

Scientific Career Development

Training of future generations of scientists and technologists is a priority and the CNB continues attracting young people who wish to pursue a scientific career. In the 2021-2022 period, 41 PhD students obtained competitive fellowships (e.g., INPhINIT, FPU, FPI) to realise their PhD thesis at our institute, and 45 students obtained their PhD degree under a CNB scientist's supervision. Our centre hosted 73 undergraduate and 99 master's students from Spanish and international universities, allowing them to experience first-class biotechnology research in a lab setting. In addition, 35 short-term trainees and visiting scientists chose the CNB for its outstanding training opportunities. Moreover, CNB researchers actively participate in some of the best university and master degree programmes in Spain. We have already celebrated the 8th edition of the "CNB course on introduction to research" for undergraduate students. In collaboration with the CSIC and funding from the Severo Ochoa Centres of Excellence Program, we offered fellowships to attract brilliant master students.

Our PhD training programme is fully established. The PhD Student and Training Committees, with the support of the Scientific Culture Unit, organise an annual programme of events to promote career development. In our effort to improve the excellence of the PhD Training Program, in 2023 we are launching the new Thesis Advisory Committee (TAC), based on the Salzburg Principles. This tool is established in internationally recognised research institutes, and has two main goals: (i) provide a complete individual quality assessment of PhD researchers for their professional growth and thesis achievements and (ii) help to detect earlier conflicts and problems that otherwise might truncate the thesis success and satisfaction of PhD researchers and supervisors.

Around 20% of our personnel are postdoctoral researchers, a task force that drives the excellence of our research and participate in the training of younger students. Our centre attracted 14 talented young scientists through international, national and regional calls such as Marie Skłodowska-Curie Actions from the European Commission, Juan de la Cierva, Ramón y Cajal, la Caixa Junior Leader, and Talent Attraction Programmes. At the end of 2022 we launched a new Postdoctoral Researchers Committee to improve their structure, visibility and involvement in CNB's scientific activities. In collaboration with the CNB Training Committee, they will work on the implementation of a specific Postdoctoral Training Program to enhance the career development of the scientists at this stage including soft-skills, professional career and complementary training.

TRAINING COMMITTEE

Inés Antón
Yolanda Carrasco
Sandra Fonseca
Vicente Rubio
Álvaro San Millán
Juan José Sanz
Javier Tamames
Mark van Raaij
Miguel Vicente

PHD RESEARCHERS COMMITTEE

Alfonso Aguilera
Lorena Bragg
Alberto Fuster
Margarita Ferriz
Arturo García Vesga
Sofía Gardeta
Álvaro Gómez
Andoni Gómez
Diego Jiménez
Javier López-Ibáñez

Leticia Lucero
Moisés Maestro
Iris Martínez
Kateryna Matveyeva
Santiago Michavila
Micaela Navarro
Sara Otaegi
Andrés París
Sergio Pipaon
Martín Sastre



Undergraduate and master students fellowships

CSIC introduction to Research Fellowships (JAE INTRO)

7 JAE INTRO

Irene Bragado García
Alba Carballo Castro
Gema Castillo García
Carlos Quero Dotor
Margarita Roda Herrera
Ainhoa Romo Valera
Paula Vázquez Utrilla

6 JAE INTRO ICU

Beatriz Deltoro Bernardes
Álvaro López-Maroto Quiñones
Inés Muniesa Martínez
Ismael Nizialek Puerto
Uxia Pérez de José
Adrián Sansiñena Rodríguez

6 JAE INTRO Severo Ochoa Excellence Center

Inés Carmen Almena Domínguez
Enrique Álvarez Coruña
Diego Crespo Roche
Oier Lauzirika Zarrabeitia
Ariadna Villanueva Marijuán
Marta Villarejo Torres

New PhD candidates

1 Fundacion Jesús Serra Fellowship

Ana Fernández Barrecheguren

2 Fundación La Caixa Fellowship

Alfonso Aguilera Vera
Darío López García

1 FIS Programme Ministry of Science and Innovation

Brenda Martínez Gonzalez

25 FPI Programme Ministry of Science and Innovation

Martín Albacete Rodríguez
Julio César Aragón Lago
David Astorgano López
Paula Carballeira Peñacoba
Gema Castillo García
Emma Diaz Piñero
Marta García López
Álvaro Gargantilla Becerra
Jesús Hurtado Tamayo
Daniel Alejandro Marchán Torres
Isabel Martín Blecua
Eva María Martín Cuevas
Altea Martín Martínez
Miguel Martín Salgado
Samuel Martínez Alcalá
Juan Manuel Martínez Romero
Kateryna Matveyeva
Santiago Michavila Puente-Villegas
Daniel Mora Diego
Alba Esteli Murillo Sánchez
Elena Nonnast Fornieles
Sergio Pipaón Alcibar
Juan Rivas Santisteban
Noelia Santander Acerete
Víctor Venturini Juarez

6 FPU Programme Ministry of Education, Culture and Sport

Tamara Alonso Blanco
José María Fernández Palacios
Silvia López Borrego
Sara Otaegi Ugartemendia
Cesar Palacios Cuéllar
Ángel Ruiz Enamorado

6 FPI Severo Ochoa Programme Ministry of Science and Innovation

José Manuel Aguilera Porcar
María Luz Blasco Santamaría
Francisco Javier Canalejo Molero
Adrián Fernández Rego
Alicia Lou Gracia
Eva Álvarez Medrano



Doctoral Theses

45 researchers obtained their PhD under the supervision of CNB researchers in the years 2021 and 2022.

2021

Lucía Agudo Alguibe

Aplicación de la biología de sistemas para mejorar las propiedades biotecnológicas de la cianobacteria *Arthrospira platensis*.

(Juan Nogales Enrique, José Luis García López)

Guillermo Albericio

Análisis de los mecanismos centrales de regulación de los progenitores cardíacos Bmi1+ en ratón adulto.

(Antonio Bernad, Carmen Mora)

Carolina Allende Ballesteros

Análisis estructural y aplicaciones biotecnológicas del nanocontenedor de encapsulina de *Brevibacterium linum*.

(José R. Castón, Javier María Rodríguez)

Alejandro Asensio Calavia

Engineering of *E. coli* bacteria for protein translocation into target mammalian cells and its *in vivo* application in tumor therapy.

(Luis Ángel Fernández, Beatriz Álvarez González)

Diego Carlero Carnero

Bases estructurales y moleculares de la proliferación viral. Mecanismo de replicación y transcripción en gripe A.

(Jaime Martín-Benito Romero)

Victoria Castro Illana

Cellular models of persistent hepatitis C virus infection reveal non-reversible transcriptomic alterations after infection clearance by direct-acting antiviral treatment. (Pablo Gastaminza, Celia Perales)

Sergio Díaz Díaz

Insights on the mode of inheritance of eQTLs and on the contribution of stabilizing and directional selection in shaping the evolution of the phosphate starvation transcriptome in *Arabidopsis*.

(Javier Paz-Ares)

Karolina Gmurczyk

The evolutionary analysis of Cdc13 protein between yeast exemplified by *Saccharomyces cerevisiae* and *Candida glabrata*.

(Fernando Moreno Herrero)

Guillermo Gómez García

Regulación de la secuencia de inserción ISPpu9 de *Pseudomonas putida* KT2440.

(Fernando Rojo, Renata Moreno)

Natalia González Mancha

Characterisation of SNX27 function in immune synapse formation and activation in T lymphocytes.

(Isabel Mérida)

Eva María Martín Cuevas

Discrete step analysis of DNA condensation by SMC proteins using Magnetic Tweezers.

(Fernando Moreno Herrero)

Fernando Martín Fernández

Estudio de la conectividad interhemisférica del cuerpo calloso.

(Marta Nieto López)

Natalia Martín González

Mechanics of Adenovirus: role of core proteins and environmental conditions in virion uncoating.

(Carmen San Martín, Pedro J. de Pablo)

Cristian Mateo Elizalde

Molecular mechanisms underlying arsenic tolerance and ER stress response in plants.

(Antonio Leyva)

Andrea Montero Atalaya

Análisis funcional de las variantes S192Y y R402Q del gen de la tirosinasa y su implicación en Albinismo Oculocutáneo de tipo I.

(Lluís Montoliu)

Rosa Ana Navajas Morillas

Análisis proteómico cualitativo y cuantitativo por espectrometría de masas en tándem para la identificación de biomarcadores de naturaleza proteica asociados a preeclampsia.

(Alberto Paradela)

Jesús Osuna Pérez

Mitochondria drive a bacteria-induced metabolic reprogramming in CD4+ T cells that orchestrates CD8+ T cell responses.

(Esteban Veiga Chacón)

Marta Pérez Illana

Structure of two stable, complex capsids: enteric and avian adenoviruses.

(Carmen San Martín)

Yadileiny Portilla Tundidor

Estudio de la influencia en los procesos de internalización, tráfico intracelular y biodegradación de nanopartículas superparamagnéticas de óxido de hierro de los recubrimientos empleados para su uso en biomedicina, y de la corona proteica que se forma sobre estos recubrimientos en entornos biológicos.

(Domingo F. Barber)

Sergio Rivas Muñoz

Análisis de la vía protumoral WIP-YAP/TAZ mediante proteómica y transcriptómica diferencial.

(Inés M Antón, Francisco Wandosell)



Elena Sanchez Martin-Fontecha

Mechanisms involved in the degradation of the strigolactone receptor DWARF14 in *Arabidopsis thaliana*. (Pilar Cubas)

Mateo Seoane Blanco

Structure and function of Salmonella virus epsilon15 and Campylobacter virus F358 tailspikes. (Mark J. van Raaij)

Adrián Vega Pérez

Response of peritoneal macrophages to infection and tumor metastasis. (Carlos Ardavín)

2022

Laura Broto Campo

Estudio del establecimiento de infecciones persistentes por el virus de la bursitis infecciosa. (José F. Rodríguez)

Carmen Campos Silva

Analysis of extracellular vesicles in cancer immunomodulation and liquid biopsy. (Mar Valés Gómez)

Chang-Yu Chang

Evolutionary engineering of microbial communities. (Álvaro Sánchez)

Antonie Cossa

Bacterial morphology analysis by cryo-soft X-ray tomography and cryo-(scanning) transmission electron microscopy. (José María Carazo, Carlos Oscar Sorzano, Veronique Arluison)

Cesar Omar Domínguez Márquez

Spatial confinement of an ethanologenic route into *Bacillus subtilis* functional membrane microdomains to improve ethanol bioproduction. (Daniel López)

Alberto Fernández Oliva

De la biología celular a los tratamientos antivirales: Estudio del flujo de lípidos y la dinámica mitocondrial como dianas terapéuticas frente a bunyavirus. (Cristina Risco Ortiz)

Alberto Fuster Pons

Disección genómica y ambiental de la variación natural para el patrón de tricomas en Cardamine. (Carlos Alonso Blanco)

Raquel García Ferreras

Mecanismos moleculares y aplicaciones terapéuticas de la transfagocitosis mediada por linfocitos. (Esteban Veiga Chacón)

Arturo García Vesga

Single molecule optical microscopy for the quantitative study of protein-lipid interactions. (Jose Requejo-Isidro)

José Manuel Honrubia Belenguer

Relevancia del motivo PBM de la proteína E en la replicación y virulencia de los coronavirus. (Luis Enjuanes, F. Javier Gutierrez Alvarez)

Pablo Laborda Martínez

Understanding evolution to tackle antibiotic resistance in *Pseudomonas aeruginosa*. (José Luis Martínez, Sara Hernando-Amado)

Aleksandra Lazarova

Modulación de la actividad de iyo y rima para entender la autorrenovación y diferenciación de células madre en plantas. (Enrique Rojo)

Bran López Luengo

Acción de las oxilipinas en la inmunidad vegetal: nuevos integrantes en las rutas de señalización. (Carmen Castresana)

Moisés Maestro López

Biochemical and structural characterization of a complex involved in chaperone mediated proteasomal degradation. (Jorge Cuéllar, José M. Valpuesta)

Javier Mendía García

Hybrid single-stranded – double stranded DNA substrates for magnetic tweezers experiments. (Fernando Moreno Herrero, Francisco de Asis Balaguer Pérez)

Elena Pedrero Vega

Caracterización del fenotipo de semi-dependencia a antibióticos ribosomales en un aislado clínico de *Staphylococcus aureus*. (Daniel López)

David Střelák

Acceleration of image processing algorithms for single particle analysis by electron microscopy. (José María Carazo, Carlos Oscar Sorzano, Ludek Matyska)

Amaia Talavera Gutiérrez

A study of the Death-Inducer Obliterator (Dido) function in somatic cell reprogramming to pluripotency. (Carlos Martínez-A)

Elena Velázquez Muñoz

Recombination-independent genomic editing and Chromosomal site-focused diversification of Gram-negative bacteria. (Víctor de Lorenzo)

Jean CC Vila

On the evolutionary ecology of microbial metabolic niche construction. (Álvaro Sánchez)

Li Wang

Human coronavirus-host interactions: pathogenesis and antiviral response. (Sonia Zúñiga, Luis Enjuanes)

Pablo Yubero Bernabé

Trade-offs in the architecture and predictability of complex phenotypes. (Juan F Poyatos)

Postdoctoral and Research Fellows

In the last two years, our center has attracted 14 early career researchers through international, national and regional calls such as Marie Skłodowska Curie Actions, from the European Commission, Juan de la Cierva, Ramón y Cajal and Talent Attraction Programmes.

3 RAMON Y CAJAL PROGRAMME

Ministry of Science and Innovation

Selena Giménez Ibañez
Esther Ortega Portero
Pablo David Scodeller

4 MARIE SKLODOWSKA CURIE ACTIONS

European Commission

Eduardo González Grandío
James Michael Krieger
Sonia Marcela Villegas Plazas
Marta Ukleja

5 JUAN DE LA CIERVA PROGRAMME

Ministry of Science and Innovation

Francisco de Asís Balaguer Pérez
Lara Del Campo Milán
Rafael Laso Pérez
Elena Pajares Martínez
Alonso Sánchez Cruz

2 LA CAIXA JUNIOR LEADER PhD FELLOWSHIPS

La Caixa Foundation

Cristina Díez Vives
Alfonso Santos López

4 FUNDACIÓN JESÚS SERRA FELLOWSHIPS

María Antonia Ávila
James Pelletier
Luis Seoane
Adrián Valli

1 AECC FOUNDATION FELLOWSHIP

Alejandra Gutiérrez



Biophysical studies on synthetic oligomeric proteins to correlate cooperativity, binding and macromolecular assembly

Luis Alberto Campos Prieto

Ramón y Cajal Fellow

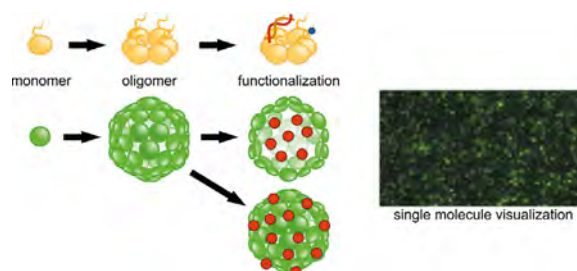
MASTER STUDENT

Ana Paula Lóbez

Proteins are involved in the majority of biological events, forming macromolecular assemblies with sometimes complex geometrical structures. In recent years, big efforts have been made in the design of non-natural protein assemblies with new geometries and functionalities for multiple applications.

I have focused my scientific interest in the rationalized modification of proteins to obtain designed assemblies. Thus, I have created a synthetic hexameric ring by mutations of a monomeric protein, which can be regulated using different activators, and studied their functionalization with different molecules. Finally, I have designed modified viral capsids, useful for delivery. These models have been fluorescently labelled for dynamic and structural experiments using single molecule techniques.

Scheme representing the designed oligomerisation and functionalisation of de novo hexamers (top) and modified viral capsids (bottom). All processes can be followed by single molecule techniques (right).



SELECTED PUBLICATION

Campos LA. Mutational analysis of protein folding transition states: phi values. *Methods Mol Biol* 2022, 2376: 3-30.



Light signalling and plant adaptation to the environment

Sandra Fonseca

2021, Ramón y Cajal Fellow
2022, Investigador Distinguido

PhD RESEARCHERS
(Co-supervised with Vicente Rubio)

Esther Cañibano
Martín Albacete

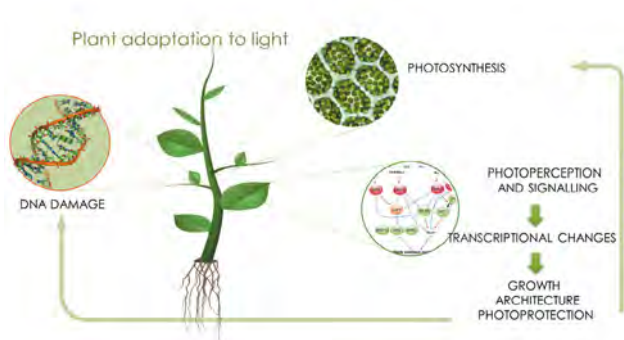
MASTER STUDENT

Alexandra Oliveira

UNDERGRADUATE STUDENT

Alicia Arenas

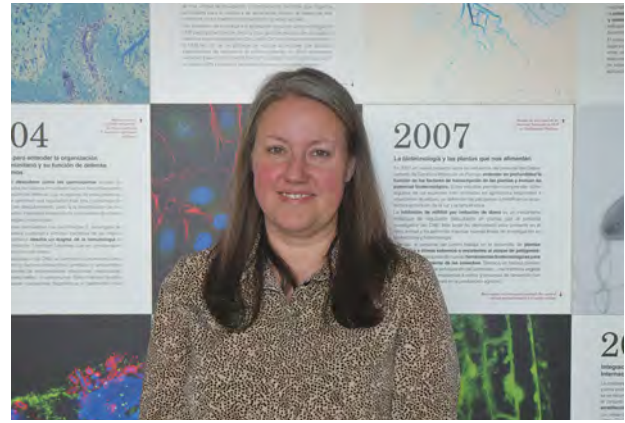
As sessile photoautotrophic organisms, plants evolved sophisticated strategies to perceive light environmental signals and to transduce them into molecular signalling networks. Though light is essential for plant growth and development, often plants have to cope with damaging or excessive light conditions, which generate stress and limits growth. We aim to understand the molecular mechanisms that allow plants to integrate beneficial and damaging effects of light and respond to them with striking plasticity. We are especially interested in the events that lead to coordinated transcriptional changes during light adaptation as changes in chromatin states, transcription factor stability and protein homeostasis. To understand the molecular mechanisms that coordinate these processes we are using genetic, genomic, biochemical and proteomic tools.



SELECTED PUBLICATIONS

Cañibano E, Bourbousse C, Garcia-Leon M, Wolf L, Garcia-Baudino C, *et al*. DET1-mediated COP1 regulation avoids HY5 activity over second-site targets to tune plant photomorphogenesis. *Mol Plant* 2021, 14(6): 963-982.

Lee B-D, Yim Y, Cañibano, E, Kim S-H, García-León M, *et al*. CONSTITUTIVELY PHOTOMORPHOGENIC1 promotes seed germination by destabilizing RGA-LIKE2 in Arabidopsis. *Plant Physiol* 2022, 189(3): 1662-1676.



Molecular mechanisms regulating plant resistance against phytopathogenic bacteria

Selena Giménez-Ibáñez

Ramón y Cajal Fellow

POSTDOCTORAL RESEARCHER

Loreto Espinosa Cores

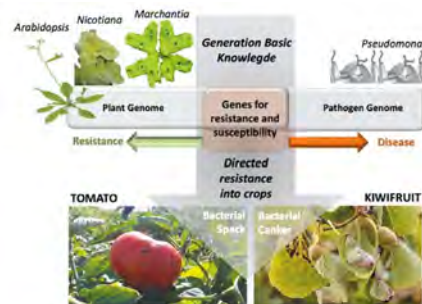
PhD RESEARCHER

(Co-directed with R. Solano)

Santiago Michavila

Our research uses on one side, model plants such as *Arabidopsis* and the liverwort *Marchantia*, to uncover the basic molecular mechanisms controlling hormonal plant immunity and how *Pseudomonas* bacteria infects hosts through its repertoire of effectors and phytotoxins. On the other side, this generated basic knowledge is directed to study these processes on crops, and to deliver novel strategies for crop protection against two of the most important disease caused by phytopathogenic *Pseudomonas*, the bacterial speck disease of tomato, caused by *P. syringae* pv. *tomato*, and the bacterial canker of kiwifruit, caused by *P. syringae* pv. *actinidiae*, by using biotechnology, genome editing, genetic breeding and searching for anti-infective potential novel chemicals among others.

Research Workflow of Molecular Mechanisms Regulating Plant Resistance Against Phytopathogenic Bacteria

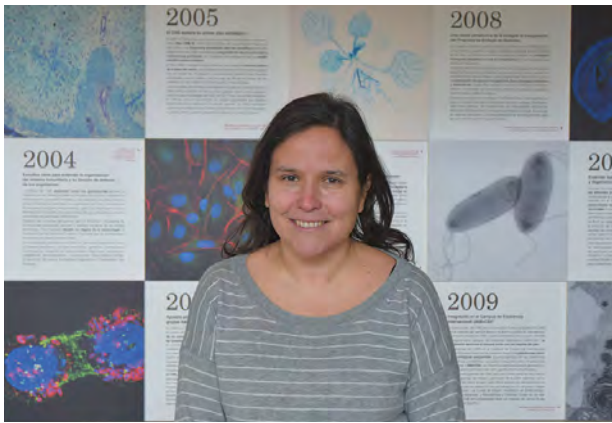


SELECTED PUBLICATIONS

Pardal AJ, Piquerez SJM, Dominguez-Ferreras A, Frungillo L, Mastorakis E, *et al*. Immunity onset alters plant chromatin and utilizes EDA16 to regulate oxidative homeostasis. *PLOS Pathog* 2021, 17(5):e1009572.

Gimenez-Ibanez S, Espinosa-Cores L, Solano R. Reversible acetylation fine-tunes plant hormone signaling and immunity. *Mol Plant* 2022, 15(9):1415-1417.

Redkar A, Gimenez Ibanez S, Sabale M, Zechmann B, Solano R, Di Pietro A. *Marchantia polymorpha* model reveals conserved infection mechanisms in the vascular wilt fungal pathogen *Fusarium oxysporum*. *New Phytologist*, 2022, 234(1):227-241.



Effect of viral and host factors on innate immunity, respiratory virus replication and pathogenesis

Marta López de Diego

Atracción de Talento Fellow

POSTDOCTORAL RESEARCHERS

Vanessa Rivero Perdomo

Raúl López Fernandez

Laura Villamayor Coronado

TECHNICIAN

Sandra Gómez López

PHD RESEARCHERS

Darío López García

Paula Vázquez Utrilla

UNDERGRADUATE STUDENT

Laura Palomo Sánchez-Grande

Influenza viruses and coronaviruses are respiratory pathogens causing drastic health and economic consequences for many animal species, including humans.

In our group we analyse virus host-interactions, particularly the innate immune responses induced after respiratory virus infections, since these host responses affect viral replication and pathogenesis. Our final goal is to use the knowledge generated to develop new antivirals to fight these and other viral infections, and to analyse viral and host genetic factors affecting the severity of respiratory virus diseases. As such we are (i) analysing the cellular functions of interferon-stimulated genes and the effect of these genes on virus infections, (ii) studying the functional effects of mutations on influenza virulence genes on virus replication, and pathogenesis, (iii) evaluating the effect of genetic polymorphisms on innate immune response genes in the severity of viral diseases, and (iv) developing antivirals targeting innate immune response proteins and viral proteins.

SELECTED PUBLICATIONS

Saiz ML, DeDiego ML, López-García D, Corte-Iglesias V, Baragaño Raneros A, *et al.* Epigenetic targeting of the ACE2 and NRP1 viral receptors limits SARS-CoV-2 infectivity. *Clin Epigenetics* 2021, 13(1):187.

Nogales A, Villamayor L, Utrilla-Trigo S, Ortega J, Martínez-Sobrido L, DeDiego ML. Natural selection of H5N1 avian influenza A viruses with increased PA-X and NS1 shutoff activity. *Viruses* 2021, 13(9):1760.

Chiem K, Martínez-Sobrido L, Nogales A, DeDiego ML. Amino acid residues involved in inhibition of host gene expression by influenza A/Brevig mission/1/1918 PA-X. *Microorganisms* 2021, 9(5):1109.

DeDiego ML, Portilla Y, Daviu N, López-García D, Villamayor L, *et al.* Iron oxide and iron oxyhydroxide nanoparticles impair SARS-CoV-2 infection of cultured cells. *J Nanobiotechnology* 2022, 20(1):352.

Chiem K, López-García D, Ortega J, Martínez-Sobrido L, DeDiego ML, Nogales A. Identification of amino acid residues required for inhibition of host gene expression by influenza virus A/Viet Nam/1203/2004 H5N1 PA-X. *J Virol* 2022, 96(5):e0040821.



Molecular mechanisms of transcription-replication conflicts (TRCs) in eukaryotes

Esther Ortega

Ramón y Cajal Fellow

TECHNICIAN

Eduardo Muñoz

PHD RESEARCHER

Jose Manuel Aguilera

MASTER STUDENTS

Chiara Saccanis

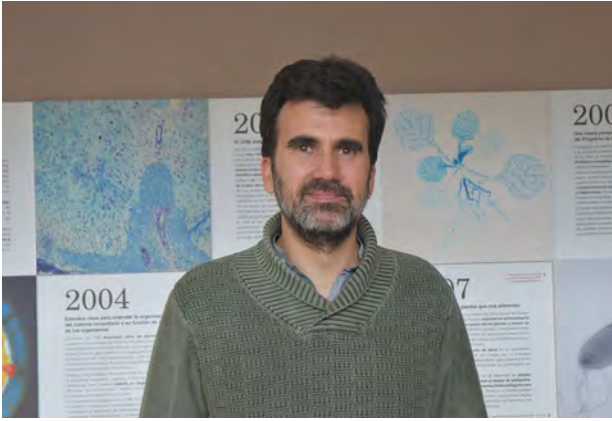
Zisis Millioris

Our group has been established in 2021 and aims to understand the molecular established mechanisms that maintain eukaryotic genome stability during DNA replication, using a combination of biochemical, biophysical, cellular and structural techniques.

DNA replication and RNA transcription are two essential processes required for accurate cell function and the propagation of genetic information. As both machineries need to access to the same DNA substrate, efficient coordination between these two processes is essential to maintain the integrity of the genome. However, these machineries can meet in space and time, causing transcription-replication conflicts (TRCs), which are a main cause of genomic instability. In eukaryotic organisms, TRCs interfere with the progression and stability of the replication forks and also trigger the accumulation of dangerous recombinant DNA structures (as R-loops) which slows down or stalls replication forks due to the physical impediments that prevents its advance. Stalled forks are a threat for DNA duplication and genome stability, causing neurodegeneration and cancer. Our group is focused on understanding the role of several factors important in the resolution of TRCs. We aim to elucidate how human Senataxin and PCNA_unloading complexes protect the integrity of the replication machinery and resolve R-loops structures formed during these TRCs.

SELECTED PUBLICATION

Cvetkovic M.A, Ortega E, Bellelli R, Costa A. Multiple roles of Pol epsilon in eukaryotic chromosome replication. *Biochem SocTrans* 2022, 50(1): 309–320.



Chloroplast protein quality control (chloroquality)

Pablo Pulido

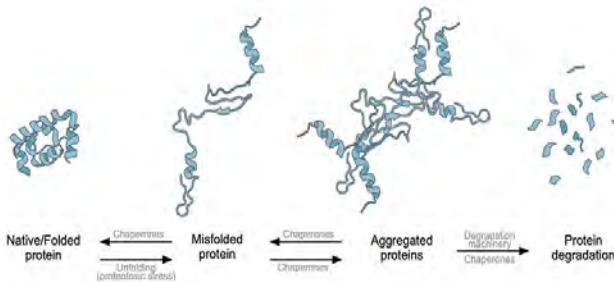
Atracción de Talento Fellow

POSTDOCTORAL RESEARCHERS

Bran Lopez Luengo
Jorge Vicente Conde

Protein quality control (PQC) systems are formed by chaperones and proteases that together regulate the correct folding and activity of proteins in every compartment of the cell, including chloroplasts. Misfolded or aggregated proteins are either recycled by chaperones (such as DNAJ and HSP70) or degraded by proteases (such as CLP) in chloroplasts. In our group we aim to elucidate and engineer the molecular machinery that protect proteins in chloroplasts allowing plants to cope with adverse environmental conditions such as high temperature or drought. These abiotic stresses are the leading cause of yield loss in crops in the current context of climate change.

Currently we are focused on the study of chloroplast DNAJE type of assembly factors of photosynthetic complexes and their role in plant stress tolerance. Besides, we have identified novel components of the chloroplast-to-nucleus retrograde signalling pathway that regulate plant survival under protein aggregation within the organelle



SELECTED PUBLICATION

Llamas E, Pulido P. A proteostasis network safeguards the chloroplast proteome. *Essays Biochem* 2022, EBC20210058.

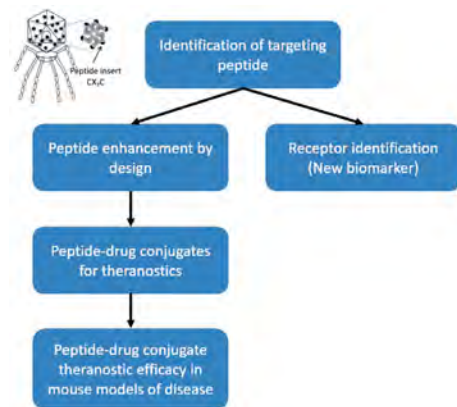


Peptide-guided theranostics

Pablo Scodeller

Ramón y Cajal Fellow

Targeting peptides can be used to carry relevant cargo to specific tissue or cells in the disease, to improve treatment and diagnosis. Targeting peptides provide selectivity, versatility, deep tissue penetration, low immunogenicity and ease and low cost of synthesis. The aim of the Peptide-Guided Theranostics Lab is to identify new targeting peptides and perform precision delivery for cancer, immunomodulation, and Alzheimer's disease, by designing peptide-guided theranostics that can be translated to the clinic.



SELECTED PUBLICATIONS

Figueiredo P, Lepland A, Scodeller P, Fontana F, Torrieri G, *et al.* Peptide-guided resiquimod-loaded lignin nanoparticles convert tumor-associated macrophages from M2 to M1 phenotype for enhanced chemotherapy. *Acta Biomater* 2021 133: 231-243.

Ewert KK, Scodeller P, Simón-Gracia L, Steffes VM, Wonder EA, *et al.* Cationic liposomes as vectors for nucleic acid and hydrophobic drug therapeutics. *Pharmaceutics* 2021, 13(9): 1365.

Lepland A, Malfanti A, Haljasorg U, Ascituo EK, Pickholz M, *et al.* Depletion of mannose receptor-positive tumor-associated macrophages via a peptide-targeted star-shaped polyglutamate inhibits breast cancer progression in mice. *Cancer Res Comms* 2022, crcres.0043.2022.

Simón-Gracia L, Scodeller P, Fisher WS, Sidorenko V, Steffes VM, *et al.* Paclitaxel-Loaded cationic fluid lipid nanodiscs and liposomes with brush-conformation peg chains penetrate breast tumors and trigger Caspase-3 activation. *ACS Appl Mater Interfaces* 2022, 14(51): 56613-56622.

Simón-Gracia L, Loisel S, Sidorenko V, Scodeller P, Parizot C, *et al.* Preclinical validation of tumor-penetrating and interfering peptides against Chronic Lymphocytic Leukemia. *Mol Pharm* 2022, 19(3): 895-903 .



Plant-virus coevolution

Adrian A. Valli

Ramón y Cajal Fellow

MASTER STUDENT

Alberto Angulo Roiz

TECHNICIAN

Irene Gonzalo Magro

UNDERGRADUATE STUDENT

Adrian Zhou

PhD RESEARCHERS

Rafael García López

Alfonso González de Prádena

(co-supervised with JA García)

Our group studies plant-virus coevolution with the aim of (i) understanding the arms race taking place when viruses infect plants, (iii) discovering new layers of antiviral responses exerted by hosts, and (ii) developing innovative strategies to fight viruses affecting the production of relevant crops. To do that, we pay special attention to RNA viruses of the *Potyviridae* family, the most relevant group of plant RNA viruses. For studies carried out over the last two years, we follow a multidisciplinary approach that includes (i) synthetic biology to build and manipulate viral infectious clones; (ii) genomics/transcriptomics studies aiming to decipher the effects of plants over viruses, and vice versa; (iii) metabolomics studies by HPLC-MS/MS to untangle plant physiological changes due to viral diseases, (iv) viral ecology to understand the interaction occurring between plants and viruses in the field.

Some of our recent findings are:

- The host-specific role of viral-derived ITPases expressed by potyvirids infecting plants from the *Euphorbiaceae* family in nature.
- The potential antiviral activity of non-canonical nucleotides produced by plants.
- The presence of an inheritable antiviral RNA-based immune system against pararetroviruses in certain plants.

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SELECTED PUBLICATIONS

Valli A, García Lopez R, Ribaya M, Martínez FJ, García Gómez D, *et al.* Maf/ham1-like pyrophosphatases of non-canonical nucleotides are host-specific partners of viral RNA-dependent RNA polymerases. *PLOS Pathog* 2022, 18(2): e1010332.

Valli A, Gonzalo I, Sanchez D. Rearranged endogenized plant pararetroviruses as evidence of heritable RNA-based immunity. *Mol Biol Evol* 2022, 40(1):msac240.