IrsiCaixa
Institut de Recerca de la Sida

Obra Social "la Caixa"

Generalitat de Catalunya
Departament de Salut

IrsiCaixa 2017

Annual Report

Contents

About IrsiCaixa

The **IrsiCaixa AIDS Research Institute** is an international landmark and leading centre for research into the eradication of HIV/AIDS and related diseases. It also tackles other challenges facing biomedicine today, such as the microbiome and emerging infectious diseases.

IrsiCaixa was created as a private non-profit foundation in 1995 with the support of "la Caixa" Banking Foundation and the Department of Health of the Generalitat of Catalonia. Its director is **Dr. Bonaventura Clotet**.

The fact that both **IrsiCaixa** and the Fight AIDS 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 the various stakeholders with an interest in HIV leads to novel solutions that facilitate progress towards eradication of this disease.

IrsiCaixa applies a combined approach to eradicating AIDS, based on five strategic lines: prevention, eradication and functional care; the microbiome; novel treatments and resistance to antiretrovirals; immunopathogenesis; and other diseases.

IrsiCaixa also participates in clinical trials to evaluate novel therapeutic strategies and actively cooperates with low-income countries in the global fight against the pandemic. It places special emphasis on the formal training of young scientists, on innovation and on the transfer of knowledge generated in its laboratories.

Letter from the Director

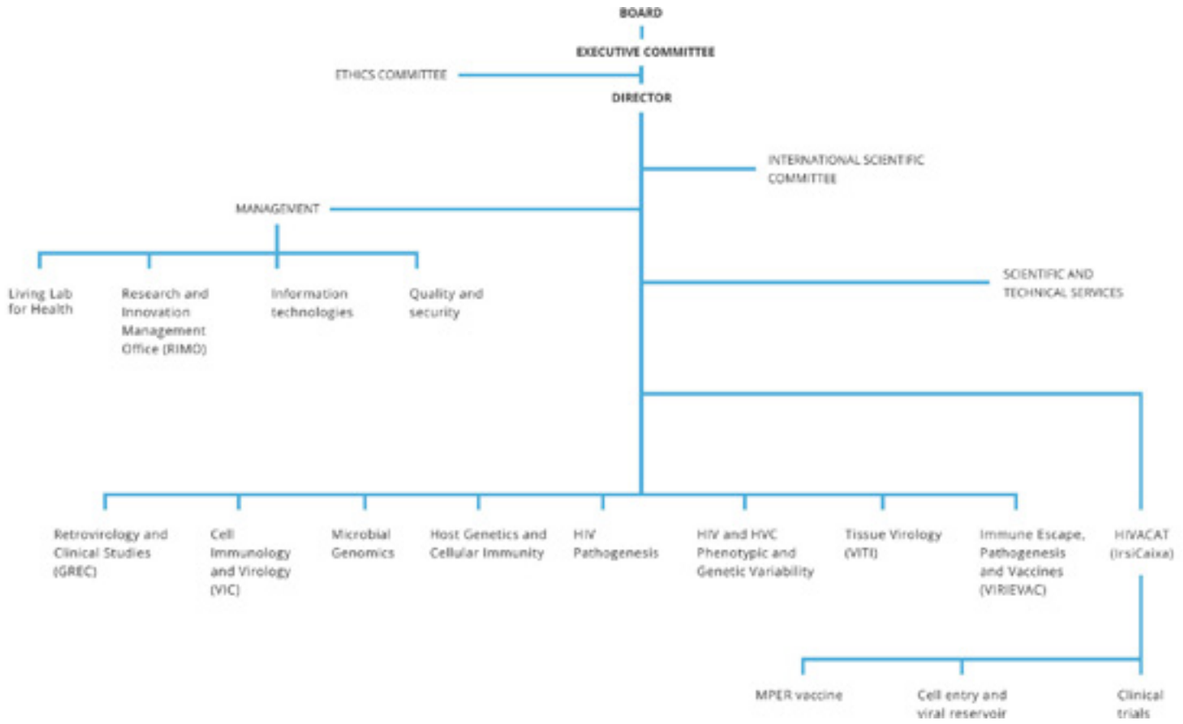
IrsiCaixa continued, in **2017**, to develop its research agenda aimed at contributing to global efforts to eradicate HIV infection. Aside from the implementation of planned actions aimed at furthering our lines of research, **2017** was notable for the following:

— International alliances of the Microbial Genomics group have been strengthened through collaborations with key international groups and organization of The Barcelona Debates on the Human Microbiome **2017**.
— PASeq, a web server developed by **IrsiCaixa** researchers, was launched to facilitate use of next-generation sequencing for viral genotyping and polymorphism analyses. Since the beta version was launched, some 3,000 samples from around the world have been sequenced.
— New applications have been developed for virus-like particles (VLPs), initially developed as a preventive HIV vaccine strategy. In 2017, applications beyond infectious diseases were explored, such as molecular visualization, cancer treatment and animal health, in collaborations with the Barcelona Supercomputing Centre, the Vall d'Hebron Oncology Institute and HIPRA.
— Eradication studies have been consolidated within the framework of an IciStem international consortium (funded by amfAR) project, as evidenced by the Dominique Dormont Prize awarded, at the International AIDS Society annual conference, to **Dr. Salgado** for her research into factors related to stem-cell transplantation that could lead to a potential cure for HIV infection.
— Progress has been made in developing compounds in spin-offs:
  • Aelix Therapeutics SL: first clinical trials using HTI and amplification of available vectors with GMP production of the chimpanzee adenovirus (ChAd) vector.
  • AlbaJuna Therapeutics SL: GMP production of immunoglobulins for use in clinical studies.
— Living Lab for Health has consolidated its participation in new European and national initiatives aimed at promoting responsible, participatory and open innovation and research in society.

In the immediate future, it will be of crucial importance to be able to access the resources necessary to implement a research agenda as ambitious, complex and successful as ours. The difficulties in raising funds (fewer calls, smaller budgets and greater competition) cannot be compensated for by increasingly smaller and fewer philanthropic and private sector contributions. To meet this challenge, we need to develop collaborations with **IrsiCaixa** in the form of public-private partnerships, so as to raise the funds necessary to maintain our competitiveness worldwide.

Bonaventura Clotet
IrsiCaixa Director

Organizational Structure



Board

President
Head of the Generalitat de Catalunya department responsible for health policy

Vice-president
Appointee of "la Caixa" Banking Foundation
Josep Vilarasau i Salat

Members
Appointee of the Director of the Catalan Health Service (CatSalut)
Albert Barberà i Lluis

Appointee of the Generalitat de Catalunya department responsible for research
Iolanda Font de Rubinat Garcia

Representatives of the Generalitat de Catalunya department responsible for health policy
Antoni Andreu i Périz
Jordi Casabona i Barbarà
Joan Guix i Oliver
Manel Puig i Domingo

Representatives of "la Caixa" Banking Foundation
Jaume Giró i Ribas
Jaume Lanaspa i Gatnau
Esther Planas i Herrera
Àngel Font i Vidal
Marta Casals i Virosque

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

Secretary
Marta Casals i Virosque

Executive Committee

For "la Caixa" Banking Foundation
Sra. Esther Planas i Herrera (President)
Sra. Marta Casals i Virosque (Secretary)
Sr. Àngel Font Vidal

For the Generalitat de Catalunya department responsible for health policy
Sr. Jordi Casabona i Barbarà
Sr. Manel Puig i Domingo
Sr. Albert Barberà i Lluis

Director

Dr. Bonaventura Clotet

Financial Manager

Lourdes Grau

Administration
Arnau Creus
Cristina Mesa
Penélope Riquelme

Information Technologies
Julián Eslava

International Scientific Committee

Dr. Brigitte Autran
Professor of Medicine (Immunology) at the Pierre and Marie Curie University (UPMC) (Paris, France) and Director of the Department of Immunology and of the Biology and Medical Pathology Division of the Pitié-Salpêtrière University Hospital (Paris, France).

Dr. Charles Boucher
Professor at the Department of Virology of the Erasmus Medical Center at Erasmus University (Rotterdam, Netherlands).

Dr. Daria Hazuda
Merck Vice President, Infectious Diseases Discovery and Chief Scientific Officer, MRL Cambridge Exploratory Science Center (Cambridge, Massachusetts).

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

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

Dr. Jürgen Rockstroh
Professor of Medicine and Head of the Outpatient HIV Clinic at the University of Bonn (Germany).

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

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

Dr. Bruce Walker
Director of the Ragon Institute of MGH, MIT and Harvard University (USA) and researcher at the Harvard Howard Hughes Medical Institute.


eppendorf
Centrifuge 5810 R

Key figures

Total **staff**

75

By sex

71% ♀

29% ♂

Funding

28 public

39 private

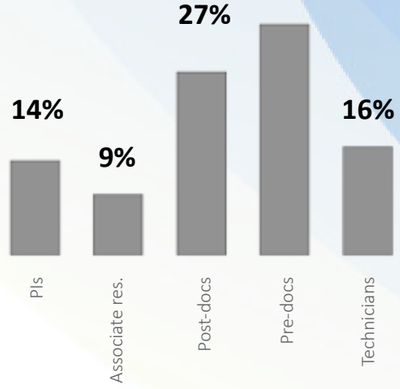
8 external

Staff by **categories**

Research, Administration and Support **17%**

Scientific and Technical Services **8%**

Research staff **75%**



Theses read 2017

2

Elisabet Gómez - Cell Virology and Immunology (VIC) and Tissue Virology (VITI)

Lucía Pastor - Cell Virology and Immunology (VIC)

Publications 2017

86

Awarded **projects** 2017

22

Highlights 2017

January

The VIC group publishes the article *Proteoliposomal formulations of an HIV-1 gp41-based miniprotein elicit a lipid-dependent immunodominant response overlapping the 2F5 binding motif*. During 2017 immunogen redesign is completed and presented in VLPs so as to improve its protective capacity.

February

The BCN02 therapeutic vaccine clinical trial demonstrates prolonged virus control after interrupted antiretroviral treatment in a substantial proportion of study participants.

April

Living Lab for Health launches two European projects, CRISH and InSPIRES, to promote participatory and inclusive research.

Javier Martínez-Picado is appointed to the Delaney Collaboratory to Cure HIV-1 Infection by Combination Immunotherapy (BEAT-HIV Collaboratory).

Roger Badia receives a researcher contract in the first Strategic Research and Innovation Plan for Health (PERIS) call.

May

José A. Esté, Chair of the 30th International Conference on Antiviral Research (Atlanta, USA).

June

VIRIEVAC group publishes an article, in *Scientific Reports*, that identifies new mutations used by HIV to develop resistance to antiretrovirals.

Living Lab for Health organizes the Co-ResponsaVIHlitat talk at CosmoCaixa, with some 400 participants.

VIRIEVAC presents its latest data on new HIV resistance mechanisms against protease inhibitors in an oral presentation at the 15th European Meeting on HIV & Hepatitis.

Elisabet Gómez is awarded her doctorate cum laude, completed while working with the VIC and VITI groups.

IrsiCaixa organizes the third B.Debate on the Human Microbiome at CosmoCaixa, bringing together leading global microbiology experts.

July

María Salgado receives the IAS/ANRS Dominique Dormont Prize at the International AIDS Society annual conference.

WHO publishes three reference documents on worldwide control of resistant HIV, in whose development **IrsiCaixa** collaborated.

August

The European Patent Office grants **IrsiCaixa** the European patent for *Methods for identifying HIV neutralizing antibodies* (EP2893349), invented by **Jorge Carrillo** and **Julià Blanco**. This is the first patent granted to **IrsiCaixa** by one of the three most important patent agencies in the world (EPO, USPTO and JPO).

September

The *Just the Essentials* campaign is presented by "la Caixa" Banking Foundation with **Bonaventura Clotet**, **Roger Paredes** and **Beatriz Mothe** in attendance.

October

Ester Ballana is appointed principal investigator of a Health Research Fund (FIS) project for the development of markers of susceptibility to antitumour drugs.

Lucía Pastor from the VIC group obtains her doctorate, graded excellent with an international mention.

November

Beatriz Mothe receives the Professional Excellence Award from the College of Physicians of Barcelona.

Analysis of immune impairment induced by HIV has given rise to various publications, including four associated with the GAMA study produced by the VIC group. The GAMA study, which started in 2012 and is now in the data analysis phase, will yield relevant insights into acute HIV infection.

Living Lab for Health launches a new European project, called Fit4Food, aimed at facilitating a transformation of the food and nutrition science and innovation system so as to meet EU strategic goals by 2030.

Marc Noguera presents PASeq at the International HIV Drug Resistance and Treatment Strategies conference. PASeq is a web server that, by automating bioinformatic analyses of resistance tests based on massive sequencing, makes these tests affordable.

The Host Genetics and Cellular Immunity group obtains an important US NIH grant (P01), worth some four million USD, which will support **IrsiCaixa**'s already very close collaboration with the University of Miami and the University of California Davis.

Research Groups

Viral Immune Evasion and Vaccines (VIRIEVAC)

Networks
- Thematic AIDS Research Networks (ISCIII RETIC RIS RD16/0025/0041)
- Recognized Group SGR2014/211. Clinical and Basic AIDS Research Group
- Member of the American Society for Microbiology **(JGP)**
- Member of the International AIDS Society **(JGP)**

Awarded projects 2017
Translational study of inhibitory receptors in HIV-1 infection (PI17/00164): identification of novel immunotherapeutic targets to reverse T-cell immune exhaustion.
Funding body(ies): Carlos III Health Institute (ISCIII)
2018- 2021
Research supervisor(s): **Julia García Prado**

LKR155762 Combine use of vaccines an immune check blockers to boost CTL activity against the reservoir.
Funding body(ies): MSD
2017- 2018
Research supervisor(s): **Julia García Prado**

Awards and recognition
Expert participation in the Human Resources Assessment Committee for Sara Borell and Miguel Servet grants for the Carlos III Health Institute (ISCIII) **(Julia García Prado)**

Master's theses
Characterization of HIV viral isolates in viremic non-progresspr adults and children.
Name: **Clara Francés**
Master in Advanced Immunology, Autonomous University of Barcelona (UAB) and University of Barcelona (UB)
Submitted: June 2017
Grade: Excellent

Principal investigator

Julia García Prado
jgarciaprado@irsicaixa.es

Dr. Prado has a degree in Biochemistry and a PhD in Immunology (2005) with honours from the Autonomous University of Barcelona (UAB). In 2006 she received a prestigious Marie Curie (ERC) grant to carry out research at the University of Oxford (UK). Awarded a Miguel Servet contract in 2010 — recently renewed — she is now listed as among the top ten national researchers in Spain. Since 2010 she has been a supervisor of undergraduate and postgraduate students at different universities and, since 2011, she has taught on the Master's in AIDS Pathogenesis and Treatment course. She is a reviewer for international scientific journals (*PlosPathogens, Retrovirology, Antiviral Therapy*) and of projects and human resources for the South African Medical Research Council and the Carlos III Health Institute (ISCIII). She has published 39 articles in international scientific journals (H-index 19) and has made 61 presentations at national and international conferences.

Team
Post-doc researcher(s)
Marta Colomer
Alba Ruiz de Andrés

Pre-doc researcher(s)
Óscar Blanch

Laboratory technician(s)
Esther Jiménez
Ruth Peña

Presentation
Our group was established in early 2013 with the aim of identifying patterns of viral evasion from host immunity and determining the implications for infectious disease progression.

The group's primary research focus is HIV-1, characterized by a great adaptive capacity exercised through multiple strategies of evasion against host immunity. This evasive capacity is a major obstacle to the design and development of new drugs and vaccines. Our challenge is to discover mechanisms of viral evasion from immune response by identifying new viral factors and key immune mechanisms.

Our group has developed three main lines of research to date: (1) mechanisms of HIV-1 infection immune evasion in extreme progression phenotypes; (2) identification of cellular responses during antiretroviral treatment of HIV-1 infection; and (3) identification of immune mechanisms and their application to the control of persistent viral infections and the development of new immunotherapies.

The results of these studies are crucial for the development of new therapeutic strategies and drugs aimed at controlling and preventing HIV-1 infection. All our projects — strongly multidisciplinary and with translational potential for clinical practice — tackle the interconnection between molecular virology and cellular immunology.

2017 milestones
Milestones in the past year within **IrsiCaixa**'s strategic lines were as follows:

— Immunopathogenesis. Studies of elite controllers and viremic non-progressors. Collaboration with the National AIDS Network (RIS) in the field of HIV-1 elite controllers has led to publication of a scientific article (Pernas et al, JVI, 2017, under review).

— New treatments and resistance to antiretrovirals. Identification of new mechanisms of resistance to antiretroviral drugs. This line has given rise to a scientific article (Codoñer et al, SciRep, 2017) and to a presentation at the 15th European Meeting on HIV & Hepatitis (Rome, Italy).

— Prevention, eradication and functional cure. This year has seen the continuation of two funded projects (PI14/01058 and MDS LKR 136618). In vitro models of HIV-1 reactivation have been implemented to analyse the functionality of CD8+ response regarding elimination of the viral reservoir in the presence of latency-reactivating molecules. These studies, which have attracted the interest of the international scientific community, have resulted in two posters displayed at the HIV & Cancer Forum and IAS 2017 (Paris, France) and at GESIDA (Vigo, Spain).

Our studies indicate that agents that reactivate HIV-1 latency induce specific immune recognition of the reactivated cells, but that immune factors are essential for effective recognition of the reactivated cells. We are currently finalizing a scientific article and filing a patent for the method. We are also evaluating the role of cellular restriction factors in controlling the viral reservoir and their potential as new targets for the development of gene therapy strategies. An additional post-doctoral researcher has been recruited for this area.

Perspectives for 2018
— Establishment and consolidation of the research team and incorporation of new staff.

— Continuation with current work in terms of advancing research to identify natural infection control mechanisms with a view to developing new immunotherapies and, by improving cellular response, advancing research into drugs to control or eliminate the viral reservoir.

— Expansion of funding at the European level for our emerging group of young researchers.

Graduate theses
Molecular epidemiology of the transmission of viral variants in new HIV-1 infeccions.
Name: **Àuria Eritja Sanjuan**
Degree in Biomedical Sciences, University of Lleida (UDL)
Grade: Excellent

Microbial Genomics

Networks
- Thematic AIDS Research Networks (ISCIII RETIC RIS RD12/0017/0002)
- Recognized Group SGR2014/211. Clinical and Basic AIDS Research Group
- EuroSIDA
- European Society of Antiviral Research (ESAR)
- WHO ResNet
- International Antiviral Society-USA (IAS-USA)
- Centre for Personalised Medicine Managing Infectious Complications in Immune Deficiency (PERSIMUNE)

Awarded projects 2017

Influence of the gut microbiome on HIV-1 eradication mediated by a kick-and-kill strategy.
Funding body(ies): Spanish Ministry of the Economy, Industry and Competitiveness, Carlos III Health Institute (ISCIII)
Jan 2017- Dec 2019
Research supervisor(s): **Roger Paredes**
Other linked IrsiCaixa groups: Host Genetics and Cellular Immunity

An open-label study of the safety, pharmacokinetics and pharmacodynamics of ABX464 in HIV-1 seronegative and seropositive adults.
Funding body(ies): ABIVAX
Jan 2017- Dec 2018
Research supervisor(s): **Roger Paredes**, Ross D Cranston
Other linked IrsiCaixa groups: Retrovirology and Clinical Studies, Tissue Virology
Other participating bodies: Fight AIDS Foundation

Scholarship for overseas stay.
Funding body(ies): EMBO
Nov 2017- Jan 2018
Research supervisor(s): Mahmoud A. Ghannoum, **Roger Paredes**

Principal investigator

Roger Paredes
rparedes@irsicaixa.es

Roger Paredes is a doctor in Medicine and Surgery from the Autonomous University of Barcelona (UAB). Funded by a post-doctoral scholarship from "la Caixa", he specialized in HIV resistance at Brigham & Women's Hospital and Harvard Medical School in Boston (USA). He has demonstrated the clinical utility of new methods of sequencing HIV in both high- and low-income countries. He is a member of the WHO HIV ResNet Steering Group, the principal advisory group to WHO in the field of resistance, and a member of the International Antiviral Society-USA, which annually publishes an international reference list of antiretroviral resistance mutations. He is co-creator of the Rega algorithm for interpreting resistance to antiretrovirals, has participated in updating the algorithm at Stanford University and is a virologist to the EuroSIDA European cohort. His group does pioneering research into the role played by the gut microbiome in HIV infection pathogenesis and chronic inflammation. He combines his research with a medical care role in the HIV Unit of the Germans Trias i Pujol University Hospital.

Team

Associate researcher(s)
Marc Noguera

Post-doc researcher(s)
Maria Casadellà
Yolanda Guillén

Pre-doc researcher(s)
Javier Rivera
Muntsa Rocafort

Laboratory technician(s)
Mariona Parera

Computer technician(s)
Cristina Rodríguez

Visiting researchers
Seth Inzaule (Amsterdam Institute for Global Health and Development); **Fernando Lázaro** (Hospital La Paz – Madrid); **Emma-Elizabeth Ilett** (University of Copenhagen - Denmark); **Justinn Hamilton Renalias** (Autonomous University of Barcelona).

Presentation

Our goal is to advance in the development of more effective and personalized treatments for microbial-based human diseases, through a better understanding of the biological determinants of health and disease. Our main areas of research are as follows:

1. Investigating the role of the gut microbiome in human health and disease
Via sequencing we study the role played by the human gut microbiota in different states of health:
— We analyse the influence of the gut microbiome in the ability of HIV-1 infected individuals to achieve adequate immune reconstitution, control HIV-1 replication and limit chronic inflammation.
— We characterize co-evolution of the gut microbiome and the immune system following acute HIV-1 infection.
— We study how the human microbiome may affect response to the AIDS vaccine and how vaccines and other strategies for eliminating HIV-1 affect the microbiome.

2. Developing and evaluating interventions
— Improving response to the HIV/AIDS vaccine
— Mitigating the chronic complications of HIV/AIDS infection.

3. Improving genotypic viral diagnostic tools to maximize antiretroviral efficacy
As a pioneer in next-generation sequencing of HIV-1 in Europe, we lead a number of studies to evaluate the clinical value of ultrasensitive tests of HIV-1 resistance and tropism in response to antiretroviral treatment.

4. Defining HIV-1 global clinical epidemiology
We work with leading European clinical cohorts (ESAR and EuroSIDA) in investigations of effects of the virus on response to treatment, clinical progression to AIDS and death.

2017 milestones and perspectives for the future

During 2017, our group continued to advance knowledge of the causes and clinical and health implications of resistance to antiretroviral treatments. We also progressed in studies of the microbiome and HIV infection pathogenesis.

1. Antiretroviral resistance
— Translational research: Two multicentre studies have clarified that the test of HIV-1 tropism in PBMCs is useful in guiding changes to treatment for individuals with the suppressed virus. However, this test cannot predict who will develop clinical complications derived from HIV-1 infection in the following year.
— Bioinformatics: We have developed PASeq as an open web server — suitable for users without knowledge of bioinformatics — for automated high-quality analyses of HIV sequences obtained using the new mass sequencing methods. This is a fundamental step in advancing the fight against resistant HIV worldwide.
— Public health and policy: As members of the WHO HIV Steering Group, we participated in the launch, in July 2017, of three key documents aimed at redirecting the global fight against HIV/AIDS: HIV Drug Resistance Report 2017, Guidelines on the Public Health Response to Pretreatment HIV Drug Resistance and Global Action Plan on HIV Drug Resistance 2017-2021.

2. Microbiome
— Our group has become a world reference for the microbiome and HIV. Our findings that suggest a strong association between microbiome composition and risk factors for HIV acquisition have been confirmed by several international cohorts. Work is ongoing on deciphering the nature of intestinal dysbiosis in HIV infection using shotgun metagenomics, which characterizes the microbiome by species and enables microbial function to be determined for individuals with and without HIV-1.
— With support from the Glòria Soler Foundation, we are working on developing new diagnostic markers of chronic inflammation and intestinal dysbiosis in HIV-infected persons and on developing new probiotic candidates. We are investigating interaction between the microbiome and kick-and-kill strategies to eradicate HIV and the impact of antiretroviral therapy on the microbiome. We have also begun work, in collaboration with US centres, on animal models of HIV infection.

Other participating bodies: Center for Medical Mycology and Mycology Reference Laboratory (Dermatology) at Case Western Reserve University and University Hospitals-Cleveland Medical Center

Host Genetics and Cellular Immunity

Networks
- Thematic AIDS Research Networks (ISCIII RETIC RIS RD12/0017/0002)
- Recognized Group SGR2014/211. Clinical and Basic AIDS Research Group
- Co-investigator for the FIPSE cohort of HIV-positive liver transplants beneficiaries **(CB)**

Projects
RETIRE-HIV.
Funding body(ies): US NIH/NIAID
2017- 2021
Research supervisor(s): **Christian Brander**
Other participating bodies: University of Miami, University of California at Davis

Regulation of the immune response by HIV-specific CD4+ T-cells.
Funding body(ies): Carlos III Health Institute (ISCIII)
2018- 2020
Research supervisor(s): **Alex Olvera**

Awards and recognition
Christian Brander: Organizing Committee of the R4P (Research for Prevention) Programme (Madrid 2018)
Christian Brander: Steering Committee of the HIVACAR project
Christian Brander: Scientific Advisory Board for the GREAT project
Beatriz Mothe: Professional Excellence Award from the College of Physicians of Barcelona
Beatriz Mothe: Protagonist of the Just the Essentials campaign ("la Caixa" Banking Foundation)

Graduate theses
The role of HLA-E expression profiles in the in vivo control of HIV.
Author: **Clara Duran**
Degree in Biotechnology, University of Vic-Central University of Catalonia (UVic-UCC)
Tutor(s): **C. Brander, M. Ruiz-Riol**
Grade: Excellent

Principal investigator

Christian Brander
cbrander@irsicaixa.es

Christian Brander graduated from the University of Bern (Switzerland) in 1994 with a PhD in Immunology, having studied exogenous antigen re-presentation and HLA and T-cell-mediated hyper-reactivity to penicillin. He spent the next 13 years at Harvard University, where he investigated cellular immunity to viral infections and the impact of host genetics on the immune response. A senior Institute for Research and Advanced Studies (ICREA) research professor since 2008, he has continued his research into host genetics and cellular immunity to viral infections, including HIV, HCV and herpesviruses such as EBV and KSHV. He is curator of the Los Alamos HIV Immunology database, scientific director of the Catalan HIVACAT programme for the development of effective preventive and therapeutic HIV vaccines and an associate lecturer at the University of Vic-Central University of Catalonia (UVic-UCC). Dr. Brander was rated among the most highly cited researchers of 2014 and 2015 by Thompson Reuters.

Team

Associate researcher(s)
Beatriz Mothe

Post-doc researcher(s)
Samandhy Cedeño
Anuska Llano
Alex Olvera
Marta Ruiz Riol
Sandra Silva Arrieta

Pre-doc researcher(s)
Miriam Rosás
Bruna Oriol

Clinical cohort coordinator / Clinical researcher
Pep Coll

Presentation
Our research focuses on the study of the cellular immunity against viral infections in hosts with compromised immunity. These studies include longitudinally followed, HIV-infected individuals as well as HIV-infected and uninfected individuals who receive an organ transplant. We also aim to identify markers of biological control of HIV to improve our understanding of HIV immunopathogenesis. Identifying immunological correlates of HIV control also supports our attempts to define biomarkers related to HIV-associated neurofunctional impairment.

Over the last years, our group has developed a therapeutic vaccine immunogen that resulted in the creation of AELIX Therapeutics as a spin-off in 2015. The ongoing clinical studies are complemented by analyses in individuals who have been exposed to HIV but remain uninfected. These studies aim at deciphering key parameters and mechanisms of natural resistance to HIV that could contribute to the development of preventive vaccines.

We also study possible factors governing HCV evolution and immune determinants of organ rejection in HIV-infected liver transplant recipients. These studies are also expanded to the clinical setting where the organ recipient as well as the organ donor are HIV-infected. A kidney transplant model is also used to determine the effects that ablative pre-transplant conditioning treatment has on the repertoire of post-transplant T-cells and to evaluate how this repertoire contributes to the control of opportunistic infections associated with post-transplant lymphoproliferative diseases and other malignant disorders.

2017 milestones and perspectives for the future
We have continued to advance the HTI T-cell immunogen, now entering the clinical trial phase. In these studies, HTI is included in different vectors and combinations of vectors, including RNA, DNA and MVA. The clinical grade production of chimpanzee adenovirus vector (ChAd) expressing HTI is underway as well and will allow us to assess how this vector can boost vaccine responses even further. To date, the ChAd vector, together with different RNA-based vaccine formulations has demonstrated very strong immunogenicity in animal models.

In 2017, we completed immunological analyses of a clinical trial conducted in Lima, Peru that compared the immunogenicity of a MVA-B vaccine delivered either intramuscularly or via a transcutaneous administration. The data were complemented by transcriptomic analyses and studies of the microbiota in faecal and skin samples. The Peruvian collaboration has also led to the identification of new HLA class II alleles associated with slow HIV disease progression and of the definition of new T-cell response targets restricted by these alleles, both potentially helping to advance the development of effective HIV vaccines. As a consequence of these studies, we have been able to successfully apply for competitive funding (US NIH and ISCIII) for the 2017-2021 period, which will allow us to further explore T cell responses restricted by HLA class II alleles and to study the role of T-cells restricted by HLA-E. The assessment of T-cell receptor usage by HIV-specific T cell responses were initiated this year in collaboration with the CNAG in Barcelona, employing single-cell transcriptomic analyses aimed at obtaining detailed information on the T-cell receptor repertoire in HIV infection.

Thanks to the support by the Glòria Soler Foundation, we have essentially completed the analyses of samples collected in the BCN02 clinical trial. In this trial, early-treated HIV-infected individuals received a therapeutic vaccination and a treatment to reactivate the dormant virus and then stopped their antiretroviral treatment. During 2017, when participants were monitored to detect possible viral rebound, we observed prolonged control of viral replication in 5 of the 14 subjects that stopped treatment. Preliminary results presented at various international conferences have been received with great interest and we are not completing these analyses with additional in vitro studies.

Progress has also been made in identifying plasma factors associated with control of HIV and whose expression is epigenetically regulated as a result of HIV infection. The IL27 cytokine and its specific receptor have been found to be associated with viral load and, more importantly, with the size of the HIV viral reservoir. These results have been validated in additional cohorts and have been compared with data from HIV uninfected individuals, identifying IL27 as a possibly important determinant of an effective HIV-specific immune response. On the basis of these findings we are currently evaluating additional markers for their potential relation with in-vivo control of HIV and the pathological consequences of HIV infection (including neuro-function). For these studies, our group works with two local cohorts of HIV-infected individuals and also uses blood and spinal fluid samples obtained from a cohort in San Francisco.

During 2017, we have also completed our study on how in-vitro inhibition of O-linked glycosylation affects HIV replication. Our findings suggest that glycosylation is a viral defence mechanism that carries a potentially significant fitness cost for the virus. As inhibition of O-linked glycosylation greatly enhances viral replication, this strategy has also been used to improve viral outgrowth kinetics, enabling better characterization of the replication component viral reservoir in HIV-infected individuals.

Continuing work in liver transplant recipients has enhanced understanding of both viral evolution in HCV-infected individuals and the impact of host and donor genetic factors on survival and organ rejection. In 2017, the group identified genetic markers in the IL28 genes in patients and donor organs that have an impact on liver fibrosis after transplantation and organ rejection On the basis of these data, we have also been able to establish a link between strong pre-transplant allo-reactivity and organ rejection. For the transplantation work, we have also progressed our collaboration with a clinical site in Cape Town in South Africa where the first cohort of HIV-positive-to-HIV-positive transplant studies had been initiated and which offers a unique opportunity to study virological and immunological parameters of successful transplantation in this context.

HIV Pathogenesis

Networks
- Thematic AIDS Research Networks (ISCIII RETIC RIS RD12/0017/0002)
- Recognized Group SSGR2014/121. HIV Pathogenesis
- European Epitranscriptomics Network (CA COST Action CA16120)

Awards and recognition
José Esté: President of the International Society for Antiviral Research (2016-2018)
Edurne García: FI-Gencat grant 2016-2018

Awarded projects 2017
Validation and development of an effective biomarker for antimetabolite response.
Funding body(ies): Spanish Health Research Fund (FIS)
Jan 2018-Dec 2020
Head investigator: **Ester Ballan**a
Other participating bodies: Germans Trias i Pujol University Hospital (HUGTP), Josep Carreras Foundation

Principal investigator

José Esté
jaeste@irsicaixa.es

Dr. José Esté's laboratory focuses on the study of cofactors associated with HIV-1 infection and the relationship with AIDS pathogenesis. Dr. Esté, with a degree in Medical Sciences from the Katholieke Universiteit Leuven, has directed 13 doctoral theses in the last ten years, has filed four patents in the last five years and has participated in the publication of over 160 papers. His research group has received external funding since 1999, including under national and European projects and contracts with pharmaceutical companies.

Dr. Esté is Chairperson of the International Society for Antiviral Research and participates in the organization of various international meetings. He is the editor of Antiviral Research and a member of the editorial boards of Antimicrobial Agents and Chemotherapy and the Journal of Biological Chemistry, among others. He acts as an expert consultant to the Research Executive Agency of the European Commission and participates in various international project evaluation panels.

Team

Associate researcher(s)
Ester Ballana

Post-doc researcher(s)
Roger Badia
Eva Riveira-Muñoz

Pre-doc researcher(s)
Marc Castellví
Edurne García
Maria Pujantell

Presentation
The HIV Pathogenesis group focuses on four main lines of research:

1. Identification of new cellular cofactors of viral infections
Our work over the past few years has focused on the study of cell targets as an antiviral intervention strategy and on validation of these targets in cohorts of HIV-positive patients. This work has allowed us to build a portfolio of cellular factors at different stages of development, ranging from new target identification/validation and approved drug monitoring to technology transfers through reports to pharmaceutical companies or patent registration.

2. Study of viral entry and between-cell transfer mechanisms
HIV needs cell activation and inter- and intra-cellular signalling mechanisms to ensure productive replication and the establishment of chronic infection. Chemokines and other cytokines induce maturation, survival and proliferation of lymphocyte cells targeted by HIV and also regulate the expression of chemokine receptors (CXCR4 and CCR5), which act as the main co-receptors of HIV entry and the intracellular signalling that leads to virus-induced cell death. In the entry process, and particularly in cell-to-cell transmission, different receptors play a key role. Chemokines and cytokines modulate expression in the cell surface and activate the cells necessary for viral replication. Our aim is to deepen understanding of both the mechanisms of interaction between HIV and the target cell admitting HIV entry and the subsequent viral replication process.

3. New antiviral drug development
We continue to screen and characterize the antiviral activity of new compounds, placing special emphasis on compounds active against viral strains resistant to other drugs and on validating new therapeutic targets based on cell viral infection cofactors.

4. Coinfection as a model for studying the virus-host relationship
The role of mucosal immunology and host genetic factors in susceptibility to HPV is poorly understood. Pre-existing HPV infection may act as a cofactor for HIV-1 transmission and infection through cellular and molecular mechanisms that generate an environment conducive to coinfection. We propose to study the expression of HIV infection cofactors modulated by early infection events or HPV reactivation in infected cell models and in patients coinfected to varying degrees. Our project results will lay the foundations for new treatment, prophylaxis and prevention strategies for sexually transmitted viral infections.

2017 milestones
We plan to continue work underway and to improve both the quantity and quality of our publications. Significant efforts have been invested in applying for and obtaining competitive funding to improve the quantity and quality of our scientific output and to acquire more staff. Accepted in 2017 was a new Spanish Health Research Fund (FIS) project to continue with the development of SAMHD1 as a possible therapeutic marker. Funding was also granted for research staff under the Strategic Research and Innovation Plan for Health (PERIS) and by the Agency for Administration of University and Research Grants (AGAUR), to **Roger Badia** and **Edurne Garcia-Vidal**, respectively.

The group now has five projects receiving external funding. All our researchers are funded or are principal investigators of projects. **Dr. Esté** continues to be an expert advisor to the Research Executive Agency of the European Commission and Chairperson of the International Society for Antiviral Research.

Perspectives for 2018
Basic research is and will continue to be a cornerstone in generating the knowledge necessary to discover new and effective strategies to cure HIV, AIDS and other infectious diseases. Our goal is to continue our research into HIV cellular cofactors and restriction factors so as to determine mechanisms of action and determine their possible role in the formation of viral reservoirs in patients. Preliminary results will enable possible therapeutic targets to be identified that will limit or reduce the viral reservoir, induce immunity to HIV and maybe even assist in HIV eradication. Based on preliminary results, the group is confident that it will be able to contribute to both understanding HIV/AIDS immunopathogenesis and identifying new therapy and immune reconstitution alternatives.

Retrovirology and Clinical Studies (GREC)

Networks

- Recognized Group SGR2014/211. Clinical and Basic AIDS Research Group
- Thematic AIDS Research Networks (ISCIII RETIC RIS RD12/0017/0002)
- Member of the American Society for Microbiology **(JMP)**
- Member of the International AIDS Society and the Scientific Working Group on HIV Cure at IAS **(JMP)**
- Member of the Forum HIV Cure Project **(JMP)**
- Member of the US Consortium for Functional Glycomics **(JMP)**
- Member of the Catalan Biology Society (Virology Group) **(JMP)**
- Member of the Spanish Virology Society **(JMP)**
- Member of the Spanish Infectious Diseases and Clinical Microbiology Society (GESIDA-SEIMC)

Awarded projects 2017

Allogeneic Stem Cell Transplantation in HIV-1 Infected Individuals.
Funding body(ies): amfAR Foundation for AIDS research (ARCHE Programme) Ref: 109552-61-RGRL
Mar 2017- Feb 2018
Research supervisor(s): **Javier Martínez-Picado**

Call for scholarships and grants for the training of doctors under the National Programme for University Teacher Training 2015 (FPU15/03698).
Funding body(ies): Spanish Ministry of Education, Culture and Sport
Jun 2017- Apr 2020
Research supervisor(s): **Javier Martínez-Picado**

Evaluation of mechanisms mediating anti-viral activity of PT compounds.
Funding body(ies): POP TEST Oncology LLC
Mar 2017- Sept 2017
Research supervisor(s): J**avier Martínez-Picado, María Carmen Puertas**

An open-label study of safety, pharmacokinetics and pharmacodynamics of ABX464 in HIV-1 seronegative and seropositive adults.
Funding body(ies): ABIVAX
2016–2019
Research supervisor(s): Dr. Ross Cranston
Other participating bodies: Fight AIDS Foundation
Other linked IrsiCaixa groups: Microbial Genomics, Tissue Virology

Principal investigator

Javier Martínez-Picado
jmpicado@irsicaixa.es

El **Dr. Javier Martinez-Picado** is a Catalan Institute for Research and Advanced Studies (ICREA) researcher at **IrsiCaixa** and associate lecturer at the University of Vic-Central University of Catalonia (UVic-UCC). He obtained his PhD on Bacterial Genomics from the University of Barcelona (UB) in 1996 and was subsequently contracted by Massachusetts General Hospital in Boston as a researcher at Harvard Medical School, where he engaged in research into AIDS. In 2000 he obtained a position as a Spanish Ministry of Health biomedical researcher assigned to the Germans Trias i Pujol University Hospital, where he focused on translational aspects of HIV-1 infection. He is a member of several scientific, industrial and academic committees, has published some 150 papers in international journals (H-index 45), has presented findings at numerous conferences (some 160 papers and 130 keynote speeches) and has directed eight doctoral theses (with three more currently underway).

Team

Associate researcher(s)
Nuria Izquierdo-Useros

Post-doc researcher(s)
Maria Salgado

Pre-doc researcher(s)
Susana Benet
Cristina Gálvez
Sara Morón-López (to September 2017)
Daniel Pérez-Zsolt
Maria Pino (to April 2017)

Laboratory technicians
Silvia Bernal
Itziar Erkizia
Mª Carmen Puertas

Cohorts and project management
Judith Dalmau

Biostatistician(s)
Víctor Urrea

Visiting researcher(s)
David Bejarano (University of Heidelberg, Germany), **Marie-Angélique de Scheerder** (University of Ghent, Belgium), **Ángel Bayón** (master's student, University of Barcelona)

Presentation

Our group focuses on translational studies of HIV-1 infection and on investigating, through both basic and applied research, potential new HIV/AIDS therapeutic strategies. The group works closely with the HIV outpatient unit at the Germans Trias i Pujol University Hospital, attending some 2,000 individuals with the infection. Its research programme focuses on four priority areas: (1) HIV cure; (2) HIV pathogenesis mediated by dendritic cells; (3) extreme HIV infection phenotypes; and (4) new therapeutic strategies.

2017 Milestones

1. HIV-1 cure

— Consolidation of an international cohort of HIV-positive patients treated with allogeneic stem-cell transplants for severe haematologic disease (IciStem). This is the only therapeutic intervention to date that is capable of significantly reducing the viral reservoir.
— Given the good penetration in the male reproductive tract, further study of the new inhibitor of viral integration, dolutegravir, which inhibits viral replication with a dynamic similar to that in blood plasma, thereby facilitating HIV elimination from this anatomical compartment considered a potential viral reservoir.
— Study of new immunotherapies with blocking monoclonal antibodies (α-PD-1 and α-PD-L1) in HIV-positive patients with oncological disease in order to assess effects at the tumoral and viral levels.
— Evaluation of drugs with new antiviral action mechanisms for their ability to reduce the viral reservoir.
— Evaluation of impact on the size of viral reservoirs of therapeutic vaccines with and without viral latency reactivators.
— Development of a new gene therapy for elimination of the CCR5 viral receptor through TALENs.
— Development of a new nanoparticle technology aimed at myeloid cells to induce viral reactivation and promote a cytotoxic response.

2. Myeloid cell role in viral pathogenesis

— Translation of knowledge acquired regarding the Siglec-1 receptor to other infectious pathologies, including Ebola and tuberculosis.
— Characterization of primary cervical myeloid cells that interact with HIV-1 via Siglec-1.
— Generation of blocking monoclonal antibodies to inhibit the Siglec-1 receptor.

3. Extreme HIV infection phenotypes

— Study of patients who spontaneously control viral replication for more than ten years without antiretroviral treatment.
— Study (in adults and children) of the factors involved in the non-progressive viremic phenotype, which, in emulating the natural host with SIV infection (sooty mangabey monkeys), presents high viremia but no pathogenesis.
— Characterization of patients with extremely low viral reservoirs receiving antiretroviral treatment.
— Study of methylation of the complete genome in association with HIV infection and disease progression.

Perspectives for 2018

Our programmes will lead to the development of new strategies for treatment and cure of HIV/AIDS. Regarding the entire set of programmes, the group aims to do the following: (1) quantify the size and analyse the role of the viral reservoir by developing virological monitoring tools for the blood and tissues of patients on antiretroviral therapy; (2) study clinical interventions aimed at reducing viral reservoirs and controlling viral persistence; (3) generate new therapeutic agents to block HIV-1 and Ebola cell-cell transmission via myeloids, specifically by interrupting virus-Siglec-1 interaction; (4) build nanoliposomes that specifically target Siglec-1 as expressed in dendritic cells as a drug-release mechanism, latency reactivation agent or viral immunogen; (5) continue exploring the role of virus-host interactions in extreme HIV-1 infection phenotypes; (6) explore therapeutic applications of factors underlying the viremic non-progressor phenotype, whose profile is similar to that of the natural host in having an immune system that is not affected by high levels of viremia; and (7) study cellular protection against HIV-1 infection in individuals who remain uninfected despite exposure to the virus.

Awards and recognition

Maria Salgado: IAS/ANRS Dominique Dormont Prize, awarded by the International AIDS Society (July 2017)

HIV and HCV Genetic and Phenotypic Variability

Networks
- Thematic AIDS Research Networks (ISCIII RETIC RIS RD12/0017/0002)
- Recognized Group SGR2014/92. HIV and HCV Genetic and Phenotypic Variability

Awarded projects 2017
HCV genetic variability in acute hepatitis C infection in HIV-positive men who have sex with men in Western Europe.
Funding body(ies): European AIDS Treatment Network (NEAT)
Oct 2017- Dec 2018
Participating bodies: IrsiCaixa, Fight AIDS Foundation, Bonn University Hospital (Germany)
Research supervisor(s): **M.A. Martínez**

Master's theses
Study of the mechanism responsible for altering HIV-1 viral replication caused by a change in gag gene use of codons.
Author: **Víctor Forteza Krättli**
Tutor(s): **M. Nevot, M.A. Martínez**
Master in Advanced Immunology, Autonomous University of Barcelona (UAB)
End date: Sept 2017
Grade: Excellent

Principal investigator

Miguel Ángel Martínez
mmartinez@irsicaixa.es

Author of 106 research papers published in journals indexed in PubMed (mostly in the HIV field) and three worldwide patents. Director of nine doctoral theses. Editor of *Antimicrobial Agents and Chemotherapy* (American Society for Microbiology, ASM) and member of the editorial board of Antiviral Research (International Society for Antiviral Research, ISAR). Author of ten book chapters and guest editor of *RNA Interference and Viruses: Current Innovations and Future Trends* (Caister: Norfolk, UK, 2010). For ten years, Chairperson of the Virology section of the Catalan Biology Society (attached to the Institute of Catalan Studies, IEC). Recipient in 2006 of the International AIDS Society (IAS) award for the most cited basic-research author in the journal *AIDS*.

Team

Post-doc researcher(s)
Sandra Franco
Maria Nevot

Pre-doc researcher(s)
Ana Jordán

Presentation
The main goal of our group is to understand the molecular bases underlying HIV and HCV evolution and variation. A better understanding of HIV and HCV evolutionary dynamics would enable a definition of the factors that contribute to immune evasion, immune persistence and the emergence of variants resistant to new antivirals. Studies of HIV and HCV variation can potentially contribute to the design of new antiviral strategies, bearing in mind the high mutation rates.

Our group is developing a strategy based on a new technology called synthetic attenuated virus engineering (SAVE), which recodes and synthesizes parts of the viral genome while maintaining the amino-acid sequence present in the wild-type virus and attenuating virulence. This technique has been successfully used to develop attenuating poliovirus and influenza virus vaccines (Martinez et al, Trends in Microbiology, 2016).

Deoptimization of different moieties of the HIV-1 gag and pol genes has enabled the development of variants of HIV-1 with attenuated phenotypes in MT-4 cells and PBMCs obtained from healthy donors (Martrus et al. Retrovirology 2013; Nevot et al. 2017).

The study of viruses is a pioneering endeavour in the new research field of synonymous genome recoding and, together with synthetic biology, is giving rise to interesting basic biology applications and the development of novel therapies. Despite great progress in research into viral genome recoding and attenuation, several questions as yet remain unanswered. A priority would be to decipher the mechanism through which synonymous mutations affect the virus phenotype.

2017 milestones and perspectives for the future
Our group is currently studying the stability of attenuated viruses and the possibility of obtaining a new attenuated virus by deoptimizing other viral genes. Recoding has been done by introducing different codon pairs in the gag (1502 nucleotides), pol (3011 nucleotides) and env (2069 nucleotides) regions of HIV-1 (pNL4-3). Only synonymous substitutions have been introduced. The recoded segments have the same amino-acid sequence as the wild-type virus but have different arrangements of synonymous codon pairs. That these viruses have an attenuated phenotype depends, on the one hand, on the presence of mutations in certain gag, pol or env regions that do not allow synonymous nucleotide changes — whether because they affect the secondary RNA structure or because of their effect on the translation of the corresponding messenger — and on the other hand, on base pair content (e.g., the presence of CpG and/or TPA).

An important issue is to develop a protocol for culture production of HIV-1 infected tissue (MT-4 cells) from transfection of synthetic DNA fragments (produced by chemical synthesis or PCR) in the absence of infectious virus clones. We have produced infectious virus from one or more DNA fragments (up to six fragments have been tested) covering the complete HIV-1 genome. Preliminary results indicate that the stability of the different viral variants is associated with the loss of replicative capacity and, more importantly, with the number of mutations introduced, which, in turn, determine the phenotypic stability of viruses whose biological effectiveness is reduced. Massive sequencing of individual clones (viral quasispecies) has yielded information on the sequence space explored by different viral variants.

An unexplored aspect of HIV-1 genetic architecture is how choice regarding use of synonymous codons influences the diversity and evolutionary capacity of the virus. To be clarified is whether the HIV-1 genome sequences are optimized not only in the amino-acid sequences but also in the viral RNA and proviral DNA sequences. We have explored whether viruses recoded in the pol region — with 13% of synonymous mutations that alter codon pair usage but not viral replicative capacity — are able to develop genotypic and phenotypic resistance to viral protease inhibitors in a similar way to wild-type viruses. Our results show that viruses recoded in the pol region show a pattern of resistance to protease inhibitors that is different from that of the wild-type virus (Nevot et al 2017, in press). Our results confirm that the virus recoded in their use of codon pairs occupy a sequence space that is different from that of the wild-type virus. Note that even though the recoded viruses show different patterns of resistance, their phenotypic resistance is similar to that of the wild-type virus, suggesting that the recoded virus is, in mutation terms, equally as robust as the wild-type virus. These results have been reported in the first published study on the evolutionary capacity of an enzyme recoded in its use of synonymous codons.

We have also explored the impact of the use of synonymous codons in terms of an ability to both express the Env viral protein and to replicate the virus. The six env-HIV-1 gene codons AGG, GAG, CCT, ACT, CTC and GGG were synonymously changed to CGT, GAA, CCG, ACG, TTA and GGA, respectively, generating a new Env protein, with results showing that the ability to replicate HIV-1 is affected by codon use. Also observed was that mutations in the Env 3 coding region can induce lethality. Ex-vivo expression experiments have shown that Env protein translation is affected. Our results underline the importance of synonymous substitutions in the configuration of the viral phenotype.

We plan to continue using and deepening our knowledge of the SAVE technology. We also plan to study the possible effect of bias in the use of codon pairs in HIV-1 and HCV translation and evolutionary capacity, as well as the stability of recoded viral variants. These variants will also be used to identify functional redundant RNA elements in the coded sequences for HIV-1 and HCV. Because synonymous recoding is directed to a basic function like translation, our hypothesis is that bias in the use of codons, codon pairs or dinucleotide composition potentially has a general application in terms of altering the phenotypes of viruses and organisms.

Cell Virology and Immunoly (VIC)

Networks

- Recognized Group SGR2014/211. Clinical and Basic AIDS Research Group
- Thematic AIDS Research Networks (ISCIII RETIC RIS RD12/0017/0002). The group actively participates in the detection and characterization of widely neutralizing broad-spectrum antibodies for different patient groups in the Vaccination Programme and also participates in WP4 and WP5 of the Immunogenicity Programme.
— HIVphagy. The group participates in the PICS consortium, which studies the role of autophagy in HIV infection.
- EUROMENE. The group participates in this Cost Action funded by H2020 (European Commission) for the study of myalgia encephalomyelitis/ chronic fatigue syndrome (ME/CFS), contributing with its knowledge regarding immunological factors associated with this disease.

Awarded projects 2017

Development of a HIV vaccine platform based on high-density antigenic VLPs.
Funding body(ies): Spanish Ministry of the Economy, Industry and Competitiveness, Carlos III Health Institute (ISCIII)
Jan 2018- Dec 2020
Research supervisor(s): **Julià Blanco**
Other participating bodies: Germans Trias i Pujol Research Institute Foundation.
Other linked IrsiCaixa groups: Host Genetics and Cellular Immunity

Pharma-Factory.
Funding body(ies): European Commission (H2020)
Jan 2017- Oct 2021
Research supervisor(s): Julian Ma (St George's Hospital Medical School, London), **Julià Blanco**

Principal investigator

Julià Blanco
jblanco@irsicaixa.es

Dr. Blanco's group has conducted in-depth studies of the HIV envelope protein and its role in viral transmission and CD4 cell death and has also developed various tools for analysing the function of this protein both in vitro and in vivo. The immunological and virological knowledge generated has allowed the group to develop different tools aimed at studying the following: (1) immunological alterations that induce HIV in infected individuals (immune activation, immunosenescence, immune dysfunction); (2) antibody response to the HIV envelope and new natural and synthetic antibodies with therapeutic applications; and (3) vaccinations based on the envelope protein presented in the form of proteoliposomes or VLPs. **Dr. Blanco** is, along with **Dr. Carrillo** and **Dr. Clotet**, a scientific director of the spin-off AlbaJuna Therapeutics, SL, founded in 2016, which develops HIV vaccine platforms that may have applications beyond HIV infection.

Team

Associate researcher(s)
Jorge Carrillo

Post-doc researcher(s)
Carmen Aguilar
Luis M. Molinos
Mª Luisa Rodríguez

Pre-doc researcher(s)
Montserrat Jiménez
Lucía Pastor
Ferran Tarrés

Laboratory technician(s)
Silvia Marfil

Biostatistician
Víctor Urrea

Visiting researcher(s)
Santa Rasa (Rigas Stradina Universitate, Augusta Kirhensteina Mikrobiologijas un virusologijas Instituts- Latvia)

AlbaJuna Therapeutics team

Post-doc researcher(s)
Ester Aparicio
Francesc Cunyat
Cristina Lorca

Presentation

Our group focuses on studies of the HIV envelope protein, the only viral protein exposed to the outside of the HIV particle. It is, therefore:
— the viral factor that determines virus spread and the target protein for neutralizing humoral response
— the main determinant of CD4 cell destruction and the resulting chronic inflammation.

These two aspects of the viral envelope have shaped our activity in recent years. We have invested significant efforts in studies of the humoral response to the viral envelope, developing new tests to identify protective and non-protective responses, optimizing technologies to isolate natural human antibodies and designing and producing synthetic antibodies for application in treatments. We have also developed a VLP platform and a proteoliposome platform to produce anti-HIV vaccines that generate protective antibodies.

CD4 cell destruction, chronic inflammation and immune system ageing (known as inflamm-ageing) have been studied through the analysis of different cohorts of HIV-infected patients, for whom we have extensively characterized the viral envelope function and cell production and destruction mechanisms (thymic production, activation, immunosenescence and cell death mechanisms such as apoptosis and autophagy). Our group has also developed new tools for analysing these data (OurFlow software).

The ultimate goal of our research is to develop vaccines that protect against HIV infection and to develop therapeutic strategies (based on antibodies or inflamm-ageing modulators) that contribute to functional cure or eradication of HIV in infected individuals.

2017 milestones and perspectives for the future

Vaccine development
In 2017 we patented the invention of new VLPs for the development of vaccines (patent EP1638234.4). These VLPs, based on the fusion of immunogens with the Gag viral protein, are a potentially excellent platform for the development of new vaccines against HIV and other pathogens. The new patent reflects potential applications to different viral or bacterial infectious diseases and to oncology. The development of these applications was assisted by the recruitment of post-doctoral researcher **Carmen Aguilar**.

Antibody characterization
New antibodies, whose identification is managed by **Dr. Jorge Carrillo**, have been isolated from HIV-positive individuals. The characterization of these antibodies is already underway and collaborations with other institutions (BSC) have been established in order to develop the project in optimal technical conditions.
The development of recombinant antibodies is ongoing within the framework of the spin-off AlbaJuna Therapeutics, SL, whose activity continues in the discovery phase.

Immune impairment in persons with HIV
During 2017, with the active assistance of **Víctor Urrea**, we further developed the OurFlow software (project DTS15/00185) as a key tool for rapidly analysing complex immunological data (multicolour flow cytometry). This software has enabled us (in a project undertaken with the Microbial Genomics group) to respond to key questions regarding the immune system-gut microbiota relationship and the earliest immunological events in HIV infection as analysed in the GAMA study. The OurFlow software has also opened up participation of our group in different clinical studies (INDOOR, RALATOR, Cohort>60).

Other participating bodies:
AlbaJuna Therapeutics, SL

Doctoral theses

Identification of immune biomarkers for use in early HIV detection and monitoring in Sub-Saharan Africa.
Author: **Lucía Pastor**
Defended: 11 Oct 2017
Department of International Health, University of Barcelona (UB)
Director(s): **Julià Blanco,** Denise Naniche
Grade: Excellent with International Mention

Functional characterization of T-lymphocytes in HIV-positive individuals with poor immunological recovery. Study of the mechanisms involved in the immunodiscordant response to antiretroviral treatment.
Author: **Elisabet Gómez**
Defended: 29 June 2017
Department of Cell Biology, Physiology and Immunology, Autonomous University of Barcelona (UAB)
Director(s): **Julià Blanco, Cecilia Cabrera**
Grade: Excellent *cum laude*

Master's theses

Characterization of humoral response in HIV-1 infection controllers and non-controllers.
Author: **Edwards Pradenas**
Tutor(s): **Julià Blanco**
Master's Degree in Advanced Immunology, Autonomous University of Barcelona (UAB) and University of Barcelona (UB)
Grade: Excellent

Tissue Virology (VITI)

Networks
- Thematic AIDS Research Networks (ISCIII RETIC RIS RD12/0017/0002)
- Recognized Group SGR2014/211. Clinical and Basic AIDS Research Group

Projects
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-guérin (BCG).
Funding body(ies): Archivel Farma, SL
2017- 2020
Research supervisor(s): **Cecilia Cabrera**

An Open-Label Study of the Safety, Pharmacokinetics, and Pharmacodynamics of ABX464 in HIV-1 Seronegative and Seropositive adult subjects.
Funding body(ies): ABIVAX
2017- 2018
Research supervisor(s): **Cecilia Cabrera**

Doctoral theses
Functional characterization of T-lymphocytes in HIV-positive individuals with poor immunological recovery. Study of the mechanisms involved in the immunodiscordant response to antiretroviral treatment.
Author: **Elisabet Gómez**
Defended: 29 June 2017
Department of Cell Biology, Physiology and Immunology, Autonomous University of Barcelona (UAB)
Director(s): **Julià Blanco, Cecilia Cabrera**
Grade: Excellent *cum laude*

Principal investigator

Cecilia Cabrera
ccabrera@irsicaixa.es

Cecilia Cabrera graduated in Biological Sciences from the University of Barcelona (UB) in 1994 and obtained her PhD in Biological Sciences from the Autonomous University of Barcelona (UAB) in 2001. After a period of postdoctoral studies at **IrsiCaixa**, in 2005 she obtained a Miguel Servet contract (ISCIII) as a biomedical researcher at the Germans Trias i Pujol University Hospital, where she was confirmed as an established researcher in 2010. Her research, initially focused on evaluating the initial stages of the viral replication cycle, is currently aimed at evaluating the pathogenic effects of HIV in the lymphoid tissue of infected individuals. In collaboration with the Department of Urology of the Germans Trias i Pujol University Hospital, **Dr. Cabrera** has extended her research to superficial bladder cancer and the role played by the immune system in responding to treatment. She has published some 40 papers in international scientific journals, has participated in numerous national and international conferences, has benefited from ongoing public and private funding for her research and collaborates with several national and international groups. In the teaching area, she is a lecturer on the microbiology degree course at the Autonomous University of Barcelona (UAB) and has been the director of one doctoral thesis and co-director of a second doctoral thesis.

Team

Pre-doc researcher(s)
Elisabet Gómez
Sònia Pedreño
Roberto Martínez

Laboratory technician
Elisabet García

Presentation
The group focuses its activities on three main research lines:

HIV pathogenesis in lymphoid tissue
HIV infection can be viewed as a mucosa-associated disease whose pathogenesis develops 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, featured by gradual destruction of CD4 T-cells in peripheral blood, a high degree of immunological activation and massive production of pro-inflammatory cytokines.

The mechanisms of destruction of CD4 T-cells and the reasons for GALT incomplete immune recovery, despite antiretroviral treatment and unlike what is observed in peripheral blood, is a current topic of debate. This difference between blood and tissue has highlighted the importance of assessing the effect of both the virus and antiretroviral therapy on lymphoid tissue, as this is where latent viral infection (the viral reservoir) is established. Therefore, studies in this area can contribute to achieving total eradication of the virus. Our group evaluates viral pathogenic effects (for HIV and SIV) and the impact of antiretroviral drugs on the tissue of HIV-positive individuals with different levels of viral and/or immune control as well as in ex vivo models of healthy donor tissue.

Functional evaluation of the immune system of individuals with poor immune recovery
Massive destruction in GALT is one of the possible causes of poor immune recovery after antiretroviral treatment, observed in 15%-30% of people infected with HIV. These immunodiscordant responders present a maturation of the altered T-cell compartment and greater inflammation and immunosenenesce, ultimately resulting in higher morbidity and mortality. Having collaborated in immunophenotype characterization of immunodiscordant individuals, the group's current focus is on functional characterization of the immune system of these individuals and on studying the role played by CMV co-infection in their poor immunological recovery and poor clinical response.

Urinary bladder cancer
Bladder cancer is one of the most prevalent cancers in the world. Around 80% of patients present with superficial bladder cancer confined to the mucosa. The standard treatment for this cancer is the intravesical administration of BCG (*Mycobacterium bovis* mycobacterium) and, although the mechanism of action is not fully understood, it is thought that it activates the immune system and attracts immune cells to the bladder wall. BCG potentially prevents the appearance of new tumours but, despite its effectiveness, many patients fail to respond and no alternative is as yet available. Our group is working to improve current treatment by developing new therapeutic strategies and identifying biomarkers that would predict response to treatments.

2017 milestones and perspectives for the future
In 2017, the results obtained in different lines of work were as follows:

HIV pathogenesis in lymphoid tissue
— Determination of autophagy in tonsil cells using different techniques. This has enabled us to evaluate the changes that occur in autophagy after HIV infection.
— Demonstration that, in lymphoid tissue, cell death is a complex process that implies both non-inflammatory death (apoptosis and autophagy) and inflammatory death (pyroptosis).
— Description of the effects of cell death inhibition on HIV pathogenesis. Evaluation of the effects of different drugs modulating autophagy, apoptosis and pyroptosis in infection will allow us to determine if these processes could be new therapeutic targets.

Immunodiscordant responders
— Determination of the effect of the humoral immune response against CMV in immune recovery. Immunodiscordant individuals present higher levels of IgG antibodies against CMV in plasma than individuals with adequate immune recovery. This increase in IgG levels is the result of a greater number of CMV reactivations, which suggests that co-infection with CMV is an important factor in high mortality/morbidity rates for these patients.
— Determination of cellular immune system functionality and characterization of the specific cellular response. Despite having a phenotypically very altered T-cell compartment, immunodiscordant individuals preserve their polyclonal and HIV-specific responses. In contrast, specific responses to CMV are much higher in immunodiscordant patients than in immunoconcordant or HIV-negative individuals. This reinforces the idea that co-infection with CMV plays a significant role in the inadequate immune recovery of these individuals.
— Determination of the role played by autophagy in immune recovery. T-cell autophagic response is reduced in immunodiscordant patients. Characterization of the autophagy process in other patient cohorts would improve understanding of the role played by this process in the immune recovery of HIV-infected individuals.

Bladder cancer
— Therapeutic strategies for improving treatment with BCG. A phase I clinical trial has been launched to study the possibility of strengthening the immune system of individuals with superficial bladder cancer before they receive intravesical BCG, so as to improve clinical efficacy of the treatment.
— Study of treatment response biomarkers. A cohort of individuals with superficial bladder cancer has been established in order to study possible blood, urine and tissue biomarkers of response to treatment.

RESEARCH MANAGEMENT

Scientific and Technical Services

Sample Conservation and Processing Service

The **IrsiCaixa** Retrovirology Laboratory, which began operations in 1993, processes and preserves biological samples from HIV-infected patients for use in research projects.

Over the years, the laboratory has processed and conserved samples for numerous projects and clinical trials sponsored by **IrsiCaixa** and external national and international sponsors. This activity has developed into a platform that aims to aid research requiring human samples.

Currently, the service routinely processes and stores samples for 33 active studies and maintains a large sample collection for research into HIV and other infections (registered with the National Registry of Biobanks, No. C0000814).

Sequencing Service

Since its launch, **IrsiCaixa** has used the 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. In this context, the need arose to create the Sequencing Service so that all patients could have access to this technique.

The Sequencing Service commenced operations in 1999 as a healthcare service receiving 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.

The Sequencing Service, in collaboration with the Germans Trias i Pujol Institute for Health Science Research (IGTP), is currently implementing next-generation sequencing technologies, which are more sensitive in identifying possible low-level resistance to drugs and potentially have an important role to play in the success of antiretroviral treatments.

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

Coordinator
Lidia Ruiz

Sample Conservation and Processing Service
Eulàlia Grau
Rafi Ayen
Lucía Gómez

Sequencing Service
Teresa Puig
Cristina Ramírez

Assistant
Susana Esteban

TYPES OF SAMPLES COLLECTED

30,894
cells

61,937
plasma

10,728
serum

24,541
other

TOTAL: 128,100

876 SAMPLES ANALYSED

557
public centres

319
private centres

Research and Innovation Management Office

The Office of Research and Innovation Management (RIMO) fosters the sharing of procedures and tools developed to support and manage projects developed by both **IrsiCaixa** and Living Lab for Health research groups, while ensuring their adaptability to the specific needs of each group.

RIMO works closely with **IrsiCaixa** and Living Lab to identify emerging needs, provide support to management, optimize mechanisms and tools and maximize synergies.

This year, renewed efforts have been invested in obtaining funding through participation in projects financed by major international public agencies in Europe and the USA, as well as through grants to researchers as a complement to existing resources. Access to specific training and to expert consultants with whom we have long-distance alliances has already materialized in NIH funding in the last quarter of 2017 and should allow us to further improve our support and management services.

Head
Mireia Manent

Team
Judith Dalmau
Chiara Mancuso

Patents

Published
Title: HIV antibody derivatives with dual antiviral and immunomodulatory activity.
Inventor(s): **Jorge Carrillo**, **Bonaventura Clotet**, **Julià Blanco**
Patent number: WO 2017085563 A1
Date granted: 26/05/2017
Organization: **IrsiCaixa**
Exploiting company(ies): AlbaJuna Therapeutics, S.L.

Filed
Title: Virus Like Particles with high density coating for the production of neutralizing antibodies.
Inventor(s): **Luis Molinos**, **Jorge Carrillo**, **Julià Blanco**
Application number: EP1638234.4
Applicant(s): **IrsiCaixa**

Title: Fc-fusion protein derivatives with high dual HIV antiviral and immunomodulatory activity.
Inventor(s): **Jorge Carrillo**, **Bonaventura Clotet**, **Julià Blanco**
Application number: 62504411 (P1607ES-US)
Applicant(s): AlbaJuna Therapeutics, S.L

Granted
Title: Methods for Identifying HIV Neutralizing Antibodies.
Inventor(s): **Jorge Carrillo**, **Julià Blanco**
Patent number: EP2893349
Date granted: 14/07/2017
Organization: **IrsiCaixa**

Living Lab for Health

In 2017, **IrsiCaixa**'s Living Lab for Health continued with its tasks focused on promoting more open and inclusive research and innovation, in line with new trends defined by the EU under the umbrella of Responsible Research and Innovation (RRI), Open Innovation and Open Science.

Living Lab projects fall into one of two categories:

— Participatory processes that promote the involvement of different social actors in research and governance through anticipation and co-creation methodologies.
— Educational programmes aimed at reducing the gap between research and education.
— RRI training to researchers, healthcare professionals, patients and other stakeholders.

Head
Rosina Malagrida

Education
Josep Carreras

Institutional communications
Júlia Bestard

Projects in 2017

Living Lab has continued to work on national and European projects already underway and has started work on new European projects, as follows:

— EnRRICH (Enhancing RRI through Curricula in Higher Education) is an EU-funded project to promote RRI training in higher education and to create a Science Store that will facilitate participatory and collaborative research by master's students and so respond to needs not covered within the scientific community.

— InSPIRES (Ingenious Science Stores to Promote Participatory Innovation, Research and Equity in Science) is an EU-funded project aimed at developing Science Stores, under the umbrella of the RRI, by creating spaces for co-creation by different social actors, including university students and lecturers, scientists, civil society organizations, industry and public policymakers.

— CRISH (Co-creating Innovative Solutions for Health) is an EU project funded by EIT Health aimed at facilitating RRI training and co-creation in different European cities.

— Fit4Food (Fostering Integration and Transformation for Food 2030) is an EU-funded project for the transformation of RD&I into food and nutrition by implementing a system-level RRI programme.

— Xplore Health is a project, developed in coordination with "la Caixa" Banking Foundation (with the support of the Amgen Foundation), aimed at reducing the gap between health research and secondary education and at training future citizens in RRI competencies.

Xplore Health

- 137,586 website visits
- 13,751 Facebook followers
- 2,800 Twitter followers
- new module on vaccination

Lines of action 2017

— Co-ResponsaVIHlitat. This project, participated in by some 680 social actors, aims to develop an RD&I Agenda for HIV and STI prevention using collaborative and participatory methodologies.

Co-ResponsaVIHlitat

- 10 participating research centres, universities and public health entities
- 6 participating civil society organizations
- 680 participants
- 400 CosmoCaixa conference attendees

— HIV/AIDS Community Advisory Committee (CAC). This external body facilitates communication and dialogue between the scientific community and HIV-affected groups and individuals at risk. It provides **IrsiCaixa** and its researchers with a broader and complementary perspective on the impact, consequences and feasibility of their research. During 2017, the CAC met every two months.

— RRI and co-creation training for professionals. Living Lab offers training to researchers, healthcare personnel, public policymakers and patients from various universities and research centres throughout Europe. Training can be customized and is also offered for doctoral, master's and undergraduate courses. Living Lab also participates in national and international conferences, seminars and workshops.

RRI training for professionals

- 1,197 participants in RRI courses and talks for professionals

— Training in RRI for secondary education. Living Lab has developed new educational resources on vaccination, has run face-to-face and online courses for teachers and has coordinated participation of secondary schools in Co-ResponsaVIHlitat.

— HIV/AIDS outreach programme. **IrsiCaixa** continues to offer reflection and dissemination sessions regarding HIV prevention at CaixaForum and CosmoCaixa events in Barcelona. These sessions are complemented by the LaboCosmoCaixa (jointly organized by "la Caixa" Banking Foundation and **IrsiCaixa**) activity, aimed at encouraging young people to do research with a vaccine candidate developed by IrsiCaixa. This programme was held for the seventh time this year.

IrsiCaixa Outreach

- 1,694 HIV/AIDS open day attendees
- 5,641 website visits

Living Lab also coordinate **IrsiCaixa**'s institutional communications (see next section).

Institutional Communications

The Institutional Communications area aims to give visibility to the research carried out in **IrsiCaixa**'s laboratories. Media impact in 2017 was relatively greater in 2017, with 376 mentions made in Spanish TV, radio and press — well above the 228 mentions of 2016 and the 260 mentions of 2015. The increase was mainly due to the media repercussions of a press campaign in February regarding the successful BCN02-Romi clinical trial — coordinated by **IrsiCaixa** and carried out in collaboration with other institutions — whose preliminary results regarding a therapeutic vaccine against AIDS were reported this year. A full-scale campaign was run that included a press conference held at Palau Macaya in Barcelona.

Another successful campaign was *Just the Essentials*, launched in September by "la Caixa" Banking Foundation. The main protagonists were the director of **IrsiCaixa**, **Bonaventura Clotet**, and **Maria Salgado**, winner of the Dominique Dormont Prize 2017, which was awarded during the International AIDS Society annual conference held in July in Paris.

In 2017, seven press releases were made, to which can be added five other news stories and five Blog365 posts that were shared on the website and in institutional social networks.

IrsiCaixa has increased its presence in social networks by creating a corporate page on Linkedin and a YouTube channel. The sustained growth of recent years has been maintained in Twitter, with the number of followers growing from 2,796 in 2016 to 3,500 in 2017.

376

press, radio and TV impacts

33.20%

increase in website sessions

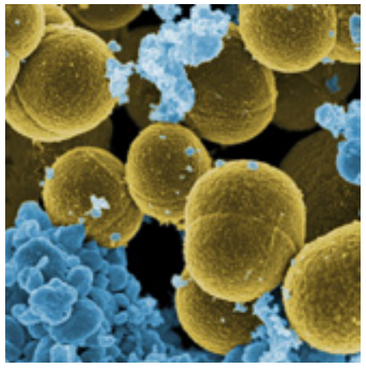
The new institutional website, presented at the end of 2016, has been further enhanced by adjustments aimed at optimizing its functionality and improving the user's experience. Traffic data endorse the success of the new website: the number of sessions in 2017 was 33.20% higher than in 2016 (33,579 and 25,210 sessions, respectively) and the number of users accessing the website in 2017 was 36.55% higher than in 2016 (22,054 and 16,151 users, respectively).

At the close of the year, coinciding with World AIDS Day on 1 December 1, **IrsiCaixa** launched its new newsletter. With a platform in three languages, our goal is to diversify our channels and reach as many audiences as possible.

Collaborations

SEAT

During 2017, **IrsiCaixa** began a strategic collaboration with SEAT to study the impact of diet and health on the gut microbiome and the gut's response to interventions to improve diet and health. This research, carried out in collaboration with the SEAT Health Care and Rehabilitation Centre (CARS), the Fight AIDS Foundation and Hospital Clínic de Barcelona, will yield crucial information for the design of new strategies to improve the health of workers and people in general.



NIAID/RML

Glòria Soler Foundation

The **Glòria Soler Foundation** is a private, nonprofit organization created in 2015 by Josep Suñol i Soler, son of Josep Suñol i Garriga and Glòria Soler i Elías. Its mission is — by providing material and human resources to prestigious institutions with proven track records — to promote solidary and innovative programmes that have an important impact in the scientific, social and humanistic fields.

The **Glòria Soler Foundation**, committed to encouraging collaboration through lines of action based on ongoing dialogue, also looks to the future by building pioneering experiences in healthcare, scientific research and the humanities.

In 2016, the **Glòria Soler Foundation** signed an agreement with **IrsiCaixa** to develop a project aimed at deciphering the relationship between the gut microbiome and HIV that has led to significant discoveries. Thanks to this contribution, the **IrsiCaixa** Microbial Genomics group, using shotgun-sequencing techniques, has demonstrated the correlation between immune deficiency progression associated with HIV and a reduced gene and functional diversity of gut microbes. The loss of microbial gene diversity is characterized by a reduction in methane-producing organisms and an increase in genes that detoxify endogenous toxic reagents derived from oxygen (ROS) and nitrogen (RNS).

Presentation of these results at international conferences has led to collaborations with groups with a long history and track record in this field. Short-chain fatty acid (acetate, butyrate, propionate, valerate, isobutyrate, and isovaleric) content in faecal samples have been estimated and analysed in collaboration with the group led by Nichole Klatt, principal investigator of the Center for Innate Immunity and Immune Disease at the University of Washington.

Early results show that individuals with a less diverse gene pool have higher levels of butyrate, a metabolite essential to the growth of the cells that form the intestinal epithelium.

Faecal metabolome was analysed on a large scale in collaboration with Rovira i Virgili University (Tarragona). Gas chromatography and mass spectrometry were used to characterize the metabolic profile of the 156 faecal samples collected for the project. At present, around 300 metabolites of microbial origin per sample have been identified. These results are being analysed as we acquire the necessary knowledge to correctly interpret them.

A longitudinal study of gut flora was launched to run parallel to the HIV-1 therapeutic vaccine clinical trial led by **Christian Brander**'s group at **IrsiCaixa**. A total of 85 faecal samples are available, provided by 12 individuals who participated in the BCN02-ROMI trial, which has also received funding from the **Glòria Soler Foundation**. Analysis of the corresponding sequencing data, which will begin shortly, aims to identify microbial changes in the guts of these patients during immune response activation at different stages of the clinical trial.

Finally, collaboration has begun with Dr. Jason M. Brenchley, leader of the parasitic disease group at the US NIH, a worldwide reference for the microbiome and HIV. The aim of this project is to characterize faecal microbes in macaque monkeys before and after exposure to SIV, related to HIV and the cause of AIDS in simians. These samples will be shotgun-sequenced in the first quarter of 2018.

Training

IrsiCaixa has been committed from the outset to training young researchers and developing successful careers in the biomedical research area. This goal is realized as follows:

— Work placements for undergraduate and master's students
— Placements for students completing their undergraduate or master's theses
— Training of pre-doctoral students
— Training of post-doctoral researchers
— Continuing professional development for staff
— Visiting researcher placements. Particularly welcome are trainee researchers interested in learning from **IrsiCaixa** research groups.

CURRENTLY IN TRAINING

8 undergraduate and master's students

18 pre-doctoral researchers

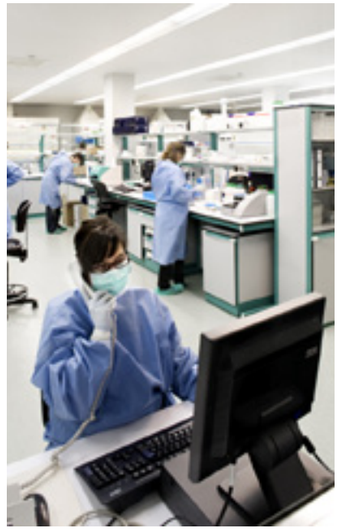
17 post-doctoral researchers

TRAINING ACTIVITIES

11 research results meetings

76 attendances at conferences

Research trainee	Host Group	Institution	City, country	Date
Alberto Crespo	Host Genetics and Cellular Immunity	Universidad Complutense de Madrid	Madrid, Spain	6 March-8 April
Seth Inzaule	Microbials Genomics	Amsterdam Institute for Global Health and Development	Amsterdam, Netherlands	1 January-31 May
Fernando Lázaro	Microbials Genomics	Hospital La Paz	Madrid, Spain	20 April-31 July
Emma-Elizabeth Ilett	Microbials Genomics	University of Copenhagen	Copenhagen, Denmark	17 July-21 July
David Bejarano	Retrovirology and Clinical Studies (GREC)	University of Heidelberg,	Heidelberg, Germany	1 March-10 March
Marie-Angélique De Scheerder	Retrovirology and Clinical Studies (GREC)	University of Ghent	Ghent, Belgium	11 April-15 April
Santa Rasa	Cell Virology and Immunology (VIC)	Rigas Stradina Universitate	Riga, Latvia	24 March-31 March
Suzanne Esther Marieke Van Der Stap	Living Lab for Health	Universiteit van Amsterdam	Netherlands	12 July-14 July



INTERNAL TRAINING

— Weekly meetings in which **IrsiCaixa** group members present their results. These strengthen individuals' ability to structure and defend experimental data before a closed audience of experts in the area.
— Fortnightly research results meetings in which members of each **IrsiCaixa** group present their results. These strengthen individuals' ability to structure and defend experimental data before a closed audience of experts in different areas.
— Seminars. **IrsiCaixa** and other Can Ruti Campus groups regularly organize open seminars with invited internationally renowned researchers.
— National and international conferences. All staff are encouraged to participate in and to present their results at scientific meetings and conferences. In 2017, 76 works were presented at conferences.
— Specialization courses and training in experimental techniques.
— Journal clubs. Weekly meetings where **IrsiCaixa** staff present an article of relevance to their own experimental work. This develops critical vision regarding published data.
— Stays at other research centres. **IrsiCaixa** actively fosters the mobility of staff in training so that they are exposed to new techniques and methodologies and can establish project collaborations with other centres. In 2017, 6 pre-doctoral students undertook stays in foreign research centres.

Research trainee	Group	Institution	City, Country	Date
Míriam Rosàs	Host Genetics and Cellular Immunity	Karolinska Institutet	Estocolm, Suècia	23-26 abril
Bruna Oriol	Host Genetics and Cellular Immunity	Karolinska Institutet	Estocolm, Suècia	23-26 abril
Javier Rivera	Microbials Genomics	Biomathematics & Biostatistics Scotland	Edimburg, Regne Unit	1-15 novembre
Muntsa Rocafort	Microbials Genomics	Center for Medical Mycology	Cleveland, Estats Units	1 novembre-31 gener 2018
Cristina Gálvez	Retrovirology and Clinical Studies (GREC)	Imperial College London	Londres, Regne Unit	1-31 maig
Silvia Bernal	Retrovirology and Clinical Studies (GREC)	University of Pittsburgh	Pittsburgh, USA	30 octubre - 3 novembre

CHAIR OF AIDS

In 2013, **IrsiCaixa** signed an agreement with the Fight AIDS Foundation and the University of Vic-Central University of Catalonia (UVic-UCC) to create the Chair of AIDS and Related Diseases. The Chair, headed by **Dr. Bonaventura Clotet,** was created to enhance collaboration between the three institutions in the interest of fostering biomedical research at the UVic-UCC and promoting the teaching and training of new researchers and healthcare professionals.

Although HIV and AIDS are considered to be the core elements in this initiative, the Chair also covers research into related conditions such as ageing, hepatitis, cancer and chronic fatigue.

Activities under the auspices of the Chair in 2017 were as follows:

— *The eradication of AIDS is now possible* (conference). 28 February 2017. Aula Magna UVic-UCC. **Bonaventura Clotet**
— *Update on AIDS and metagenomics* (continuous professional development). 23 May 2017. Conference Hall at Vic General Hospital (Vic Hospital Consortium). Talks were as follows:
• *Antiretroviral drugs and their development since 1987*, **Bonaventura Clotet**
• *Rapid progression,* **Javier Martínez-Picado**
• *Ageing and comorbidities,* **Eugènia Negredo**
• *Immune recovery with cART: what to do when it fails?* **Julià Blanco**
• *Resistance to antiretrovirals*, **Roger Paredes**
• *Microbiome and HIV,* **Marc Noguera**
• *Therapeutic vaccines*, **Bonaventura Clotet**
— Talk as part of the welcome to the first cadre of UVic-UCC Faculty of Medicine students. 29 September 2017. Teatre l'Atlàntida, Vic. **Bonaventura Clotet**.
— *Clinical trials: design, types and stages* (seminar). 6 November 2017. UVic-UCC Faculty of Medicine. **Beatriz Mothe**.

Clinical Trials

1. CONTROLLERS

Cohort study of HIV-positive elite controllers and non-progressors. Prospective follow-up.

Summary and objectives: Cohort study with prospective follow-up of HIV-positive individuals with an undetectable or very low viral load in the absence of antiretroviral treatment (known as elite or viremic controllers). The aim is to study the virological and immunological mechanisms involved in spontaneously controlling the HIV virus in order to develop new therapeutic vaccines. There is no clinical intervention other than the extraction of additional biological samples.

Study type: Observational
Design: Cohort, prospective
Recruitment: Open
Start-end: 03/06/2009- /
Sponsor: IrsiCaixa
Principal investigator(s): Dr. Beatriz Mothe
Participating centre(s): Germans Trias i Pujol University Hospital (Fight AIDS Foundation), Hospital Vall d'Hebron, prisons
CEIC Code: EO-09-042

2. Early_cART

Cohort study of individuals with documented acute/recent HIV-1 infection initiating antiretroviral therapy from diagnosis.

Summary and objectives: Prospective cohort study to monitor individuals with documented acute/recent HIV-1 infection initiating early-stage antiretroviral therapy. The objective is to have a clinical platform of candidates for clinical trials of therapeutic vaccination and eradication strategies and also to prospectively obtain biological samples from the outset of antiretroviral therapy to study initial transmission of HIV, immune response, the establishment of viral reservoirs and changes in the gut microbiome. There is no clinical intervention other than the extraction of additional biological samples and the collection of faecal samples.

Study type: Observational
Design: Cohort, prospective
Recruitment: Open
Start-end: 24/07/2014- /
Sponsor: IrsiCaixa
Principal investigator(s): Dr. Beatriz Mothe
Participating centre(s): Germans Trias i Pujol University Hospital (Fight AIDS Foundation)
CEIC Code: PI-14-072

3. Seronegative_genotyped

Biobank of biological samples from HIV-negative individuals with known HLA genotype for experimental use in immunological studies related to AIDS research.

Summary and objectives: Prospective cohort of healthy volunteers whose HIV seronegative status and high-resolution HLA genotype is documented, for whom biological samples (plasma and PBMCs) — stored in the IrsiCaixa Retrovirology Laboratory biobank — are available for use in the study of immunological aspects of HIV infection and related diseases.

Study type: Observational
Design: Cohort, prospective
Recruitment: Open
Start-end: 30/10/2009- /
Sponsor: IrsiCaixa
Principal investigator(s): Dr. Beatriz Mothe
Participating centre(s): Germans Trias i Pujol University Hospital (Fight AIDS Foundation)
CEIC Code: EO-09-070

4. BCN02-ROMI

Safety and efficacy of HIVconsv vaccines administered in combination with romidepsin in achieving viral control after interruption of antiretroviral therapy in HIV-positive individuals treated from diagnosis.

Summary and objectives: The BCN02-ROMI clinical trial evaluates the effectiveness of a kick-and-kill eradication strategy based on use of the most immunogenic therapeutic vaccines known to date (HIVconsv) and the most powerful viral latency reactivation drug currently available (romidepsin). HIV-positive individuals treated from diagnosis and previously vaccinated in the BCN01 trial represent an ideal group in which to demonstrate the effectiveness of this strategy that combines viral reservoir reduction with viral rebound control once treatment ends. Investigated by means of a populational pharmacokinetics/pharmacodynamics analysis are the relationship between romidepsin levels, in-vivo effects on induced expression of reservoir HIV and the impact on the immune system. Results will enable optimization of the romidepsin dose and will identify markers to help assess the efficacy of currently studied eradication strategies.

Study type: Interventional
Design: Open-label, multicentre
Recruitment: Closed (n=15)
Phase: I
Start-end: 02/2015- 10/2017
Sponsor: IrsiCaixa
Principal investigator(s): Dr. Beatriz Mothe, Dr. José Moltó
Participating centre(s): Germans Trias i Pujol University Hospital (Fight AIDS Foundation), Hospital Clínic de Barcelona, BCN Checkpoint
CT Code: NCT02616874
EUDRA Code: 2015-002300-84

5. iHIVARNA-02

Phase IIa multicentre, double-blind, placebo-controlled clinical trial to evaluate the safety and immunogenicity of the new iHIVARNA-01 therapeutic vaccine in HIV-infected patients.

Summary and objectives: Phase IIa multicentre, double-blind, placebo-controlled clinical trial of the iHIVARNA therapeutic vaccine candidate. Included are 70 individuals with chronic fully suppressed HIV-1 infection, randomized to receive either three intranodal consecutive doses of the iHIVARNA vaccine containing 900 g of the HTI immunogen plus 300 g of the adjuvant TriMix (n=40) or three doses of placebo (n=15). Two weeks after the last vaccination, the antiretroviral treatment is interrupted, viral rebound is monitored for 12 weeks; if viral rebound occurs, the treatment is resumed. Objectives include studying vaccine administration safety, immune response and viral control once treatment stops.

Study type: Interventional
Design: Double blind, placebo-controlled, multicentre
Recruitment: Closed
Phase: IIa
Start-end: 04/04/2017- 28/02/2018
Sponsor: Erasmus MC, Rotterdam (Netherlands)
Principal investigator(s): Dr. Rob Gruters
Participating centre(s): Erasmus MC, Rotterdam (Netherlands), Hospital Clínic de Barcelona, Germans Trias i Pujol University Hospital (Fight AIDS Foundation), IrsiCaixa (Badalona, Spain), Instituut voor Tropische Geneeskunde (Antwerp, Belgium), Vrije Universiteit Brussel/UZ Brussel (Belgium)
NCT Code: NCT02888756

6. AELIX-002

Phase I randomized, double blind, placebo-controlled clinical trial to assess the safety, tolerance and immunogenicity of DNA.HTI vaccines administered in combination with MVA.HTI to 15 HIV-positive patients diagnosed and treated from an early stage.

Study type: Interventional
Design: Double blind, placebo-controlled, multicentre
Recruitment: Closed (n=15)
Phase: I
Start-end: 07/07/2017- 31/05/2018
Sponsor: Aelix Therapeutics, SL
Principal investigator(s): Dr. Beatriz Mothe
Participating centre(s): Germans Trias i Pujol University Hospital (Fight AIDS Foundation), IrsiCaixa (Badalona, Spain)
NCT Code: NCT03204617

7. BCG-INMUNO-RESP

Prediction and improvement of clinical response to intravesical BCG treatment of superficial bladder cancer.

Summary and objectives: To evaluate correlation between recurrence/progression and synthetic/local immune response to BCG before and after intravesical therapy and to identify biological markers that predict clinical response to this treatment.

Study type: Observational
Design: Pilot study
Start-end: 2015- /
Sponsor: IrsiCaixa
Principal investigator(s): Dr. Cecilia Cabrera
Participating centre(s): Germans Trias i Pujol University Hospital (Fight AIDS Foundation).

8. IciStem (amfAR)

Clinical observational study to evaluate the effect of allogenic transplants in HIV-positive patients with malignant haematological diseases.

Summary and objectives: A European consortium co-led by IrsiCaixa has been created to study the effect of allogenic transplants in HIV-infected patients with malignant haematological diseases. To date 17 patients have been recruited from different European countries, including Spain, Holland, Germany, Belgium and Italy. The main objective is to study the impact of this intervention on the viral reservoir and its potential for eradicating HIV infection.

Study type: Clinical observational
Design: Multicentre
Start-end: 01/07/2014- /
Sponsor: University Medical Center Utrecht (Netherlands)
Principal investigator(s): Dr. Javier Martinez-Picado, Dr. Annemarie Wensing

9. RIPIM

Clinical trial to evaluate the impact of intensification with raltegravir in HIV-positive patients with full viral suppression in monotherapy with protease inhibitors. .

Summary and objectives: Pilot phase III, proof-of-concept, open-label clinical trial, with the aim of evaluating the impact of intensification with raltegravir on both the persistent viral reservoir and immune activation in patients receiving treatment with protease inhibitors as monotherapy. Included are 41 patients who, after 8 weeks of baseline monitoring, are treated and followed up for 24 weeks.

Study type: Clinical trial
Design: Pilot, proof of concept, open-label
Phase: III
Start-end: 28/10/2011-
Sponsor: IrsiCaixa
Principal investigator(s): Dr. Javier Martinez-Picado

10. INDOOR

Clinical trial to evaluate HIV reservoir dynamics after patients receiving treatment based on protease inhibitors are switched to dolutegravir.

Summary and objectives: Phase IV open-label randomized clinical trial that aims to comprehensively evaluate the viral reservoir in CD4+ T-cells in peripheral blood and lymphoid tissue obtained from biopsies of the ileum and to prospectively analyse changes in immune activation and inflammation after switching to dolutegravir.

Study type: Clinical trial
Design: Randomized, open-label
Phase: IV
Start-end: 01/06/2015- /
Sponsor: IrsiCaixa
Principal investigator(s): Dr. Javier Martinez-Picado, Dr. Manel Crespo, Dr. Linos Vandekerckhove

11. LoViReT

Clinical observational study to evaluate predictors of extremely low viral reservoirs.

Summary and objectives: Clinical observational study to screen some 400 patients for cellular proviral DNA in order to create a cohort of 20-30 patients with extremely low viral reservoirs. The factors involved in these reservoir levels and their possible application to treatment strategies will be exhaustively studied.

Study type: Clinical observational
Start-end: 01/01/2015- /
Principal investigator(s): Dr. Javier Martinez-Picado

12. Siglec-1

Clinical observational study to evaluate the effect of SIGLEC-1 mutations in cases of HIV and Micobacteri tuberculosis co-infection.

Summary and objectives: Clinical observational study involving genetic screening of some 4,000 individuals to select patients with mutations in the gene encoding SIGLEC-1 in order to evaluate clinical effect and pathogenesis of HIV and Micobacteri tuberculosis co-infection.

Study type: Clinical observational
Start-end: 01/01/2015- /
Principal investigator(s): Dr. Javier Martinez-Picado, Dr. Nuria Izquierdo-Useros

13. **Durvast**
Clinical trial to evaluate the effect of durvalumab (MEDI4736) in HIV-positive patients with advanced solid tumours.
Summary and objectives: Phase II clinical trial to evaluate the effect of durvalumab (MEDI4736) in HIV-positive patients with advanced solid tumours.
Phase: II
Start-end: 01/01/2015- /
Principal investigator(s): **Dr. Javier Martinez-Picado**

14. **RUTIVAC-1**
Phase I randomized, double-blind, placebo-controlled clinical trial to evaluate the immunomodulating effect of RUTI® in individuals with high-grade superficial bladder cancer treated with intravesical Bacillus Calmette-Guerin (BCG).
Summary and objectives: This phase I clinical trial is designed to evaluate and collect safety information on systemic and mucosal immune response to RUTI® administered to individuals with high-grade superficial bladder cancer.
Design: Double blind, placebo-controlled, randomized
Phase: I
Start-end: 2017–2019.
Sponsor: Archivel Farma, SL
Principal investigator(s): **Dr. Cecilia Cabrera**
Participating centre(s): Germans Trias i Pujol University Hospital (Urology Department), Fight AIDS Foundation (CRO)
CEIC Code: AC-16-048-CEIM
EUDRA Code: 2016-004311-12

15. **AbiVax 005**
Open-label study of the safety, pharmacokinetics and pharmacodynamics of ABX464 in HIV-1 seronegative and seropositive adults.
Summary and objectives: Clinical trial to evaluate distribution of ABX464 and its main metabolite (N-Glu) in various compartments in HIV-1 seronegative and seropositive adult subjects.
Phase: Ib
Start-end: Q4 2016- /
Principal investigator(s): **Dr. Ross Cranston**

16. **LT-EC**
Analysis of the presence of infectious viruses in the blood of elite non-progressing controllers.
Summary and objectives: A clinical trial to study host and virus characteristics in elite controllers of more than ten years in order to explore and better understand pathogenic mechanisms and spontaneous control of infection.
Study type: Clinical observational
Start-end: 01/01/2017- /
Principal investigator(s): **Dr. Cecilio López-Galíndez** (CNM-ISCIII)

17. **VNP**
HIV adult and pediatric viremic non-progression: clues from immune preservation for the cure.
Summary and objectives: Clinical trial to study the factors associated with the viremic non-progressor phenotype that maintains health and immunity despite a high viral load.
Study type: Clinical observational
Start-end: Q4 2014- /
Principal investigator(s): **Dr. Philip Goulder, Dr. Javier Martinez-Picado, Dr. Julia Garcia-Prado**

The final cycle of The Barcelona Debates on the Human Microbiome 2017. From Microbes to Medicines — organized by B·Debate (an initiative of Biocat and "la Caixa" Banking Foundation), led by **IrsiCaixa** and held in CosmoCaixa — showcased works that exemplified how the microbiota is becoming an essential part of modern medicine.

Microbiome and HIV
Nichole Klatt from the University of Washington presented data from a study he had published in *Science* on vaginal dysbiosis, i.e., the change from a physiological vaginal flora predominated by *Lactobacillus spp*. to a flora with an abundance of other species such as *Gardnerella spp.* or *Prevotella spp.* A vaginal microbicide based on tenofovir was far less efficacious in *Gardnerella*-dominant women with HIV-1 than in *Lactobacillus*-dominant women with HIV-1, as *Gardnerella* absorb tenofovir, which is then not available to block HIV-1 entry. This is the first evidence that the microbiota can influence HIV-1 transmission. The study launches an area for research into the role played by microbes in the drug metabolism that will acquire great importance in the coming years.

Dr. Fernández-Real from the University of Girona presented results of recent

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work demonstrating that one effect of metformin — the drug most commonly used to treat adult diabetes — is to modify the gut microbiota so as to favour bacteria more capable of metabolizing sugars in the diet.

The **IrsiCaixa** Microbial Genomics group presented data demonstrating that the gut microbiome in people with HIV-1 is modified to adapt to the oxidative stress caused by the infection. This adaptation leads to an increase in bacteria more capable of tolerating oxygen and nitrogen free radicals. Adaptation to oxidative stress, which is much more evident in people with a significantly impaired immune system, favours increases in certain bacterial virulence factors and brings about changes in an individual's antibiotic resistance profile. An interesting observation is that the patterns of change observed in HIV infection are similar to those of other diseases where there is inflammation of the gut.

Microbiota and cancer
Laurence Zitvogel from INSERM presented data showing that certain gut microbiota bacteria can stimulate the response to the new immunomodulatory drugs used to treat certain types of cancer. He also suggested that antibiotic treatment could alter the response to some of these new immunomodulatory drugs and so affect patient survival.

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These and other issues related to the role played by the microbiota in healthy ageing, neurodegenerative diseases (such as Parkinson), inflammatory bowel disease and other human health areas were the focal points of an event that annually brings together some 200 people interested in the science of the microbiome and its translation to the medicine of the 21st century.

Publications and Presentations

Publications

Original publications

1. Adland E, Hill M, Lavandier N, Csala A, Edwards A, Chen, Marek Radkowski F, Paraskevis D, Avila-Rios S, Borrow P, Mori M, Pfafferott K, Rockstroh J, Bonn clinician16, Brander C, Mothe B, Martinez-Picado J, Tudor-Williams G, Frater J, Stryhn A, Buus S, Reyes Tehran G, John M, MACS people, Carrington M, Goulder P. **Differential immunodominance hierarchy of cd8+ t cell responses in hla-b*27:05 and b*27:02-mediated control of hiv-1 infection**. In press in *Journal Virology*. IF: 4.663

2. Andrei G, Carter K, Janeba Z, Sampath A, Schang LM, Tarbet EB, Hodge RAV, Bray M, Este JA. **Highlights of the 30th International Conference on Antiviral Research**. *Antiviral Research*. Volumen: 145, Páginas: 184-196. IF: 4.271

3. AIDS-defining Cancer Project Working Group for IeDEA and COHERE in EuroCoord; AIDS-defining Cancer Project Working Group for IeDEA and COHERE in EuroCoord. (Paredes R). **Comparison of Kaposi Sarcoma Risk in Human Immunodeficiency Virus-Positive Adults Across 5 Continents: A Multiregional Multicohort Study**. *Clin Infect Dis.* 2017 Oct 15;65(8):1316-1326. doi: 10.1093/cid/cix480. IF: 8.216

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Conference presentations

Verhofstede C, Vandamme AM, Lemey P, Van Laethem K. **A21 HIV-1 sub-subtype F1 outbreak among MSM in Belgium**. *Virus Evol*. 2017 Mar 5;3(Suppl 1). pii: vew036.020. doi: 10.1093/ve/vew036.020. eCollection 2017 Mar. PubMed PMID: 28845274; PubMed Central PMCID: PMC5565986. IF:__/__

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Collaborative publications

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7. Pett SL, Amin J, Horban A, Andrade-Villanueva, Losso M, Porteiro N, Madero JS, Belloso W, Tu E, Silk D, Kelleher A, Harrigan R, Clark A, Sugiura W, Wolff M, Gill J, Gatell J, Clarke A, Ruxrungtham K, Prazuck T, Kaiser R, Woolley I, Alberto Arnaiz J, Cooper D1, Rockstroh JK, Mallon P, Emery S; MARCH study group. **Week 96 results of the randomized, multicentre Maraviroc Switch (MARCH) study**. *HIV Med*. 2017 Jul 13. doi: 10.1111/hiv.12532. IF: 3.257

1. O-glcnac Glycosylation of HIV synthetic epitopes reduces cytotoxic T cell recognition. Gemma Arsequell, Gregorio Valencia, Christian Brander, Àlex Olvera. EuroCarb 2017. Barcelona (Spain). 2-7 to 6-7-2017. Poster presentation.

2. MDA5 blocks hcv but not hiv-1 replication in parental and rig-i-defective hepatoma cells. Ester Ballana, Maria Pujantell, Sandra Franco, Eva Riveira-Muñoz, Roger Badia, Bonaventura Clotet, Cristina Tural, Miguel Angel Martinez, José A. Esté. 23rd Conference on Retroviruses and Opportunistic Infections. Seattle, USA.

3. Epstein-Barr virus load in plasma is an early biomarker of HIV-related lymphomas. Baptista MJ, Muncunill J, Hernandez-Rodriguez A, Dalmau J, Garcia O, Tapia G, Moreno M, Sancho JM, Martinez-Picado J, Ribera JM, Feliu E, Mate J, Navarro JT. International Conference on Malignant Lymphoma. Lugano (Switzerland). June 14-17, 2017. Poster presentation.

4. Activation of mature dendritic cells via PKC agonist induces HIV-1 reactivation of latently infected cells. Benet S, Erkizia I, Martinez-Picado J, Izquierdo Useros N. 8th HIV Persistence during Therapy Workshop. Miami, USA. December 12-15, 2017.

5. Persistence of HIV DNA in tissues early after transplantation with CCR5Δ32 stem cells (Abstract 320). Bosman K, Nijhuis M, Bruns A, Salgado M, Hütter G, Brosens L, Martinez-Picado J, Kuball J, Wensing A. 23rd Conference on Retroviruses and Opportunistic Infections. International Antiviral Society–USA (IAS USA). Seattle, USA. February 13-16, 2017. Poster presentation.

6. HIV-1 envelope glycoproteins isolated from Viremic non-progressors HIV-infected individuals are fully functional and cytophatic. Blanco J. III CONGRESO - GEHEP 2017. Sevilla (Spain). 28 -30 September 2017. Invited speaker.

7. Accelerated immunosenescence and inflammaging. Blanco J. Comprehensive Management of Aging in HIV-Infected Subjects. 2nd edition of the International Workshop. Buenos Aires (Argentina). 2-3 November 2017. Invited speaker.

8. HIV-1 Gag reduce PI-susceptibility in the absence of protease resistance mutations. Óscar Blanch-Lombarte, José Ramón Santos, Ruth Peña, Esther Jiménez-Moyano, Alba Ruiz, Roger Paredes, Bonaventura Clotet, Julia G Prado. IX Congreso GeSIDA. Vigo (Spain). November 28 - December 1. Poster presentation.

9. Virological failure to protease inhibitors in Monotherapy is linked to the presence of signature mutations in Gag without changes in HIV-1 replication. Óscar Blanch-Lombarte, Jose Ramón Santos, Ruth Peña, Esther Jiménez-Moyano, Alba Ruiz, Roger Paredes, Bonaventura Clotet and Julia G Prado. 15th European meeting on HIV-1 and Hepatitis. Roma (Italy). June 7-9. Oral presentation.

10. Identificación de las claves en la vacuna terapéutica frente al VIH: ¿tan cerca/lejos como parece? Christian Brander. IX Congreso Nacional de GESIDA. Vigo (Spain). 29-11-2017. Invited speaker.

11. Predictors of HIV control and their use for HIV vaccine design. Christian Brander. ENABLE (EuropeaN Academy for BiomedicaL SciencE 2017. 1st European PhD and Postdoc symposium. Barcelona (Spain). 15-11 to 18-11-2017. Keynote Address.

12. Immune correlates and biomarkers of HIV control after therapeutic vaccination and treatment interruption. Christian Brander. World Immune Profiling Congress 2017. Barcelona (Spain). 12-10-2017. Invited speaker.

13. Memory B cell dysregulation in HIV-1 infected Individuals. Carrillo J, Negredo E, Puig J, Molinos-Albert LM, Rodríguez de la Concepción ML, Curriu M, Massanella M, Navarro J, Crespo M, Viñets E, Millá F, Clotet B, Blanco J. IX GESIDA 2017. Vigo (Spain). 28 November- 1 December 2017. Poster presentation.

14. Resident memory CD4+ T cells in cervical tissue are highly permissive to HIV infection. Jon Cantero-Pérez, Alba Ruiz, Antoni Tarrats, Julio Garrido, Alba Hernández-Gallego, Laia Pérez-Roca, Irian Lorencés, Julia G Prado, María J. Buzón, Meritxell Genescà. IX Congreso GeSIDA. Vigo (Spain). 28 November - 1 December. Poster oral (PO-23).

15. Primary Resistance to Integrase Strand-Transfer Inhibitors in Spain. Maria Casadellà. 2nd Spanish HIV Clinical Forum. Málaga (Spain). 10-11 May 2017. Oral presentation.

16. Deep sequencing for HIV-1 clinical management. Maria Casadellà. Association for Molecular Pathology Meeting 2017. Salt Lake City (USA). November 18 2017. Oral presentation.

17. Gag-protease coevolution analyses define structural surfaces in the HIV-1 matrix and capsid involved in resistance to Protease Inhibitors. Francisco M Codoñer, Ruth Peña, Esther Jimenez-Moyano, Maria Pino, Thomas Vollbrecht, Bonaventura Clotet, Javier Martinez-Picado, Rika Draenert and Julia G. Prado. 15th European meeting on HIV-1 and Hepatitis. Roma (Italy). June 7-9. Poster presentation (P-32).

18. Myeloid Cells from Human Cervical Tissue Express Siglec-1 and Capture HIV-1. Cantero-Pérez J, Perez-Zsolt D, Erkizia I, Pino Claveria M, Hernández-Gallego A, Pérez-Roca L, Lorencés I, Garrido J, Tarrats A, Martinez-Picado J, Izquierdo-Useros N, Genescà M. 18th International Congress of Mucosal Immunology (ICMI 2017). Washington D.C. (USA). July 19-22, 2017. Oral presentation.

19. Allogeneic stem cell transplantation in HIV-1-infected individuals - the role of lymphocyte populations (Abstract TULBPEB23). Eberhard JM, Körner C, Salgado M, Jensen B, Kwon M, Díez JL, Hütter G, Rocha V, Sáez-Cirión A, Nijhuis M, Schulze zur Wiesch J, Wensing A, Martinez-Picado J, for the IciStem Consortium. 9th IAS Conference on HIV Science. Paris (France). July 23-26, 2017. Oral presentation.

20. Allogeneic stem cell transplantation in HIV-1 infected individuals: The role of lymphocyte populations. Eberhard JM, Körner C, Salgado M, Jensen B, Kwon M, Díez JL, Hütter G, Rocha V, Sáez-Cirión A, Nijhuis M, Schulze zur Wiesch J, Wensing A, Martinez-Picado J, for the IciStem Consortium. The joint Annual Meeting of the German Society of Infectious Diseases (DGI) and the German Center for Infection Research (DZIF). Hamburg (Germany). September 28-30, 2017. Oral presentation.

21. Resistant mutations at baseline do not predict the response to new DAAs in HCV/HIV-1 coinfected patients with advanced liver fibrosis. S Franco, L Díez, J López, B Clotet, C Tural, MA Martinez. XIV Congreso Nacional de Virología. Cádiz (Spain). June 11-14. Poster presentation.

22. Towards a Natural HIV Sterilizing Cure: Super Elite Controllers. Gálvez C, Salgado M, Rodriguez C, del Romero J, Casado C, Pernas M, López-Galindez C, Martinez-Picado J. IX Congreso Nacional GeSIDA. Vigo (Spain). November 28-December 1, 2017. Oral presentation.

23. Chronically Treated HIV+ Subjects Can Naturally Harbor Extremely Low Viral Reservoir. Gálvez C, Dalmau J, Urrea V, Clotet B, Leal M, García F, Martinez-Picado J, Salgado M. 8th HIV Persistence during Therapy Workshop. Miami (USA). December 12-15, 2017. Oral presentation and poster.

24. Host factors associated to control of HIV-reservoir in elite-controller patients (Abstract

MOPEA0043). García M, López-Fernández L, Mínguez P, Morón-López S, López-Bernaldo JC, Benguría A, Górgolas M, Cabello A, Fernández M, De la Hera FJ, Estrada V, Barros C, Restrepo C, García MI, Martínez-Picado J, Benito JM, Rallón N. 9th IAS Conference on HIV Science. Paris (France). July 23-26, 2017. Poster presentation.

25. A phase II exploratory study of durvalumab (MEDI4736) in HIV-1 patients with advanced solid tumors. M. Gonzalez-Cao, J. Martinez- Picado, M. Provencio, B. Clotet, O. Juan, J. Dalmau, T. Moran, A. Meyerhans, J. de Castro7, J. Blanco, R. Bernabe, N. Karachaliou1, J. Garcia-Corbacho10, R. Blanco, C. Brander, J. Carrillo, MA. Molina, R. Rosell on behalf of the Spanish Lung Cancer Group. ESMO 2017. Madrid (Spain) 8-9 to 12-9-2017. Poster Presentation

26. The human gut microbiome in HIV infection. Yolanda Guillén. 7º Congresso Pandemias na era da globalizaçao. Coimbra (Portugal). 8-9/06/2017. Oral presentation.

27. Nadir CD4+ T-cell count strongly predicts gut disbyosis in HIV infection. Y. Guillén, M. Noguera-Julian, J. Rivera, M. Casadellà, M. Rocafort, M. Parera, C. Rodríguez, J. Carrillo, B. Mothe, J. Coll, J. Navarro, M. Crespo, C. Brander, E. Negredo, J. Blanco, M.L. Calle, B. Clotet, R. Paredes, The Meta-HIV Study Group. International AIDS Society 2017. Paris (France). 12-10-2017. Poster presentation.

28. 1208TiP - A phase II exploratory study of durvalumab (MEDI4736) in HIV-1 patients with advanced solid tumors. M. Gonzalez-Cao J. Martinez-Picado M. Provencio Pulla B. Clotet O. Juan J. Dalmau T. Moran A. Mayerhans J. De Castro J. Blanco R. Blanco R. Bernabe Caro N. Karachaliou J. Garcia-Corbacho M.A. Molina C. Brander R. Rosell. ESMO 2017. Madrid (Spain). 8-12 September 2017 Poster presentation.

29. Preserved immune functionality and high CMV-specific T-cell responses in HIV-infected individuals with poor CD4+ T-cell immune recovery. Elisabet Gómez-Mora, Elisabet García, Victor Urrea, Marta Massanella, Jordi Puig, Eugenia Negredo, Bonaventura Clotet, Julià Blanco & Cecilia Cabrera. IX Congreso GeSIDA. VIgo (Spain). 28 Nov-1 Dec. Poster presentation.

30. What natural human Siglec-1 knockouts tell us about HIV-1 pathogenesis. Izquierdo-Useros N. AC31 International meeting: "Innate Immunity and Inflammation during HIV and Viral Hepatitis Infections". Paris (France). December 15, 2017. Invited speaker.

31. Synonymous changes in the codon usage of HIV-1 gp160 strongly reduce the virus replication capacity. A Jordan-Paiz, M Nevot, S Franco, MA Martinez. XIV Congreso Nacional de Virología. Cádiz (Spain). June 11-14. Oral presentation.

32. Synonymous recoded env gene induce lethality and loss of protein expression in HIV-1. A Jordan-Paiz, M Nevot, S Franco, MA Martinez. XVI Jornada de Virología. Barcelona (Spain). December 4. Oral presentation.

33. Expression of the marker CD32a within the B cell follicle of lymph nodes is restrained to productively HIV-infected cells. Luque-Ballesteros L, Serra-Peinado C, Grau-Expósito J, Genescà M, Astorga A, Morales R, Navarro J, Curran A, Burgos J, Ocaña I, Torrella A, Planas B, Badía R, Ribera E, Castellví J, Martinez-Picado J, Falcò V, Buzón MJ. IX Congreso Nacional GeSIDA. Vigo (Spain). November 28-December 1, 2017. Oral presentation.

34. Risk factors of acute rejection after liver transplantation in HIV+/HCV+ patients. C Manzardo, S Arrieta, A Rafecas, S Franco, S del Campo, E Cordero, J Peñafiel, A Rimola, C Brander, JM. Miro. 23rd Conference on Retroviruses and Opportunistic Infections. Seattle (USA). February 13-16, 2017. Poster presentation.

35. A phase II exploratory study of durvalumab (MEDI4736) in HIV-1 patients with advanced solid tumors. Marfil S, Hebman V, Marrero-Hernandez S, Márquez-Arce D, Cabrera-Rodríguez R, Varela MS, Casado C, Cabrera C, Urrea V, Pernas M, Clotet B, López-Galíndez C, Biard-Piechazyck M, Valenzuela A, Blanco J. IX Congreso GeSIDA. Vigo (Spain). 28 November- 1 December 2017. Oral presentation.

36. Nuevas herramientas de Ingeniería Genómica para el tratamiento del SIDA. Martín JM, Vallejo S, Salgado M, Gálvez C, Martín V, Fleischer A, Palomino E, Martínez Picado J, Bachiller D. IX Congreso Nacional GeSIDA. Vigo (Spain). November 28- December 1, 2017. Oral presentation.

37. Stem cell transplantation in HIV-1-infected patients. Martinez-Picado J. HIV and Hepatitis Nordic Conference. Stockholm (Sweden). September 28, 2017. Invited speaker.

38. IciStem: HIV cure by Stem Cell Transplantation. Martinez-Picado J. 16th European AIDS Conference. Milano (Italy). October 25-27, 2017. Invited speaker.

39. Immune response and HIV cure. Martinez-Picado J. 16th European AIDS Conference. Milano (Italy). October 25-27, 2017. Chair.

40. Avances en curación/remisión. Martinez-Picado J. IX Congreso Nacional GeSIDA. Vigo (Spain) November 28 - December 1, 2017. Chair.

41. Allogeneic Stem Cell Transplantation in HIV-1 infected individuals; the IciStem Consortium. Martinez-Picado J. 4th Utrecht HIV Cure Symposium Utrecht (The Netherlands). November 20, 2017. Oral speaker.

42. HIV Cure Strategies. Martinez-Picado J. 8th HIV Persistence during Therapy Workshop. Miami (USA). December 12-15, 2017. Chair and invited speaker.

43. Genome-wide methylation is associated with HIV-1 infection and disease progression (Abstract 228). Moron-Lopez S, Dalmau J, Urrea V, Lopez M, Puertas MC, Mothe B, Brander C, Esteller M, Berdasco M, Martinez-Picado J. 23rd Conference on Retroviruses and Opportunistic Infections. Seattle (USA). February 13-16, 2017. Poster presentation.

44. Viral control induced by HIVCONSV vaccine & romidepsin in early treated individuals (Abstract 119LB). Mothe B, Moltó J, Manzardo C, Coll J, Puertas MC, Martinez-Picado J, Hanke T, Clotet B, Brander C). 23rd Conference on Retroviruses and Opportunistic Infections. Seattle (USA). February 13-16, 2017. Oral presentation late breaker.

45. Effect of switching to integrase inhibitor on the HIV reservoir in ileum biopsies. Moron-Lopez S, Urrea V, Navarro J, Puertas MC, Torrella A, Salgado M, Gálvez C, Planas B, Vandekerckhove L, Blanco J, Crespo M, Martinez-Picado J. 8th HIV Persistence during Therapy Workshop. Miami (USA). December 12-15, 2017. Poster presentation.

46. Epstein-Barr virus load in plasma is an early biomarker of HIV-related lymphomas. Muncunill J, Baptista MJ, Hernandez-Rodriguez A, Dalmau J, Garcia O, Tapia G, Moreno M, Sancho JM, Martinez-Picado J, Ribera JM, Feliu E, Mate J, Navarro JT. 22nd European Hematology Association Conference.Madrid (Spain). June 22-25, 2017. Poster presentation.

47. Evolvability of HIV-1 is influenced by the codon pair usage. M Nevot, M Parera, G Martrus, MA Martinez. 22nd International Bioinformatics Workshop on Virus Evolution and Molecular Epidemiology (VEME). Lisboa (Portugal). August 27-September 1, 2017. Poster presentation.

48. La recodificación sinónima del gen gag modifica su expresión proteica en el virus de la inmunodeficiencia humana tipo 1. M Nevot, A Joradan-Paiz, S Franco, MA Martinez. IX Congreso Nacional GeSIDA. Vigo (Spain). 28 November - 1 December 2017. Oral presentation.

49. Modulation of HIV-1 replication capacity by synonymous mutations introduced in the gag region. M Nevot, A Joradan-Paiz, S Franco, MA Martinez. XIV Congreso Nacional de Virología. Cádiz (Spain). June 11-14. Poster presentation.

50. PASeq.org: One-click, Cloud-based Web Service for NGS-based HIV genotyping Data Analysis. Noguera M. International HIV Drug Resistance and Treatment Strategies Workshop. Johannesburg (South Africa). 8-10/11/2017. Oral presentation.

51. DNA methylation profiles identify epigenetically regulated host factors associated with immune control of HIV infection. Oriol-Tordera B, Berdasco M, Llano A, Mothe B, Carrillo J, Galvez C, Blanco J, Martinez-Picado J, Ganoza C, Clotet B, Calle ML, Sanchez-Pla A, Sanchez J, Ruiz-Riol M, Esteller M, Brander C. EMBO Conference on Epigenetics and Infection 2017. Paris (France). 13-6 to 16-6-2017. Poster presentation.

52. Plasma IP-10 levels as a surrogate of virological failure in treated HIV-patients. L. Pastor, A. Casellas, M. Rupérez, J. Carrillo, L. Luis, E. Macete, R. Paredes, J. Blanco, D. Naniche. IAS 2017 - 9th IAS Conference on HIV Science. International AIDS Society. Paris (France). 23- 26 July 2017. Poster presentation.

53. APC from human cervical mucosa express Siglec-1 and mediate viral capture via recognition of viral membrane gangliosides. Perez-Zsolt D, Cantero-Pérez J, Erkizia I, Pino M, Hernández-Gallego A, Pérez-Roca L, Lorencés I, Garrido J, Tarrats A, Martinez-Picado J, Genescà M, Izquierdo-Useros N. CSH Retroviruses. Cold Spring Harbour (USA). May 22-27, 2017. Oral presentation.

54. Activity of SAMHD1 in cycling cells permissive to HIV-1 infection. Maria Pujantell1, Roger Badia, Javier Torres-Torronteras, Luis Menéndez-Arias, Ramón Martí, Albert Ruzo, Eduardo Pauls, Bonaventura Clotet, Ester Ballana, and José A. Esté, Eva Riveira-Muñoz. ICAR 2017. Atlanta (USA).

55. Inflammatory and Regulatory Cytokine Profiles in HIV+-to-HIV+ Renal Transplant Recipients. Stefan Rautenbach, Marta Marszalek, Christian Brander, Sandra Silvia-Arrieta, Guadalupe Gómez, Marta Bofill, Alex Sanchez, Elmi Muller, Clive M. Gray. European Immunogenetics and Histocompatibility Conference 2017. Mannheim (Germany). 30-5 to 2-6-2017. Poster presentation.

56. Impacto de los polimorfismos rs1799864 y rs1801157 en los genes CCR2 y CXCL12 en la baja recuperación inmunológica de pacientes VIH+ con tratamiento antirretroviral exitoso. Rallón N, Resino S, Blanco J, Pacheco Y, Benito JL. IX Congreso Nacional GeSIDA. Vigo (Spain). 28 November- 1 December 2017. Poster presentation.

57. Polimorfismos en los genes IFNγ e IL19 incrementan la probabilidad de respuesta inmunodiscordante en pacientes VIH+ que inician cART con bajos recuentos de CD4. Rallón N, Resino S, Blanco J, Pacheco Y, Benito JL. IX Congreso Nacional GeSIDA. Vigo (Spain).

58. Balance selection in microbiome studies. Javier Rivera. 38th Annual Conference of the International Society for Clinical Biostatistics. Vigo (Spain). 8-13/07/2017. Oral presentation.

59. Kernel regression for CoDa analysis in microbiome studies. Javier Rivera. XVI Conferencia Española de Biometría 2017. Sevilla (Spain). 13-15/09/2017. Oralpresentation.

60. Early cART of HIV-1 infected subjects preserves an=viral func=on of CD8+ T cells. Miriam Rosás, Beatriz Mothe, Gemma Hancock, Hongbing Yang, Christian Manzardo, Pep Coll, Christian Brander and Lucy Dorrell. Conference on Retroviruses and Opportunistic Infections 2017. Seattle (USA). 13-2-2017 to 16-2-2017. Poster Presentation.

61. Human Gut Microbial Gene Richness Correlates with HIV infection. Muntsa Rocafort, Marc Noguera-Julian, Yolanda Guillén, Mariona Parera, Maria Casadellà, Isabel Bravo, Josep Coll, Julià Blanco, Bonaventura Clotet, Roger Paredes. Conference on Retroviruses and Opportunistic Infections 2017. Seattle (USA). 13-2-2017 to 16-2-2017. Poster presentation.

62. Kinetics of CTL recognition of latently infected cells after HIV-1 inducible reactivation. A. Ruiz, O. Blanch-Lombarte, E. Jimenez-Moyano, R. Peña, M. Genescà, P. Goulder, B. Clotet, J. G. Prado. IX Congreso Nacional GeSIDA. Vigo (Spain). 28 November- 1 December. Poster-Oral (PO-16).

63. Rapid CTL recognition of HIV-1 latently infected cells depends on the levels of inducible viral reactivation and CTL activation status. A. Ruiz, O. Blanch-Lombarte, E. Jimenez-Moyano, R. Peña, M. Genescà, P. Goulder, B. Clotet, J. G. Prado. Nom congrés: HIV Cure & Cancer Forum. Paris (France). 22-23 July. Poster presentation (PB20#128).

64. Rapid CTL recognition of HIV-1 latently infected cells depends on the levels of inducible viral reactivation and CTL activation status. A. Ruiz, O. Blanch-Lombarte, E. Jimenez-Moyano, R. Peña, M. Genescà, P. Goulder, B. Clotet, J. G. Prado. 9th IAS Conference on HIV Science. Paris (France). 22-23 July. Poster presentation (MOLBPEA15).

65. HIV-seroreversion dynamics after allogeneic stem cell transplantation. Salgado M, González V, Rivaya B, Kwon M, Gálvez C, Nijhuis M, Bandera A, Badiola J, Jurado M, Jensen B, Kaiser R, Wensing A, Diez JL, Martinez-Picado J, for the IciStem Consortium. 8th HIV Persistence during Therapy Workshop. Miami (USA). December 12-15, 2017. Oral presentation.

66. Achievement of full donor chimerism with episodes of alloreactivity contributes to reduce the HIV reservoir after allogeneic stem cell transplantation (Abstract OA5-1). Salgado M, Kwon M, Gálvez C, Nijhuis M, Schulze zur Wiesch J, Bandera A, Knops E, Badiola J, Jensen J, Saez-Cirión A, Jurado M, Kaiser R, Hutter G, Rocha V, Kobbe G, Wensing A, Diez JL, Martinez-Picado J, for the IciStem Consortium rivera. 9th IAS Conference on HIV Science. Paris (France). July 23-26, 2017. Oral presentation.

67. Murine model to predict viral rebound in HIV+ allotransplanted subjects (Abstract 11). Salgado M, Kwon M, Galvez C, Nijhuis M, Vilaplana C, Bandera A, Badiola J, Jurado M, Wensing A, Diez JL, Martinez-Picado J, for the IciStem Consortium. 9th IAS Conference on HIV Science. Paris (France). July 23-26, 2017. Poster presentation.

68. Is it possible an HIV cure with stem cells allotransplants? Salgado M. IX Congreso Nacional GeSIDA. Vigo (Spain). November 28 - December 1, 2017. Invited speaker.

69. Productive HIV-1 infection upregulates CD32 in vitro and in vivo. Serra-Peinado C, Grau-Expósito J, Genescà M, Luque-Ballesteros L, Astorga A, Gálvez C, Castellví J, Willekens R, Ocaña I, Burgos J, Navarro J, Curran A, Ribera E, Montaner L, Falcó V, Martinez-Picado J, Buzon MJ. 8th HIV Persistence during Therapy Workshop. Miami (USA). December 12-15, 2017. Oral presentation.

70. Toxicity study in C57/BL6 mice after repeated intramuscular administration of the HIV-1 therapeutic prime-boost vaccine combination DNA.HTI and MVA.HTI. Araceli Tortajada, Caroline

Brennan, Christian Brander, Antonio Guzmán. 53th Congress of the European Societies of Toxicology. Eurtox 2017. Bratislava (Slovak Republic).10-9 to 13-9-2017. Poster Presentation.

Invited lectures

1. **Bryostatin-1 action on mature dendritic cells promotes HIV-1 reactivation of latently infected cells**. Benet S, Nieto-Garai JA, Erkizia I, Bilbao E, Prado JG, Martinez-Picado J, Lorizate M, Izquierdo-Useros N. 4th Madrid Meeting on Dendritic Cells and Macrophages. Madrid (Spain). March 27-28, 2017. Oral presentation.

2. **Definition of biomarkers and immune correlates of HIV control: implications for therapeutic HIV vaccine development**. Christian Brander. Seminar Series. Barcelona (Spain). 7-2-2017. Invited speaker.

3. **Challenges and opportunities conducting research with US NIH grant funding outside the US**. Christian Brander. NIAID, NIH Post Award Grants Policy and Management Training. Barcelona (Spain). Barcelona (Spain). 6-6-2017. Invited speaker.

4. **Viruses as DC Riders: What natural human Siglec-1 knockouts tell us about HIV-1 pathogenesis**. Izquierdo-Useros N. DC Day. Barcelona (Spain). June 6, 2017. Invited speaker.

5. **Definition of biomarkers and immune correlates of HIV control: implications for therapeutic HIV vaccine development**. Christian Brander. Ciclo de Reuniones Cientificas 2017. Lima (Perú). 6-9-2017. Invited speaker.

6. **Viruses as DC Riders: What natural human Siglec-1 knockouts tell us about HIV-1 pathogenesis**. Izquierdo-Useros N. Madrid (Spain). November 15, 2017. Invited speaker.

7. **Stem cell therapy to cure HIV infection: so close, so far.** Martinez-Picado J. Aarhus (Denmark). January 31, 2017. Invited speaker.

8. **HIV-1 or the art of teasing the immune system**. Martinez-Picado J. Hamburg (Germany). June 8, 2017. Invited speaker.

9. **HIV Immunopathogenesis**. Martinez-Picado J. Hot topics in HIV: Vaccines, Immune recovery and Eradication. Barcelona (Spain). October 5, 2017. Invited speaker.

10. **Allogeneic transplantation of hematopoietic progenitors and the cure of HIV infection**. Martinez-Picado J. Madrid (Spain). October 17, 2017. Invited speaker.

11. **Review of Previous Intensification Studies**. Martinez-Picado J. HIV Intensification workshop. Philadelphia (USA). December 5, 2017. Invited speaker.

12. **Population pharmacokinetics of romidepsin as a latency reactivating agent in HIV-infected adults.** Cristina Pérez, Marta Valle, Beatriz Mothe, Cristina Miranda, Magí Farré, Anabel Barriocanal, Christian Manzardo, Christian Brander, Bonaventura Clotet, José Moltó for the BCN02¬Romi study group. Poster presentation.

13. **Identification of relevant microbial balances using compositional data analysis**. Javier Rivera The Barcelona Debates on the Human Microbiome 2017. From Microbes to Medicines. Barcelona (Spain). 29-30/06/2017. Poster presentation.

14. **Hepatitis C Virus-related Orthotopic Liver Transplantation in HIV- and HIV+ organ Recipients**. Sandra Silva- Arrieta. Ciclo de Reuniones Cientificas 2017. Lima (Perú). 6-9-2017. Invited speaker.

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