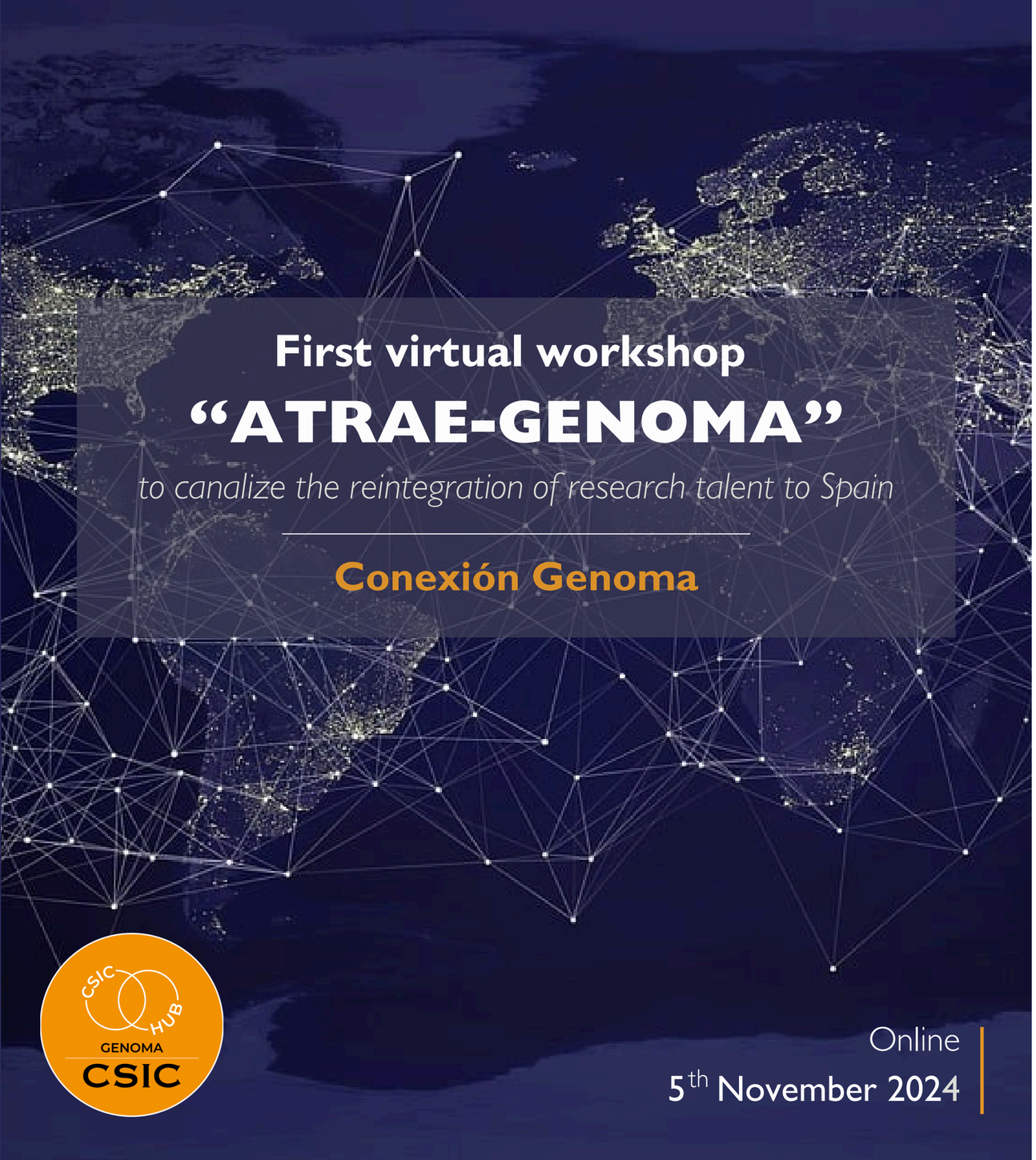

First virtual workshop

"ATRAE-GENOMA"

to canalize the reintegration of research talent to Spain

Conexión Genoma

CSIC HUB GENOMA CSIC

Online

5th November 2024

PROGRAMME

10:00 - 10:10 **Welcoming and workshop presentation**
Crisanto Gutiérrez (CBMSO) and **Josefa González** (IBB)

Session I: Biotechnology and evolution

Chairs: Mar Castellano (CBPG) and Lluis Montoliu (CNB)

10:10 - 10:40 **Laura Gómez Valero** | Institut Pasteur (France)
From amoeba to humans: the emergence and evolution of waterborne pathogens

10:40 - 11:10 **Maria Leyva** | Agriculture and Food Development Authority (Ireland)
TBD

11:10 - 11:40 **Coffee break**

11:40 - 12:10 **Ana Catalán** | Ludwig Maximilians University (Germany)
The genomic basis of adaptations

12:10 - 12:40 **Sergio Menchero** | The Francis Crick Institute (UK)
One organism, multiple clocks: Understanding asynchronous development in evolution and restrictive environments

12:40 - 13:10 **Miriam Merenciano** | Laboratory of Biometry and Evolutionary Biology (France)
Exploring the role of transposable elements in adaptation and lifespan

13:10 - 14:30 **Lunch break**

Session 2: Biomedicine

Chairs: Chairs: Nuria Flames (IBV) and Alvaro Rada (IBBTEC)

14:30 - 15:00 **Luís Arnes** | University of Copenhagen (Denmark)
Pancreas Cell Plasticity: How Developmental Regulators Fuel Pancreatic Cancer's Onset and Spread

15:00 - 15:30 **Beatrice Borsari** | Yale University (EEUU)
Bridging the genome-phenome gap with multi-scale molecular, cellular, and digital traits

15:30 - 16:00 **Lorena Aguilar Arnal** | Instituto de Investigaciones Biomédicas (Mexico)
Dissecting the role of NAD+ metabolism in regulating dynamic gene expression programs

16:00 - 16:30 **Samuel Peña-Llopis** | University Hospital Essen (Germany)
Translational Genomics in kidney cancer and uveal melanoma

SPEAKERS

Laura Gómez Valero | Institut Pasteur (France)

Throughout my entire scientific career, I have consistently combined the use of both in-silico and experimental approaches to study bacterial genome evolution. Before and during my PhD, I analyzed the genome evolution of various endosymbiotic and pathogenic bacteria. My work on these organisms contributed to explaining the tempo and mode of genomic reduction that free-living bacteria undergo when becoming intracellular organisms. Later, during my postdoctoral research at Institut Pasteur, I continued working on genome analysis, particularly focusing on the bacterial pathogens Legionella. During this time, I started to address evolutionary and epidemiological questions at both intra- and interspecific level. Since then, my research has primarily focused on Legionella genomics using both in-silico and wet lab biology techniques. My research work allowed me to obtain a research position at Institut Pasteur through a competitive recruitment process and where I conduct my research since then. Among other discoveries, my work has revealed an unexpectedly large and unique repository of secreted proteins containing eukaryotic-like elements in the Legionella genus that have been acquired from organisms belonging to different domains of life. This finding has provided insight into how reshuffling and gene acquisition from environmental eukaryotic hosts may contribute to the emergence of human pathogens. Furthermore, my results have given guidance to projects for the entire lab and also other labs around the world. Recently, I initiated a new project based on genomics and metagenomics analyses to better understand the evolution of Legionella and its genome in the environment. This project aims to decipher the impact of microbiome and water parameters on Legionella, as well as on other opportunistic waterborne pathogens such as Pseudomonas and Nontuberculous mycobacteria. The main question we want to address is: what are the relationships between bacteria, fungi and protists that constitute the drinking water microbiome, and what is the impact of key physiochemical water parameters? We want to answer this question reaching the characterization of the water microbiome at species level and studding their associated genomic traits. We will also isolate amoeba, known host of waterborne pathogens, to specifically study their microbiome and horizontal gene transfer events among amoeba related organisms. The knowledge acquired from this research will provide a better understanding of the threat microbes may present in drinking water. Considering also the accelerated pace of climatic change, the data obtained will be essential to understand how microbial communities change in response to environmental and disaster stress and the implications this might have on human health.

Ana Catalán | Ludwig Maximilians University (Germany)

I am an evolutionary biologist using genomics and transcriptomics to unravel the evolutionary forces shaping genomes and traits. I have gathered international research experience and have a deep knowledge in molecular biology and bioinformatics. I have been awarded several research grants which have served me to develop a novel system, which focuses on research in fireflies, to investigate evolutionary patterns. Fireflies, bioluminescent beetles, are popular but understudied insects.

I am generating genomic resources of European and Neotropical species to investigate the genomic architecture of key innovations, demographic history and local adaptation events and to fit models on species delimitation. Overall, I am working on generating an integrative research approach, merging genomics, transcriptomics, morphometrics and natural history, for the study of genomes and phenotypes.

Sergio Menchero Fernández | The Francis Crick Institute (UK)

Developmental biology has been the common denominator of my academic career guided by different transcriptomic, epigenomic and evolutionary perspectives. During my PhD studies in Miguel Manzanares' laboratory (CNIC, Madrid), I focused on early mouse development and how the totipotent embryo transitions until the first lineages are segregated (Rayon, Menchero et al. 2016; Menchero et al. 2019). As a postdoc, I moved to James Turner's laboratory at the Francis Crick Institute (London, UK) to work on X-chromosome inactivation in marsupials as a paradigm to study epigenomic regulation and convergent evolution (Courtois, Menchero et al, unpublished). While learning about marsupial development, I became interested in their quick development and how they prioritise the differentiation of specific tissues relevant for the immediate survival of neonates. I characterised these temporal shifts of development in the opossum, Monodelphis domestica (Menchero et al, 2024, preprint).

My future work aims to elucidate the mechanisms that make embryos allocate more resources to the more relevant tissues for their survival. Understanding how embryos overcome developmental constraints could impact our insight into the connection between embryo development and the environment. In eutherians, including humans, the exposure of embryos to constricting environments also leads to asynchronous development and restricted growth. In response, the embryo prioritises the development of key organs in a process known as organ sparing. I will combine work in opossums and in a mouse model of intrauterine growth restriction to understand the strategies that have evolved in mammals to develop under restrictive conditions and that could be relevant for human health.

Miriam Merenciano | Laboratory of Biometry and Evolutionary Biology (France)

I did a Ph.D. in Genetics at the Institute of Evolutionary Biology (IBE-CSIC) under the supervision of Dr. Josefa González. Following a postdoctoral position at IBE from 2020 to 2021, I joined the Laboratory of Biometry and Evolutionary Biology (LBBE, France) in 2022 to work with Dr. Cristina Vieira. In the same year, I was awarded a Marie Sklodowska-Curie postdoctoral fellowship (MSCA), which allowed me to continue my research at LBBE up to the present. Throughout my research career, I have focused on the role of transposable elements (TE) in adaptation and longevity. I found that a specific TE element of the fruit fly Drosophila melanogaster confers resistance to cold and bacterial infection. To support these findings, I developed a methodology for precisely deleting TE insertions from natural populations using the CRISPR/Cas9 homology-directed repair technique. Additionally, I have investigated the role of age-related misregulation of Y chromosome-associated TEs in the sex gap in longevity between males and females across different Drosophila species and humans. Currently, I am interested in exploring the role of TEs in the rapid invasion of the crop pest D. suzukii and investigating whether TEs are involved in transgenerational epigenetic inheritance of adaptive traits in this species. Furthermore, I am collaborating on the international citizen science project Melanogaster Catch the Fly!, which is the first European citizen science network focused on the genomics of adaptation.

Luís Arnes | University of Copenhagen (Denmark)

My research interests center on understanding pancreatic cellular plasticity in the contexts of development and disease. During my postdoctoral studies, I discovered that noncoding RNAs emerging from enhancer elements are essential for the specification of pancreatic lineages. This finding introduced a paradigm shift in pancreatic developmental studies and was among the first to identify noncoding RNA regulators of lineage specification. These studies sparked my interest in exploring the role of pervasively transcribed RNA molecules in gene expression, genome organization, and cell fate decisions.

By integrating molecular and computational biology, I demonstrated that cellular states in pancreatic cancer are dynamic and that noncoding RNAs regulate the transitions between these states, each with distinct tumor-propagating capacities and clinical response.

In 2019, I established my laboratory at the University of Copenhagen. Over the past five years, I have built a strong scientific program embedded within Denmark's translational pancreatic research ecosystem. We have developed preclinical models to study various aspects of pancreatic physiology in both homeostatic and pathological states, using a range of tools, including mouse genetics, human pluripotent stem cells (hPSCs), human tissue explants, and organoids. My group's research focuses on two major areas:

- Pancreatic cell plasticity: Tissue dynamics in fibrosis and cancer.
- Regulation of gene expression by noncoding RNAs: The interplay between transcription and genome organization in determining cell fate.

Our mission is to identify the molecular underpinnings of cell fate decisions in pancreas regeneration and cancer, which will provide us with better tools to identify early-stage lesions and to develop novel and more specific targets with therapeutic potential. I envision that targeting cellular plasticity will allow preventive and targeted therapy. We collaborate with oncologists and pathologists to shape our research according to patient needs and translate our findings to clinical settings.

Beatrice Borsari | Yale University (EEUU)

I obtained my BSc in Biotechnology and MSc in Bioinformatics from Università di Bologna, Italy (2014 and 2016), and my PhD in Biomedicine from Universitat Pompeu Fabra, Spain (2021). My doctoral thesis, supervised by Dr. Roderic Guigó at the Centre for Genomic Regulation (CRG), focused on the impact of the epigenome on gene regulatory programs during tissue development and cell diQerentiation. During my PhD I have also served as the principal data analyst for the CRG team within the ENCODE Consortium. After completing my PhD, I went on to receive postdoctoral training in the lab of Dr. Mark Gerstein at Yale University (USA, 2022-present). Here I co-led the ENCODE-GTEx project (EN-TEx), which released the first multi-tissue personal epigenomes of four human donors. In the framework of this project, I also developed transferQTL, a machine learning model that predicts the activity of expression quantitative trait loci (eQTLs) across multiple tissues, oQering insights into tissues like the heart and lungs which are often challenging to study due to their limited availability. Additionally, I currently participate in two international consortia: the Impact of Genome Variation on Function and the developmental Genotype Tissue Expression projects.

Over the last years, substantial eQorts have focused on decoding genomic information to improve our understanding of human biology and disease. Furthermore, as the cost of genome sequencing keeps decreasing, we expect that personalized genomics will soon guide clinical decisions and therapeutic approaches. Consequently, it is important to fully understand how the instructions encoded in the genome translate into specific organismal traits and diseases (i.e., macroscopic phenotypes). My research focuses on two complementary aspects of (epi)genome biology to accelerate the use of personalized genomics in the biomedical field:

- Exploring the broader influence of the epigenome on cellular biology beyond gene regulation, focusing on the crosstalk between epigenetic marks and cellular metabolism.
- Investigating the relationship between genetic variants, endophenotypes, and macrophenotypes. I aim to explore the interplay between genetics, behavioral traits, and neuropsychiatric disorders by utilizing digital phenotypes collected from wearable devices.

Lorena Aguilar Arnal | Instituto de Investigaciones Biomédicas (Mexico)

I have researched and published extensively on mechanisms of metabolic control, with a particular focus on transcriptional and epigenetic regulation in highly dynamic biological systems, such as circadian rhythms and cellular differentiation. As PI or Co-Investigator on several national and international funded projects, together with my team we have uncovered critical molecular mechanisms of energy metabolism control at the transcriptional level. Using mouse models, I led several projects to decipher links between metabolism and circadian gene expression, and recently defined that the hepatic content of the metabolite dinucleotide of nicotinamide and adenine (NAD+) is a druggable target to correct obesity-associated metabolic diseases, as it can synchronize the hepatic molecular clock and reinforce circadian rhythms in transcription. Metabolic diseases are an intense subject of research in my lab, and we recently uncover a connection between the 3D architecture of the genome and the development of fatty liver disease, mediated by a molecular interplay between the circadian clock and lipid-responsive transcription factors such as CEBPb. Furthermore, we have acquired solid expertise in single-cell approaches. At this regard, we have recently disentangled subcellular properties of redox metabolism regulating the progress of adipogenic differentiation from human primary cells, using advanced molecular biology and microscopy techniques with a multidisciplinary approach. We have also successfully implemented and analyzed scRNAseq experiments in embryonic stem cells and neural progenitors to decipher cellular heterogeneity imposed by the NAD+-dependent histone deacetylase SIRT1, which controls metabolic transitions in neurogenesis, and we plan to expand this knowledge to understand the developing brain using human midbrain organoids (unpublished data). I aim to continue working on these lines of research, defining molecular connections between metabolism, epigenetic regulation and transcriptional control in mammals, using advanced techniques and multidisciplinary approaches in close collaboration with experts in different fields.

Samuel Peña-Llopis | University Hospital Essen (Germany)

Dr. Samuel Peña-Llopis is a Group Leader in Translational Genomics at University Hospital Essen, Germany. He was formerly postdoc at Harvard University, UT Southwestern Medical Center (UTSW) and the German Cancer Research Center (DKFZ). His research team focuses on elucidating the aggressiveness and vulnerabilities of tumors with mutations in the epigenetic modifier BAP1 using a combination of bioinformatics, molecular biology and pre-clinical model approaches using patient-derived tumor organoids to identify novel therapies with the aim of translating them into the clinic.