PloS One*. 2022;17(12):e0276618.

64. Marin S, Val AM, Peligero MB, Rodríguez-Bernuz C, Pérez-Ricart A, Vilaró Jaques L, et al. **Safety of Short-Term Treatments with Oral Chloroquine and Hydroxychloroquine in Patients with and without COVID-19: A Systematic Review**. *Pharmaceuticals* (Basel, Switzerland). 2022;15(5).

65. Martin HA, Kadiyala GN, Telwatte S, Wedrychowski A, Chen TH, Moron-Lopez S, et al. **New Assay Reveals Vast Excess of Defective over Intact HIV-1 Transcripts in Antiretroviral Therapy-Suppressed Individuals**. *Journal of Virology*. 2022;96(24):e0160522.

66. Martinez de Lagran M, Elizalde-Torrent A, Paredes R, Clotet B, Dierssen M. **Lamivudine, a reverse transcriptase inhibitor, rescues cognitive deficits in a mouse model of down syndrome**. *Journal of Cellular and Molecular Medicine*. 2022.

67. Martinez MA, Tural C, Franco S. **Circulating MicroRNAs as a Tool for Diagnosis of Liver Disease Progression in People Living with HIV-1**. *Viruses*. 2022;14(6).

68. Martinez MA. **What Should Be Learned From Repurposed Antivirals Against SARS-CoV-2?**. *Frontiers in Microbiology*. 2022;13:843587.

69. Mazuelas H, Magallón-Lorenz M, Fernández-Rodríguez J, Uriarte-Arrazola I, Richaud-Patin Y, Terribas E, et al. **Modeling iPSC-derived human neurofibroma-like tumors in mice uncovers the heterogeneity of Schwann cells within plexiform neurofibromas**. *Cell Reports*. 2022;38(7):110385.

70. Millat-Martinez P, Gharbharan A, Alemany A, Rokx C, Geurtsvankessel C, Papageourgiou G, et al. **Prospective individual patient data meta-analysis of two randomized trials on convalescent plasma for COVID-19 outpatients**. *Nature Communications*. 2022;13(1):2583.

71. Miranda MNS, Pingarilho M, Pimentel V, Martins MDRO, Kaiser R, Seguin-Devaux C, et al. **Trends of Transmitted and Acquired Drug Resistance in Europe From 1981 to 2019: A Comparison Between the Populations of Late Presenters and Non-late Presenters**. *Frontiers in Microbiology*. 2022;13:846943.

72. Miro JM, Torres A, Paredes R. **New Antivirals and Immune Therapies for COVID-19 Infection**. *Archivos de Bronconeumologia*. 2022.

73. Mode AM, Magaji UF, Nzoniwu NA, Tangaza MH, Tanimu FI, Dandare SU, et al. **Coadministration of L-alanine and L-glutamine ameliorate blood glucose levels, biochemical indices and histological features in alloxan-induced diabetic rats**. *Journal of Food Biochemistry*. 2022;e14420.

74. Moltó J, Graterol F, Curran A, Ramos N, Imaz A, Sandoval D, et al. **Removal of doravirine by haemodialysis in people living with HIV with end-stage renal disease**. *The Journal of Antimicrobial Chemotherapy*. 2022.

Publications

75. Moyano A, Blanch-Lombarte O, Tarancon-Diez L, Pedreño-Lopez N, Arenas M, Alvaro T, et al. **Immunoescape of HIV-1 in Env-EL9 CD8+T cell response restricted by HLA-B*14:02 in a Non progressor who lost twenty-seven years of HIV-1 control.** Retrovirology. 2022;19(1):6.

76. Noël-Romas L, Guillén Y, De Leon M, Knodel S, Birse K, Manzardo C, et al. **Gut microbiome signatures linked to HIV-1 reservoir size and viremia control**.*Microbiome*. 2022;10(1):59.

77. Oriol-Tordera B, Esteve-Codina A, Berdasco M, Rosás-Umbert M, Gonçalves E, Duran-Castells C, et al. **Epigenetic landscape in the kick-and-kill therapeutic vaccine BCN02 clinical trial is associated with antiretroviral treatment interruption (ATI) outcome**. *EBioMedicine*. 2022;78:103956.

78. Pedreño-López S, García E, Guerrero D, Gómez-Mora E, Molina Mateu L, Orera Pérez F, et al. **Modulation of the autophagic pathway inhibits HIV-1 infection in human lymphoid tissue cultured ex vivo**. *Scientific Reports*. 2022;12(1):7439.

79. Pérez-González A, Represa M, Coll P, Potel C, Rodríguez-Rivero S, Flores EV, et al. **Real-life cohort experience after implementing HIV pre-exposure prophylaxis for one year in northwest Spain**. *Frontiers in Public Health*. 2022;10:1005622.

80. Pérez-Yanes S, Pernas M, Marfil S, Cabrera-Rodríguez R, Ortiz R, Urrea V, et al. **The Characteristics of the HIV-1 Env Glycoprotein Are Linked With Viral Pathogenesis**. *Frontiers in Microbiology*. 2022;13:763039.

81. Pradenas E, Trinité B, Urrea V, Marfil S, Tarrés-Freixas F, Ortiz R, et al. **Clinical course impacts early kinetics, magnitude, and amplitude of SARS-CoV-2 neutralizing antibodies beyond 1 year after infection**. *Cell Reports Medicine*. 2022;3(2):100523.

82. Pradenas E, Ubals M, Urrea V, Suñer C, Trinité B, Riveira-Muñoz E, et al. **Virological and Clinical Determinants of the Magnitude of Humoral Responses to SARS-CoV-2 in Mild-Symptomatic Individuals**. *Frontiers in Immunology*. 2022;13:860215.

83. Raïch-Regué D, Muñoz-Basagoiti J, Perez-Zsolt D, Noguera-Julian M, Pradenas E, Riveira-Muñoz E, et al. **Performance of SARS-CoV-2 Antigen-Detecting Rapid Diagnostic Tests for Omicron and Other Variants of Concern**. *Frontiers in Microbiology*. 2022;13:810576.

84. Raïch-Regué D, Resa-Infante P, Gallemí M, Laguia F, Muñiz-Trabudua X, Muñoz-Basagoiti J, et al. **Role of Siglecs in viral infections: A double-edged sword interaction**. *Molecular Aspects of Medicine*. 2022;101113.

85. Revollo B, Viñuela L, de la Mora L, García F, Noguera-Julián M, Parera M, et al. **Integrase resistance emergence with dolutegravir/lamivudine with prior HIV-1 suppression**. *The Journal of Antimicrobial Chemotherapy*. 2022.

86. Rodon J, Elosua-Bayes M, Risco C, Sachse M, Pino M, Gumber S, et al. Author Correction to: **SARS-CoV-2 interaction with Siglec-1 mediates trans-infection by dendritic cells**. *Cellular & Molecular Immunology*. 2022.

87. Rogers AJ, Wentworth D, Phillips A, Shaw-Saliba K, Dewar RL, Aggarwal NR, et al. **The Association of Baseline Plasma SARS-CoV-2 Nucleocapsid Antigen Level and Outcomes in Patients Hospitalized With COVID-19**. *Annals of Internal Medicine*. 2022;175(10):1401-1410.

88. Romero-Martín L, Duran-Castells C, Olivella M, Rosás-Umbert M, Ruiz-Riol M, Sanchez J, et al. **Disruption of the HLA-E/NKG2X axis is associated with uncontrolled HIV infections**. *Frontiers in Immunology*. 2022;13:1027855.

89. Romero-Martín L, Tarrés-Freixas F, Pedreño-López N, de la Concepción MLR, Cunyat F, Hartigan-O'Connor D, et al. **T Cell Responses in Chronic HIV Infection Are Associated With Virus Control and Antibody Isotype Switching to IgG**. *Frontiers in Immunology*. 2022;13:928039.

90. Rosás-Umbert M, Gunst JD, Pahus MH, Olesen R, Schleimann M, Denton PW, et al. **T cell immunity**. *Nature Communications*. 2022;13(1):6473.

91. Roso-Llorach A, Serra-Picamal X, Cos FX, Pallejà-Millán M, Mateu L, Rosell A, et al. **Evolving mortality and clinical outcomes of hospitalized subjects during successive COVID-19 waves in Catalonia, Spain**. *Global Epidemiology*. 2022;100071.

92. Roure S, Pérez-Quílez O, Vallès X, Valerio L, Fernández-Rivas G, Rivaya B, et al. **A simple new screening tool for diagnosing imported schistosomiasis**. *Public Health in Practice* (Oxford, England). 2022;3:100245.

93. Roure S, Pérez-Quílez O, Vallès X, Valerio L, López-Muñoz I, Soldevila L, et al. **Schistosomiasis Among Female Migrants in Non-endemic Countries: Neglected Among the Neglected? A Pilot Study**. *Frontiers in Public Health*. 2022;10:778110.

94. Sachse M, Tenorio R, Fernández de Castro I, Rodon J, Losada A, Avilés P, et al. **Unraveling the antiviral activity of plitidepsin by subcellular and morphological analysis**. Antiviral Research. 2022;105270.

95. Senserrich J, Guallar-Garrido S, Gomez-Mora E, Urrea V, Clotet B, Julián E, et al. **Remodeling the bladder tumor immune microenvironment by mycobacterial species with changes in their cell envelope composition**. *Frontiers in Immunology*. 2022;13:993401.

96. Serra Mitjà P, Centeno C, Garcia-Olivé I, Antuori A, Casadellà M, Tazi R, et al. **Bronchoscopy in Critically Ill COVID-19 Patients: Findings, Microbiological Profile, and Coinfection**. *Journal of Bronchology & Interventional Pulmonology*. 2022;29(3):186-190.

97. Simões D, Ehsani S, Stanojevic M, Shubladze N, Kalmambetova G, Paredes R, et al. **Integrated use of laboratory services for multiple infectious diseases in the WHO European Region during the COVID-19 pandemic and beyond**. *Euro surveillance: bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*. 2022;27(29).

98. Sirera G, Videla S, Saludes V, Castellà E, Sanz C, Ariza A, et al. **Prevalence of HPV-DNA and E6 mRNA in lung cancer of HIV-infected patients**. *Scientific Reports*. 2022;12(1):13196.

99. Suñer C, Coma E, Ouchi D, Hermosilla E, Baro B, Rodríguez-Arias MÀ, et al. **Association between two mass-gathering outdoor events**

Publications/ Conference presentations & talks

and incidence of SARS-CoV-2 infections during the fifth wave of COVID-19 in north-east Spain: A population-based control-matched analysis. *The Lancet Regional Health Europe.* 2022;15:100337.

100. Suñer C, Ouchi D, Baro B, Rodríguez-Arias MÀ, Puig J, Clotet B, et al. **Re-examining the importance of mask-wearing at mass gathering events-Authors' reply**. *The Lancet Regional Health Europe.* 2022;18:100425.

101. Suñer C, Ubals M, Tarín-Vicente EJ, Mendoza A, Alemany A, Hernández-Rodríguez Á, et al. **Viral dynamics in patients with monkeypox infection: a prospective cohort study in Spain**. *The Lancet Infectious Diseases.* 2022.

102. Tarín-Vicente EJ, Alemany A, Agud-Dios M, Ubals M, Suñer C, Antón A, et al. **Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: a prospective observational cohort study**. *The Lancet* (London, England). 2022;400(10353):661-669.

103. Tarragó-Gil R, Gil-Mosteo MJ, Aza-Pascual-Salcedo M, Alvarez MJL, Ainaga RR, Gimeno NL, et al. **Randomised clinical trial to assess the impact of oral intervention with cetylpyridinium chloride (CPC) to reduce salivary sars-cov-2 viral load**. *Journal of Clinical Periodontology.* 2022.

104. Tarrés-Freixas F, Trinité B, Pons-Grífols A, Romero-Durana M, Riveira-Muñoz E, Ávila-Nieto C, et al. **Heterogeneous Infectivity and Pathogenesis of SARS-CoV-2 Variants Beta, Delta and Omicron in Transgenic K18-hACE2 and Wildtype Mice**. *Frontiers in Microbiology.* 2022;13:840757.

105. Trigueros M, Pradenas E, Palacín D, Muñoz-López F, Ávila-Nieto C, Trinité B, et al. **Reduced humoral response 3 months following BNT162b2 vaccination in SARS-CoV-2 uninfected residents of long-term care facilities**. *Age and Ageing.* 2022;51(5).

106. Ubals M, Tarín-Vicente EJ, Oller X, Mendoza A, Alemany A, Hernández-Rodríguez Á, et al. **Evaluating the accuracy of self-collected swabs for the diagnosis of monkeypox**. *Clinical Infectious Diseases: an official publication of the Infectious Diseases Society of America.* 2022.

107. Usai C, Pailler-García L, Lorca-Oró C, Fernández-Bastit L, Roca N, Brustolin M, et al. **Agreement and differential use of laboratory methods for the detection and quantification of SARS-CoV-2 in experimentally infected animals**. *Frontiers in Microbiology.* 2022;13:1016201.

108. Valenzuela-Fernández A, Cabrera-Rodríguez R, Casado C, Pérez-Yanes S, Pernas M, García-Luis J, et al. **Contribution of the HIV-1 Envelope Glycoprotein to AIDS Pathogenesis and Clinical Progression**. *Biomedicines.* 2022;10(9).

109. Varona JF, Landete P, Lopez-Martin JA, Estrada V, Paredes R, Guisado-Vasco P, et al. **Preclinical and randomized phase I studies of plitidepsin in adults hospitalized with COVID-19**. *Life Science Alliance.* 2022;5(4).

110. Vergara-Alert J, Izquierdo-Useros N. **An anti-SARS-CoV-2 metabolite is reduced in diabetes**. *Nature Metabolism.* 2022.

111. Violán C, Torán-Monserrat P, Quirant B, Lamonja-Vicente N, Carrasco-Ribelles LA, Chacón C, et al. **Kinetics of humoral immune response over 17 months of COVID-19 pandemic in a large cohort of healthcare workers in Spain: the ProHEpiC-19 study**.*BMC Infectious Diseases.* 2022;22(1):721.

112. Wensing AM, Calvez V, Ceccherini-Silberstein F, Charpentier C, Günthard HF, Paredes R, et al. **2022 update of the drug resistance mutations in HIV-1**. *Topics in Antiviral Medicine.* 2022;30(4):559-574.

113. Xie G, Moron-Lopez S, Siegel DA, Yin K, Polos A, Cohen J, et al. **Common and Divergent Features of T Cells from Blood, Gut, and Genital Tract of Antiretroviral Therapy-Treated HIV+ Women**. *Journal of Immunology.* 2022;208(7):1790-1801.

114. Xie J, Prats-Uribe A, Feng Q, Wang Y, Gill D, Paredes R, et al. **Clinical and Genetic Risk Factors for Acute Incident Venous Thromboembolism in Ambulatory Patients With COVID-19**. *JAMA Internal Medicine.* 2022.

115. Yeregui E, Masip J, Viladés C, Domingo P, Pacheco YM, Mallolas J, et al. **T-Cell Reconstitution in PLHIV on Suppressive Antiretroviral Therapy**. *International Journal of Molecular Sciences.* 2022;23(4).

116. Zargari Marandi R, Jørgensen M, Ilett EE, Nørgaard JC, Noguera-Julian M, Paredes R, et al. **Pre-Transplant Prediction of Acute Graft-versus-Host Disease Using the Gut Microbiome**. *Cells.* 2022;11(24).

International congresses

1. Ainsua Enrich E, Pedreño López N, Rodríguez de la Concepción ML, Ávila Nieto C, Pradenas Saavedra E, Marfil Verchili S, García Prado J, Mothe Pujadas B, Brander C, Izquierdo Useros N, Massanella Luna M, Blanco Arbués J, Clotet Sala B, Carrillo Molina J. **Response to SARS-CoV-2 vaccination in patients with Antibody Deficiency Disorders**. *ECCMID European Congress of Clinical Microbiology & Infectious Diseases.* Lisbon, Portugal, 23-26 April 2022. Poster.

2. Bayón Gil A, Dalmau Moreno J, Urrea Gales V, García Guerrero MC, Gálvez Celada C, Salgado Bernal M, Martínez Picado J, Puertas Castro MC. **Immune preservation in HIV+ Viremic Non-Progressors is associated with downregulation of type-I IFN pathway and reduced activation of cytotoxic compartments**. *AIDS 2022 - IAS - International AIDS Society.* Montreal, Canada, 29 July-02 August 2022. Poster # A-AIDS-2022-04473.

3. Blazquez Bondia C, Parera Sallent M, Català Moll F, Casadellà Fontdevila M, Paredes Deiros R, Noguera Julian M. **Probiotic effects on immunity and microbiome in HIV-1 discordant patients**. *International Human Microbiome Congress (IHMC).* Online, 8-10 November 2022. Poster.

4. Borgognone A, Elizalde Torrent A, Casadellà Fontdevila M, Romero Martín L, Escribà Bel T, Parera Sallent M, Català Moll F, Noguera Julian M, Brander C, Olvera van der Stoep A, Paredes Deiros R. **Vaccination with HIV T cell immunogen induces alterations in the mouse gut microbiota**. *International Human Microbiome Congress (IHMC).* Online, 8-10 November 2022. Poster.

5. Brander C. **The HIVACAT Therapeutic HIV vaccine development**. *Ragon Institute Round Table Series*, 23 March 2022. Invited talk.

6. Brander C. **Advances in Therapeutic HIV Vaccine Development**. *Vaccine Technology*

Conference presentations & talks

VIII, 13-16 June 2022. Invited talk.

7. Brander C. **Impact of the HLA-E/NKG2x axis in COVID-19 disease progression**. *AIDS 2022 - IAS - International AIDS Society*. Montreal, Canada, 29 July-02 August 2022. Oral communication.

8. Brander C. **Effective HIV Control after Therapeutic Vaccination in the Aelix-002 trial**. *World Vaccine Congress Europe*. Barcelona, Spain, 12 October 2022. Oral communication.

9. Brander C. **Immune Correlates of Virus Control in the AELIX-002 Therapeutic HIV Vaccine Trial**. *PAVE Delaney Consortium Meeting*, 29 November 2022. Invited talk.

10. Carrillo J. **Structurally guided stabilization of Spike glycoproteins for the development of novel SARS-CoV-2 vaccines**. *Joint annual meeting of the French Society for Immunology and the French Association of Cytometry*. Nice, France, 22-24 November 2022. Invited talk.

11. Ezeonwumelu IJ, García Vidal E, Oriol Tordera B, Ruiz Riol M, Massanella Luna M, Clotet Sala B, Badia Córcoles R, Riveira Muñoz E, Ballana Guix E. **IRF7 regulates HIV-1 latency reversal independent of cytokine signaling blockade**. *Viruses 2022 - At the Leading Edge of Virology Research*. Online, 5-8 April 2022. Poster.

12. Ezeonwumelu IJ, García Vidal E, Oriol Tordera B, Ruiz Riol M, Massanella Luna M, Clotet Sala B, Badia Córcoles R, Riveira Muñoz E, Ballana Guix E. **IRF7 regulates HIV-1 latency reversal independent of cytokine signaling blockade**. *Conference on Retroviruses and Opportunistic Infections CROI 2022*. Seattle, USA, 12-16 February 2022. Poster.

13. Ezeonwumelu IJ, Riveira Muñoz E, Felip Falgàs E, García Vidal E, Gutiérrez Chamorro L, Massanella Luna M, Ballana Guix E, Badia Córcoles R. **Pharmacological inhibition of IKK induces reactivation of latent HIV-1**. *Viruses 2022 - At the Leading Edge of Virology Research*. Online, 5-8 April 2022. Poster.

12. Martínez de la Sierra MA, Franco Cirera S. **Reducing HIV-1 HXB2 env gene CpG frequency increases virus replication capacity**. *Conference on Retroviruses and Opportunistic Infections CROI 2022*. Seattle, USA, 12-16 February 2022. Poster #00182.

13. González Navarro I, Gálvez Celada C, Garrido Sanz L, Urrea Gales V, Martínez Picado J, Salgado Bernal M. **HIV-1-infected individuals with extremely low reservoir under ART are characterized by reduced viral diversity and higher levels of hypermutations in their viral reservoirs**. *10th International Workshop on HIV Persistence during Therapy*. Miami, USA, 13-16 December 2022. Poster #PP3.13–00189.

14. Gutiérrez Chamorro L, Felip Falgàs E, Ezeonwumelu IJ, Clotet Sala B, Ballana Guix E. **CDK inhibitors impact HIV-1 susceptibility by modulating in vivo immunologic response**. *Conference on Retroviruses and Opportunistic Infections CROI 2022*. Online, 12-16 February 2022. Poster.

15. Gutiérrez Chamorro L, Felip Falgàs E, Riveira Muñoz E, Ballana Guix E. **SAMHD1 expression determines proinflammatory signalling and immune infiltration capacity in 3D breast cancer in vitro models**. *EACR 2022 Congress-Innovative Cancer Science: Translating Biology to Medicine*. Sevilla, Spain, 20-23 June 2022. Poster #EACR22-0807.

16. Malagrida Escala R. **A participatory system analysis approach to co-design accompanying interventions for more effective SARS-CoV-2 prevention in schools**. *Living Knowledge Conference*. Groningen, Netherlands, 30 June 2022. Oral communication.

17. Malagrida Escala R. **Students as key agents to address our complex and persistent problems**. *40th Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID)*. Athens, Greece, 13 May 2022. Oral communication.

18. Malagrida Escala R, Pino Cebrián M. **Transforming the System of Promotion of Healthy and Sustainable Diets**. *Microbe 2022*. Washington, 9-13 June 2022. Poster #1989.

19. Martínez de la Sierra MA, Franco Cirera S. **HCV-DAA Therapy Affects Circulating Levels Of MiRNAs In HIV-1/HCV Coinfected Subjects**. *Transformative Innovation Policy Conference 2022*. Online, 19 January 2022. Oral communication.

20. Martínez Picado J, Puertas Castro MC. **The multitask effort of measuring viral persistence**. *HIV Cure Symposium*. Ghent, Belgium, 19 January 2022.

21. Massanella Luna M. **Inflammation and ageing: ¿Myth or reality?** *Aging in HIV (7ª Edición), Fundación Huésped*. Online, 17 November 2022. Invited talk.

22. Massanella Luna M. **New immunological insights for destroying the HIV reservoir**. *European Congress of Clinical Microbiology and Infectious Diseases*. Online, 23-26 April 2022. Invited talk.

23. Massanella Luna M. **Inflamación y envejecimiento**. *Excellence Highlights in HIV, Jornadas cientificas de Gilead*. Online, 24 December 2022 - 24 January 2023. Invited talk.

24. Massanella Luna M. **Covid post-agudo y Long COVID: Fisiopatología e inmunopatología**. *Enfermedades infecciosas emergentes: factores ambientales y lecciones de COVID-19, LINCGLOBAL*. Online, 25 November 2022 - 27 January 2023. Invited talk.

25. Morón López S. **Intact HIV transcripts are rare in ART-suppressed individuals**. *28th Conference on Retroviruses and Opportunistic Infections*. Online, 12-16 February 2022 - 27 January 2023. Poster.

26. Muñoz Basagoiti J, Pérez Zsolt D, Ouchi Vernet D, Raïch Regué D, Trinité B, Pradenas Saavedra E, Blanco Arbués J, Clotet Sala B, Izquierdo Useros N. **Cetylpyridinium chloride mouthwashes to reduce the shedding of viable viable SARS-CoV-2.** *28th Conference on Retroviruses and Opportunistic Infections*. Online, 12-16 February 2022 - 27 January 2023. Poster.

27. Puertas Castro MC, Garcia Guerrero MC, Mothe Pujadas B, Martínez Picado J. **Differential decay dynamics of the inducible pool of HIV-1 infected CD4+ T cells and proviral DNA upon ART initiation revealed by the novel VIP-SPOT assay**. *10th International Workshop on HIV Persistence during Therapy*. Miami, USA, 13-16 December 2022. Poster #PP1.19–00109.

28. Puertas Castro MC, Mothe Pujadas B. **Measuring the impact of early 3BNC117**

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intervention at ART initiation on the productive reservoir in a cohort of diverse viral subtypes: results from the VIP-SPOT assay in the eCLEAR trial . *10th International Workshop on HIV Persistence during Therapy.* Miami, USA, 13-16 December 2022. Oral communication #OP1.9–00042.

29. Rodríguez de la Concepción ML, Riveira Muñoz E, Ballana Guix E, Blanco Arbués J, Massanella Luna M, Grau Segú E, Clotet Sala B, Carrillo Molina J. **Small Form Factor Flow Virometer for SARS-CoV-2**. *Optical Sensors and Sensing Congress.* Vancouver, British Columbia, Canada, 11-15 July 2022. Oral communication.

30. Romero Martín L, Duran Castells C, Ruiz Riol M, Olvera van der Stoep A, Brander C. **Impact of chronic HIV infection on NK cell response through the HLA-E/NKG2X axis**. *AIDS 2022.* Montréal, Québec, Canada, 27 July - 2 August 2022. Poster.

31. Romero Martín L, Massanella Luna M, Olvera van der Stoep A, Brander C. **COVID-19 severity is related to exhausted NK cells with impaired HLA-E sensing**. *Keystone Symposia - Viral Immunity.* Keystone, Colorado, USA, 28 June - 2 July 2022. Poster.

32. Senserrich Velasco J. **Tumour immune microenvironment is dictated by mycobacterial species and their cell envelope composition in a bladder cancer model**. *42th Congress of the European Society of Mycobacteriology.* Bologna, Italy, 26-29 June 2022. Poster.

33. Senserrich Velasco J, Pedreño López S, García Rodríguez E, Clotet Sala B, Cabrera Navarro C. **The pan-caspase inhibitor Q-VD-OPh drives cells into an anti-viral state through Type I IFN activation**. *Innate immunity in host-pathogen interactions, EMBO.* Heidelberg, Germany, 17-20 July. Poster.

34. Trinité B, Pradenas Saavedra E, Urrea Gales V, Marfil Verchili S, Tarrés Freixas F, Ortiz López R, Rovirosa Martí C, Izquierdo Useros N, Noguera Julian M, Carrillo Molina J, Paredes Deiros R, Massanella Luna M, Clotet Sala B, Blanco Arbués J. **SARS-COV-2 neutralizing response beyondone year after infection**. *28th Conference on Retroviruses and Opportunistic Infections.* Online, 12-16 February 2022 - 27 January 2023. Poster.

National congresses

1. Aguilar-Gurrieri C, Barajas Molina A, Rovirosa Martí C, Urrea Gales V, de la Iglesia Zaragoza N, Clotet Sala B, Blanco Arbués J, Carrillo Molina J. **Alanine-based spacers promote a more efficient antigen processing and presentation of neoantigen polypeptide vaccines**. *EACR 2022-Innovative cancer science: Translating biology to medicine.* Sevilla, 20-23 June 2022. Poster.

2. Ainsua Enrich E, Pedreño López N, Ávila Nieto C, Rodríguez de la Concepción ML, Pradenas Saavedra E, Trinité B, Marfil Verchili S, Escribà Bel T, Jiménez Moyano E, Peña Poderós R, Cedeño Briceño S, García Prado J, Mothe Pujadas B, Brander C, Izquierdo Useros N, Massanella Luna M, Blanco Arbués J, Clotet Sala B, Carrillo Molina J. **Kinetics of T cell immune responses elicited after three mRNA COVID-19 vaccine doses in predominantly antibody-deficient individuals**. *Congreso de la Sociedad Española de Immunología.* León, 22-24 September 2022. Poster.

3. Blanco Arbués J. **Nuevas tecnologías para nuevas vacunas**. *11º Congreso de la AEV Asociación Española de Vacunología.* Lleida, Spain, 20-22 October 2022. Invited talk.

4. Blanco Arbués J. **Second generation vaccines against SARS-CoV-2: HIPRA vaccine**. *XII Jornadas de Enfermedades Emergentes, FUITB.* Barcelona, Spain, 25-26 May 2022. Invited talk.

5. Blanco Arbués J. **Immunity against SARS-COV-2 variants. Protective mechanisms and implications for vaccination programs**. *Jornada de la Societat Catalana d'Immunologia.* Barcelona, Spain, 19 May 2022. Invited talk.

6. Benet S, Blanch Lombarte O, Ainsua Enrich E, Pedreño López N, Muñoz Basagoiti J, Raïch Regué D, et al. **Limited humoral and specific T-cell responses after SARS-CoV-2 vaccination in PWH with poor immune reconstitution**. *GESIDA 2022.* Sitges, Spain, 29 November 2022. Poster.

7. Brander C. **CD4/CD8 ratio ≥0.5 is a risk factor of acute rejection in HIV-infected LT recipients**. *GESIDA 2022.* Sitges, Spain, 29 November 2022. Poster.

8. Ezeonwumelu IJ, García Vidal E, Riveira Muñoz E, Felip Falgàs E, Gutiérrez Chamorro L, Calba Iñiguez I, Massanella Luna M, Clotet Sala B, Ballana Guix E, Badia Córcoles R. **Pharmacological inhibition of IKK to tackle latency and hyperinflammation in chronic HIV-1 infection**. *XXI Virology meeting 2022, Societat Catalana de Biologia, Secció de Virologia.* Barcelona, Spain, 21 November 2022. Oral communication #O.17.

9. Franco Cirera S, Martínez de la Sierra MA. **Normalization of circulating plasma levels of miRNAs in HIV-1/HCV co-infected patients following direct acting antiviral-induced sustained virologic response at week 12**. *XVI Congreso Nacional de Virología, Sociedad Española de Virología.* Málaga, Spain, 6 September 2022. Poster #P13.2HVI.

10. Izquierdo Pujol J, Morón López S, Dalmau Moreno J, Puertas Castro MC, Martínez Picado J. **PBMC immunophenotyping and plasma inflammatory profile of children with Long COVID**. *XXI Jornada de Virologia, Societat Catalana de Biologia.* Barcelona, Spain, 21 November 2022. Oral communication.

11. Izquierdo Useros N. **Pan-antiviral strategies and the future ahead**. *MedChem.* Barcelona, Spain, 6-9 July 2022. Invited talk.

12. Izquierdo Useros N. **Pan-antiviral strategies and the future ahead**. *BioForo UPV/EHC CSIC Insitituto Biofisika.* Bilbao, Spain, 8 June 2022. Invited talk.

13. Izquierdo Useros N. **Pan-antiviral strategies and the future ahead**. *IBUB Seminars.* Barcelona, Spain, 9 May 2022. Invited talk.

14. Izquierdo Useros N. **When antigen-presenting cells go viral. Coronaviruses,**

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retroviruses, filoviruses and beyond. *Department Seminar Series CNB CSIC.* Online, 12 January 2022. Invited talk.

15. Izquierdo Useros N. **Could antivirals halt long COVID? Plitidepsin: Mechanisms of action.** *Condición Post-COVID-19: Un largo camino hacia la recuperación.* Barcelona, Spain, 21 April 2022. Invited talk.

16. Muñoz López FM. **Deep characterization of the post-COVID-19 condition.** *COVID-19 from basic knowledge to vaccine development, Societat Catalana d'Immunologia.* Barcelona, Spain, 19 May 2022. Oral communication.

17. Pedreño López N. **Characterization of vaccine-induced humoral responses elicited after three mRNA COVID-19 doses in patients with predominantly antibody-deficiencies.** *Congreso de la Sociedad Española de Immunología.* León, Spain, 22-24 September 2022. Poster.

18. Pérez Zsolt D, Raïch Regué D, Muñoz Basagoiti J, Gallemí Rovira M, Clotet Sala B, Izquierdo Useros N. **In vitro screening platform to quickly assess the antiviral and immunomodulatory activity of potential anti-SARS-CoV-2 compounds.** *XXI Jornada de Virologia - Virology Meeting 2022.* Barcelona, Spain, 21 November 2022. Oral communication.

19. Pons Grifols A, Tarrés Freixas F, Riveira Muñoz E, Pérez Zsolt D, Muñoz Basagoiti J, Raïch Regué D, Izquierdo Useros N, Ballana Guix E, Carrillo Molina J, Clotet Sala B, Trinité B, Blanco Arbués J. **Development and characterization of a new human ACE2 knock-in mouse model for SARS-CoV-2 infection and pathogenesis.** *XXI Jornada de Virologia - Virology Meeting 2022.* Barcelona, Spain, 21 November 2022. Oral communication.

20. Raïch Regué D, Pérez Zsolt D, Muñoz Basagoiti J, Gallemí Rovira M, Carrillo Molina J, Blanco Arbués J, Clotet Sala B, Izquierdo Useros N. **ß-Cyclodextrins as affordable antivirals against coronavirus infection.** *XXI Jornada de Virologia - Virology Meeting 2022.* Barcelona, Spain, 21 November 2022. Oral communication #O.11.

21. Raïch Regué D, Pérez Zsolt D, Muñoz Basagoiti J, Gallemí Rovira M, Tarrés Freixas F, Carrillo Molina J, Blanco Arbués J, Clotet Sala B, Izquierdo Useros N. **ß-Cyclodextrins as affordable antivirals against coronavirus infection.** *XXI Jornada de Virologia - Virology Meeting 2022.* Barcelona, Spain, 21 November 2022. Oral communication #O.11.

22. Salgado Bernal M. **Estrategias de cura en la infección por VIH**. *XIII Congreso GESIDA.* Sitges, Spain, 27 November - 1 December 2022. Invited talk.

23. Salgado Bernal M. **Terapia celular con CAR-T para la curación del VIH**. *XIII Congreso GESIDA.* Sitges, Spain, 27 November - 1 December 2022. Invited talk.

24. Salgado Bernal M. **Nuevos avances hacia la curación del VIH**. *XIII Congreso GESIDA.* Sitges, Spain, 27 November - 1 December 2022. Invited talk.

25. Senserrich Velasco J. **Tumour immune microenvironment is dictated by mycobacterial species and their cell envelope composition in a bladder cancer model**. *III Jornada de Microbiologia.* Barcelona, Spain, 25 May 2022. Poster.

26. Senserrich Velasco J. **Tumour immune microenvironment is dictated by mycobacterial species and their cell envelope composition in a bladder cancer model**. *MycoNET Meeting.* Madrid, Spain, 20-22 May 2022. Poster.


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