



CAREER DEVELOPMENT AND GENDER BALANCE, TOP PRIORITIES

The CRG Gender Balance Committee gets down to business with numerous proposals for the second half of 2015

Two new initiatives to support and promote the careers of young researchers have been recently launched. Firstly, following its success last year, the second year of the Mentoring Programme has now been launched. This program, which is exclusively for post-docs, aims to help them in their professional development through the support and guidance of a senior researcher. Feedback from the previous year emphasizes how the relationship of trust between mentor and mentee helps to increase awareness and confidence in oneself and opens up a range of new ideas, horizons and unimaginable challenges.

Secondly, a new program will start for women scientists who are at a crucial point in their careers and personal lives, both of which require a high level of dedication. Based on the successful German program developed by the Nobel

prize winner Christiane Nüsslein-Volhard, the Women Scientists Supporting Grant (WOSS) specifically aims to support ambitious women scientists who have the potential to achieve a leading position but who also have responsibilities associated with motherhood. PhD students and postdocs who meet these requirements can apply throughout the year. After selection by an external panel, successful candidates will receive financial support to allow them to combine doing cutting-edge research with motherhood.

Both of these proposals are aimed at closing the gap to having equal opportunities for men and women in research. Many situations have to be taken into account before implementing specific actions, and these programs address the needs that have been detected at the CRG for supporting high-quality, innovative research and top-level scientific careers. <

SPAIN JOINS ELIXIR

On October 23rd, the ELIXIR Board unanimously accepted Spain and France as full members of ELIXIR, the largest infrastructure of life science data in Europe. ELIXIR's aim is to manage, exploit, and distribute the massive amounts of information generated currently by biomedical re-

search. Entering this partnership will allow Spain to strengthen its ties with Europe and to lead large-scale projects in biomedicine, such as those related to human genomic diseases.

Until now, Spain had participated in ELIXIR as an Observer country. Spain is represented within ELIXIR by the National Institute of Health Carlos III

(ISCIII), under the Ministry of Economy and Competitiveness. The National Bioinformatics Institute (INB), which acts as the Spanish scientific node, will coordinate the Spanish scientific partner institutions. These comprise top-level institutions such as the CNIO, the UPF, the IRB Barcelona, the BSC-CNS and the CRG, which includes the CNAG. <

EDITORIAL



Pablo Cironi

Head of the Technology
and Business
Development Office

CONTRIBUTING TO A SUSTAINABLE ECONOMIC DEVELOPMENT, AN ISSUE FOR ALL

Generating discoveries and inventions is only the first stage in the long process of transferring knowledge to society through commercialization. Similar to research, the knowledge transfer process also requires a strategic vision, long-term support, strong financial resources, and talented people. It requires professionals able to understand the scientific results generated, to define possible products that meet a market need, and to envisage, define, and lead a series of different stages in a strategic manner. It is therefore essential to have dynamic and expert professionals able to provide solutions to different problems and needs. This knowledge transfer process involves also different players at different stages, intellectual property experts, business development managers with experience in academic and business environments, entrepreneurs, investors specialized in the sector and the engagement of established companies.

Catalonia is well positioned nationally, as it has world-renowned research centres, it has different organizations aimed to boost and enrich the local business ecosystem and is the region with the most investment funds specialized in the life science sector in Spain. Nevertheless, this is not enough. In order to move research-based inventions forward through value creation, we need to increase early-stage investment funding and to attract experienced and talented entrepreneurs. The latter, are key players to promote the ideas from the academic setting into companies in order to de-risk the projects and secure subsequent investments. Taking this into account and based on a new strategy for promoting and commercializing early stage inventions, we have launched the new CRG Technology and Business Development Office (TBDO). In this new stage, we aim to contribute to the process of value creation by supporting proof of concept projects and by developing new business strategies. As many of the inventions made at the CRG are still far from the market, various experienced players need to be involved to support the process and push these forward into feasible and business-oriented projects.

Part of the value creation process for these technologies comes from establishing companies. Consequently, the TBDO has launched various initiatives to forge entrepreneurship and support entrepreneurs through training programs, such as the Bio-Business School, coaching programs, the S2B Concept Challenge, and through the Entrepreneur-in-Residence (EiR) program, which brings experienced entrepreneurs to the CRG to stimulate the scientist to think out of their comfort zone. This comprehensive strategy aims to stimulate the entrepreneurial ecosystem at CRG and also to contribute to our regional economic growth by leveraging innovation.

Granted, Barcelona is not Boston or Silicon Valley, but neither of these cities built their ecosystems in a day—or even in a decade. If we take the right direction now, we will be able to witness the change. <

FEATURING CRG

UNDERSTANDING CELLULAR MACHINERIES

The CRG celebrated the 14th edition of its Annual Symposium with “Cellular Machineries” (October 22–23). Scientists have come a long way towards understanding various parts of cellular machineries and their impact on cellular behaviour and tissue organization. Still, there are major challenges to address, as the tim-

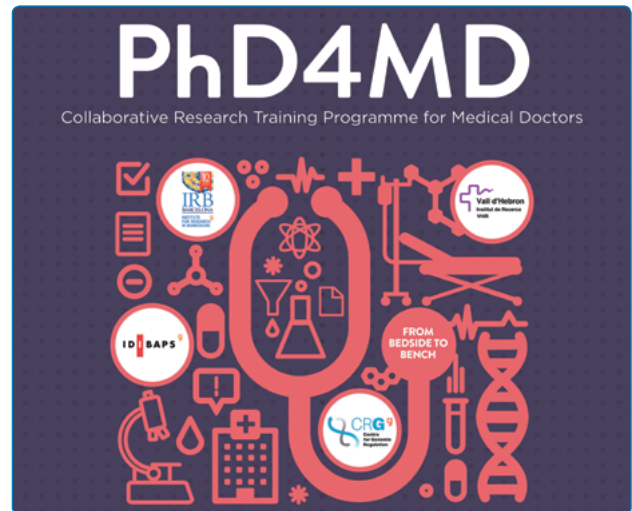
ing, quantity, and location of cellular events are under the control of a multitude of players and pathways. World-leading scientists who use a variety of approaches presented their latest results in this field and discussed the basic principles of how a cell works, and how this affects the function and physiology of tissues and whole organisms. Once again, Barcelona was a focal point for life science research at the international level, highlighting the value that the biomedical scientific community brings to existing in the city. <

FEATURING CRG

KICKSTARTING THE PH4MD PROGRAMME

The three physicians Eva Calvo, Juan Miguel Cejalvo, and Alberto Indacochea were selected for the PhD for Medical Doctors Programme PHD4MD (PhD4MD) this October. This programme is organised by the Centre for Genomic Regulation (CRG), the Institute for Research in Biomedicine (IRB Barcelona), the August Pi i Sunyer Biomedical Research Institute (IDIBAPS) (linked to the Hospital Clínic de Barcelona), and the Vall d'Hebron Research Institute (VHIR) (linked to the Clínic Vall d'Hebron University Hospital). Over the next three years, the selected candidates will develop their theses on a translational research project.

In addition to outstanding CVs, the candidates share a dedication to helping patients beyond medical practice. During their residencies, all three witnessed how biomedical research has contributed in recent years to advancing diagnostic techniques, treatments, and patient wellbeing. All of them are now willing to put their knowledge and talent to the service of biomedical research of excellence, which they will undertake in these four centres in Barcelona.

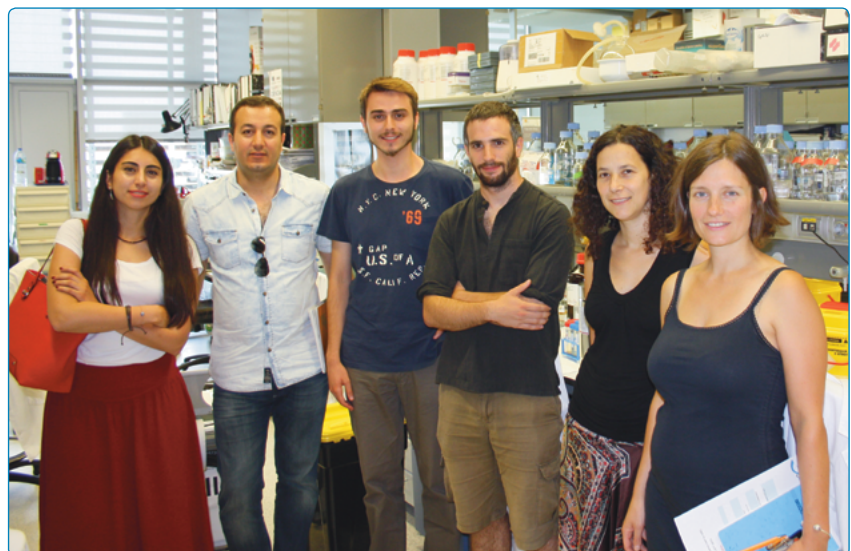


Two of the three physicians participating in this programme will be at CRG: Alberto Inacochea will join the CRG Regulation of Protein Synthesis in Eukaryotes laboratory, led by Fátima Gebauer, and the Pathology and Molecular Oncology team at VHIR, led by Matilde Leonart; and Eva Calvo will be working in Miquel Casas' group at VHIR and in the CRG Genomics and Disease group, led by Xavier Estivill. <

INSIDE

REPRESENTATIVES OF THE ANKARA CHAMBER OF COMMERCE VISIT CRG

Last August, two representatives of the Ankara Chamber of Commerce–Projects & European Union Department visited the CRG. They were here to see first-hand the experiences of Burak Kizil, a Turkish student who spent the summer in the Cellular and Systems Neurobiology laboratory with a grant from the Ankara Chamber of Commerce. Burak has been participating in the project “Neuronal connectome of human epilepsy” as part of the larger project “Imaging, Analysis and Modelling of Epilepsy (IAME)”, developed by Linus Manubens within the laboratory of Mara Dierssen. <



The representatives were initially interested in following Burak's project and to get to know both his mentor and the host institution, to assess the success of the scholarship program. Both the proj-

ect and CRG left them enthusiastic and impressed. After getting to know CRG better during their visit, they were very open to the possibility of formalizing new and future collaborations. <



FEATURING CRG

SUMMER AT CRG

Beach or mountain? Everyone makes summer vacation plans, but for some young people, spending their vacation doing research fits in with having fun and disconnecting from daily life.

Each year, CRG hosts and participates in various summer science programs for young people. For instance, the center offers the “CRG Summer Internship Programme” for university students, which aims to boost the interest of young people in scientific careers and give them the opportunity to experience research in an international laboratory. In this 3rd edition, ten participants of different nationalities worked side-by-side with CRG scientists in 10 of the 30 research groups. “For most students, this experience will be absolutely decisive for their career. Participating in this program shows them the real daily life in a laboratory and allows them to discover how to work in an international research center. It is a very intense and enriching experience for everyone—for the participants, their mentors, and their lab co-workers,” said Imma Falero, CRG academic officer.

In addition to its own program for college students, CRG has participated from the beginning in the “Joves i Ciència” (“Youth and Science”) program, organized since 2008 by the Fundació Catalana La Pedrera. This program is geared towards high school students and aims to foster interest in science careers. This program selects young people who excel



academically and who show an aptitude for and an interest in scientific research. They participate in a 3-year program that includes a stay in the Pyrenees to carry out a research project and two stays in either a Spanish or international research centres. Marta Solis, the CRG outreach officer, said, “Spending three consecutive summers doing research is, for many, a unique life experience that further strengthens their motivation and interest in science. In addition, it offers a stimulating and very realistic view of what it means to have a research career, which will be very useful when they decide whether science is the choice for their future.”

Participating in and leading initiatives such as these are already yielding results, as they contribute to forming new generations of scientists. We already have some success stories, such as those of Ana Alcaine and Oriol Pich, who began their scientific adventure in the Pyrenees summer camps at sixteen and now, in their early twenties, are working in the CRG laboratories of Luciano Di Croce and Fyodor Kondrashov, respectively. This shows that enjoying summers of mountain and beach is not incompatible with science!

FEATURING CRG



Alba Guembe, participant at the Joves i Ciència Program at Monnatura Pirineus

“As a high school student, taking part in the genetic research project of Joves i Ciència was certainly a new experience. I learned that even if the results are unexpected, it does not mean that something went wrong; you just

need to open your mind in order to make sense of them. I learned a lot, and I am very grateful for having had the opportunity of being introduced to scientific research.”



Karl Wotton and Eva Jiménez, CRG postdoctoral researchers and tutors at the Joves i Ciència Program at Monnatura Pirineus

“We spent two weeks in Planes de Son teaching the evolution and biodiversity field course surrounded by pirinean nature. This is a unique and exciting teaching experiences and the kids (and us) loved it. We contribute to the knowledge of the biodi-

versity of this landscape through the International Barcode of Life project and nine very talented kids become citizen scientists for a fortnight. Sharing their excitement as they saw their results is a great feeling.”



Mireia Colom, participant at the Joves i Ciència Program within the Regulation of Protein Synthesis in Eukaryotes group

“This has been one of the best experiences I've ever had. Not only have I learned laboratory techniques, I have also experienced two different perspectives of what it means to work in a laboratory: being frustrated when things don't go well and being happy

when you get good results, the importance of support from co-workers, and the overall good working environment in laboratories. I learned that errors can also be good, and that by all means you have to pursue what you really want if you are passionate about it.”



Polina Shichkova, participant at the CRG Summer Internship Program in the Evolutionary Genomics group

“I am very happy to work on serious problems together with great scientists in Fyodor's lab. I believe we grow faster when we look to the giants. Moreover, passion, desire, and hard work are key features for

success. Here, I was working on four projects, and I gave a talk about my results at a group meeting. Finally, the really cool things here are the inspiring atmosphere and nice and smart people.”



Jerome Solon, group leader and tutor at the CRG Summer Internship Program

“I supervised four students within the CRG summer internship programme, two developed an experimental project and two a theoretical one. There was an amazing synergy between the students and their scientific interaction was fantastic. They all

succeeded to shape innovative projects that will serve as a seed for new projects in the lab. I believe they have learned fundamental skills to pursue their formation in scientific research.”



BUSINESS & INNOVATION

AN RNA BIOMARKERS PROJECT WINS THE S2B CONCEPT CHALLENGE

Coinciding with the launch of the renewed Technology and Business Development Office at the CRG, the winner of the Science to Business Concept Challenge (S2B) was announced on September 18.

The S2B aims to address critical healthcare and market needs, while stimulating CRG entrepreneurship to create innovative strategies to address them. The 2015 edition awarded the project presented by Rory Johnson, staff scientist and Ramon y Cajal



fellow at the Computational Biology or RNA Processing laboratory. The project, based on non-invasive RNA biomarkers to support treatment decisions in chronic lymphocytic leukaemia (CLL), will be supported by the TBDO team. <

2ND EDITION OF THE BIO BUSINESS SCHOOL

The Bio Business School was once again a great success. In this second edition, participants were able to take advantage of the experience and examples presented by several renowned speakers, including Teresa Tarragó, entrepreneurial founder and CEO of Iproteos; Els Beirnaert, senior manager of New Ventures in the VIB; Jose Antonio Mesa, from La Caixa Capital Risk; Keith Curtis, Office of Business



Development at Harvard; Carla Snoeck and Jan Demolder, IP experts at VIB; and the TBDO team at CRG.

During the course, participants were able to explore and discuss in detail top-

ics such as the importance of identifying the potential in research at an early stage, modes of intellectual property protection, licensing, and the different business models and entrepreneurship. These lectures were accompanied by workshops and case studies that were developed during the course.

Participants agreed that the course was instructive, useful, and very practical. Additionally, many of them stressed the importance that initiatives like this can have on their scientific career. <

A COMPANY CREATED BY CRG ALUMNI WINS THE STARTUP COMPETITION 2015

S-Biomedic, a biotech company co-founded by Veronika Oudova and CRG Alumni Bernhard Paetzold and Marc Güell, has been awarded the Healthcare and Biotech Startup Competition Prize. This news was announced last month in Madrid during the South Summit 2015 meeting, which celebrated entrepreneurship and innovation. This biotech startup company uses cutting-edge technology to produce live probiotic cosmetics helping in acne recovery or skin aging. The CRG alumni co-founding this company were previously in the Design of Biological Systems laboratory led by Luis Serrano and were advised by the Technology Business and Development Office. <

NEW ENTREPRENEURS IN TOWN

Four entrepreneurs have recently joined the CRG through a new program launched at the TBDO. The CRG Entrepreneur-In-Residence (EiR) Program is designed for experienced and successful entrepreneurs who are willing to launch a start-up based on technology and know-how already available at CRG, or to take new technologies and know-how to the next level, by leveraging CRG scientific support and infrastructure.

Different approaches are being taken by the four new entrepreneurs. Ion Aracena is now collaborating with the TBDO team to mine the CRG innovation capital and technology portfolio in search for business opportunities in the field of microbiome research. Victor Llorente is searching for business opportunities based on innovative technologies in the software and medical sectors. Xavier Gallego will test a next-generation video tracking system that he has recently developed, which is able to automatically detect complex rodent behaviours under any environmental condition. Finally, Cristian Martí is looking for business opportunities in the digital health market, where genetics and software play an important role.

More information: tbdo.crg.eu/entrepreneurs/entrepreneur-in-residence <

CRG & SOCIETY

COMMUNICATING FRONTIER SCIENCE AT 100xCIENCIA

The Severo Ochoa centres of excellence in Spain organised the “100xCiencia: Communicating frontier science” event from October 7–9. This international meeting brought together renowned international science journalists and outstanding scientists and representatives from the Severo Ochoa institutes. The aim of the meeting was to spread the knowledge of the science carried out by the main R&D centres in Spain, to strengthen their ability to com-

municate, and to discuss the popularization of science and its impact in the media and society. Both groups—scientists and journalists—gained a unique opportunity to understand each other and to collaborate for a common goal: to share the scientific knowledge with society. <



THE TREE OF LIFE EXHIBITION LANDS IN GIRONA

“Tree of Life. The complexity of life: from the cell to a living organism” is an itinerant scientific picture exhibition which shows images produced by CRG scientists. It will be shown from 13 October to 14 November at the Espai Santa Caterina in the Catalan Government building in Girona. This initiative has been possible thanks to the research carried out by CRG investigators, but also to the support of the Banc Sabadell Foundation and funding from the Ministry of Economy and Competitiveness, in the framework of the Severo Ochoa Centre of Excellence programme 2013–2017. So, in case you were not able to visit the exhibition when it was in Barcelona, do not miss the opportunity to enjoy both the great exhibition and the wonderful city of Girona! <

BACK TO SCHOOL... AND TO CRG

September marked a new school year, and the CRG, as it does every year, submitted its proposal for school activities to the educational community. The CRG offer is varied and has new items, such as workshops on the cell for primary schools, guided tours, workshops and role play for high school students, and training for teachers. This time, we are offering 20 workshops for 500 primary students as well as 40 activities for secondary students designed for more than 1,300 participants. What is not new is the speed with which these activities are reserved—we had to place our “booked out” sign on the website within minutes after opening the reservations. No one wants to miss out! <



EU-LIFE

STIMULATING TRANSLATIONAL RESEARCH

Most would agree that transforming lab findings into clinical applications should be an important goal for biomedical research. Yet it is widely acknowledged that this process needs to be faster and more effective. To address this, thirteen European research institutions in life sciences within the EU-LIFE Alliance have now shared their experiences, made recommendations, and identified measures to promote translational research. Their conclusions appeared in the September issue of the journal *Trends in Molecular Medicine*.

“We all have the same challenge: to provide scientific freedom to our researchers while also translating fundamental findings into innovative applications in medicine. By sharing experienc-

es, thoughts and actions, we identified some good practises and guidelines that we want to share with the scientific community and relevant stakeholders,” explains Michela Bertero, chair of the Translational Research working group in EU-LIFE and head of the International and Scientific Affairs Office at the CRG.

The authors first identified the different major phases of the research process. Based on this, they were able to draw up a list of five measures that they believe would improve, promote, and stimulate translational research. The authors pointed out that not all the responsibility for stimulating translational research falls on the research institutes: policy makers and funding agencies must also have key roles. To this end, they also included a list of seven recommendations for policy makers and funding agencies, such as creating specific evaluation and rewarding systems for scientists doing translational research and promoting cultural changes among all players. <



STUDYING YEAST PROVIDES NEW INSIGHT TO GENOME EVOLUTION

Toni Gabaldon and Marina Marcet-Houben have proposed a new theory to explain the origin of whole genome duplication at the beginning of the yeast lineage. They studied the origins of the whole genome duplication in yeast to gain a more thorough understanding of this phenomenon, which is thought to have played a key role the evolution and adaption of the species. Their results, which were published in *PLoS Biology*, unexpectedly show that the appearance of duplicated genes was not caused by a simple duplication of the whole genome but rather by a hybridization of two different species. Their proposal, which is at odds with the currently most widely accepted theory in the scientific community, provides new insight into this key process during genome evolution and the origins of species.

They have now revealed that, for yeast, hybridization was indeed behind the duplication of some genes. The researchers analyzed genomic data with computational tool, based on cutting-edge computational methods, and designed by the Gabaldón group, to study the phylogenetic trees of yeast families. To their surprise, they found that the age of some duplicated genes seemed to be much greater than that predicted by the theory of whole genome duplication. Rather than supporting a genome duplication event at the time when yeast evolved to have twice the number of chromosomes, their data indicated that the duplicated genes had begun to diverge long before. This result suggested the possibility of hybridization between species.

The hybridization hypothesis has strong implications on how we interpret the origin and evolution of duplicated genomes. Being able to “look” at 100 million-year-old eukaryotic genomes will now allow us to deepen our knowledge about genomes as well as about the evolutionary mechanisms that lead to diversifying and acquiring new function. <

TRANSLATING BRAIN SIGNALS INTO SOUND

Researchers from CRG, the research company Starlab, the group BR::AC (Barcelona Research Art & Creation) of the University of Barcelona, and the Institut Hospital del Mar d'Investgacions Mèdiques (IMIM) have developed a device that produces sounds from brain signals. This highly interdisciplinary team is led by Mara Dierssen, head of the Cellular & Systems Neurobiology group at CRG. Its ultimate goal is to develop an alternative communication system for people with cerebral palsy to allow them to communicate their emotions. Scientists are carrying out the Brain Polyphony project, which is still in its pilot phase, with volunteers who are either healthy or who have physical and/or mental disabilities, working together with the association Pro-Personas con Discapacidades Físicas y Psíquicas (ASDI) from Sant Cugat del Vallès.



Most of the systems that are currently available or are being tested require a certain level of motor control, for example by using eye movement. This represents a major constraint for people with cerebral palsy, who often suffer from spasticity or who are unable to control any aspect of their motor system, making it impossible for them to use these systems. A further limitation is that most of these other devices do not allow real-time analysis of the signals but rather require information post-processing. The proposal put forth by the Brain Polyphony researchers now allows real-time analysis, starting from the moment the user puts on the interface device.

Brain Polyphony was the result of an internal initiative of the CRG, which seeks to promote multidisciplinary approaches and mainstreaming of basic research focused on patients and society, especially at an early stage. <

QUEEN OR WORKER? FLEXIBILITY BETWEEN ROLES

Two insect species from Latin America, the dinosaur ant and the red paper wasp, were used to uncover the molecular mechanisms underpinning queen and worker roles in social insects. Researchers from the University of Bristol, the Babraham Institute, and CRG analysed individual wasp and ant brains from queens and workers of both species to see whether caste differences could be explained by variations in how the genome is 'read' and regulated.

As published in *PNAS*, the two species revealed much more than honeybees about how queen and worker castes evolve in insect societies. Unlike honeybees, who as larvae are irreversibly fated to be a queen or worker, paper wasps and dinosaur ants are able to switch role from worker to queen at any point in their life. This flexibility is thought to represent the first stages of caste evolution, when the simplest societies formed.



*Dinosaur ant, *Dinoponera quadriceps**
Author: Chris Tranter



Aggressive interactions between dinosaur ants
Author: Claire Asher

The authors found that castes were differentiated by subtle but non-random arrangements of gene networks. Their results suggest that there is no single master gene regulating caste differentiation, but rather that genes for simple social behaviour act in interconnected networks involving many genes with small effects.

The researchers also looked at whether epigenetic modifications to DNA might be regulating these subtle gene networks. Surprisingly, they found no evidence that queen- and worker-specific gene expression is driven by DNA methylation, and that overall these genomes lack strong epigenetic signatures. Solenn Patalano, lead author of the paper and CRG alumni currently at the Babraham Institute, said, "We suggest that this absence of molecular commitment keeps the genome open and responsive, facilitating the behavioural plasticity we see in these species."

The work illustrates the relevance of genomic approaches, including genome and transcriptome sequencing, to understand animal behaviour. They help to uncover the genetic basis underlying behavioural traits. <

A SWITCH FOR HEALTHY HEART MUSCLE

The heart is arguably the hardest working muscle in our body and without its incessant, regular beating, our organs would be starved of life-giving nutrients. Yet how the heart grows from a thin layer of cells in the embryo into this powerful and symbolic organ has remained largely unknown.

Now CRG researchers have discovered a unique genetic switch that appears to guide stem cells so they develop into specialised heart muscle. The findings, which are published in the journal *Cell Stem Cell*, could help to reveal the underlying causes of heart defects in congenital heart diseases. They may also lead to new ways of controlling stem cells in the laboratory to grow cellular repair kits for patients with damaged hearts.

Led by Dr Luciano Di Croce, the research team found a protein (Mel18) responsible for regulating a piece of cellular machinery that applies temporary silencers to the DNA in developing cells. This protein is normally active in a group of embryonic stem cells in the mesoderm - a layer in the embryo that develops into all the muscles and red blood cells in the body.

By acting on a protein complex known as PRC1—a member of the Polycomb family of protein complexes that remodel the structure of chromosomes—Mel18 is able to silence certain genes, which seems to set the developing cells down a pathway towards differentiation into specialised heart muscle cells. However, the researchers found that Mel18 also serves another unexpected function, namely, turning on particular genes as the cardiac cells begin to develop in the mesoderm. Together this dual functionality appears to result in the growth of healthy heart tissue.

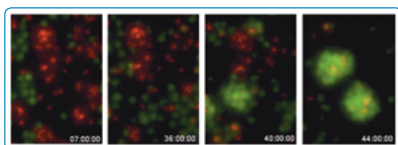
Harnessing Mel18 also could potentially to make it easier to grow functioning heart cells in the laboratory from induced pluripotent stem (iPS) cells. iPS cells are formed by reverting adult cells (rather than embryonic cells) back to a more embryo-like state and are a valuable source of cells for research and, potentially, for clinical use in treating patients. <

TURNING ONE IMMUNE CELL INTO ANOTHER

All it takes is one molecule to reprogram an antibody-producing B cell into a scavenging macrophage. This transformation is possible because the C/EBPα transcription factor “short-circuits” the cells so that they re-express genes reserved for macrophage development. The findings appeared in *Stem Cell Reports*, the journal of the International Society for Stem Cell Research.

Over the past 28 years, researchers have shown that a number of specialized cell types can be forcibly converted into another, but the science of how this change takes place is still emerging. Based on experiments led by the first author of the study, Chris van Oevelen, B cell transdifferentiation takes place when C/EBPα binds to two regions of DNA that act as gene expression enhancers. Whereas one of these regions is normally active in immune cells, the other is only turned on when macrophage precursors are ready to differentiate. This indicates that the convergence of these two enhancer pathways can cause the B cell to act like a macrophage precursor, thus triggering the unnatural transdifferentiation.

Senior author of the study Thomas Graf and collaborators are interested in this specific pathway because C/EBPα-induced B cell-to-macrophage transdifferentiation can convert both human B cell lymphoma or leukaemia cells into functional, non-cancerous macrophages. So, induced transdifferentiation could become therapeutically relevant, if a drug could be found that can replace the transcription factor—not to mention that understanding the mechanisms of the process would help labs worldwide who use this transdifferentiation approach to generate cells “a la carte” for regenerative purposes. <



KEY GENETIC EVENT UNDERLYING FIN-TO-LIMB EVOLUTION

A study of catsharks reveals how alterations in the expression and function of certain genes in limb buds underlie the evolution of fish fins to limbs. The findings by researchers from the Tokyo Institute of Technology, the CRG, and their collaborators are reported in the journal *eLife* and give new insight into how fish evolved to live on land in the form of early tetrapods. The first four-legged, land-living creatures – known as early tetrapods – evolved from fish, following the transformation of fins into limbs. This fin-to-limb evolution is a crucial, yet so far unsolved, example of how morphological changes can dramatically alter life on Earth. Now, researchers have revealed how genetic alterations governing the patterning of skeletal structures in fins may have led to the evolution of limbs and the rise of early tetrapods.

A key regulator protein controlling the balance of anterior and posterior fields of limb buds of tetrapods is *Gli3*. This protein is expressed in the anterior part of limb buds and regulates the expression of a number of genes providing cells with information about their position along the anterior-posterior axis. To determine whether shifts in the balance of anterior and posterior fields occurred during fin-to-limb evolution, Koh Onimaru, a postdoctoral researcher in James Sharpe’s lab, and his colleagues carefully compared the expression, function, and regulation of genes involved in anterior-posterior patterning in pectoral fins of catsharks with those of mice. They found that, in pectoral fin of catshark embryos, *Gli3* expression was intensified posteriorly, and that the balance of the anterior and posterior fields was shifted. This indicates that a major genetic shift (posteriorisation) occurred as tetrapods evolved. <

BY THE COMPANY THEY KEEP

High-throughput experiments revealed novel aspects of gene regulation that are coordinated by multiple associations of transcription factors. In a recent work published in *Nucleic Acids Research*, CRG researchers Davide Cirillo, Teresa Botta-Orfila, and Gian Gaetano Tartaglia studied the relationship between the availability of transcription factor protein partners and their ability to associate with DNA regions. They found that combinatorial recruitment is a fundamental feature for explaining cell-specific expression of genes. Such results have been integrated into an original approach to predict protein-DNA interactions, called PAnDA (Protein And DNA Associations). PAnDA algorithm (http://s.tartagliolab.com/new_submission/panda) predicts the DNA binding ability of transcription factors in human cells using motif counts, expression levels, and protein-protein interaction networks. The algorithm achieves >80% accuracy in classifying transcription factors binding events in high-throughput experiments. For >400 experiments, their observations were statistically robust and accurately described by a theoretical framework, which will be extremely useful for future studies.

The most innovative aspect of their work is that it introduces a cell-specific view of transcription factors networks, which opens up the way for efficient and effective manipulation of cellular processes. Their findings are of great practical relevance to a number of research lines, from engineering gene expression to somatic stem cell reprogramming. The authors hope that the study will raise new fundamental questions and will inspire future investigations on topics like the evolution of regulatory networks and the formation of macromolecular complexes. <

SHAKING UP THE FOUNDATIONS OF EPIGENETICS

Cells of multicellular organisms contain identical genetic material (the genome) yet can have drastic differences in their structural arrangements and functions. This variation of the distinct cell types comes from the differential expression of genes, which is controlled by interplay between different regulators within the cells, such as transcription factors, the transcription machinery, and the “epigenetic” modifications (which do not change the underlying genetic code) that occur on the DNA and protein factors within chromatin.

In a study co-directed by Roderic Guigó, CRG senior group leader, and Montserrat Corominas, at the University of Barcelona, scientists show that the chromatin marks are irrelevant for regulating genes that are expressed in a punctual manner during development. The results of this study contrast sharply with the generally accepted view of the key roles that these epigenetic marks play in regulating gene expression.

Scientists found that, unexpectedly, some highly-expressed genes did not have the epigenetic marks on their chromatin. When they analyzed the data from the modENCODE project, they realized that the genes that were regulated during development were indeed expressed even

though they lacked the chromatin marks one would expect.

The work from these two research groups in Barcelona now offers novel information for understanding embryonic development, by focusing on a set of genes that act during development and are specific to certain tissues. It has been published in the October issue of *Nature Genetics* and is featured on the cover with an illustration by Luisa Lens, which was inspired by the results of the Catalan teams as well as by the Salvador Dali painting “Paisaje de mariposa. *El gran masturbador en paisaje surrealista con ADN* (Butterfly landscape. The great masturbator in a surrealist landscape with DNA).” <

ALUMNI



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Wyss Institute, Harvard
University

Chemical engineer by training, I did my PhD in the Systems Biology group of Luis Serrano between 2007 and 2010, studying one of the simplest organisms that exist, *Mycoplasma pneumoniae*. I came to CRG after starting my thesis in Germany. I always like to proudly explain that the move from a well-established institute such as EMBL in Heidelberg to a more recently-formed one such as CRG did not lead in any way to a reduction in the quality of research. My experience was very satisfactory, as I received support not only from my group but also from the CRG organizational structure. This support was both experimental, from core facilities, and non-experimental, with help in scholarships, technology transfer, communication, among other things.

I am now completing my postdoc in the synthetic biology laboratory of George Church at Harvard, where I have worked on synthesizing a genome that is recoded to create microorganism biocontent, and on the humanization of the pig genome to create compatible tissue. Recently, I have also participated in marketing some of the technologies developed in the laboratory (www.egenesisbio.com, www.sbiomedic.com). The latter, S-Biomedic, was co-founded with Veronika Oudova and Bernhard Paetzold, also CRG alumni and fellow co-workers during my thesis in the Luis Serrano group.

In retrospect, after working in various institutions in the world, I believe that CRG stands out because of its high quality of research and its multidisciplinary and international nature. Additionally, I think that the combination of cutting-edge science with this special location makes it quite unique in the world.

In short, a great place to live, work, and grow as a scientist. <



WELCOMES

A warm welcome to:

Enrique Vidal (Chromatin and Gene Expression); Amy Guillaumet and Maria Méndez-Lago (CNAG); Núria Palomino (Administration – General Services); Jonas Krebs (International and Scientific Affairs); Natalia Sánchez, Alexandros Armaos, and Fernando Cid (Gene Function and Evolution); Anne Daulny (Coordination of Cytokinesis with Chromosome Segregation); Melania Tudor (Administration – Communications); Ní Chárthaigh and Alberto Indacochea (Regulation of Protein Synthesis in Eukaryotes); Moritz Bauer (Epigenetic Reprogramming in Embryogenesis and the Germline); Antonio Torres and Thomas Spruce (Transcriptomics of Vertebrate Development and Evolution); Júlia Domingo and Pablo Baeza (Genetic Systems); Claire Lastrucci and Daniel Shaw (Design of Biological Systems); Lorena Espinar (Genome Architecture); German Demidov and Francesc Muyas (Genomic and Epigenomic Variation in Disease); Caterina Coll (Regulation of Alternative pre-mRNA Splicing during Cell Differentiation, Development and Disease); Karen Sarkisyan and Ekaterina Putintseva (Evolutionary Genomics); Martina Pesaresi (Reprogramming and Regeneration); Álvaro Aranguren (Organelle Biogenesis and Homeostasis); Audald Lloret (EGA); Carla Illas (Administration – Reception); and Silvia Galán (Structural Genomics).

FAREWELLS

Our best wishes to:



Johannes Jaeger was leading the Comparative Analysis of Developmental Systems at the EMBL-CRG Systems Biology Research Unit. He has now moved to Klosterneuburg, Austria, where he is currently the Scientific Director of the Konrad Lorenz Institute (KLI). KLI is an international center for advanced studies in theoretical biology, with a focus on the development and evolution of biological and cultural complexity.

Alicia Broto (Design of Biological Systems); Marc Sitges (EGA); Felix Campelo (Intracellular Compartmentation); Jürgen Mayer and Vivekraj Senthivel (Multicellular Systems Biology); Joao Curado, Marco Mariotti, Amadís Pagès and Sarah Djebali (Computational Biology of RNA Processing); Arnau Bria (Scientific Information Technologies); Marina Isabel Núñez (Histology Unit); Laura Vives (Sequencing Unit); Nicolas Boulanger and Colin Kingswood, Beatriz Fontal, Maria Soler and Maria Mendez (CNAG); Núria Palomino (EiPMC); Daniela Sanges (Reprogramming and Regeneration), Marina García (Regulation of Protein Synthesis in Eukaryotes); Jain Payal (Epigenetic Events in Cancer); Daniel Poglayen (Transcriptomics of Vertebrate Development and Evolution); Chiara Di Vona (Gene Function); Silvia Rodríguez (Gene Function and Evolution); Berta Verd and Diego Bárcena (Comparative Analysis of Developmental Systems);

DIARY

13/11/2015

CRG Proteomics Symposium

Applying proteomics to life sciences: from ions to biology
PRBB Auditorium,
Dr. Aiguader 88
08003 Barcelona (Spain)
www.crg.eu/en/proteomics_symposium_2015

25-27/05/2015

Meeting

RNA Biology in Cancer and Other Diseases
PRBB Auditorium,
Dr. Aiguader 88
08003 Barcelona (Spain)
www.crg.eu/en/event/rna-biology-cancer-and-other-diseases

04-06/04/2016

NGS'2016

NGS'16 Barcelona: Genome Annotation
CRG, Dr. Aiguader 88
08003 Barcelona (Spain)
<http://www.iscb.org/ngs2016>

03-08/04/2016

Whole-cell Modeling

CRG, Dr. Aiguader 88
08003 Barcelona (Spain)
www.crg.eu/event/coursescrg-whole-cell-modeling