In recent months, certain large research consortia that include CRG researchers have presented their results. In November, the Mouse ENCODE consortium published a set of articles in top quality journals including *Nature*, *Genome Research*, and *Genome Biology*. Mouse ENCODE, sibling of the ENCODE consortium, is a collaboration aimed at decoding the functional elements of the mouse genome in order to improve translational research. A month later, the Avian Phylogenomics consortium also presented its results via a large numeral of papers in several high impact journals, with eight appearing in a *Science* special issue. Once again, the CRG has been placed firmly on the international scientific map as playing a key role in high-profile science.

It is clear that scientific journals are committed to publishing the results of big research projects and the coverage they receive in the traditional media is also fairly extensive. The researchers themselves are in two minds about this kind of project (see the article by Toni Gabaldón on page 2), but in general, participation in ventures of these dimensions is quite positive.

Fortunately, there is room in research for all kinds of initiatives, from the most intimate, the labour of a single researcher or a collaboration between a small circle of scientists, right up to large consortia, involving hundreds of people. This range of possibilities means the most interesting subjects can be approached from various points of view. Here too, diversity plays a key role, because each person does the science in their own particular way and, for the moment, the publishing groups continue to respect all the options.

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**SPAIN, A FULL MEMBER OF ELIXIR**

Spain will become a full member of ELIXIR, the European bioinformatics infrastructure created to optimise the biological data obtained from life sciences research. Spain is participating in ELIXIR through the National Bioinformatics Institute (INB), a platform of the National Institute of Health Carlos III (ISCIII), whose central node is hosted at the CNIO. Six INB institutions are taking part in ELIXIR: the CNIO, CRG, IRB Barcelona, UPF, BSC and CNAG.

ELIXIR coordinates storage and access, as well as developing the software needed to understand biological data. According to ELIXIR, “for the first time, we are creating infrastructure – a kind of highway system – that integrates research data from all corners of Europe and ensures the provision of a seamless service that is easily accessible to all,” and which “will facilitate discoveries that benefit humankind.” Spain provides ELIXIR with key services in the areas of biocomputing and bioinformatics, including the assessment of bioinformatic methods, genomic and biomedical data analysis, and data mining. Furthermore, the Spanish ELIXIR team is co-leading the development of the European Genome-phenome Archive (EGA) database, the main repository for genomic data of biomedical interest, which is an essential component of the bioinformatics infrastructure for analysing data on rare diseases.
Big research consortia carry out projects, often known as “big science”, which because of their size or complexity need many groups with complementary experience. The work dynamics of these projects is very special. The logistics deriving from the large number of groups, data, types of information and a complex flow of work, require significant coordination. Telephone conferences are typical, outside normal working hours, with many participants, and involving long discussions on logistical problems and not as much science as we would like. Writing articles can end up being a total saga and, although the subject tends to be attractive for the big journals, the large number of authors somewhat waters down its impact on your CV. You may even find that the person assessing you considers it a purely technical contribution that says nothing about your worth as a scientist.

Despite all this, as a scientist it is a unique opportunity to work towards resolving a problem of a magnitude and complexity that a single group would never be able to tackle, to work together with the best groups in the world in their respective fields, to expand your network of future collaborators, and to have a say in which direction the next big step in your field will be taken in. As a professional, starting a scientific discussion on a new and complex problem, with international experts in complementary fields to yours, is a very satisfactory experience. I think that the only important danger of big consortia is that a group could over-specialise in a particular topic if they just take part in these big projects. Science closer to home, where a couple of groups tackle a subject that is easier to deal with, is also exciting and has the advantage that the logistics are more straightforward. For a start, discussions can take place over coffee and not via an impersonal teleconferencing.

THE MORE, THE MERRIER

INSIDE

THE VIDEOGAME “BRAINFUL LEGENDS” IS TO GO AHEAD THANKS TO CROWDFUNDING

Lidia Montes

The money the project needs has been collected through the web platform Precipita

The ‘Brainful Legends’ project, whose objective is to develop a videogame to mentally stimulate disabled people, has collected more than 19,600 euros through the crowdfunding platform Precipita. This figure has surpassed the minimum amount required by the developers to carry out the project by more than 4,000 euros. However, it has not reached the optimal figure of 25,000 euros for launching the videogame.

Thanks to the donations received, a group of CRG researchers led by Mara Dierssen, in collaboration with neuropsychologists and neuropharmacologists from the IMIM as well as the videogame developers at the University of Barcelona, will be able to take this videogame project forward to stimulate the mental capacity of people with intellectual disabilities.

“We want to develop a demo for kids and adolescents with Down’s syndrome, giving it a multi-touch control and developing a computer interface that will let us to know how brain activity changes while the videogame is being played” explained the leader of the initiative, Mara Dierssen, a researcher at the CRG.

The campaign for collecting donations was launched last October, through the Precipita website, a crowdfunding platform that promotes the collective funding of science. The combination of this online resource and supporting activities publicising the project has raised the amount needed to launch and forge ahead with ‘Brainful Legends’.
CATALAN “LA MARATÓ” FOUNDATION FUNDS MULTIPLE SYSTEM ATROPHY PROJECT

Gian G. Tartaglia, CRG group leader in the Gene Function and Evolution laboratory, is part of the “Catalan Network of Multiple System Atrophy: biomarkers and pathophysiology” project, coordinated by Dr. Josefa Maria Martí Domènech, from the IDIBAPS biomedical institute. They have just received close to 300,000€ from the Catalan “La Marató” Foundation, which organises an annual telethon to raise funds for scientific research. Last year it focused on neurodegenerative disorders and raised more than 11 million euros that will go towards funding 44 research projects.

The purpose of the project is to build a Catalan registry of Multiple Systems Atrophy (MSA) patients to enable better clinical and neuropathological characterisation of this neurodegenerative disorder. This will allow scientists to identify the proteins and microRNAs involved in the disease and study these elements as possible diagnostic biomarkers.

NEW ROOMS AVAILABLE
Josep Queralt

Autumn saw an increase in the number of rooms at the CRG. There is now a study area available for use in the new “altell” located at the end of the corridor, on the 6th floor of the north wing (in front of Juan Valcárcel’s lab).

Additionally, and located in the same “altell”, are two new seminar rooms equipped with a projector and whiteboard. These seminar rooms are easy to book through the intranet booking system. You will find them under the numbers 778.01 and 778.02.
THE CRGopts for Health and Safety Training to prevent accidents in the workplace. To do this the H&S team is organising several basic courses aimed at giving people guidance about the risks they are exposed to both while they work and in the place they work. This training should raise our awareness as we plan our tasks and remind us to include safety in our day-to-day work as well as helping us reflect on both our personal and collective responsibility. By doing this we are aiming to achieve the milestone of 0 accidents - 0 incidents.

In 2014 we held 4 courses as part of the Self-protection Plan (courses on life-saving, resuscitation, and fire, as well as a workshop for the emergency teams) in which more than 100 people participated. Six health and safety training sessions were held, covering different fields (data viewing screens, occupational hazards related to experiments, cryogenics, ionising radiation, lasers and eye protection), where a total of 217 people took part. On top of this, the Health and Safety office gave the welcome training course to a further 100 people.

THE 2015 CRG AWARDS GO TO...
Joaquim Calbo, Michela Bertero

Last year the CRG once again launched two open competitions for innovative and collaborative projects among junior and senior researchers working at the institute.

These calls aim to encourage “thinking-out-the-box”, or rather “thinking-out-of-your-own-lab”, pushing researchers to seek out collaboration with other groups either at the CRG or further afield, in neighbouring hospitals and companies.

Congratulations go to:
2nd Emergent Translational Research call: Toni Gabaldon, “CoLong: Long, non-coding RNAs as novel biomarkers in colorectal cancer” in collaboration with the University Hospital Parc Taulí in Sabadell; and Mara Dierssen, “Brain Polyphony: Neurosonification of EEG signals as a tool for diagnosis and rehabilitation in motor and/or cognitive disabled patients” in collaboration with Starlab Living Science and the University of Vic.

1st Call for Collaborative Projects between Junior Researchers: Linus Manubens and Jim Swoger, “Imaging, Analysis & Modelling of Epilepsy (IAME)”; and José Luis Sardina-Ortega, Bruno di Stefano, Mirko Francesconi, and Tian Tian, “Determinants in transition of embryonic stem cells between preimplantation ‘naïve’ state and postimplantation ‘primed’ state”. <
I did my PhD in the Thomas Seuffertelin’s lab at the University of Ulm, Germany, where I investigated the compartment-specific function of a protein kinase that is overexpressed in pancreatic cancer, known as Protein Kinase D. During my PhD I met Vivek Malhotra who inspired me to study the Golgi apparatus. I started my post doc in his lab from where we moved to the CRG in 2007.

Starting my work at the CRG, I realised for the first time what it means to be in an institute with a perfect infrastructure including core facilities for imaging, proteomics, bioinformatics, and so on. It enables you to do any experiment you like, which is paradise for a researcher.

For me it was also very important to be active in a research surrounding with leading experts in their fields who were very open to discussing things and collaborating. Doing science in such an environment was very stimulating, exciting and provided the support for me to be productive and publish papers. The CRG was basically my home for 4 years and 6 months because I literally spent the day and sometimes also the night there. My personal life suffered at that time because my husband, family and friends were in Germany.

However, this was compensated for by a lab space with an ocean view and a “research family” in Vivek’s lab that collaborated closely and discussed scientific as well as personal problems at any time of the day or night. To be at the CRG in Vivek’s lab was also key in my getting a position at the Max Planck Institute of Biochemistry in Germany. Although I now have an outstanding position, I still miss the scientific atmosphere and the people in the lab at the CRG.

From my point of view, success in science depends on several factors and since I have not yet reached the status of a permanent position it is not easy to give recommendations to younger scientists. If science is a part of you and not just a job, you should push on and fight for it. In my experience, there are crucial points that you should keep in mind:

1. Research a topic that fascinates you
2. Try to get a position in a cutting-edge laboratory with a supportive PI (support is 50% of success).
3. The most important thing is, in my opinion, to struggle and work very hard and always give more than your best in order to publish outstanding papers.
4. Take time for yourself and your friends and relax from time to time. <
In October the CRG held its first EMBO Practical Course. This inaugural edition of the EMBO Practical Course “Targeted proteomics: Experimental design and data analysis” was a very successful event and there will be a second edition before the end of this year.

Here we present a short interview with one of the keynote speakers as well as some comments and thoughts from organisers, speakers and participants.

**Communications:** What makes targeted proteomics so special?

**Michael MacCoss:** Targeted proteomics is special because it is driven by the development and validation of assays of importance as opposed to a large list of items found in a sample.

**C:** Has genomics led to proteomics? Or are both complementary approaches?

**M.M.:** Genomics definitely helps enable proteomics by providing a list of genes that encode for proteins. However that doesn’t tell us how the protein is modified, how much of the protein is expressed, where the protein is localized, what the activity or function of the protein is, etc.

**C:** Is proteomics the key for personalised medicine?

**M.M.:** Lots of things will need to come together to use modern methods to improve patient care. I think having molecular phenotypes that can be measured precisely and associated with disease and outcome will become a part of personalised medicine. Our interest is in helping improve peptide measurements so that they can become reliable and precise enough to be a good phenotypic measure. However, many molecular measurements including mRNA and metabolites will probably play an important role in precision health care.

**C:** Which are the main current challenges of today’s proteomics techniques?

**M.M.:** We really struggle to convert peptide abundances into a measure of a functional protein unit. Until we can figure out how to measure protein abundances we will have to be ok with peptide quantitation as our unit of proteomics measurement.

We are so only scratching the surface of the dynamic range of the proteome. Currently mass spectrometers are capable of performing quantitative measurements over 4 orders of dynamic range. However most samples of biological interest span 6 to 10 orders of magnitude. To overcome this dynamic range limitation will require taking a different approach.

**C:** How do you think the proteomics field will address its current limitations?

**M.M.:** As soon as I work it out I will let you know.
“I think that holding EMBO courses at the CRG and in Barcelona is very important. Organising and hosting these courses puts us on the international research map because they are recognised internationally and include the best speakers and teachers in the field. The significance of these courses and the lack of specific proteomics training is highlighted by the staggering number of applications we received. They came from all around the world and selecting the participants was not easy. I am certain that this training will help scientists find new avenues of research where proteomics plays a key role.”

“I decided to participate in this course because the programme included all the stages for the development, application and interpretation of Targeted Proteomics methods. In fact, my PhD project is about developing protein quantification methods using Targeted Proteomics, so the course suited me perfectly. It allowed me to expand my knowledge in the field and improve my skills for data processing using Skyline. I really enjoyed the course and I’m very pleased with what I learnt during those days at the PRBB. All the sessions were very interesting and they covered the subject from the basics up to advanced techniques at a good scientific level. The fact of having the experts with us during the practical sessions (Skyline tutorials) was very helpful as they could answer our questions and guide us when necessary. In addition, the social events were also very pleasant and gave us the opportunity to talk more with the speakers and participants, and visit the beautiful city of Barcelona.”

“Targeted proteomics allows the detection and quantification of proteins in a fast, sensitive and specific way. Although the technology behind targeted methods is not cutting-edge, the new applications for Selected Reaction Monitoring (SRM) are so promising that this tool was selected by *Nature* as “Method of the year” in 2012. It will be absolutely crucial for biomedical research in the future. So, well established methods for detection of specific proteins used as biomarkers will be determined and quantified in the context of clinical proteomics for the diagnosis or prognosis of certain diseases. This tool will be available in hospitals as a routine technique and new methods will be continuously developed for many different applications.”

“Targeted proteomics was of great benefit to the scientific community. Targeted proteomics is a relatively new approach. It is fast gaining worldwide recognition as critical to transforming protein-related hypotheses into proven conclusions with clinical relevance. Another relevant aspect of this topic is the role of scientific software in science and its approach in these kinds of courses. Science seems to rely on ever-increasing amounts of data, with human understanding of that data becoming the critical bottleneck. Without software to help scientists make sense of the data they are collecting, moving from experiment to conclusion and on to new hypotheses, driving more data collection, much of what is being done today in science laboratories would grind to a halt. Even when you may not be responsible for creating the data that you will eventually stake your conclusions and professional reputation on, understanding and trusting it is no less critical to success. Deep understanding of modern scientific data now often requires modern scientific software. Poor understanding or poor software can lead to years of effort wasted. Choosing and studying software may well be as important as any technique for physical sample handling and processing.”

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An international consortium including researchers from Roderic Guigó’s lab presented an exhaustive description of the mouse’s functional genome elements and their comparison with the human genome. These results have been published in four articles in *Nature* as well as other articles in journals like *Genome Research*, *Genome Biology*, and *PNAS*, among others. This research gives us the keys to explaining why certain processes and systems in mice, like the immune system, metabolism and stress response, are so different to those in humans.

Scientists have detailed the functional parts of the mouse genome and have compared them with those in humans. A whole data set has come out of this – which is now to available to the scientific community – that will be significant for research into mammalian biology as well as the study of human illness mechanisms.

“The mouse is one of the most utilised models for studying human biology and we use it for creating models of human illnesses and testing new drugs and therapies. Our study goes a long way towards validating the usefulness of this animal model and provides enormous support for its use in human illnesses. We have found that there are many well-preserved cell processes in the two species, for example, in embryonic development. Understanding these similarities will allow us to carry out more accurate studies on human biology”, explains Roderic Guigó, one of the main researchers involved in the work and coordinator of the Bioinformatics and Genomics programme at the CRG.

**NEW YEAR RESOLUTIONS:**

TRAINING, TRAINING, TRAINING!

Elias Bechara

The training unit also opened a call for PIs and Heads of Core Facilities to organise advanced courses in 2015 under the umbrella of our successful international training programme, Courses@CRG. Below is the 2015 calendar for new courses.

Please make space in your diary if you are interested in acquiring specific skills and knowledge!

**Course** | **Organiser** | **Dates**
---|---|---
NGS: Library preparation | H. Himmelbauer | February 2-6
Analysis of Exome Sequencing Data for Clinical | S. Ossowski | April 20-24
Modelling for Systems Biology | J. Sharpe | June 14-19
Advanced Proteomics Course | E. Sabido | June 29 – July 3
NGS (Wits, South Africa) | X. Estivill / M. Ramsay | September 11-14
Introductory to *C. elegans* | B. Lehner / J. Ceron | September 13-19
Chromosomal Conformation | M. Beato / F. Le Dilly / G. Verde | Sept. 27 – Oct. 2
Somatic Cell Reprogramming | P. Cosma | October 25-31
Advanced Light Microscopy | T. Zimmermann | November 2-8
Molecular Tools for Genome Editing | C. Carolis | Nov. 31 – Dec. 4

**SCIENCE @ CRG**

**HUMANS AND MICE, SO SIMILAR BUT YET SO DIFFERENT**

Elias Bechara

An international consortium including researchers from Roderic Guigó’s lab presented an exhaustive description of the mouse’s functional genome elements and their comparison with the human genome. These results have been published in four articles in *Nature* as well as other articles in journals like *Genome Research*, *Genome Biology*, and *PNAS*, among others. This research gives us the keys to explaining why certain processes and systems in mice, like the immune system, metabolism and stress response, are so different to those in humans.

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The genome is the cell’s book of instructions. All the cells in our body contain the same genomic information but each of them “reads” the gene fragments that interest them in order to carry out their function. So, neurones, hepatocytes and cardiac cells are different although their genome is the same. In order to achieve this huge variety of functions from the same genome, the cells employ a mechanism known as alternative splicing. This enables them to combine several fragments – known as exons – from the same genes in order to give rise to different proteins, similar to key words being recombined to create different phrases.

Until now, only alternative exons large enough to be detected by the available computational techniques were recognised. The authors of this study have not only been able to detect really small exons, known as “microexons”, but have also been able to determine their functions. “They are very short fragments, some even code for only one or two amino acids, but we have observed that these are essential for neurone maturation”, explains Manuel Irimia, first author of the work, from the University of Toronto and now group leader at the EMBL-CRG Systems Biology Research Unit. In the same way that a word, although very short, can change the meaning of a phrase, microexons achieve the same effect and contribute to the creation of proteins with different functions.

The work published in the journal Cell presents the group of microexons that the scientists have discovered and reveals interesting aspects of these small gene fragments. On the one hand, the researchers have seen that, although microexons are small, they play a very important role in neurone maturation. On the other, they have observed a relationship between these microexons and autism: a great number of the microexons studied are not expressed correctly in autistic individuals, including several microexons in genes that had previously been associated with this disorder.

The researchers compared the whole genome of 48 species and reconstructed the family tree of birds. They also sequenced three crocodilian genomes, the closest living relatives of birds, and traced the evolution of all their genes and other elements in their genomes. The rapid diversification of birds into many visibly different groups contrasts with the stability of the crocodiles that have remained practically the same for millions of years, and this stasis is reflected in their genomes. Crocodiles were found to have one of the most slowly evolving genomes, whereas the evolutionary clock has ticked much faster for birds.

The results of this study have been published simultaneously in 8 articles in a special edition of Science and in a further 15 articles in other renowned scientific publications. They resolve some of the mysteries surrounding bird evolution and propose a new method for phylogenetic study based on massive genome sequencing.
FEATURING CRG

1ST ROUND TABLE ON RESEARCH CENTRE FINANCES
Eva del Pinto

The CRG Finance department organised the 1st Round Table for centres involved in the Catalan government’s CERCA system, to share knowledge and doubts relating to financial issues. Participation wise this first call was a complete success and involved more than 20 centres represented by 40 attendees.

The highest priority subjects were dealt with, along with the worries that were most common among the centres. At the same time, the participants’ willingness to share their experiences and the realities of each centre proved very useful because the larger and more experienced organisations were able to address doubts and give advice to the smaller and newer centres.

CRG & SOCIETY

PREMIÈRE OF THE FILM “CELL FATE, JOURNEYS TO SPECIALIZATION”
Lidia Montes

The film “Cell fate, journeys to specialization” was screened for the first time in October in the DAI cultural centre in Heidelberg. As well as the film itself, the première included a question and answer session with Andreas Trumpp (DFKZ), aided by CRG and ICREA research professor, Thomas Graf, as a guest scientist at this event.

“Listening to the questions after the launch of the film in Heidelberg and discussing it with the audience was inspiring. There was evident interest in the subject and even the cinema manager asked a question”, declared Graf after the première in Heidelberg.

Both Graf and the team he heads up at the CRG have contributed to this film. The plot explains how the different types of cells in our bodies form, develop and specialise, while at the same time it explores the latest research that makes it possible to change one cell type into another.

This audiovisual work, directed by Patricia Delso, produced in the United Kingdom and shot in Barcelona as part of the European EuroStemCell project, was shown in the official international category of the Science Film Festival held at the Goethe Institute over November and December. An international event described by its organisers as “the greatest event of its kind” as audience numbers topped 440,000 in eleven countries in 2013.
19th CATALAN SCIENCE WEEK

November saw the 19th Science Week held in Catalonia. The CRG took part in several activities contributing to raising public interest in science and technology, particularly amongst young people.

CRG scientists Juanjo Fraire and Mariana López visited schools where they were able to talk to the students about their respective research projects, career paths and the daily routine of a scientist.

129 students also visited us for the activity “Get close to biotechnology”. They had a guided tour and attended three short talks by Cedric Magis, Linus Manubens and Lisa Johnsen.

Finally, the Electrophoresis kit was sent to about 200 students around Catalonia who were not able to come to Barcelona and decided to organise “in house” experiments thanks to the free loan of our kits.
PEOPLE @ CRG

WELCOMES
We warmly welcome:

- Chris Douglas Robert (Transcriptomics of Vertebrate Development and Evolution), Ralph Stathouders and Antonio Gómez (Hematopoietic Stem Cells, Transdifferentiation and Reprogramming), Jacopo Boni (Gene Function), Yanina Valverde (Design of Biological Systems), Mª Paula Pifarré and Martina Niksic (Multicellular Systems Biology), Joana Carlevaro and Marco Mariotti (Computational Biology of RNA Processing),
- Marta Solís (Communications and PR Department), Jennifer Semple (Genetic Systems), Marta AGostinho (EU Life Project Manager), Maria Montserrat Ruano (RRHH), and Marta Vives (Genomics and Disease).

FAREWELLS
Our best wishes to:

- Gian Gaetano Targaglia, group leader of the Gene Function and Evolution laboratory has been appointed ICREA Research Professor.
- Mara Dierssen, leader of the Cellular and Systems Neurobiology group has been appointed a member of Academia Europaea in the behavioural sciences section.
- Manuel Irimia, group leader of the Transcriptomics of Vertebrate Development and Evolution laboratory at the EMBL-CRG Systems Biology Research Unit, has been awarded an ERC Starting Grant for his project “Functions and evolutionary impact of transcriptomic novelties in the vertebrate brain”.
- Glòria Mas, postdoctoral researcher at the Epigenetic Events in Cancer laboratory led by Luciano Di Croce, has been given a grant by the BBVA Foundation.

AWARDS AND HONOURS

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DIARY

02-06/02/15 – Courses@CRG
Library Preparation for Next Generation Sequencing
CRG, Dr. Aiguader 88, 08003 Barcelona (Spain)

19-22/05/2015 – European Light Microscopy Initiative
15th International ELMI Meeting
Hotel Meliá Sitges, Sitges, Barcelona (Spain)
www.elmi2015.eu