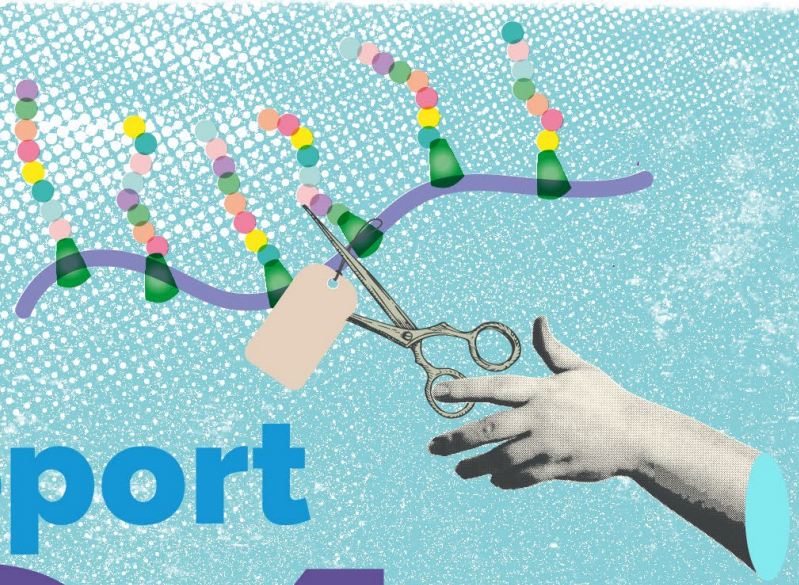
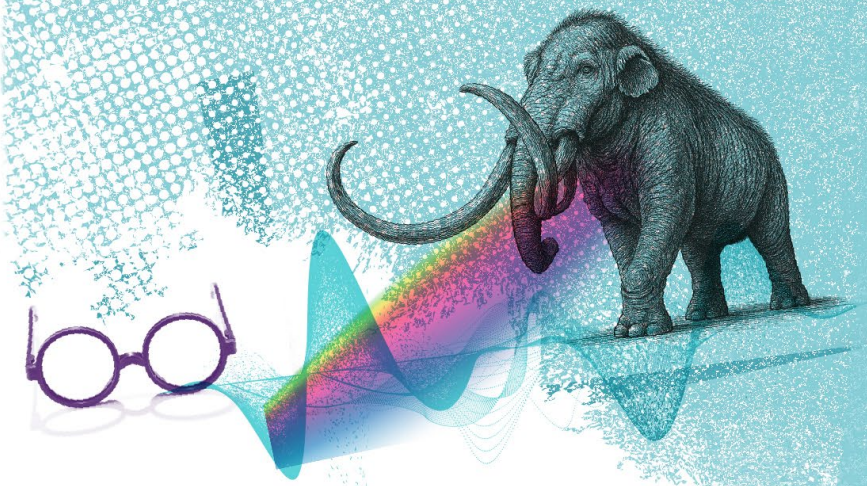
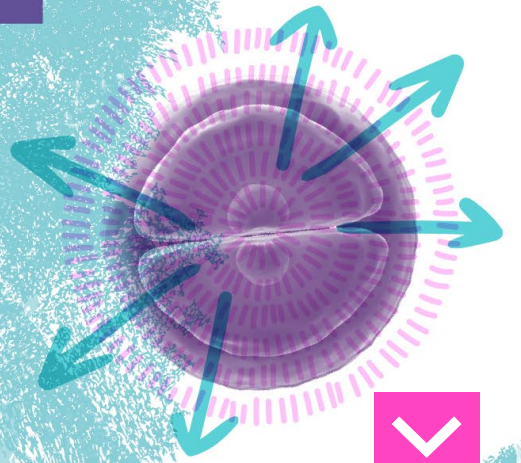


Annual Report 2024





EXCELENCIA SEVERO OCHOA

CRG Centre de Regulació Genòmica

CERCA Centres de Recerca de Catalunya

Close

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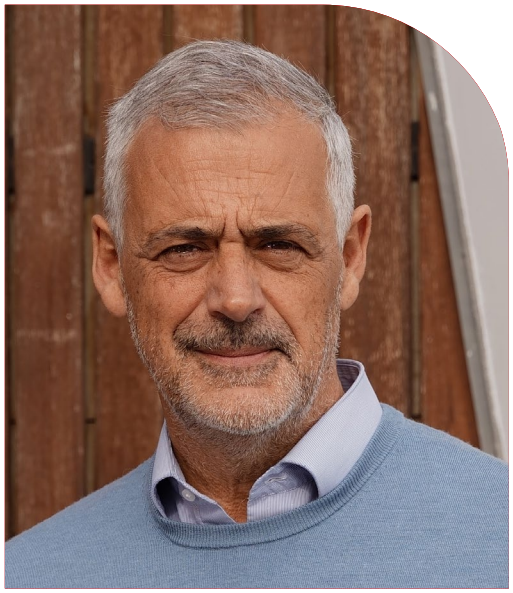
Foreword

Luis Serrano
DIRECTOR



The past twelve months have once again underscored the CRG's ability to turn bold ideas into concrete advances. Building on the momentum of our 20th anniversary, we entered 2024 with renewed purpose, expanding our scientific reach while strengthening ties with industry and academia alike.

A standout example is our new partnership with Almirall to map molecular pathways and biomarkers of atopic dermatitis, uniting the company's dermatology *know-how* with the cutting-edge proteomics of our Joint CRG/UPF Unit. Complementing this, Cytek Biosciences selected our Flow Cytometry Unit, also jointly run with the UPF, as a reference site, installing next-generation technologies that will empower many researchers worldwide.

This was also a year for ambitious, forward-looking science. Thanks to the Gordon and Betty Moore Foundation, our researchers launched the first phase of a global quest to chart cellular biodiversity, work that will lay essential groundwork for a future Biodiversity Cell Atlas. Closer to home, we joined forces with UPF and IBE to inaugurate the world's first Joint Program on Evolutionary Medical Genomics, positioning Barcelona as a hub where evolutionary insight meets precision medicine.

On a personal note, 2024 marked the start of the formal search for my successor. After more than a decade at the helm of the CRG, I have begun a carefully planned transition that will culminate in the appointment of a new Director in 2025. Guiding the CRG from a fledgling institute to one that drives discoveries on the world stage has been the privilege of a lifetime, and I am prouder than ever to see the organisation's talent, resilience, and international standing continue to grow.

In these pages you will find many more stories of discovery, new infrastructure, and successful funding bids, all made possible by the imagination and perseverance of our researchers and support staff. I am immensely proud of their achievements and confident that the seeds planted in 2024 will bear fruit for years to come.

A look back at the year

INSTITUTIONAL

EVOLUTIONARY MEDICAL GENOMICS TAKES FLIGHT

CRG, UPF MELIS and IBE launched **EvoMG**, the world's first joint programme using evolutionary principles to decipher disease mechanisms. Led by **Manuel Irimia** and backed by 360K€ from the Catalan Government, the initiative positions Barcelona as a hub for evolutionary precision medicine.

SETTING THE ETHICAL GOLD STANDARD FOR THE HUMAN CELL ATLAS

Co-chaired by **Prof. Roderic Guigó**, the HCA Ethics Working Group released a global data-sharing toolkit that harmonises consent and privacy rules across borders, ensuring discoveries from the flagship Human Cell Atlas Project benefit everyone.

CATALAN INITIATIVE JOINS THE EARTH BIOGENOME PROJECT

A 150-scientist consortium co-led by **Prof. Roderic Guigó** began sequencing 40 000 genomes in the Catalan territories, with the critically endangered Balearic shearwater delivered as the first reference genome.

FEDERATED EGA GOES LIVE

National nodes in Poland, Norway and Sweden made the first sensitive omics datasets discoverable via the **FEGA** portal co-developed by CRG, marking a new era of secure, cross-border data access.

PYRISENTINEL MAPS THE INVISIBLE LIFE OF 300 PYRENEAN LAKES

A €1.6 million EU project coordinated by **Dr. Hannah Benisty** kicked off field sampling to gauge climate impacts on high-altitude microbial ecosystems in sensitive ecosystems in the Pyrenees.

CATALAN JOINS THE LANGUAGE OF SCIENCE

CRG researchers published the first *Nature Communications* paper to hyperlink a **Catalan-language abstract**, pioneering multilingual accessibility in major journals.

INSTITUTIONAL

EQUALITY, DIVERSITY AND INCLUSION

The CRG's **Gender Equality, Diversity and Inclusion Committee** organised an inaugural *Pride Walk*, renewed its travel-grant programme, began an institute-wide inclusivity audit and, with EU-LIFE, hosted active bystander training.

CRG GOES EVEN GREENER

We continue to implement a sustainability strategy, ensuring and piloted a lab-equipment sharing scheme that cut energy use by 11 %.

NEW ALLIANCE IN CATALONIA

We joined forces with the Biomedical Research Institute of Lleida (IRBLleida) to launch a scheme that marries our fundamental expertise with IRBLleida's clinical strengths, fast-tracking discoveries from bench to bedside.

EXTERNAL REVIEWS FOR EXCELLENCE

Three independent panels examined key pillars of the CRG: Administration and Research Support staff (23–24 May), the Quantitative Cell Biology programme (30–31 May) and the Core Technologies programme (14–15 November). Each review praised the institute's scientific excellence, open-science policies and cost-effective management, concluding that the CRG remains fully competitive with the world's top biomedical centres and offering constructive input that will feed into our next strategic plan.

A NEW DIRECTION FOR THE CRG

Finally, we embarked on the journey to find a new Director for the CRG. An international and independent panel of experts have been tasked to find the person that will help steer our centre into the future.

FUNDING

BIG WINS IN CALLS FROM 'la Caixa' FOUNDATION

Pia Cosma (€1 M) builds a synthetic retina for retinitis pigmentosa; **Luis Serrano** (€1 M) engineers bacteria to attack lung metastases.

CRG CONTINUES TO BE AN POWERHOUSE IN ERC CALLS

• **AI-designed nanobodies**: Professor Luis Serrano was awarded an ERC PoC grant which aims to create an automated pipeline that couples his group's proven FoldX and ModelX algorithms with generative AI to create high-affinity nanobodies entirely *in silico*, shrinking design-to-prototype time from months to days.

• **Whole-genome diabetes test**: This ERC PoC grant by Jorge Ferrer aims to convert decades of diabetes genetics into a clinician-friendly assay: whole-genome sequencing interpreted through Ferrer-lab regulatory maps to classify ambiguous diabetes cases in children and young adults.

• **Liquid biopsy**: Eva Novoa's received a PoC to scale up **Nano-tRNAseq**, her nanopore method that sequences native tRNAs, including their chemical modifications, in a single read, one day enabling liquid biopsies that can flag tumour-specific tRNA signatures.

• **Generative AI for custom proteins**: A 1.5-million-euro ERC Starting Grant was awarded to Noelia Ferruz to build ATHENA, a new AI model which can create proteins with custom properties that do not exist in nature.

• **Cell Atlases** - A 2-million-euro ERC Consolidator Grant will help Arnau Sebe Pedrós map the evolutionary relationships between different animal cell types. Using advanced genetic tools, the group aims to map out a family tree of cell types, providing new insights into the building blocks of life.

FUNDING

WORLDWIDE CANCER RESEARCH BACKS TWO CRG PROJECTS.
Luciano Di Croce and Sara Sdelci received around 250,000 euros each to advance efforts into targeting diffuse midline glioma and the oncogene KRAS respectively, thanks to the Worldwide Cancer Research fund.

FÁTIMA GEBAUER WON A BIST IGNITE GRANT TO bRaiNA, a CRG-IBEC collaboration that will engineer messenger-RNA therapies able to slip through brain blood vessels and tackle neurological disease

MEDICAL COLLABORATIONS.
Luciano Di Croce secured 170,000 euros from private donors to discover new therapeutic compounds for diffuse midline glioma. The generous donation was made to Hospital Sant Joan de Deu and passed on to Di Croce's group to address a paediatric tumour with poor outcomes.

FEDER INFRASTRUCTURE BOOST
Through a successful bid to the European Regional Development Fund (FEDER), the CRG secured financing for four state-of-the-art instruments that will upgrade our core facilities in microscopy, flow cytometry, genomics, and protein technologies. The new equipment, due for installation in 2025, will expand capacity, increase throughput, and give our researchers and external users faster access to cutting-edge tools.

BUSINESS & INNOVATION

€2.7 M NEXTGEN-EU BOOST FOR FRAGILE X THERAPY

A CRG–Connecta–IMIM–I3PT consortium moves AI-designed drug CTH120 into Phase IIa trials, with **Dr. Mara Dierssen** leading biomarker work.

CRG–ALMIRALL TEAM UP ON ATOPIC DERMATITIS

The new collaboration couples Almirall's dermatology know-how with CRG proteomics to uncover pathways and biomarkers for next-generation therapies.

DIABETIC FOOT ULCERS

The Protein Technologies unit, together with Lincbiotech, is leading a European project funded by the European Innovation Council to develop novel molecules targeting severe conditions, including diabetic foot ulcers.

CYTEK PARTNERS WITH FLOW CYTOMETRY

A strategic agreement outfits the CRG/UPF Flow Cytometry Unit with cutting-edge spectral platforms, keeping Barcelona at the forefront of single-cell phenotyping.

COMING AND GOING

We are delighted to welcome Bernardo Rodríguez-Martín (cancer-genome structural variation) as independent fellow, **Noelia Ferruz** (AI-driven protein design) as junior group leader and **Florian Kohler** (high-throughput genomics technologies) as team leader within the Genomics Unit. Their complementary expertise adds fresh momentum to the CRG's mission and opens exciting opportunities for collaboration across our community.

We said goodbye to Bernard Payer, junior group leader of the Genome Biology Programme, who became Associate Professor at Université de Montréal, and the CHU Saint-Justine (centre hospitalier mère-enfant), in Canada.

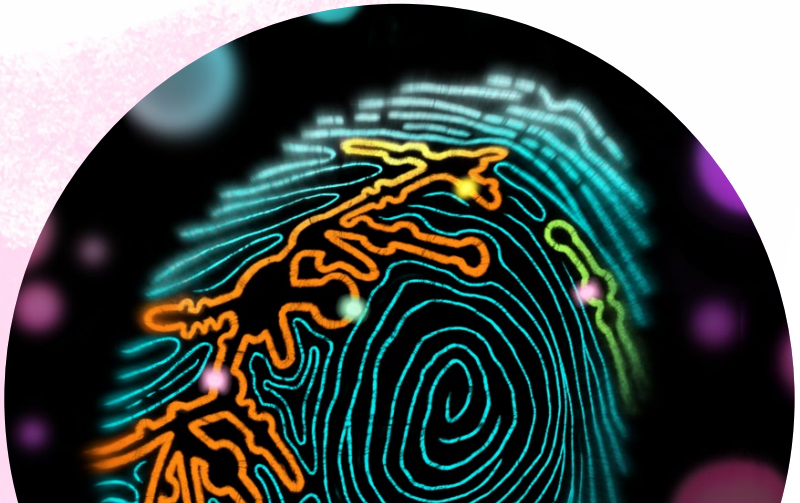
Finally, after nearly two decades at the CRG, where has done pioneering work on cell reprogramming and haematopoietic differentiation, and a scientific career spanning EMBL, Albert Einstein College of Medicine and our own institute, **Thomas Graf** is retiring. His visionary leadership, mentorship and 300-plus publications have shaped generations of scientists and firmly established the CRG as a reference in gene-regulation research. We thank him warmly and wish him an inspiring new chapter.

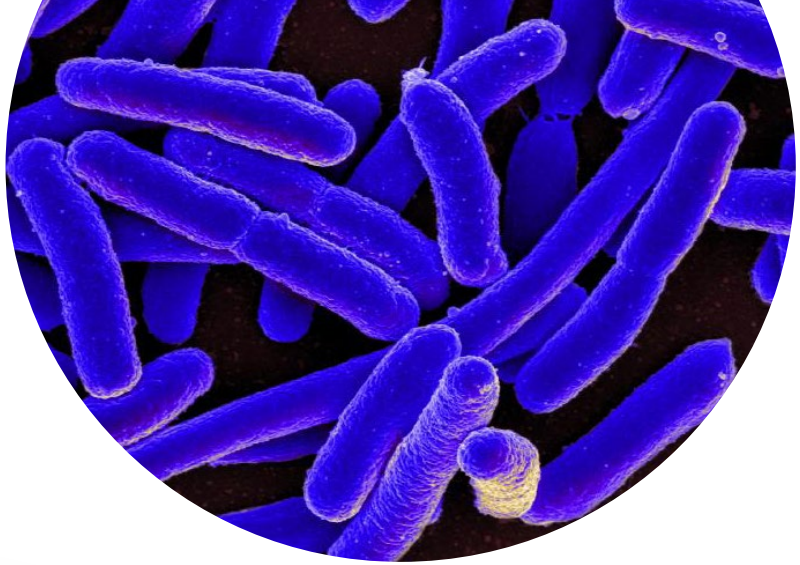
Research highlights

‘Ribosome fingerprint’ enables rapid cancer detection

Researchers led by **Dr. Eva Novoa** have revealed that tiny chemical marks on ribosomal RNA form tissue-specific “fingerprints” and that early-stage lung tumours systematically erase some of them. A nanopore-sequencing test trained on these patterns distinguished healthy from cancerous tissue with near-perfect accuracy after analysing just a few hundred molecules.

The work lays the groundwork for pocket-sized, same-day diagnostics that could catch cancers when they are still curable.





Bacteria shed ribosome tags to evade antibiotics

Under antibiotic pressure, *E. coli* rebuilds ribosomes minus key chemical tags at drug-binding sites, a stealth resistance mechanism uncovered by **Dr. Eva Novoa’s** group. Real-time nanopore sequencing showed tag loss within hours of exposure to streptomycin or kasugamycin, reducing the drugs’ grip on the ribosome.

Understanding this rapid “tag-ditching” strategy opens new avenues to block resistance before it takes hold.

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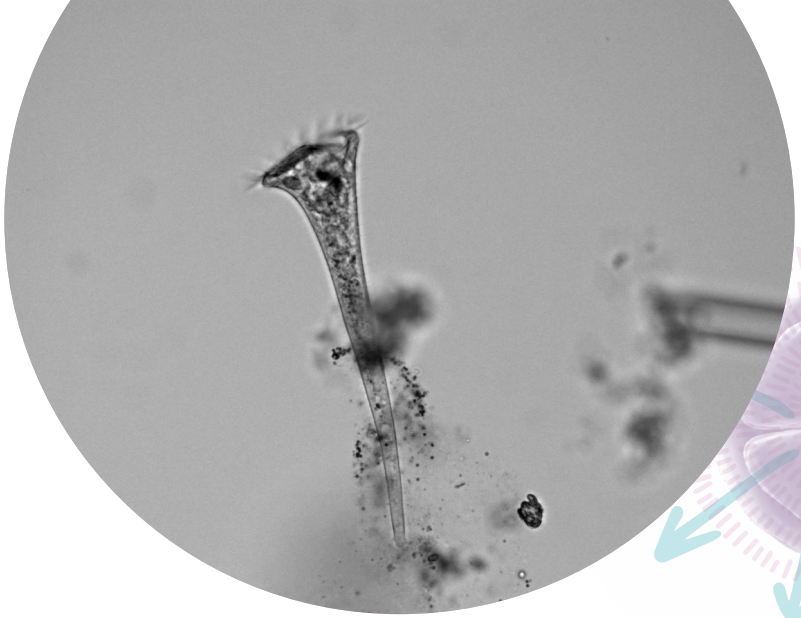
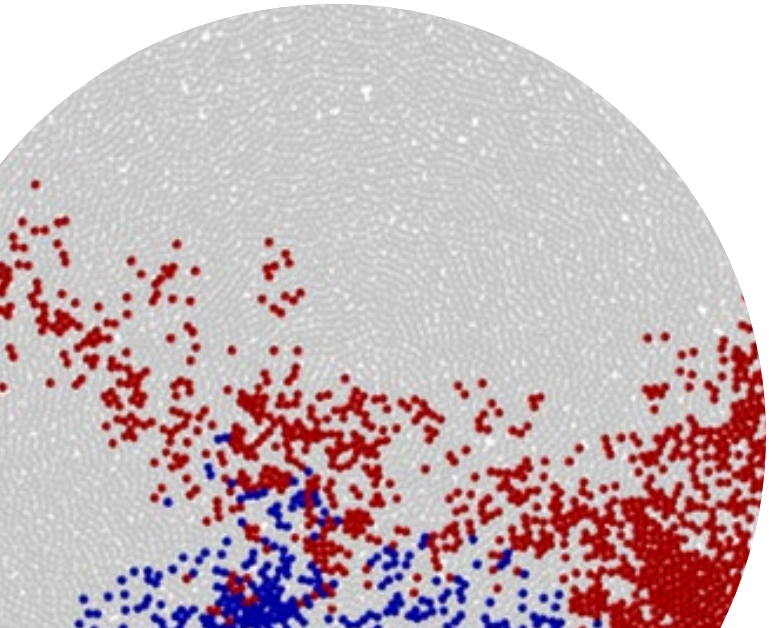


Tumours grow evenly, not from the edge

Spatial-genomics maps created by **Dr. Donate Weghorn** reveal that liver cancers expand uniformly throughout their bulk rather than racing at the rim. Mutation angles and clustering patterns matched computer-simulated "volume growth," challenging the 50-year dogma of surface-driven expansion.

The finding revises how we model tumour evolution, helping forecast where therapy-resistant clones may emerge.



Single cells show a primitive form of learning

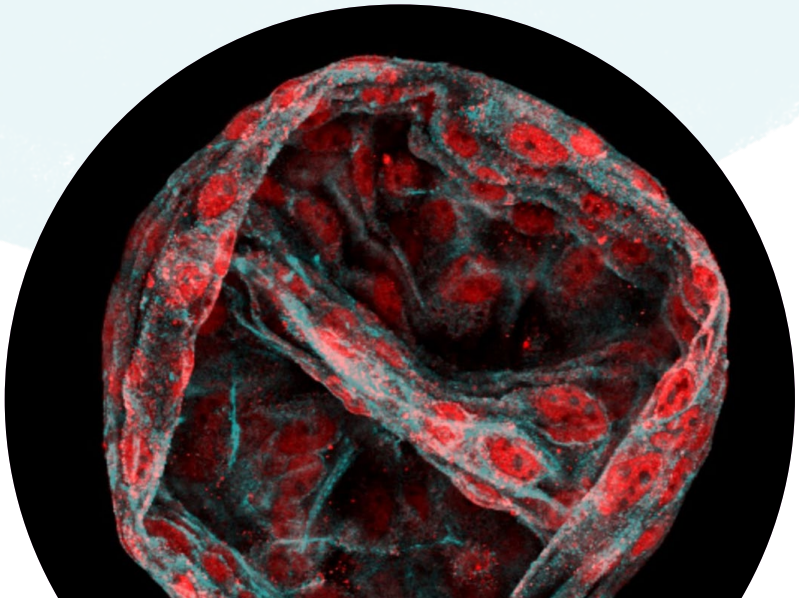
Mathematical models from **Dr. Rosa Martínez** and collaborators suggest that negative-feedback and feed-forward loops inside cells can reproduce habituation, the simplest type of learning. Simulations show molecular circuits adjusting their responses to repeated stimuli, blurring the line between neural and cellular cognition.

The insight hints that "memory" at the molecular scale could underlie phenomena such as antibiotic or chemotherapy resistance.

‘Moonlighting’ metabolic enzymes double as DNA guardians

Dr. Sara Sdelci’s team discovered that energy-pathway enzymes MTHFD2 and IMPDH2 migrate to the nucleus, where they steer chromosome segregation and DNA repair. For triple-negative breast cancer, flooding nuclei with IMPDH2 overwhelmed repair systems and killed tumour cells.

Targeting these dual-role enzymes could result in a two-pronged attack that starves cancers metabolically while sabotaging genome upkeep.



A single phospho-switch rewires the mitotic scaffold

Using a programmable *in-vitro* system, **Prof. Thomas Surrey** and colleagues showed that toggling phosphorylation on PRC1 flips the microtubule cytoskeleton between interphase and anaphase architectures in minutes. The reversible “switch” lets scientists fast-forward or rewind cell-division movies at will.

Mastering this control could inspire therapies that stall dividing cancer cells by freezing their internal roadways.

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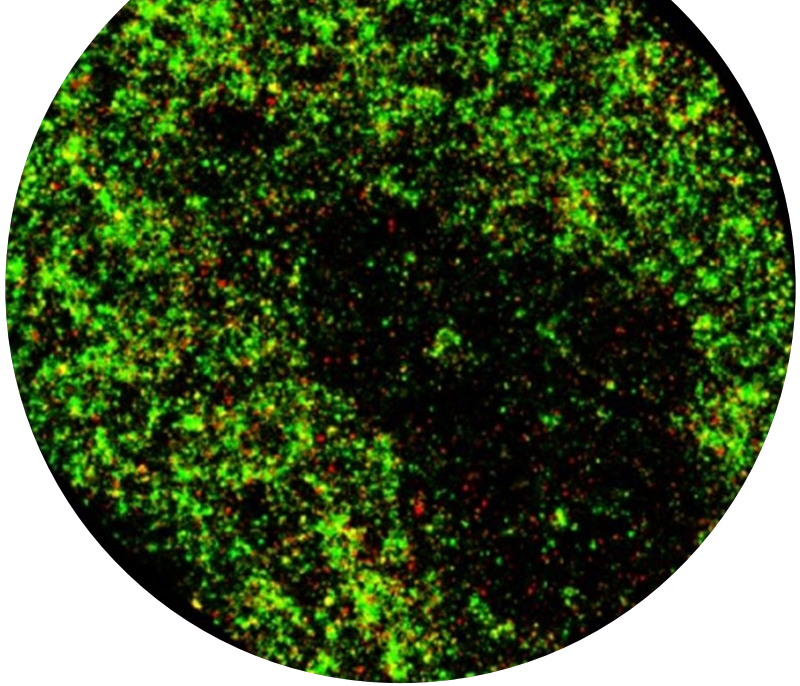
First complete blueprint of the human spliceosome

After a decade-long effort, **Prof. Juan Valcárcel** charted the specialised roles of more than 150 spliceosomal proteins, revealing a highly interconnected editing factory rather than a generic cut-and-paste machine. Perturbing one hub protein, SF3B1, rippled through a third of the network.

The atlas spotlights fresh drug targets and exposes an Achilles' heel in cancers addicted to splicing rewiring.



AI detects cancer & viruses at 20-nanometre resolution

Prof. Pia Cosma co-developed AINU, a convolutional neural network that reads super-resolution STORM images of nuclei to flag cancer cells and herpes-infected cells within an hour of infection. The model recognises subtle chromatin-organisation changes at very small scales.

AINU could accelerate stem-cell quality control today and, with faster microscopes, usher in new ultrasensitive clinical diagnostics.

Protein mutation effects add up with simple maths

Work led by **Dr. Ben Lehner** demonstrates that most amino-acid changes alter protein stability independently, so the impact of multiple mutations can be predicted by summing single effects. The rule, verified across thousands of variants, slashes the experimental search space for drug and enzyme design.

The discovery streamlines efforts to forecast disease severity and to engineer proteins for industry.

Retrotransposon misfire implicated in Down syndrome

Dr. Mara Dierssen and collaborators show that mobile DNA elements are over-active in a Down-syndrome mouse model, dysregulating genes tied to neurodegeneration. Treating mice with the antiretroviral lamivudine restored normal expression for key genes.

The study points to retrotransposon inhibitors as potential therapies for Down-syndrome-related cognitive decline.

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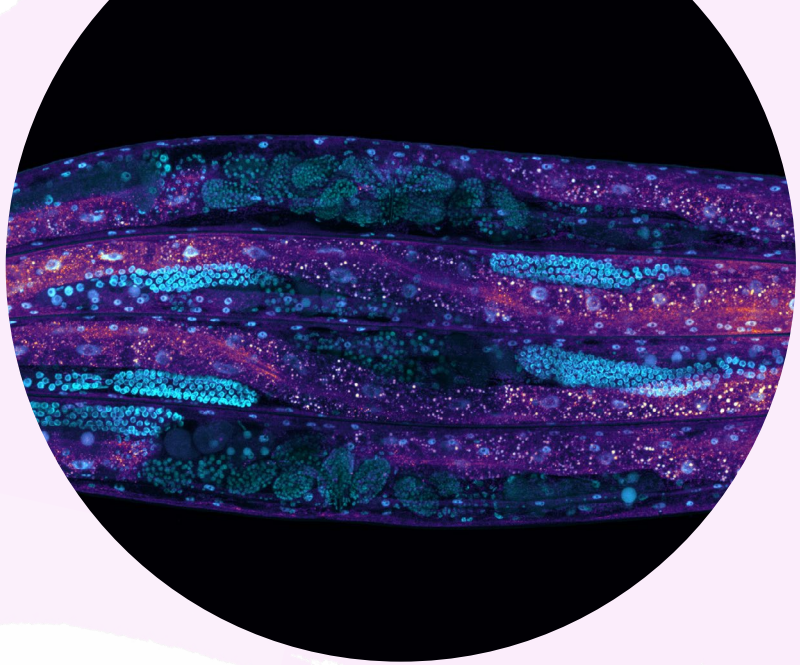

52,000-year-old ‘chromoglass’ preserves mammoth genome

An international team including **Dr. Marc A. Marti-Renom** recovered intact chromosome architecture (down to 50-nm loops) from permafrost mammoth skin. The fossilised “chromoglass” reveals 28 chromosome pairs and hair-gene activity patterns distinct from elephants.

The breakthrough inaugurates a new era of palaeogenomics, where extinct species’ genomes can be assembled scaffold-by-scaffold.

Gene ‘lottery’ makes ageing fairer in worms

Dr. Nick Stroustrup’s Lifespan-Machine assays show that random fluctuations in a network of 40-plus genes uncouple germline and somatic mRNA balances, dictating whether genetically identical *C. elegans* live 8 or 20 days. Silencing aexr-1, nlp-28 or mak-1 halves this inequality.

Modulating similar pathways in humans could extend healthy years by lifting the shortest-lived, not chasing immortality.

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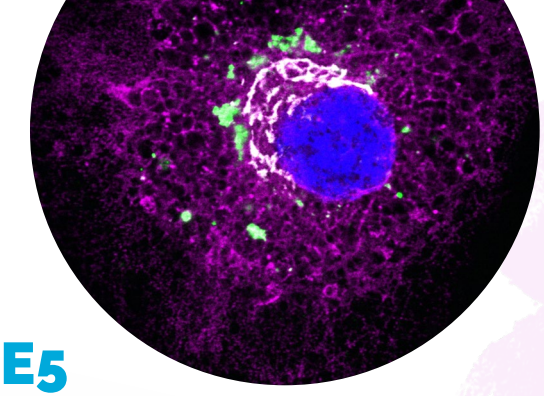


Blocking TANGO1–cTAGE5 halts collagen flood, curbs scarring

Guided by AlphaFold2 structures, **Dr. Vivek Malhotra's** group designed cell-permeable peptides that sever the TANGO1–cTAGE5 interface, bottling collagen inside fibroblasts. The effect reversed within 48 hours and reduced fibrosis in zebrafish wounds. The strategy offers a precision, reversible therapy for skin scarring, scleroderma and post-surgical fibrosis.

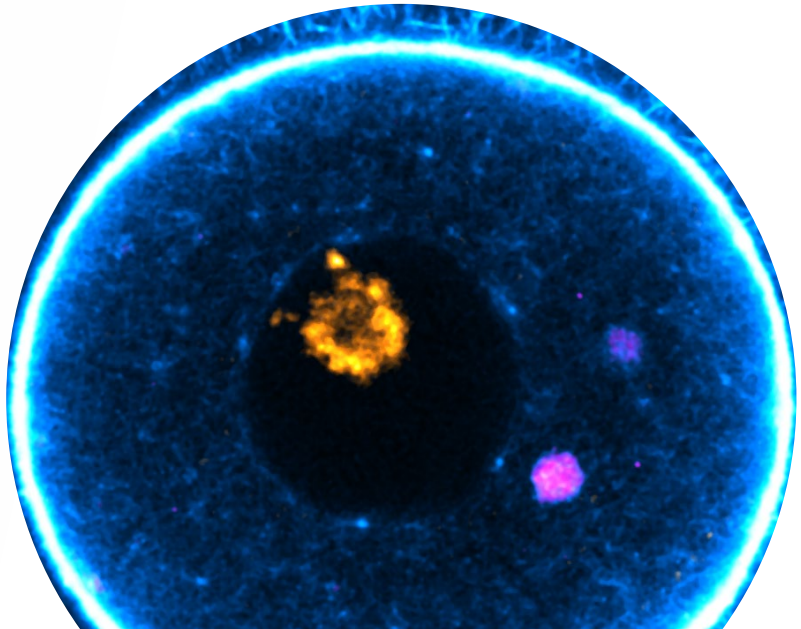
Oocytes deploy 'ELVA' superorganelles to trap toxic proteins

Dr. Elvan Böke discovered EndoLysosomal Vesicular Assemblies (ELVAs), mobile clusters that sequester misfolded proteins for decades until oocytes mature, when the aggregates are purged en masse. Disabling ELVAs ruined egg quality and derailed early embryogenesis.

The mechanism offers fresh clues to age-related infertility and may illuminate how long-lived cells like neurons manage proteotoxic stress.

Melanomas resist therapy by deleting BRAF exons

Clinical-genomics work spearheaded by **Dr. Francisco Aya Moreno** and **Dr. Juan Valcárcel** reveals that treated and even untreated melanomas excise chunks of the BRAF gene, creating altBRAFs that sidestep first-generation inhibitors. The deletions, not alternative splicing, reignite MAPK signalling. The finding advocates second-generation RAF inhibitors and deeper genomic screening to pre-empt resistance.



Research and Scientific Services

COMPUTATIONAL BIOLOGY AND HEALTH GENOMICS PROGRAMME

Coordinator: **Jorge Ferrer**

In 2024, the Programme reinforced its role at the interface of genomics, evolutionary biology and human health, contributing to high-profile international events and publications. Its research activities spanned fundamental and translational science, with advances in the functional interpretation of genetic variants, evolutionary medical genomics and technology development. These efforts reflect our continued commitment to scientific leadership and collaborative impact across disciplines.

The programme members (Frazer, Weghorn, Irimia, Dias) co-organised several events, including the Evolutionary Medical Genomics Symposium at the Society for Molecular Biology and Evolution Annual Meeting and the Inaugural Symposium of the Evolutionary Medical Genomics Program held at the CRG, while Notredame contributed to the Barcelona Nextflow Summit and the nf-core community.

Guigó's group described a new technology for sequencing transcripts in the GENCODE project (Carbonell Sala, *Nat Comm*), was awarded funds to participate in the human and non-human primate developmental GTEx project, and led the inaugural report of the Catalan initiative of the Earth BioGenome Project (Corominas, *NAR Genomics and Bioinformatics*). Notredame's lab developed a method that uses protein structures to reconstruct phylogenetic trees (Baltzis, *Nature Comm*, 2024), while Irimia's lab used transcriptomics to uncover the widespread evolution of tissue-specific expression in animals (Mantica, *Nature Ecol Evol*, 2024)

The Ferrer group co-led a large-scale analysis of genetic variants that modulate insulin secretion in humans (Madsen, *Nat Metab*) and published a review on the role of long non-coding RNAs in human disease (Ferrer, *Nat Rev Mol Cell Biol*). In parallel, Dias and Fraser published state-of-the-art recommendations for the use of machine learning in the clinical interpretation of genetic variants (Dias, *Am J Hum Genet*).

QUANTITATIVE CELL BIOLOGY PROGRAMME

Co-coordinators: **Isabelle Vernos and Vivek Malhotra (until June) and Thomas Surrey (since October)**

The Quantitative Cell Biology Programme investigates molecular mechanisms underlying the internal organisation of cells, cell division and early development. Research in the programme focuses on the dynamic nature of intracellular and tissue-level processes, which are studied using live-cell or organism imaging in combination with a variety of other methods such as genetics, biochemistry, omics technologies and mathematical modelling.

In 2024, Vivek Malhotra, who had led the programme for 16 years, stepped down as co-coordinator and Isabelle Vernos (Microtubule Function and Cell Division) took over the coordination of the programme's activities together with Thomas Surrey (Intracellular Self-Organisation).

The department has produced several publications. For example, Surrey's lab provided new insights into the microtubule nucleation mechanism (Brito, Serna, *Science*, 2024), Böke's lab (Oocyte Biology and Cellular Dormancy) discovered a new super-organelle in oocytes (Zaffagnini, *Cell*, 2024) and Malhotra's lab (Intracellular Compartmentalisation) elucidated the effect of cargo size on protein secretion (Saxena, *Dev Cell*, 2024). The new Al Jord lab (Mechanics of Organelle Remodelling) has also established itself in the programme, studying the link between cytoskeleton mechanics and the biology of the nucleus (Letort, *J Vis Exp*, 2024).

Elvan Böke was appointed ICREA Research Professor, thus becoming the fifth ICREA position in the department, and also received the EMBO Gold Medal (among other awards). Vivek Malhotra was elected member of the American Academy of Arts and Sciences and also received other distinctions.

Elvan Böke and Verena Ruprecht (Cell and Tissue Dynamics) started their ERC grants, bringing the number of active ERC grants in the department to five.

GENOME BIOLOGY PROGRAMME

Co-Coordinators: **Fátima Gebauer and Luciano Di Croce**

The Genome Biology programme focuses on investigating the mechanisms that lead to the expression of our genome during homeostasis, cell reprogramming and disease. We use quantitative 'omics' technologies, mathematical modelling, cellular biology and mouse genetics to understand chromatin organisation, transcription, splicing, mRNA translation, signalling and RNA modification. Gene expression control mechanisms are studied in the context of a variety of diseases, including cancer (leukaemia, lymphoma, pancreatic and lung adenocarcinomas, gliomas, melanoma, breast cancer), Down syndrome and fertility disorders.

The transcriptional regulation groups study the effects of dosage imbalance of chromosome 21 (Dr. Susana de la Lluna, epigenetic mechanisms in cancer and stem cells (Dr. Luciano Di Croce), single-cell epigenomics in lymphomas (Dr. Renée Beekman) and epigenetic regulation of cancer metabolism (Dr. Sara Sdelci). The RNA biology groups study the identification and control of RNA modifications (Dr. Eva Novoa), the regulation of alternative splicing (Dr. Juan Valcárcel) and the regulation of mRNA translation (Dr. Fàtima Gebauer). Cell reprogramming studies include differentiation and trans-differentiation in the hematopoietic system (Dr. Thomas Graf) and epigenetic reprogramming in embryogenesis and the germline (Dr. Bernhard Payer).

In 2024, Dr. Juan Valcárcel discovered specialised regulatory functions of the core spliceosome; Dr. Fátima Gebauer uncovered CSDE1 as a melanoma biomarker and was elected President of the RNA Society; Dr. Luciano Di Croce found an interplay between alternative splicing of PRC2 and chromatin regulation; Dr. Eva Novoa devised Nano-tRNAseq for the accurate analysis of tRNA levels and modifications and obtained ERC Proof of Concept and NIH grants; Dr. Sara Sdelci found roles for the IMPDH2 and MTFHD2 enzymes in regulating cellular processes from the nucleus and obtained several grants and awards (FERO-Mango, WWCR, AECC); Dr. Bernhard Payer described a role for the interferon gamma pathway in pluripotency and moved to the University of Montreal, in Canada; and Dr. Thomas Graf became Emeritus Professor at the CRG.

SYSTEMS AND SYNTHETIC BIOLOGY PROGRAMME

Coordinator: **Pia Cosma**

The Systems and Synthetic Biology programme uses multiple systems and scales: from microbes to entire organs and animals, from non-model animals to human genetics, evolution, neuroscience and aging to address breakthrough questions with a common intent.

We seek to explain, predict and build biological systems that lie at the base of any cell, tissue and organ function. The Systems and Synthetic Biology programme sets out to learn the foundation of life by transforming molecular, cellular and systems biology into quantitative and predictive engineering science.

2024 brought several important achievements. Nick Stroustrup's group used an innovative approach, Asych-seq, to explore how gene expression heterogeneity generates lifespan variation (Eder et al., *Cell*, 2024). Ben Lehner's group quantified protein folding stability, and by exploring sequence spaces larger than 10^{10} demonstrated that the genetic architecture of some proteins is remarkably simple (Faure et al., *Nature* 2024). All the PIs in the programme are well-funded through both local and external grants. Noelia Ferruz and Arnau Sebe were awarded ERC Starting and ERC Consolidator Grants, respectively. Nora Martin and Rosa Martinez, Independent Fellows at the Barcelona Collaboratorium for Modelling and Predictive Biology, co-organised a highly successful Collaboratorium Symposium focused on *Modelling Biology Across Scales*.

CORE TECHNOLOGIES PROGRAMME

Head: **Mònica Morales**

The Core Technologies programme is comprised of seven Technology Units that provide researchers with state-of-the-art technologies and expertise to advance research. The programme is a member of the Core Facilities Excellence Alliance "Core For Life" (www.coreforlife.eu).

In 2024, the agreement between the Flow Cytometry Unit and Cytek Biosciences was consolidated, resulting in the installation of three new spectral cytometry platforms in the first half of the year. Moreover, the BD FACSDiscover™ S8 Cell Sorter, featuring real-time imaging-based cell sorting capabilities, was installed in January 2024. Thanks to these latest additions, the CRG/UPF Flow Cytometry Unit is now among the few cytometry facilities in the world that straddles all the latest technologies in this field.

A new transversal single-cell platform was also established in 2024 with the aim of providing end users with a comprehensive, integrated and transversal service to carry out complex single-cell projects successfully. The platform is comprised of different CRG technological units that offer cutting-edge technology and specialised advice in different technological areas such as Flow Cytometry, Genomics, Protein Technologies and Bioinformatics Analysis. The studies carried out in the platform provide a higher resolution of cellular differences and a better understanding of an individual cell's function in the context of its microenvironment.

In parallel, the programme has a new team dedicated to advanced genomics technologies, focusing on the development and implementation of cutting-edge methodologies in this field. This team places particular emphasis on single-cell and spatial transcriptomics studies.

Additionally, other units have prioritised innovation, successfully securing public-private partnership grants in order to further technology development in collaboration with industry partners. Notably, the Proteomics Unit has partnered with Almirall to identify molecular pathways and biomarkers specific to atopic dermatitis, whereas the Protein Technologies Unit, together with Lincbiotech, is leading a European project funded by the European Innovation Council to develop novel molecules targeting severe conditions, including diabetic foot ulcers. These collaborations have collectively secured €670,000 in funding for the CRG.

On 14 and 15 November 2024, the Core Technologies Programme underwent its external evaluation, a process conducted every four years. The evaluation panel commended the Programme for its exceptional performance and contributions to biomedical research. The panel's positive assessment underscores the Programme's pivotal role in advancing cutting-edge technologies and supporting the scientific community.

EUROPEAN GENOME-PHENOME ARCHIVE (EGA)

Director: **Arcadi Navarro**
Team Leader: **Jordi Rambla**

The European Genome-phenome Archive (EGA), jointly managed by the European Bioinformatics Institute (EMBL-EBI) and the Centre for Genomic Regulation (CRG) in collaboration with the Barcelona Supercomputer Center (BSC-CNS), is a secure global repository for human genetic and phenotypic data. It supports biomedical research by ensuring that data are safely archived, discoverable, and accessible, in line with FAIR principles. Recognized as the world-wide reference for storing personally identifiable genomic and clinical data, the EGA has become essential for international data sharing.

The CRG's EGA team, now comprising 24 multidisciplinary professionals after the new hirings in 2024, plays a central role in this initiative. In 2022 it co-led the creation of the Federated EGA Network, which enables secure cross-border genomic data sharing. Since 2024, the network has numbered eight national nodes and has welcomed Canada as its first non-European member. The technology underpinning this network was developed by the CRG team.

In 2024, the team completed two collaborative projects and launched five new ones, contributing to a total of 12 active competitive grants. The CRG's EGA team also leads the global development of Beacon, a genomic data discovery technology, and released both the Beacon v2 API and its live implementation in 2024. They also developed several customised user interfaces for several collaborative scientific projects.

New Hirings

Two outstanding early-career scientists joined the CRG in 2024.

Bernardo Rodríguez Martín

After taking his PhD in Cancer Genomics at the University of Santiago de Compostela and the University of Vigo in Spain, in 2020 Bernardo took up a position as Postdoctoral Fellow at the European Molecular Biology Laboratory in Heidelberg, Germany, a position he held for two years. In 2021 he became Bridging Excellence Postdoctoral Fellow at both the European Molecular Biology Laboratory and at Stanford University in Palo Alto, USA, until January 2024, when he joined the Computational Biology and Health Genomics Programme at the CRG as Independent Fellow.

His team employs state-of-the-art genome sequencing in conjunction with functional multi-omics data to investigate the impact of repetitive DNA on genome function and evolution. Diverse types of repetitive DNA elements are ubiquitous in the genomic sequences of all eukaryotic organisms and account for about 50% of the human genome. Specific repeat classes, such as telomeric or centromeric repeat arrays, are crucial for preserving genome function and integrity. Repetitive DNAs also fuel genome evolution by serving as substrates for the generation of regulatory sequences and genetic variation, including disease-causing mutations. Nonetheless, owing to technological limitations for the accurate sequencing of highly repetitive sequences, the repetitive portion of the genome remains largely uncharted territory, awaiting further exploration.

To illuminate the role of repetitive DNA in genome biology, his team harnesses the latest technological advances to decode nucleotide sequences, including long-read sequencing approaches such as Oxford Nanopore and Pacific Biosciences. A central aspect of their research is the development of computational methods for annotating and characterising repeats, as well as their application to the ever-expanding volume of genomic and functional data. Through this approach, they also investigate the role of repetitive DNA in the generation of structural variants, a variant class encompassing large genetic changes, including deletions, insertions, inversions or duplications of DNA sequences.

Noelia Ferruz

Noelia obtained her PhD in Biomedicine at the Universitat Pompeu Fabra in Barcelona, Spain, in 2016. She then took up a position as Researcher at Acellera Labs in Barcelona, Spain and as Postdoctoral Researcher at Pfizer in Cambridge, USA. In 2017 she moved to the University of Bayreuth in Germany as Postdoctoral Researcher. She subsequently joined the University of Girona in Spain as Beatriu de Pinós Fellow in 2022. One year later, she moved to the Institute of Molecular Biology of Barcelona in Spain as Group Leader. Finally, in June 2024 she joined the CRG Systems and Synthetic Biology Programme as Junior Group Leader.

Her research group focuses on using computational and experimental approaches to understand and design protein functions. They have extensive experience in deep unsupervised learning and protein design, which they have applied to several projects (see https://www.aiproteindesign.com). Over the next few years, they will be expanding their focus to include the design of custom-tailored and new-to-nature protein functions. They will implement models, understand their decision-making process using XAI and improve their performance through reinforcement learning. They will also include experimental characterisation efforts, thus permitting the continual improvement of their models. They are particularly interested in leveraging their expertise to address significant challenges in the fields of healthcare and sustainability. This includes developing new proteins to treat diseases, designing enzymes for biotechnological applications and creating proteins with novel functions that can help to address environmental challenges.They believe that protein design has the potential to change the world we live in and that Artificial Intelligence lies at the core of this revolution.

Honours & Awards

VI FERO-MANGO Award in Breast Cancer

Sara Sdelci

Doctor Honoris Causa, Miguel Hernández University of Elche (UMH), Spain

Luis Serrano

XIX Prize for Biomedical Research, Fundación Banco Sabadell

Elvan Böke

Member American Academy of Arts and Sciences

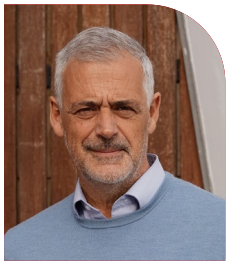
Vivek Malhotra

LifeArc Knowledge Transfer Innovation Fellowship

Eylem Aydoğdu Lohaus

EMBO Gold Medal 2024

Elvan Böke



Rei Jaume I Award in New Technologies

Luis Serrano

Full academic member of the Royal Academy of Sciences and Arts of Barcelona

Arcadi Navarro

ERC grantees at CRG

STARTING GRANTS

Elvan Böke

Arnau Sebé-Pedrós

Nicholas Stroustrup

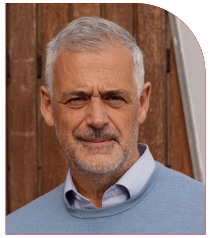
Sara Sdelci

Renée Beekman

Lars Velten

Eva Novoa

ADVANCED GRANTS



Luis Serrano

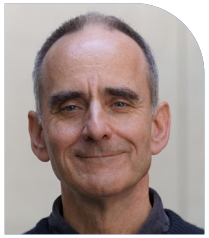
Ben Lehner

CONSOLIDATOR GRANTS

Elvan Böke

SYNERGY GRANTS

Verena Ruprecht

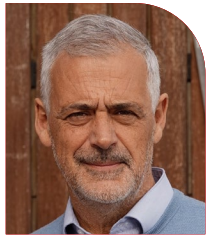


Juan Valcárcel

Vivek Malhotra

Thomas Surrey

PROOF OF CONCEPT GRANTS



Luis Serrano

Jorge Ferrer

Facts & figures

Publications

162
Total Publications

88%
Open Access Publications

81%
1st Quartile Publications

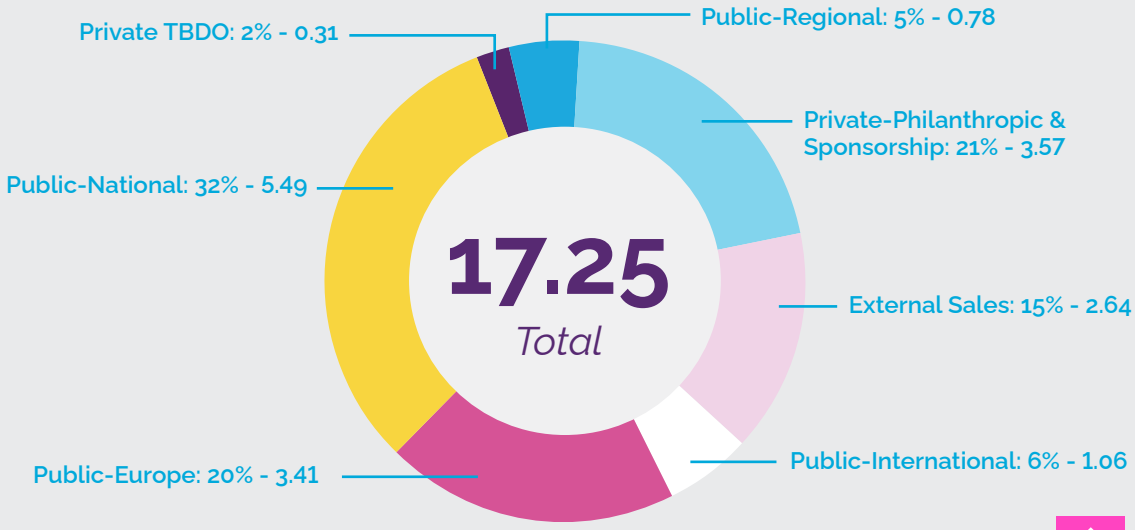
12
Average Impact Factor

Funding (M€)

44.4
Total Funding

EXTERNAL FUNDING AWARDED IN 2024

Note: This graph includes competitive funds obtained during 2024 and pending for final notice of award or grant agreement as of 31/12/2024



Projects

162
Total Ongoing Research Projects and Networks

17 *are Ongoing ERC Projects*

16 *are Ongoing Coordinated Projects*

43 *are Other Ongoing H2020 and Horizon Europe Research Projects and Networks*

11 *are International Ongoing Research Projects (non-EC)*

24
Total Ongoing Postdoctoral Fellowships

Staff

453.98*
*Total FTE**

467
Total

FTE, Full-time equivalent*

Research Staff

290.97*
*Total FTE**

300
Total

Scientific Services

68.39*
*Total FTE**

70
Total

Administration & Scientific Support

94.63*
*Total FTE**

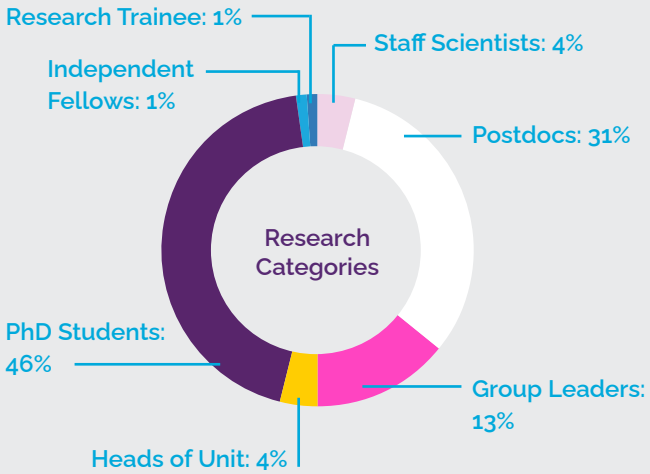
97
Total

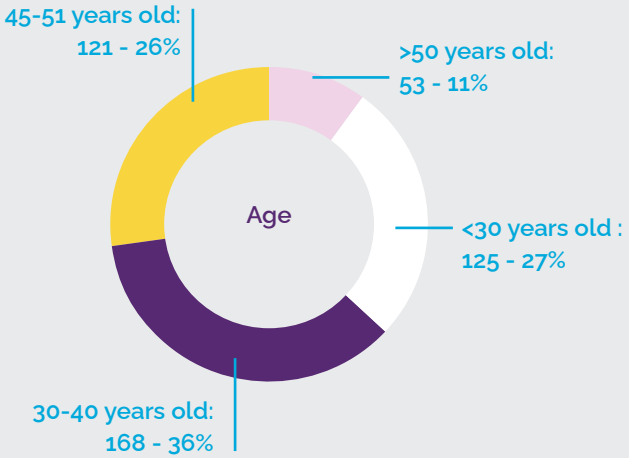
Research Groups (by 31st Dec 2024)

34
Total

32
CRG

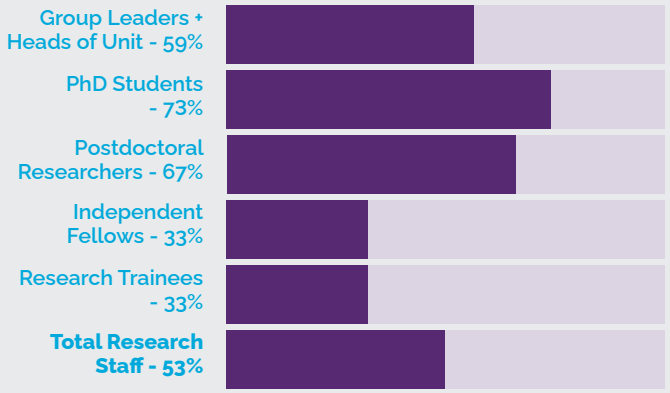
2
Dual-affiliation



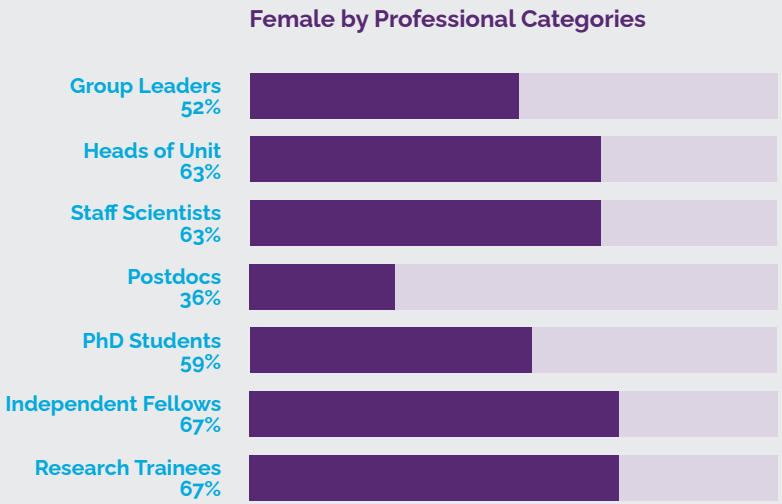


Internationality

55 nationalities represented



Gender



Applicants to our Selection Processes

48% 52%

2,063 2,241

Selected / Hired Candidates

57% 42%

92 68

% Female invited speakers

41% in 2024

(41% in 2023)

Advanced training

PhD Theses defended

23

Courses@CRG

4 *international courses*

68 *participants*

Scientific & Technology and RR Courses

39 *internal courses*

628 *participants*

Transferable & Innovation Skills Courses

10 *internal courses*

292 *participants*

Career-related Events & Training

6 *internal courses*

375 *participants*

Events

5
International Conferences

86
High-profile Seminars

Technology & business development

7
Spin-offs

25
Ongoing Valorisation Projects

32
Active Patent Families

21
Invention Disclosures

13
Services, Scientific Collaborations & Licenses Agreements

180
Other Agreements

Communications, Public Engagement & Science Education

MEDIA RELATIONS

2,178
Media Appearances

293
Print Media

1,824
Online Media

43
Radio

18
TV

SOCIAL MEDIA
(by 31st Dec 2024)

X Followers
22,709

YouTube
314,618
Channel views

2,283
Subscribers

Facebook
4,681
Likes

4,982
Followers

LinkedIn Followers
29,731

PUBLIC ENGAGEMENT AND SCIENCE EDUCATION

41
Categories of Activities Organised

5,667
Audience Reached

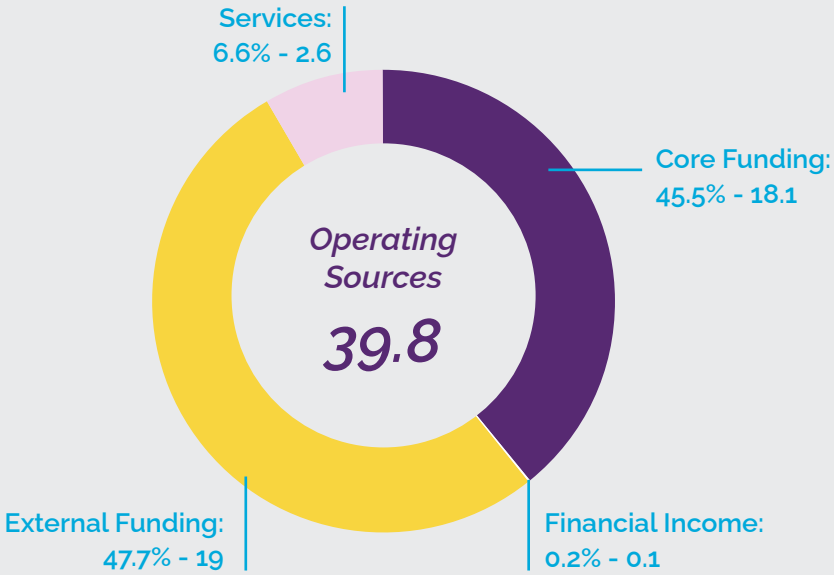
1,809
Students

3,858
General Public

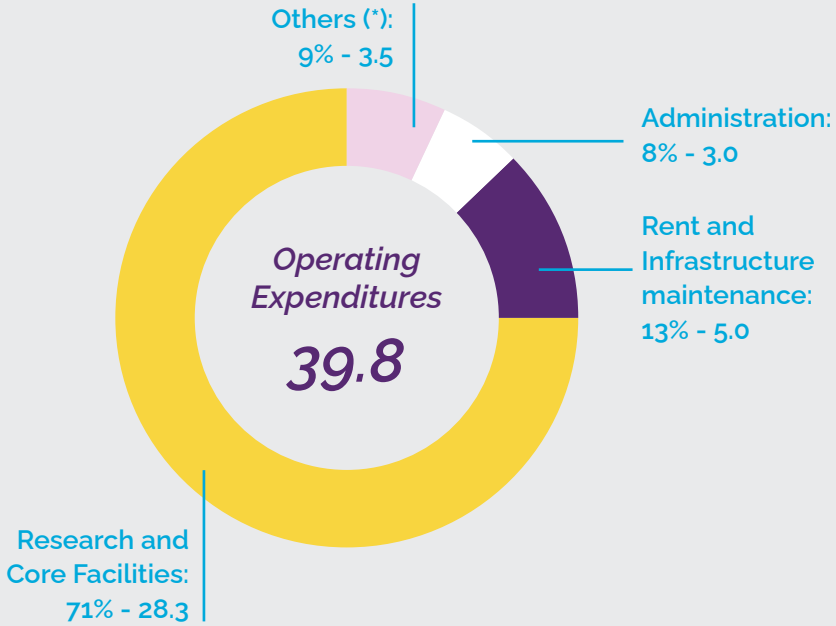
Financial report

SOURCES & USES MANAGED

Operating sources in M€



Operating expenditures in M€



(*) **Others includes:** Director's Group + SaF + TBDO + TAO + Pre-Award and Communication + 97.2k€ of Financial Expenses

Acknowledgements

TRUSTEES

Generalitat de Catalunya

Gobierno de España · Ministerio de Ciencia, Innovación y Universidades

upf. Universitat Pompeu Fabra Barcelona

Fundació "la Caixa"

Support from our trustees, public and private funders and sponsors is key to accomplishing the CRG's mission of discovering and driving knowledge for the benefit of society, public health and economic prosperity.

PUBLIC FUNDERS

European Union · European Regional Development Fund

European Union · European Research Council

Gobierno de España · Ministerio de Ciencia, Innovación y Universidades

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Generalitat de Catalunya · Departament de Recerca i Universitats

Generalitat de Catalunya · Departament de Salut

European Union · European Regional Development Fund

European Union · European Social Fund

EMBO excellence in life sciences

AGAUR · Agència de Gestió d'Ajuts Universitaris i de Recerca

Gobierno de España · Ministerio de Ciencia e Innovación · FECYT · Fundación Española para la Ciencia y la Tecnología

Barcelona Cultura · Ajuntament de Barcelona

NIH National Institutes of Health

ICREA

ciber Centro de Investigación Biomédica en Red

isc Instituto de Salud Carlos III

Note: ERDF and ESF funds have been instrumental over the years through different funding schemes and in a variety of activities in supporting our research and keeping our infrastructures state-of-the-art. Further details on the projects co-financed by these funds can be found in the ERDF AND ESF FUNDS AT THE CRG

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Scientific highlights

- Research Highlights
- Honours & Awards
- Research and Scientific Services
- ERC Researchers at CRG
- New Hirings