Annual report 2025

CRG Centre de Regulació Genòmica

EXCELENCIA SEVERO OCHOA

CERCA Centres de Recerca de Catalunya

Close

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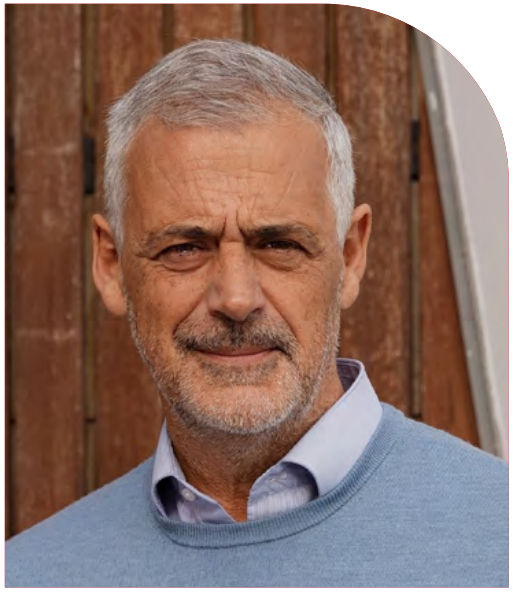
Foreword

Luis Serrano
DIRECTOR (2011–2026)



The year 2025 was one of transition, renewal and continued ambition for our institute. As I write these lines, having completed my term as Director , I look back with immense pride at what our community has achieved and with great confidence in the future of the institution.

Throughout the year, researchers continued to push the boundaries of knowledge across disciplines, from genome biology and RNA research to systems biology, tissue biology, computational biology and artificial intelligence. Our scientific excellence was recognised through major competitive grants and fellowships, including two new ERC Starting Grants, new ICREA appointments, support from the "la Caixa" Foundation, AECC, BBVA Foundation and many other funding bodies. These achievements reflect the creativity, determination and talent of our researchers at every career stage.

At the institutional level, 2025 was marked by important milestones. We expanded our presence at Barcelona's Torre MareNostrum, strengthening our commitment to computational biology and AI, received positive external evaluation of the Genome Biology Programme, and continued to reinforce our international leadership through initiatives such as the Federated European Genome-phenome Archive, which reached a new milestone with its expansion both beyond and within Europe.

A particularly significant moment for the institute was the appointment of Mónica Bettencourt-Dias as the next Director of the CRG. An outstanding scientist and experienced leader, she will officially take up the position in May 2026. I am delighted to pass the baton to her and confident that under her leadership the CRG will continue to flourish, expand its scientific impact and strengthen its position among the world's leading biomedical research centres.

Innovation remained a defining feature of our institute. New partnerships with technology providers brought cutting-edge capabilities to our scientific platforms, while the launch of the Single-Cell Transversal Platform and new collaborations in rare disease diagnostics further reinforced our commitment to translating knowledge into impact. At the same time, our community continued to advance sustainability, diversity and inclusion, recognising that scientific excellence must go hand in hand with responsible and equitable research practices.

One of the most significant collective efforts of the year was the preparation and submission of our proposal to renew the Severo Ochoa Centre of Excellence accreditation. The application mobilised researchers, support staff and leadership teams across the institute. We now know that this effort has been rewarded with a successful outcome, reaffirming the CRG's position among Spain's leading research centres.

After more than fourteen years as Director, it has been a privilege to witness the growth of the CRG into a globally recognised centre of excellence. While I now return my full attention to research, I do so knowing that the institute is entering a new chapter from a position of strength. The achievements described in these pages belong to the entire CRG community, whose dedication, curiosity and collaborative spirit continue to inspire me every day.

I would like to thank all members of the CRG, past and present, as well as our partners, funders and trustees, for their trust and commitment throughout this extraordinary journey. Above all, I wish Mónica Bettencourt-Dias every success as she takes on the leadership of the institute. I am certain that the CRG's future is bright and that the years ahead will bring new discoveries, new opportunities and even greater achievements.

A Look Back at the Year

INSTITUTIONAL

FÁTIMA GEBAUER ELECTED PRESIDENT OF THE RNA SOCIETY

The RNA Society is one of the world's leading organisations in RNA research. The appointment recognises Gebauer's longstanding scientific contributions and reinforces the CRG's international leadership in the field of RNA biology.

SAB VISIT AND GENOME BIOLOGY PROGRAMME EVALUATION

In February, the Scientific Advisory Board visited the centre and highlighted the strength and ambition of its research programmes, while in July the Genome Biology Programme received an excellent evaluation from an international panel of experts.

SWITZERLAND JOINS THE FEDERATED EGA

After the incorporation of Canada in 2024, the Federated European Genome-phenome Archive (FEGA) welcomed Switzerland in 2025, which adds the tenth node to this initiative. Coordinated in part by the CRG, the initiative strengthens global collaboration in secure genomic data sharing and supports international biomedical research.

CRG EXPANDS PRESENCE AT TORRE MARENOSTRUM

We strengthened our commitment to computational biology and artificial intelligence by establishing a new presence at Barcelona's Torre MareNostrum innovation hub. We rented an entire floor there, creating new opportunities for interdisciplinary collaboration at the interface of genomics, data science and AI. The move will also bring the Barcelona Collaboratorium into the same space, relocating the initiative from the Fundació Pasqual Maragall and further strengthening synergies between institutions working at the intersection of biomedicine, technology and innovation.

MÓNICA BETTENCOURT-DIAS APPOINTED NEW CRG DIRECTOR

In July 2025, the CRG Board of Trustees appointed Mónica Bettencourt-Dias as the new Director of the CRG. An internationally recognised cell biologist and experienced scientific leader, she will guide the institution through its next phase of scientific and organisational development. She will officially begin her mandate in May 2026.

EU-LIFE STRENGTHENS COLLABORATION AND ADVOCACY ACROSS EUROPE

As part of the EU-LIFE alliance, we contributed to expanding its influence as a network of leading life sciences research institutes across Europe. The alliance welcomed two new members, strengthening its presence to 17 institutes in 16 countries. EU-LIFE also reinforced its role in European science policy, advocating for ambitious research funding and stronger support for investigator-driven science, while promoting initiatives for postdoctoral researchers, research careers, collaboration and scientific excellence across Europe.

INSTITUTIONAL

GENDER EQUALITY, DIVERSITY AND INCLUSION (GEDI) INITIATIVES

Throughout 2025, the GEDI Committee continued promoting a more inclusive and supportive research environment through a range of initiatives and awareness activities. These included new Child and Family Care Travel Support Grants, the continuation of the Women Scientists Support (WOSS) programme, celebrations marking the International Day of Women and Girls in Science and International Women's Day, and organisation of the Pride Walk to support LGBTQIA+ visibility in science. The committee also launched an internal communication campaign to raise awareness of GEDI initiatives and foster greater community engagement across the institute.

ADVANCING SUSTAINABILITY AT THE CRG

Several CRG laboratories received LEAF (Laboratory Efficiency Assessment Framework) certification in 2025, recognising efforts to reduce waste, energy consumption and the use of single-use plastics. The achievement reflects the CRG community's growing commitment to embedding sustainable practices into everyday scientific research.

ADVANCING RESEARCH EVALUATION AND IMPACT NARRATIVES

The CRG continued contributing to international discussions on research assessment reform through initiatives such as CoARA and the CoARA Boost project INCAS. These efforts support more responsible and inclusive approaches to recognising the value of fundamental research and its long-term societal impact.

ART AND SCIENCE MEET AT THE ECABOX EXHIBITION

The exhibition *Seeing. Un ull i una caixa*, hosted at the Convent de Sant Agustí, brought together art, science and public engagement through the Ecabox project. The initiative invited audiences to reflect on perception, technology and biology, highlighting the CRG's commitment to fostering dialogue between scientific research and contemporary culture.

FUNDING

FIVE “la Caixa” INPhINIT FELLOWSHIPS AWARDED

Five PhD projects at the CRG received “la Caixa” Foundation INPhINIT fellowships in 2025. The highly competitive programme supports outstanding early-career researchers pursuing ambitious interdisciplinary research.

RENÉE BEEKMAN RECEIVES FERO FELLOWSHIP

Renée received the XXIX FERO Young Researchers Fellowship, recognising her work in cancer biology and precision medicine. The award supports innovative research aimed at improving cancer diagnosis and treatment.

AECC SUPPORTS NEW CANCER RESEARCH PROJECTS

The Spanish Association Against Cancer (AECC) awarded funding to Luciano Di Croce and Sara Sdelci, both developing innovative approaches to understand and prevent cancer metastasis. The projects aim to uncover new vulnerabilities in some of the deadliest forms of cancer.

PROJECT VITA LAUNCHES TO PROMOTE HEALTHY AGEING

Researchers from Hospital del Mar Research Institute, the CRG (Mara Dierssen) and IrsiCaixa launched Project VITA, an ambitious initiative focused on understanding healthy ageing. The project forms part of the global XPRIZE Healthspan competition.

TWO ERC STARTING GRANTS AWARDED TO THE CRG

The European Research Council awarded two new Starting Grants to newcomers Markus Höpfler and Hsiu-Chuan Lin. The prestigious grants will support pioneering research into gene regulation, cell communication and brain biology.

FUNDING FOR AGEING RESEARCH

The BBVA Foundation awarded funding to Nick Stroustrup for a project investigating the molecular roots of ageing. The research aims to uncover fundamental biological mechanisms linked to longevity and age-related disease.

FUNDING

SUPPORT FROM THE CATALAN GOVERNMENT'S *PROJECTES SINGULARS*

The CRG secured funding through this programme from the Catalan Government to develop an integrated microscopy infrastructure for the advanced study of biological samples. The initiative will strengthen technological capabilities supporting strategic research and innovation with scientific, social and economic impact.

TWO NEW DOCTORAL NETWORKS AWARDED

The CRG will coordinate two new European Doctoral Networks funded in 2025 by the Horizon Europe Marie Slodowska-Curie Actions (MSCA): EvoMG-DN, focused on evolutionary medical genomics (Manuel Irimia), and ProtAIomics, dedicated to integrating artificial intelligence into proteomics research and translational applications (Eduard Sabidó).

BUSINESS, INNOVATION AND TECHNOLOGIES

VERITAS GENETICS ACQUIRES QGENOMICS

The first CRG spin-off, qGenomics, specialised in genomic diagnostics, was acquired by Veritas Genetics. The acquisition reflects the impact of CRG innovation and entrepreneurship in advancing precision medicine technologies.

CRG INNOVATORS DAY CELEBRATES ENTREPRENEURSHIP AND TECHNOLOGY TRANSFER

This activity recognised outstanding innovation initiatives through the CRG Innovator Award and MenTT4Inn programme. The event highlighted the centre's growing entrepreneurial ecosystem and commitment to technology transfer.

NEW SINGLE-CELL TRANSVERSAL PLATFORM LAUNCHED

The Core Technologies Programme launched its new Single-Cell Transversal Platform, bringing together expertise and technologies from flow cytometry, genomics, protein technologies and bioinformatics to support advanced single-cell research. The platform provides integrated access to cutting-edge equipment and specialised support for analysing complex cellular systems at single-cell resolution, strengthening the institute's capabilities in biomedical and translational research.

NEW TECHNOLOGY PARTNERSHIPS STRENGTHEN RESEARCH INFRASTRUCTURE

New collaborations were established with leading technology providers to deploy cutting-edge equipment and co-develop innovative applications across multiple scientific platforms. The Flow Cytometry Unit partnered with Becton Dickinson Biosciences and ThermoFisher Scientific to install two new spectral cytometry platforms, while Element Biosciences deployed its latest Aviti24 sequencing platform in the Genomics Unit for access by the wider research community. The Proteomics Unit also partnered with ThermoFisher Scientific to advance single-cell proteomics applications, reinforcing the CRG's technological capabilities in genomics, proteomics and single-cell research.

COLLABORATION WITH SANT JOAN DE DÉU TO ADVANCE RARE DISEASE DIAGNOSTICS

The CRG strengthened its collaboration with Fundació Sant Joan de Déu (FSJD) and Hospital Sant Joan de Déu (HSJD) through a joint initiative focused on paediatric rare diseases and advanced genomic diagnostics. As part of the agreement, a PacBio REVIO long-read sequencing platform was transferred to the CRG to support clinical and translational research. The collaboration also included participation by the CRG's Genomics and Bioinformatics Units in the first "Únicas Hackathon", contributing sequencing and analysis expertise to help diagnose paediatric patients with suspected rare diseases lacking genetic confirmation.

COMING AND GOING

After years of important contributions in quantitative cell and developmental biology, Verena Ruprecht left the CRG to join the University of Innsbruck, in Austria.

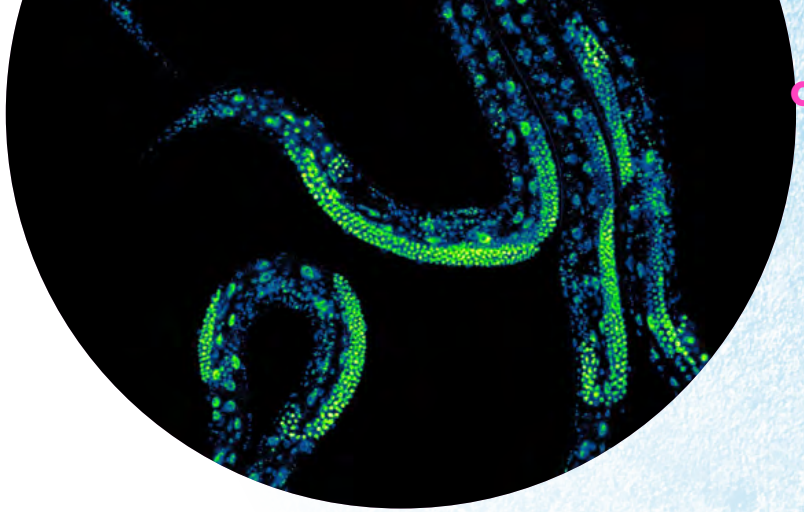
Luis-Carlos Tábara joined the CRG as a new Group Leader, to investigate how mitochondrial dynamics and mitochondrial DNA (mtDNA) copy number are regulated, and how their disruption contributes to ageing and disease. By using different techniques, his lab aims to uncover the mechanisms that maintain mitochondrial health and mtDNA balance, with the goal of identifying new strategies to prevent or treat disease.

We welcomed Markus Höpfler as a new Group Leader who will investigate how cells regulate protein production by controlling the stability and degradation of messenger RNAs (mRNAs), with a particular focus on a newly emerging mechanism called peptide-mediated mRNA decay (PMD), in which the nascent protein itself triggers degradation of the mRNA being translated.

Hsiu-Chuan Lin joined the CRG as a new Group Leader to uncover the principles that govern cell fate decisions and apply them to engineer human cells. By studying cellular processes their group seeks to understand and precisely control cell identity changes, enabling the generation of diverse human cell types and more accurate models of human biology and disease.

Jaume Bacardit was appointed the new Administrative Director, succeeding Joan Vives after his departure from the institution earlier in the year. The transition marks a new chapter in the centre's administrative leadership.

Research Highlights



Can your housemate's genes shape your gut microbes?

Working with more than 4,000 rats, the group of **Amelie Baud** showed that an animal's gut microbiome is shaped not only by its own genes but by the genes of the individuals it lives with, an "indirect genetic effect" carried by microbes that pass between individuals. Including these social effects raised the estimated genetic influence on certain bacteria four- to eight-fold.

The finding reveals a hidden route by which genes and social life intertwine, and helps explain part of the long-standing puzzle of "missing heritability" in microbiome studies.

A plant hormone dials proteins up and down for life

Nick Stroustrup and his team re-engineered the auxin-inducible degron system into a "dual-channel" tool that uses two plant-hormone triggers to control how much of a protein remains, in which tissue, and when. They tested it across more than 100,000 worms and found it works even in reproductive tissues, where such systems usually fail.

Rather than simply switching proteins off, the technique turns them up or down like a volume dial, opening new ways to study the molecular drivers of ageing and disease in a whole, living animal.

Content

Human gene maps tilt towards European ancestries

A joint BSC and CRG (**Roderic Guigó**) study used long-read RNA sequencing across a diverse human cohort uncovered tens of thousands of transcripts missing from current gene maps in people of African, Asian and American ancestry, some potentially the products of entirely new genes. Many were from genes already linked to lupus, asthma and metabolic traits.

The work shows reference gene maps must include far more ancestries if precision medicine is to work equally well for everyone, and not leave whole populations invisible to biomedical research.

Gene ‘start lines’ are a new mutation hotspot

The group of **Donate Weghorn** found that the first 100 letters after a gene’s transcription start site are 35% more prone to mutation than expected, a hotspot driven by stalling transcription machinery and DNA breaks during the rapid cell divisions just after conception, leaving heritable “scars” across the genome.

It is a rare discovery of an entirely new source of germline mutation, with direct consequences for how we read disease risk written into the genome.

Content

AI reads the tree of life to flag disease mutations

Jonathan Frazer and **Mafalda Dias**, with Harvard Medical School, built popEVE, a model that learns from evolution across thousands of species and from human population data to score how damaging a protein mutation is, even one never seen before in any person, with scores that are finally comparable across the whole proteome.

The tool can help clinicians prioritise the most damaging variants first, supporting diagnosis for ultra-rare cases.

‘Dual-feeding’ coral shrugs off Mediterranean heat

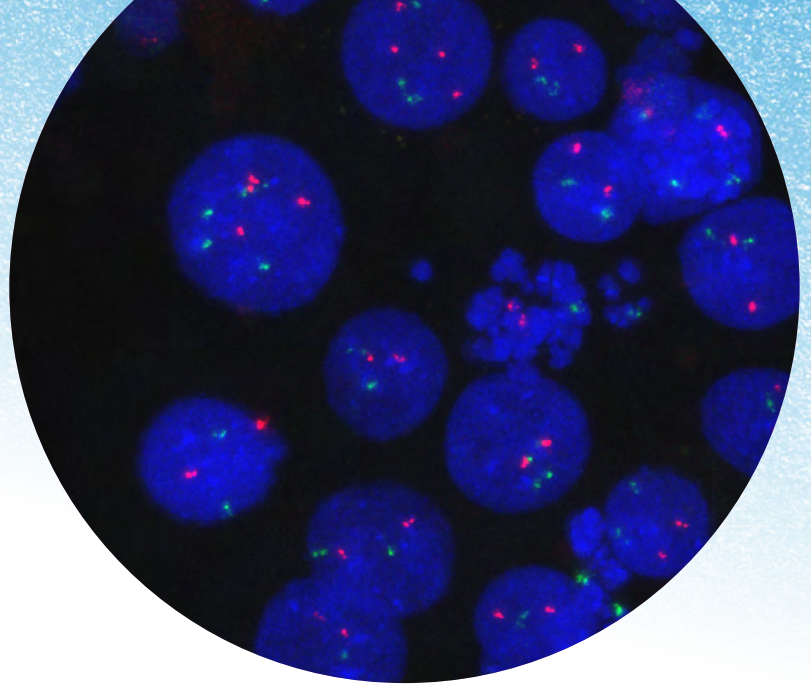
Arnau Sebé-Pedrós’ research group showed that the Mediterranean stony coral *Oculina patagonica* survives marine heatwaves by switching between two diets. They draw energy from symbiotic algae when conditions allow and feed directly on plankton when water temperatures are above 29˚C. Cell-atlas comparisons revealed this fall-back is an ancient ability conserved across corals rather than a new invention. The study is a window into how marine life may adapt to a warming world.

Content

Generative AI out-designs nature's genome editors

In a collaboration led by Integra Therapeutics and UPF, **Noelia Ferruz** used protein language models to generate entirely synthetic transposases, the "copy-and-paste" enzymes that insert large DNA sequences into the genome. They could edit human cells more efficiently than their natural counterparts.

The advance points to better, faster tools for the cell and gene therapies, including CAR-T, that underpin treatments for cancer and rare disease.



One lymphoma swap rewires 50 genes at once

Renée Beekman found that the chromosome translocation typical of mantle cell lymphoma does far more than disrupt the genes at its breakpoints: it drags a powerful regulatory element, the IGH enhancer, into a new position where it boosts the activity of around 50 genes, nearly 7% of an entire chromosome, across 50 million letters of DNA.

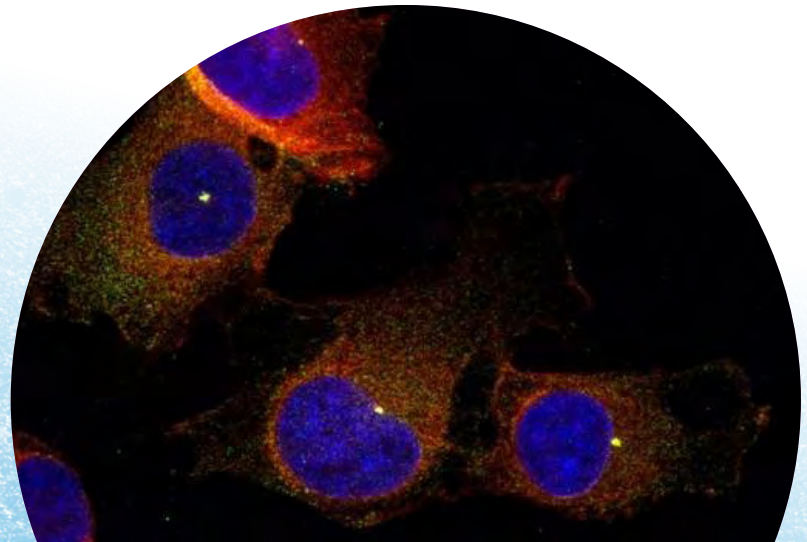
The discovery widens the search for drug targets in an incurable cancer and suggests at-risk cells could be spotted, through epigenetic profiling, before a lymphoma ever appears.

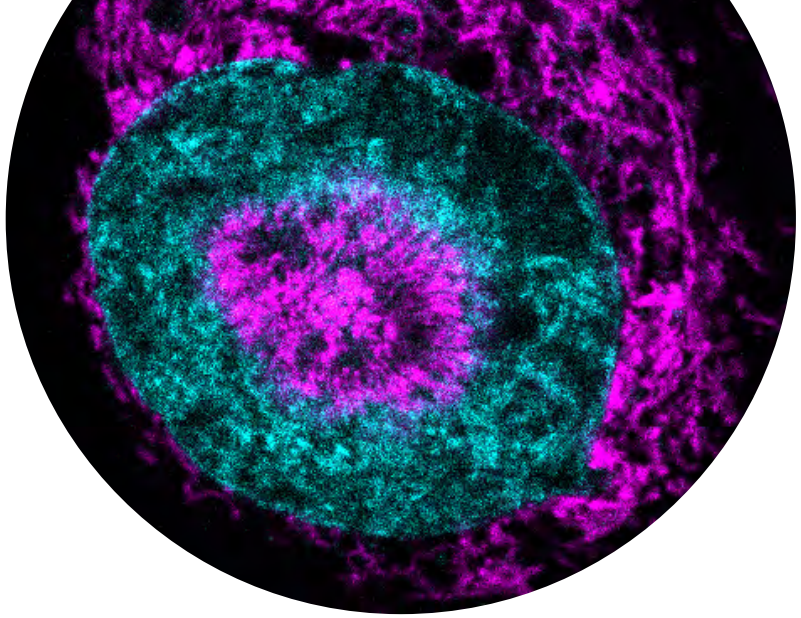
Content

Melanoma's 'sat-nav' protein is a metastasis target

Fàtima Gebauer discovered that the protein eIF2A is not a translation factor as long assumed, but a scaffold that keeps a melanoma cell's centrosome, its internal compass, correctly oriented for directed movement. Removing it stalled tumour-sphere growth and slowed migration, with barely any effect on protein production.

Because cells only become dependent on eIF2A after turning malignant, it offers a potential therapeutic window to curb metastasis while sparing healthy tissue.





Squeezed cancer cells 'power up' to survive

Using a microscope that compresses living cells to three microns wide, **Verena Ruprecht** and **Sara Sdelci** caught mitochondria rushing to the nuclear membrane to deliver a rapid surge of ATP (seen in 84% of confined cancer cells) that helps them repair DNA and endure the mechanical battering of tumours, blood vessels and the bloodstream.

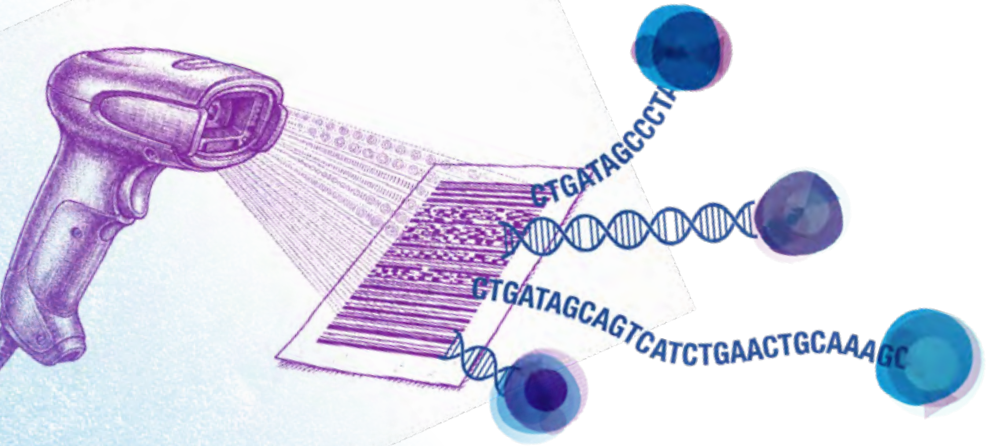
Blocking this energy scaffold could make tumours less invasive without poisoning healthy mitochondria, marking mechanical stress as an underexplored vulnerability of cancer.

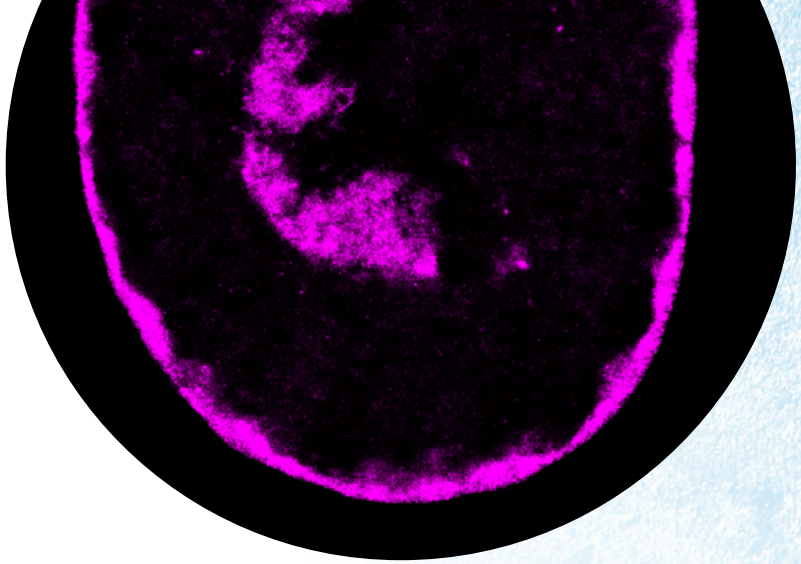
Content

Genome ‘re-read’ doubles known structural variation

In two back-to-back papers co-led with EMBL and Heinrich Heine University Düsseldorf, CRG researcher **Bernardo Rodríguez-Martín** used long-read sequencing to re-read 1,019 genomes from 26 populations, cataloguing more than 167,000 large structural variants and doubling the known structural variation in the human pangenome. More than half of the insertions were never reported before.

The work is a major step from a single “standard” genome towards a true human pangenome, better suited to personalised medicine and far less biased towards European ancestry.





Herpes virus redecorates the human genome in 3D

Combining super-resolution microscopy with Hi-C, **Pia Cosma** showed that within an hour of infection, herpes simplex virus-1 hijacks the host’s RNA polymerase, topoisomerase I and cohesin, compacting the human genome and folding it to reach the genes it needs. It’s the first proof the virus reshapes our DNA architecture deliberately.

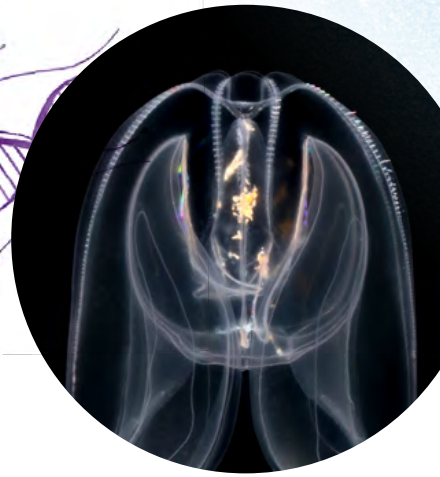
Crucially, blocking a single host enzyme, topoisomerase I, halted the takeover before the virus could make a single new particle, a potential new way to fight a virus carried by some four billion people, with no cure and rising drug resistance.

Content

DNA ‘barcodes’ reveal how our blood ages

Lars Velten, with IRB Barcelona, developed EPI-Clone, which reads naturally occurring methylation “barcodes” to trace blood stem-cell families without genetic engineering across 230,000 single cells from mice and people. It revealed that ageing blood loses diversity as a few inflammation-prone clones take over, a shift detectable from age 50 and near-universal by 60.

Because many dominant clones carry no known cancer mutation, the work reframes clonal takeover as a general feature of ageing and points to a way of flagging unhealthy blood ageing years before disease appears.



Comb jellies push genome control back 150 million years

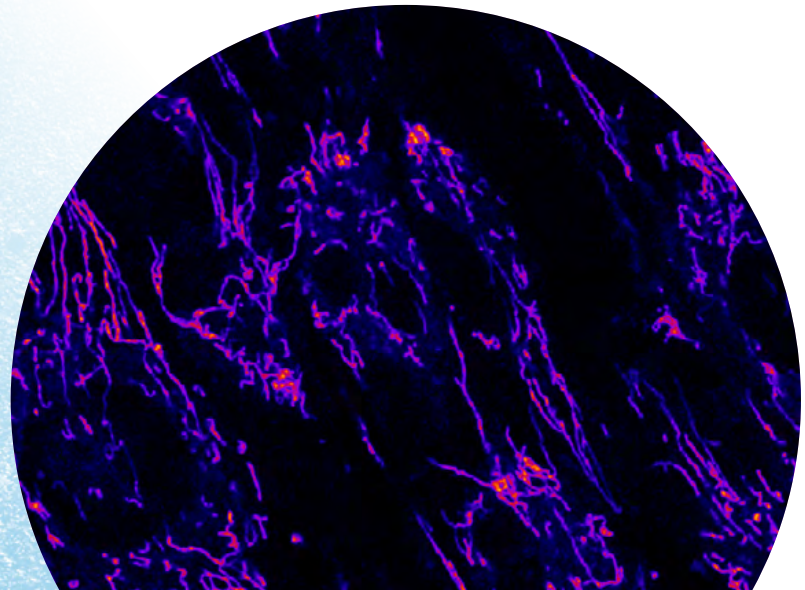
A CRG–CNAG study led by **Arnau Sebé-Pedrós and Marc A. Marti-Renom**, with first author Iana Kim, used 3D genome mapping of comb jellies, sponges, placozoans and cnidarians to show that long-distance gene control evolved 650 to 700 million years ago, around 150 million years earlier than thought.

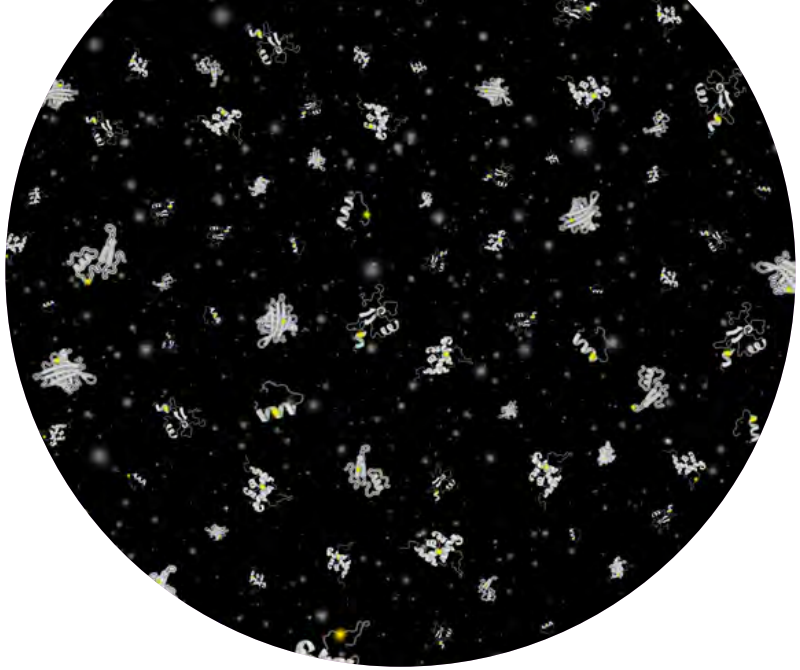
This extra regulatory layer likely let the first animals build specialised tissues without inventing new genes, repurposing their genetic toolkit “like a Swiss knife”.

Content

Fat-shuttle protein explains rare childhood crises

Marking International Rare Disease Day, the group of **Vivek Malhotra** showed that the protein TANGO2 binds and shuttles acyl-CoA fat molecules inside cells, readying them to be burned for energy. In children with TANGO2 Deficiency Disorder this fails, starving cells of usable fats and triggering life-threatening metabolic crises. The insight could sharpen diagnosis and guide targeted therapies for the disorder, and illuminate common heart, muscle and fat-metabolism conditions too.





‘Domainome’ pins heritable disease on unstable proteins

Ben Lehner built Human Domainome 1 — over half a million mutations across 522 protein domains, the largest such catalogue to date. It revealed that most disease-causing missense mutations work simply by making proteins less stable. For example, 72% of the cataract mutations tested destabilised the lens protein crystallin. The catalogue explains at the molecular level why tiny genetic changes cause heritable neurological, developmental and muscle-wasting disease.

Research and scientific services

COMPUTATIONAL BIOLOGY AND HEALTH GENOMICS PROGRAMME

Coordinator: **Jorge Ferrer**

In 2025, the Computational Biology and Health Genomics Programme pursued its core vision of understanding genomes as dynamic regulatory systems that enable us to decode evolution, development and disease. A significant development was the arrival of Hsiu Chuan Lin, whose Cell Fate Decoding and Engineering group joined the Programme with the support of both a "la Caixa" Foundation Fellowship and an ERC Starting Grant. This appointment also catalysed a new Programme initiative to develop foundation models capable of predicting the cellular effects of previously unseen genomic perturbations, spearheaded by the Dias, Frazer, Lin and Velten labs.

The year was marked by a series of high-impact studies. The Velten lab demonstrated that spontaneous DNA methylation mutations can serve as natural barcodes for tracing clonal cellular expansions in humans, a finding with broad implications for ageing and disease (Scherer, *Nature* 2025). The group also uncovered new principles governing the transcriptional programming of blood cell lineages (Fromel, Cell 2025). The Ferrer lab identified defective transcriptional and splicing programmes as core molecular lesions in type 2 diabetes, providing a potential therapeutic avenue for the disease (Bernardo *et al.*, *Cell* Metab 2025). The Rodríguez-Martín lab co-led the construction of a landmark resource on human structural variation, leveraging long-read sequencing technologies to chart genomic diversity (Schloissnig *et al.*, *Nature* 2025). Meanwhile, the Weghorn lab illuminated a previously unrecognised mutational mechanism underlying inherited disorders (Cortés Guzmán, *Nat Commun* 2025). Finally, Dias and Frazer developed a deep learning methodology for diagnostic pipelines to predict which rare mutations are likely to cause human diseases (Orenbuch *et al, Nat Genet* 2025) and are implementing analogous pipelines in real-life settings including a SENEGENE, a rare disease diagnostic initiative in Senegal.

Taken together, the achievements of 2025 reflected the breadth and ambition of the Programme, demonstrating how new technologies and fundamental discoveries in genome architecture, function and cell fate can drive progress in understanding human disease.

QUANTITATIVE CELL BIOLOGY PROGRAMME

Co-coordinators:

Isabelle Vernos and Thomas Surrey

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

In 2025, Junior Group Leader Verena Ruprecht relocated her lab (Cell and Tissue Dynamics) to the University of Innsbruck, where she obtained a position as Full Professor. Luis Carlos Tabara Rodriguez joined the department as a Junior Group Leader from the University of Cambridge (UK) to establish his new lab (Mitochondrial Dynamics).

The department produced several publications. Among others, the Malhotra lab (Intracellular Compartmentation) characterised a new acyl-CoA-binding protein, suggesting new avenues for addressing cardiomyopathies (Lujan, *J Cell Biol* 2025). The Böke lab (Oocyte Biology & Cellular Dormancy) presented the first large-scale study characterising reduced organelle activity in human oocytes (Zaffagnini, *EMBO J* 2025). The Ruprecht lab, in collaboration with the Sdelci lab from the Genome Biology Programme, found that an increase in ATP levels in the cell nucleus helps repair DNA damage during mechanical stress (Ghose, *Nat Commun* 2025). The Surrey lab (Intracellular Self-Organisation) provided new insights into how the motor protein dynein organises mitotic spindles during cell division (Colombo, *J Cell Biol* 2025; Chew, *PNAS* 2025).

GENOME BIOLOGY PROGRAMME

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

The Genome Biology Programme focuses on investigating the mechanisms that regulate the expression of the genome during homeostasis, cell reprogramming and disease. We use quantitative omics technologies, mathematical modelling, cell biology and mouse genetics to understand chromatin organisation, transcription, splicing, mRNA translation and degradation, and RNA modification. Mechanisms controlling gene expression are studied in the context of a variety of diseases, including cancer (leukaemia, lymphoma, pancreatic and lung adenocarcinomas, gliomas, melanoma and breast cancer).

Chromatin regulation groups study epigenetic mechanisms in cancer and stem cells (Luciano Di Croce), single-cell epigenomics in lymphomas (Renee Beekman), 3D genome organisation (Marc Martí-Renom, a PI at CNAG with a dual affiliation associated with the Programme), and the epigenetic regulation of cancer metabolism (Sara Sdelci). RNA biology groups study the identification and regulation of RNA modifications (Eva Novoa), alternative splicing (Juan Valcárcel), mRNA translation (Fátima Gebauer), and mRNA stability (Markus Hopfler).

In 2025, Juan Valcárcel, in collaboration with Ben Lehner, used saturation mutagenesis to reveal the regulatory architecture of alternatively spliced exons and received the Carmen and Severo Ochoa Prize. Fátima Gebauer uncovered novel non-canonical roles of translation factors in cancer cell migration. Luciano Di Croce showed that the PRC2-associated factor EPOP is required for proper Hox gene regulation and axial skeleton development in mice, and received support from WWCR to study paediatric brain tumours. Eva Novoa revealed that epitranscriptomic fingerprinting of rRNA can be used to identify the tissue of origin of tumours, and obtained an ERC Proof of Concept grant for cancer diagnosis. Sara Sdelci found that mechanical confinement modulates nuclear ATP content, with consequences for cell proliferation; received the EMBO Young Investigator Programme (YIP) and PharmaMar Argonauta awards; and launched a Marie Skłodowska-Curie Actions (MSCA) Doctoral Network. Renee Beekman discovered that chromosomal translocations can drive gene expression changes across entire chromosome arms and was awarded the XXIX FERO Young Researchers Fellowship. In collaborative work, Marc Martí-Renom found that chromatin loops are an ancestral regulatory hallmark across the animal kingdom. Susana de la Luna moved to IDIBAPS. Markus Hopfler was recruited to the Programme as a Junior PI and received an ERC Starting Grant.

SYSTEMS AND SYNTHETIC BIOLOGY PROGRAMME

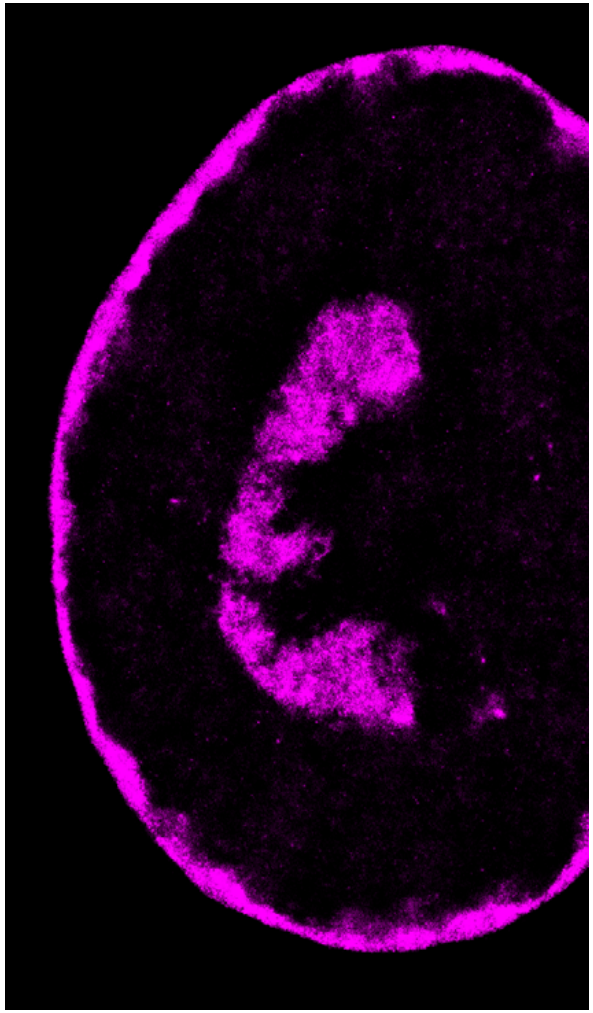
Coordinator: **Pia Cosma**

The Systems and Synthetic Biology Programme spans multiple biological systems and scales, from microbes to entire organs and organisms, and from non-model species to human genetics, evolution, neuroscience and ageing, to address fundamental biological questions through a common framework. We seek to explain, predict and engineer biological systems that underpin cellular, tissue and organ function. The Programme aims to uncover the foundations of life by transforming molecular, cellular and systems biology into a quantitative and predictive engineering science. In 2025, it continued to combine large-scale quantitative data generation with modelling and machine learning to make molecular biology more predictive and programmable, including through the Barcelona Collaboratorium for Modelling and Predictive Biology, a joint initiative with EMBL Barcelona.

Several important achievements marked 2025. Nick Stroustrup's group developed an engineered auxin-inducible degron system that enables tuneable *in vivo* control of organismal physiology, providing a new way to manipulate protein levels and dissect the molecular mechanisms of ageing and disease (Vicencio *et al.*, *Nature Communications*, 2025). Amélie Baud's group showed that the gut microbiome is shaped not only by an individual's own genes but also by the genes of its social partners, revealing a social dimension of host–microbiome genetics (Baud *et al.*, *Nature Communications*, 2025). Ben Lehner's group further advanced our understanding of protein evolution and design by showing how genetics, energetics and allostery interact in proteins with randomised cores and surfaces, strengthening the Programme's broader goal of developing predictive biology (Escobedo *et al.*, *Science*, 2025). Luis Serrano's group produced a comprehensive essentiality map of a living organism. Using *Mycoplasma pneumoniae*, they defined which genomic elements are required, tolerated or dispensable in a minimal living cell (Miravet-Verde *et al.*, *Molecular Systems Biology*, 2025). Mara Dierssen's group continued to advance the Programme's systems-level approach to neuroscience, focusing on the neurobiology of learning and memory and their perturbation in brain disorders, including intellectual disability and Down syndrome (Fernández-Blanco *et al.*, *Cells*, 2025).

The Programme also contributed to advances in AI-guided protein engineering, evolutionary genomics and host–pathogen biology. Noelia Ferruz co-authored a *Nature Biotechnology* study on protein language model-guided discovery and design of hyperactive transposases, demonstrating the potential of generative approaches to expand genome-engineering tools (Ivančić *et al.*, *Nature Biotechnology*, 2025). Arnau Sebé-Pedrós's group used comparative genomics and single-cell atlases to investigate the genomic and cellular basis of facultative symbiosis in the thermotolerant Mediterranean coral *Oculina patagonica*. Their work shed light on the mechanisms that allow some corals to survive extended bleaching events (Levy, Grau-Bové *et al.*, *Nature*, 2025). Pia Cosma's group showed how HSV-1 rewires host chromatin architecture during lytic infection by hijacking the transcriptional machinery and forming contacts between viral and host genomes (González-Almela *et al.*, *Nature Communications*, 2025). Nora Martin continued to strengthen the Barcelona Collaboratorium's modelling and predictive biology activities as an Independent Collaboratorium Fellow, developing quantitative models of evolution, genotype–phenotype maps and fitness landscapes, and contributing to the Programme's broader effort to connect mechanistic biological understanding with predictive modelling. Eric Latorre joined the Programme as a Barcelona Collaboratorium Independent Fellow to develop mathematical and computational models of cellular ageing, combining modelling with experimental design to investigate ageing mechanisms and their links to age-related disease.

The Programme also received important public recognition and funding. Arnau Sebé-Pedrós was awarded the 2025 Spanish National Research Award for Young Scientists – Margarita Salas in Biology, in recognition of his work in comparative genomics, evolutionary biology and the origins of animal cell types. Luis Serrano received the 2025 Spanish National Innovation and Design Award in the Innovative Career category, the highest national recognition for scientific and business leadership in R&D, highlighting his contributions to systems biology, protein design, technology transfer and spin-off creation. He also received the 2025 Catalan National Research Prize, which recognises his pioneering career and contributions to systems and synthetic biology. Nick Stroustrup was awarded a grant from the BBVA Foundation for a project aimed at disentangling the causal molecular mechanisms of ageing. Mara Dierssen maintains a strong public engagement profile and is part of the VITA consortium, which was selected as a semi-finalist in the XPRIZE Healthspan competition in 2025.



CORE TECHNOLOGIES PROGRAMME

Head: **Mònica Morales**

The Core Technologies Programme comprises 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 2025, the Programme entered into agreements with several technology providers, leading to the deployment of cutting-edge equipment across multiple Units and the joint development of new applications in their respective fields. In particular, the Flow Cytometry Unit established collaborations with Becton Dickinson Biosciences and Thermo Fisher Scientific, enabling the installation of two new spectral cytometry platforms. Element Biosciences deployed its latest sequencing platform, Aviti24, in the Genomics Unit for access by the wider research community, and the Proteomics Unit partnered with Thermo Fisher Scientific to co-develop single-cell proteomics applications.

During this period, the Programme successfully secured funding through the Spanish regional FEDER programme for the acquisition of four new instruments, strengthening the Protein Technologies, Flow Cytometry, Genomics and Advanced Light Microscopy Units. The equipment for the Genomics and Advanced Light Microscopy Units was acquired in 2025, while the remaining instruments will be purchased and deployed in the corresponding Units in 2026.

The new transversal single-cell platform began providing services in 2025 and has already delivered more than 100 integrated services to both internal and external users. Efforts are currently under way to integrate the Proteomics Unit into the platform, enabling the provision of single-cell proteomics and fully integrated multiomics services to end users. In parallel, the platform has introduced spatial transcriptomics services with single-cell resolution, for which demand is steadily increasing.

Additionally, innovation has remained a strategic priority across the Programme, with several Units securing public–private partnership grants, as well as European consortium-based funding, to support the development and implementation of emerging technologies.

EUROPEAN GENOME–PHENOME ARCHIVE (EGA)

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

The European Genome–phenome Archive (EGA), jointly managed by the Centre for Genomic Regulation (CRG) and the European Bioinformatics Institute (EMBL-EBI), in collaboration with the Barcelona Supercomputing Center (BSC-CNS), is a secure global repository for human genomic and phenotypic data. Recognised as the worldwide reference for sharing personally identifiable data, the EGA provides essential services for data archiving, discovery and access, in accordance with FAIR principles, to researchers around the world.

During 2025, the EGA archived and made available for re-use 926 new datasets and distributed 2,698 datasets to scientists to support their research. By the end of the year, the total volume of archived data had surpassed 20 PB, and the Helpdesk team had responded to more than 5,000 requests from researchers.

The CRG's EGA team, now comprising 24 multidisciplinary professionals, has co-led the Federated EGA Network since 2022, enabling secure cross-border genomic data sharing. In 2025, the network included nine national nodes, including Canada and Switzerland. The technology underpinning this network was developed by the CRG team.

In 2025, the team completed three collaborative projects and launched five new ones, contributing to a portfolio of 16 active competitive grants. The CRG's EGA team also leads the global development of Beacon, a genomic data discovery technology, and supported 43 Beacon instances across 13 countries during 2025 alone. In addition, the team developed new tools and deployed the Global Beacon Atlas.

Honours and Awards

ICREA Research Professor

Eva Novoa

29th FERO Young Researchers Fellowship, FERO Foundation

Renée Beekman

ICREA Research Professor

Elvan Böke

2025 Catalan National Research Award

Luis Serrano

EMBO Young Investigator

Sara Sdelci

President of the RNA Society

Fátima Gebauer

2025 Spanish National Research Award for Young Scientists – Margarita Salas in Biology

Arnau Sebé-Pedrós

2025 Spanish National Innovation and Design Award, Innovative Career category

Luis Serrano

Best Young Researcher, Argonauta Prizes, Pharmamar Foundation,

Sara Sdelci

FEBS Excellence Award

Noelia Ferruz

30th Carmen and Severo Ochoa Prize for Research in Molecular Biology, Carmen and Severo Ochoa Foundation

Juan Valcárcel

ERC grantees at CRG*

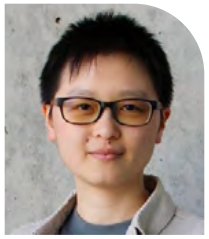
STARTING GRANTS

Arnau Sebé-Pedrós

Nicholas Stroustrup

Sara Sdelci

Renée Beekman



Hsiu-Chuan Lin

Lars Velten

Eva Novoa

Noelia Ferruz

Markus Höpfler

ADVANCED GRANTS

Luis Serrano

Ben Lehner

* Ongoing and ended projects during 2025

CONSOLIDATOR GRANTS

Elvan Böke

Arnau Sebé-Pedrós

SYNERGY GRANTS

Verena Ruprecht

Juan Valcárcel

Vivek Malhotra

Thomas Surrey

PROOF OF CONCEPT GRANTS

Luis Serrano

Ben Lehner (2)

Jorge Ferrer

Eva Novoa

Facts & figures

Publications

201
Total Publications (articles & reviews)

89%
Open Access Publications

81%
1st Quartile Publications

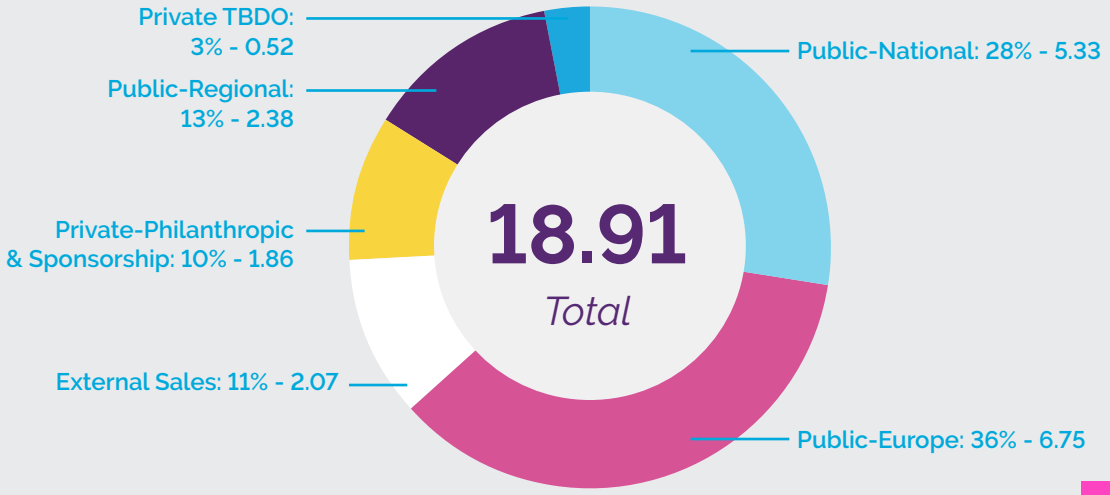
14.0
Average Impact Factor

Funding (M€)

42.5
Total Funding

EXTERNAL FUNDING AWARDED IN 2025

Note: The above graph includes competitive funds obtained during 2025 and pending for final notice of award or grant agreement as of 31/12/2025



Projects

152

Total Ongoing Research Projects and Networks

19 *are Ongoing ERC Projects*

13 *are Ongoing Coordinated Projects*

29 *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

462.85*

*Total FTE**

476

Total

* Full-time equivalent

Research Staff

297.26* *Total FTE**

307 *Total*

Scientific Services

66.90* *Total FTE**

68 *Total*

Administration & Scientific Support

98.70* *Total FTE**

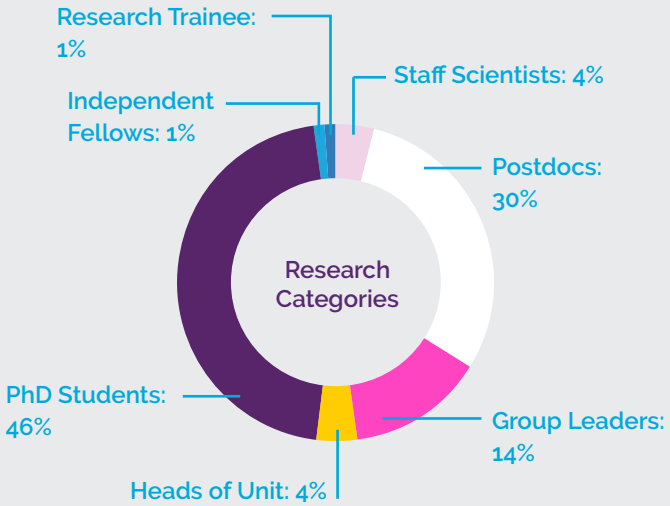
101 *Total*

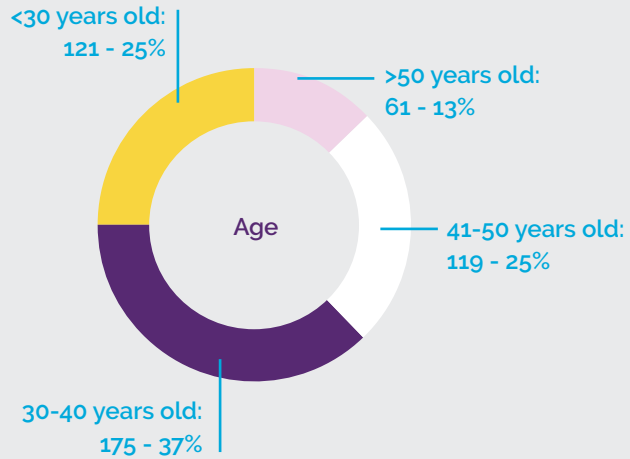
Research Groups (by 31st Dec 2025)

34 *Total*

32 *CRG*

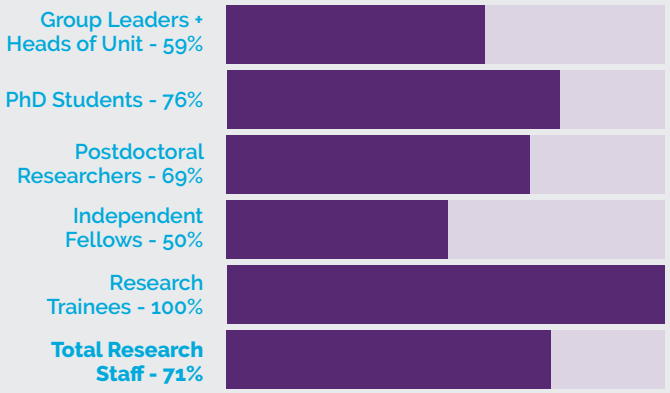
2 *Dual-affiliation*



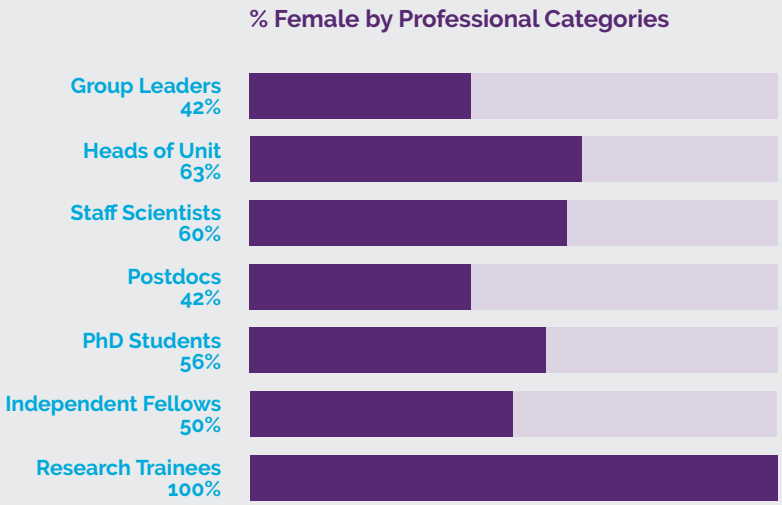


Internationality

47 nationalities represented



Gender



Applicants to our Selection Processes

45% 55%

1,192 1,449

Selected / Hired Candidates

47% 53%

42 47

% Female invited speakers

39% in 2025

(41% in 2024)

Advanced training

PhD Theses defended

24

Courses@CRG / EMBO Workshops

2 *international courses*

43 *participants*

Scientific Skills & RR Courses

48 *internal courses*

734 *participants*

Transferable Skills & Innovation Courses

18 *internal courses*

328 *participants*

Career-related Training Events

8 *internal courses*

121 *participants*

Language Courses (CA, ES, EN)

29 *internal courses*

189 *participants*

Events

10
International Conferences

65
High-profile Seminars

Technology and business development

7
Spin-offs

27
Ongoing Valorisation Projects

31
Active Patent Families

14
Invention Disclosures

7
Services, Scientific Collaborations & Licenses Agreements

186
Other Agreements

Communications, public engagement & science education

MEDIA RELATIONS

2,149
Media Appearances

239
Print Media

1,837
Online Media

51
Radio

22
TV

SOCIAL MEDIA
(by 31st Dec 2025)

YouTube
335,796
Channel views

2,403
Subscribers

Facebook
5,003
Likes

4,995
Followers

Instagram followers
2,564

LinkedIn followers
37,347

Bluesky followers
2,931

PUBLIC ENGAGEMENT AND SCIENCE EDUCATION

81
Nr. Activities Delivered

24,675
Audience Reached

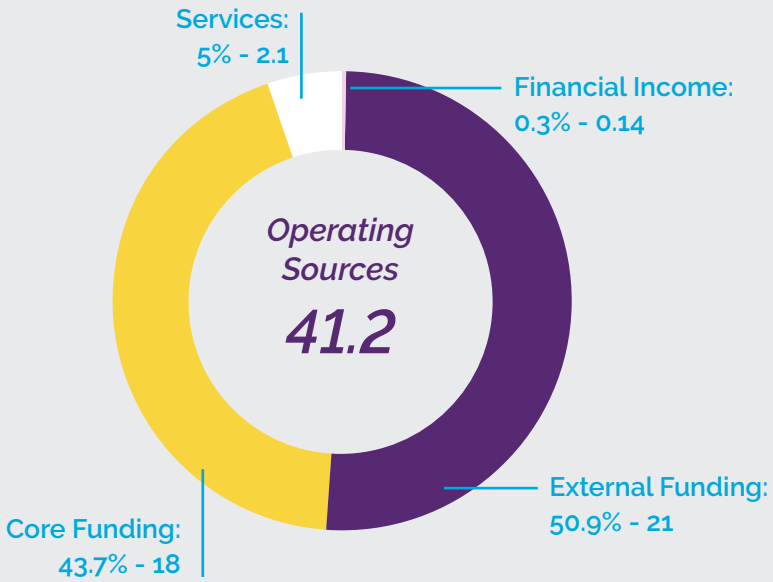
1,970
Students

22,705
General Public

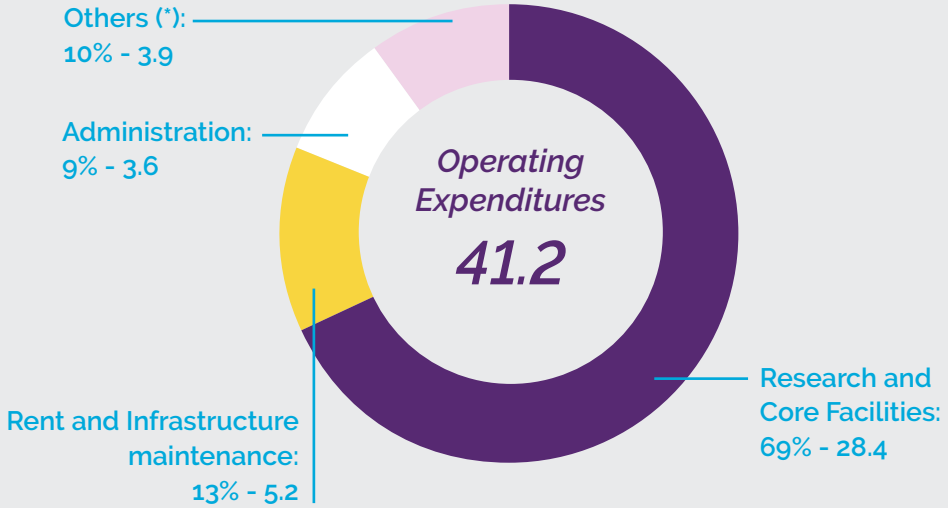
Financial report

SOURCES & USES MANAGED

Operating sources in M€



Operating expenditures in M€



(*) **Others includes**: Director's group + SaF + TBDO + TAO + Pre-award + Communications + €74.5k financial expenses

Acknowledgements

TRUSTEES

Generalitat de Catalunya

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

erc European Research Council

AGENCIA ESTATAL DE INVESTIGACIÓN

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

FECYT

BARCELONA CULTURA Ajuntament de Barcelona

NIH National Institutes of Health

ICREA

ciber CENTRO DE INVESTIGACIÓN BIOMÉDICA EN RED

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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