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EMBO encounters

PAGE 3

Science meets policy in Amsterdam

PAGES 3 | 10 | 11

The EMBO Meeting 2013

PAGE 6

Epigenetics in Asia

PAGE 21

The unseen world

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INSIDE SCIENTIFIC PUBLISHING

Announcing EMBO Press

Previous articles in *EMBOencounters* explored important topics in scientific publishing related to peer review, editorial processes and the merits of journal impact factors in assessing research. This month we are excited to announce the launch of EMBO PRESS, a new editorially independent publishing platform that will allow us to develop further EMBO scientific publications and build on the established strong reputation of our journals.

Online journals are no longer constrained to static PDFs and web presentation that mimic the appearance of printed articles. As a publisher of scientific research, EMBO strives to be at the forefront of new technologies that will allow research data to be discovered more easily through new search mechanisms, and to be published in a way that will allow their broader use – an essential consideration for all scientists, given the rapid expansion of the research literature. We will launch EMBO Press in December to further these goals.

EMBO Press is a new publishing platform for *The EMBO Journal*, *EMBO reports*, *Molecular Systems Biology* and *EMBO Molecular Medicine*. EMBO Press will embody our editorial independence and is founded on the principle that scientific publishing should be more transparent, fair, and ethical; it must support a reliable, reproducible literature.

EMBO Press is part of the transformation of research articles into enriched and accessible records of research data that will help scientists make new discoveries. Our four journals will benefit from a fresh and dynamic design that will maximize online functionality and access. The enhancements will include publication and persistent storage of source data as well as the curation of published figures with the addition of computer-readable metadata. EMBO Press will also include resources such as visually enhanced guidelines to help write a successful paper and for image and data processing.

New partnership

After ten fruitful years with Nature Publishing Group, we have decided to collaborate with Wiley and HighWire Press to support the EMBO Press platform. *EMBO Molecular Medicine* has been published in cooperation with Wiley since 2009. Wiley, one of the leading international publishers of academic content, will now support editorial production and international marketing of the four EMBO scientific journals. HighWire Press will provide an innovative online platform for the journals. Access to the Drupal open source content management system of HighWire Press opens up new possibilities for innovation in areas like data presentation, semantic interlinking, article level metrics and mobile web interfaces. Many leading journals in the life sciences rely on HighWire Press and we look forward to cooperating with these journals on technology and policy developments.

Following the launch of EMBO Press, our four journals will continue to serve their individual communities, selecting and presenting some of the very best research for publication from authors all over the world. Authors and readers will benefit from the shared policies, technology, and further innovations that EMBO Press provides, including our Transparent Process, which has enhanced the reliability and accountability of the editorial process. All the financial benefits from our publishing activities will continue to support the activities of EMBO and the scientific community.

Further details about EMBO Press are available at http://www.embo.org/embo-press and we encourage you to visit the new journal websites that will be available from December.

We are continually looking for ways to add maximum value to scientific research, and are always eager to hear feedback from you.

Maria Leptin
Director EMBO

Bernd Pulverer
EMBO Head of Scientific Publications

Thomas Lemberger
EMBO Deputy Head of Scientific Publications

HIGHLIGHTS FROM THE EMBO MEETING 2013

From lipid rafts to the role of science in policy making

THE EMBO MEETING 2013 took place at the Amsterdam RAI Exhibition and Convention Centre in The Netherlands on 21–24 September 2013. The meeting brought together more than 1000 scientists from across the world to talk about the life sciences.

Kai Simons, Research Group Leader and Director Emeritus of the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden, Germany, gave the opening lecture. In the introduction to his talk, he emphasized the excitement of doing science as well as some of the challenges. Simons helped establish *The EMBO Meeting* as part of the regular calendar of events for scientists. In his lecture, he talked about lipid rafts and the way that changes in membrane structure can influence cell function.

Chris McKay, a research scientist at NASA Ames Research Center in the United States, gave the special lecture on the second day of the meeting. McKay provided an update on the Mars Curiosity Rover mission and also gave his thoughts on other planets that might be able to support life. "The Viking mission inspired me to get involved in looking for life on other planets," said McKay. "Beyond Mars, one of my favourite candidates in the search for life in our Solar System is Enceladus." Enceladus is one of the moons of Saturn that appears to have liquid water under its surface.

The EMBO Meeting included 20 concurrent sessions that spanned topics such as cell membranes, stem cells, cancer genomics and optogenetics. Three plenary sessions included talks about the organization of the cytoplasm and the roles of health and disease of ubiquitin signaling and infectious proteins.

In a plenary session, David Eisenberg from the Institute for Genomics and Proteomics at The University of California Los Angeles Department of Energy presented two different ways of thinking about the structures of amyloid fibres. Some diseases are clearly related to the presence of these fibres. The work of his team helps to define relationships between structure and activity and is also useful in designing new drugs. Eisenberg described a structure-based procedure for design of non-natural peptides that inhibit fibre growth as well as a combined structure and computational procedure for the identification of small molecules that inhibit amyloid toxicity.

In a session on new methods in genomics, Peer Bork from EMBL described a systemic analysis of the human gut microbiome. He summarized work that has identified three types of microbial communities that exist in the gut of humans and provided an update on some of the latest results arising from large-scale studies that are being conducted in several countries across different continents. Microbial markers offer considerable potential as diagnostic tools. In the future, it might also be possible to improve health by influencing changes in the composition of the microbiome of an individual. Clear differences in the makeup of the gut microbiome exist for individuals from different countries. In some studies, these differences have been shown to reflect different usage patterns for antibiotics in each country.

On the second day of the meeting, Vishva Dixit from Genentech gave a plenary lecture. Dr. Dixit helped to define many of the key molecular events that take place during programmed cell death. His current research interests include how inflammation can contribute to cancer and other diseases. In his talk, he described the role of the protein deubiquitinase BAP-1 as a tumour suppressor and summarized some of the essential genes regulated by this protein that may contribute to disease. The loss of function of BAP-1 has similar consequences in mice and humans and is linked to the development of hereditary cancer syndrome.

In the Science Policy session, Anne Glover, Chief Scientific Adviser to the European Commission president Manuel Barroso, discussed the role of science in policy making. Scientists have an "absolute obligation" to translate their research to the public, said Glover speaking at the meeting. The session was organized by the EMBO Science Policy Programme, and moderated by Michele Garfinkel, manager of the Programme.

For further highlights of *The EMBO Meeting* 2013 see pages 10 and 11.

Poster session at The EMBO Meeting 2013

Constructive interference

OLIVIER VOINNET is Professor and Chair of RNA Biology at the Swiss Federal Institute of Technology Zürich as well as Directeur de recherche détaché du Centre National de la Recherche Scientifique (CNRS), France. In 2009, he was awarded the EMBO Gold Medal for his work on RNA silencing in plants. In *EMBOencounters*, he talks to Barry Whyte about his career and recent papers in *Nature Genetics* and *Science*.

How did you first get involved in gene silencing research?

Before my position at the CNRS in 2002, I worked with David Baulcombe, who is now Professor of Botany at the Department of Plant Sciences at the University of Cambridge. When I joined David's lab in 1996, very little was known about gene silencing; some people even thought it was an artefact of transgenesis. But we managed to develop a model system that helped work out some mechanisms and uncover a universal role for RNA silencing in antiviral defence. Our recent findings in mammals make me more inclined to believe that defence against viruses and transposons constitutes the primordial function of RNA silencing across all kingdoms of life.

This was before we knew the identity of small interfering RNAs or microRNAs?

Yes. Small interfering RNAs or siRNAs were discovered in David's group at the Sainsbury Laboratory in Norwich, England, in 1998, right in the middle of my Ph.D. These are the infamous small double-stranded RNA molecules, typically 20-25 base pairs in length, that provide sequence specificity to the whole mechanism of RNA interference. We rapidly realized that virus-derived siRNAs accumulate in virus-infected plants and that these molecules underlie the specificity of the antiviral immune system we had just discovered. I have fond memories of this time and particularly remember the perseverance of Dr. Andrew Hamilton, the postdoctoral researcher in charge of the siRNA project. He was absolutely convinced that antisense molecules had to be involved in the process and he considered all possibilities to eventually find them, even though they were such tiny molecules. This tenacious and uncompromising attitude remains one of my greatest inspirations in science, alongside the incredible support and freedom I received from David to conduct my research at an early stage. I was very fortunate to be there at the right time with the right tools.

It was really in the early 2000s that microRNAs were recognized as a distinct and large class of biological regulators, even though the first microRNA and its target had been reported many years before in *Caenorhabditis elegans*, thanks to the seminal work of Victor Ambros and, later, Gary Ruvkun. microRNAs are similar in size to small interfering RNAs and processed by the same enzyme, Dicer. They are encoded by endogenous genes and regulate cellular gene expression. They were found in many organisms, including plants, although for some reason the plant community was a bit slow to hop onto the "microRNA train." Small RNAs were breakthrough of the year in *Science* in 2002, but, from my perspective, the siRNA and miRNA breakthroughs had already been made many years before: there is a big difference between making the key discovery and generalizing a discovery. There are some interesting historical perspectives to be made about this field in this respect.

How important has work in plants been to the understanding of how RNA interference works in mammals?

The discovery of siRNAs in David's lab is certainly, in my mind, the most important contribution of the plant work to the whole field. For the first time, readily detectable molecules, the siRNAs, could be used to ascertain, initially at least qualitatively, that RNA silencing was at work in a tissue or under specific conditions. Before siRNAs were discovered, all we could do was measure the loss of mRNAs, which is not very useful to characterize a process. Using siRNAs as molecular markers expedited the elucidation of the basic mechanism of RNA silencing. This was convincingly done in animal model systems, mainly *Drosophila*. The same basic mechanism was found to function in mammalian cells where it was and continues to be studied from a gene regulatory standpoint in the framework of miRNA-mediated regulation.

Other key concepts that emerged from our plant work included the notion that many plant viruses encode suppressors of RNA silencing, as is most likely the case for most invertebrate viruses. These viral suppressors form a large array of proteins that have proved to be very useful tools to dissect the silencing mechanism itself. We and others also found, very early on, that RNA silencing moves between cells and over long distances in plants and we showed how this process forms the systemic arm of antiviral silencing, emphasizing further its analogy to an immune system. But the plant contribution to the RNA silencing field went well beyond antiviral defence. In particular, the phenomenon of small RNA-directed DNA methylation and chromatin modification was discovered and extensively characterized in plants, and this created a whole field of investigation with important ramifications in fission yeast, flies and even, possibly, mammals. Amplification of RNA silencing was also discovered and characterized in plants. Many people do not realize that Dicer was first identified in a plant genetic screen. Even the name 'ARGONAUTE', which defines a universal class of RNA silencing effector proteins, stems from the squid-like phenotype of an *Arabidopsis* mutant.

In 2002, you set up your first laboratory in Strasbourg, France. What was the biggest challenge in building up your research group?

I do not recall many big challenges but you tend to forget the difficulties when you are hungry to test your hypotheses and explore new ideas. I chose the Institut de Biologie Moléculaire des Plantes in Strasbourg because I knew the infrastructure was there to conduct the type of research I had in mind. I also benefited from a CNRS incentive, called ATIP, which provides some financial support to young principal investigators. I was very lucky to attract talented postdoctoral researchers and students so that the laboratory did very well from an early stage. We received many awards and scientific prizes and this created a foundation for further discoveries. The Agence National de la Recherche (ANR) was also created at the time, and for many French scientists this was a god-send: for the first time, French research was provided with a credible, competitive funding scheme. Particularly important were the open-calls, the "ANR Blanc," which allowed funding of basic science. The ERC system was also created at this time and our team benefited from the first competitive grants awarded in 2008. This was an incredibly productive time where we grew to a team of more than 25 researchers and expanded our research into mammalian systems.

And then you moved to Switzerland?

Yes. I had exhausted all credible and legal possibilities to maintain a group of this size in France when a clear opportunity presented itself at the Eidgenössische Technische Hochschule Zürich (ETH Zurich). I asked the CNRS for a "détachement" using a unique prerogative of permanently employed French researchers. My move coincided with the decline of the ANR, where bureaucracy, lobbying and an increasing emphasis on applied science had progressively supplanted the original, highly praised ambitions of this agency. I suppose the financial crisis that hit France and so many countries did not help, but there are still inexplicable decisions that were taken about the function and scope of funding for the ANR. Given the more recent constraints imposed on the employment of research staff in state-funded institutions, I think the current conditions deter even the most motivated of French researchers, something I witness directly in our struggle to maintain a laboratory in Strasbourg. But there is still hope: France hosts some of the brightest and innovative minds and I never cease to be amazed of how much is achieved with so little.

The level of support and trust given by Switzerland to its researchers is staggering and notable at all stages of a scientific career. The system is highly competitive and entirely based

on merit, something I also see within the ETH Zurich itself. The strong support from Swiss funding institutions is also intertwined with a clear vision that exploratory and applied sciences do reinforce one another, and that there is space for both.


Olivier Voinnet

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What has your recent work focused on?

We have many interesting projects brewing in the lab, which reflect the diversity of talented people who contribute to my laboratory. Surprisingly, defensive roles for RNA silencing have been somewhat overlooked in mammals over the years. I say surprisingly because our initial findings on plant antiviral silencing were later corroborated almost identically in invertebrates, including insects, and, more recently, in *C.elegans*; whether, likewise, defensive RNA silencing persisted in mammals is a legitimate question to ask. We have approached this question from two major angles that we had already taken in plants: antiviral defence and maintenance of genome integrity through transposon taming. Unlike most other researchers working on differentiated cells, I became convinced that multipotent or progenitor cells, which have now been characterized in many tissues of developing and adult mammals, would be primary sites of defensive RNAi. We now have papers in *Science*[1] and *PLoS Genetics* (2) that strongly support this idea for defence against viruses and transposons.

When I moved to Zürich we had just demonstrated that thousands of cellular small RNAs are transported from cell to cell and over long distances in healthy plants. We proposed at the time that this mobile component to endogenous RNA silencing could help plants to adapt their new growth and perhaps their progenies to environmental cues or stresses perceived very locally in single leaves or roots; we now have experimental evidence to support this view and have also isolated what I believe are the first components of the mechanism that physically transports small RNAs between plant cells. Intriguing observations suggest that non-cell autonomous silencing might also operate in mammals, a question my group is now pursuing as part of a major research project on extracellular RNAs that has just been funded by the National Institutes of Health in the United States.(3)

And now you have papers in *Nature Genetics* and *Science*?

The paper in *Nature Genetics*,[4] which was published a month ago, describes how we were able to reactivate and follow, for the first time, the whole mechanism by which *Arabidopsis* eventually silences an invasive retro-element with the potential to amplify itself many times in a genome. Essentially, we have deciphered the series of molecular events that lead to the silencing of the many copies that originated initially from a single-copy transposon. We could also evaluate the significant contribution of the mobilization of this transposon to the genetic diversification of its host before the transposable element became silenced permanently. This is a heavy-duty piece of work, full of genetic tricks and elaborate molecular biology experiments. We took the time to design our experiments very meticulously and we set the bar very high to decipher the whole thing from A to Z. I know our community appreciates this paper and I am proud of what was achieved here, sometimes against all the odds. I keep telling people in the laboratory that perseverance is the essence of innovative science. An obvious corollary is that exploratory science needs time and unconditional support, which brings us back to funding.

And the *Science* paper describes work in mammals?

Yes and it is yet another example of perseverance. I initiated this project many years ago, at a time when some colleagues were puzzled about my new interest in mouse embryonic stem cells (ES cells). Thanks to a very fruitful collaboration with Edith Heard at the Institut Curie in Paris, we set up the ES cell system in our laboratory, and together made some interesting observations potentially linking X chromosome inactivation and transposable elements. These findings are at the origin of our current interest in how RNA silencing contributes to silence transposons in ES, and, more widely, in multipotent cells. But Edith knew from the beginning that my real motivation to work with ES cells was to implement an experimental virus infection system because I was convinced that ES cells would be the right material to demonstrate antiviral RNAi in mammals. Mouse ES cells are also unique because, unlike differentiated cells, they can withstand the complete removal of the RNA silencing machinery, which was for me essential to conduct clear-cut genetic experiments as we had done previously in plants to decipher the molecular underpinnings of antiviral silencing.

The role for RNA silencing in mammalian defence against viruses has been hotly contested mostly because long double-stranded RNA produced by viruses, the molecule that initiates antiviral RNA silencing in plants and invertebrates, activates innate immune pathways unique to vertebrates. These pathways promote the non-specific antiviral interferon response, which most people consider so potent that it probably rendered RNA silencing superfluous in mammals. This argument was fuelled by the negative results of several labs exploring the accumulation of virus-derived siRNAs in virus-infected mammalian cells. We provide in the *Science* paper several key reasons why antiviral RNAi has remained elusive so far in mammalian cells. One reason pertains to the differentiated versus multipotent state of cells. Multipotency seems to correlate with poor interferon signalling and a tolerance to long double-stranded RNA accumulation. The second reason pertains to the use of highly virulent viruses, which, as shown previously by others and our group effectively suppress RNA silencing in plants and invertebrates. It seems obvious that you cannot use a tool to probe a phenomenon that is coincidently suppressed by the very same tool. We were not deterred by the negative results of others and persevered with our original idea, applying the knowledge we gained from our studies of plant model systems.

We have published in *Science* at the same time as a group led by my colleague and friend Shou-Wei Ding who has shown similar findings using different approaches. A staggering aspect of their work is to show that virus-derived siRNAs that immunize mice *in vivo* are identical in their distribution, biochemical properties and relative proportions to the siRNAs we detect in ES cells. This implies the existence of a previously unknown siRNA-based immune system in mammals. These are real breakthrough findings, and I cannot wait to get the results of ongoing experiments conducted in my and Shou Wei's laboratories to uncover how, when and where this immune system operates in mice. I think it is really an exciting time to be working in this research area and we have still only scratched the surface in terms of biology and, perhaps, applications.

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Epigenetic effects on coconut seeds

MARJORI MATZKE, an expert in epigenetic gene silencing and former EMBO Council Member, left her institute in Austria last year to set up a new laboratory in Asia together with her husband and fellow researcher ANTONIUS MATZKE. In *EMBOencounters*, she talks about their new research efforts and about how her life changed after moving across continents.

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Dr. Matzke, you left the Gregor Mendel Institute in Vienna exactly a year ago to join the Institute of Plant and Microbial Biology at the Academia Sinica in Taipei. Did the focus of your research also change?

It did not change too much. In Austria we worked on epigenetic gene silencing in plants and specifically RNA-directed DNA methylation in *Arabidopsis thaliana*. This is the major small RNA-mediated epigenetic pathway in plants. Here, we have additionally started to look for variations of this pathway in coconut, which is very understudied. Coconuts grow in southern Taiwan and we can get them at all stages of development. So we are dedicating more time to this "non-model" plant while still staying with the basic problem of the epigenetic gene silencing in plants and continuing our work on RNA-directed DNA methylation in *Arabidopsis*.

Why is coconut interesting for researchers?

It is an economically important plant, particularly in tropical regions. And there appears to be a lot of action in the RNA-directed DNA methylation pathway during plant reproduction and seed development. Coconut has some of the largest seeds in the plant kingdom so getting enough experimental material is not a problem. At this point, very little is known about the genetics and genomics of coconut. This research area is not very highly populated and it is fun to work with.

What are the possible applications arising from your research?

It is possible that the factors we find in this epigenetic silencing pathway can ultimately be modulated to change characteristics of the plant or its seeds or make them resistant to certain stress. This is of course a long-term goal for the future.

Why did you move to Asia?

We had worked in Austria for more than 30 years and we were ready for something new. Asia has plenty of good places to do research. We knew that Academia Sinica is a top research institution in Taiwan and that IPMB has a strong focus on basic plant science. There are not so many institutes around the world that are focused on basic plant science without expectations for applied work. When I visited Taiwan about six years ago for a conference I fell in love with this place. My husband Antonius also liked it so we are very happy to have this opportunity to work and live in Taiwan.

Last year EMBO signed a cooperation agreement with the National Science Council of Taiwan. What role does EMBO play in Taiwanese science today?

EMBO has definitely made itself visible with several well-received visits. I know young scientists who are interested in working in Europe and applying for funding opportunities like the postdoctoral fellowships made available by EMBO. The opportunities offered by the organization are slipping into the consciousness of local scientists and I am certainly doing my part to make people aware of them.

How important is the growing global orientation of EMBO in your view?

Science is a global activity and I like the fact that what you do is relevant beyond your small world. So I think it is important for EMBO to expand beyond the European borders, to attract young scientists for training in Europe, and to help reinforce the international rhythm of science.

How international is the scientific landscape in Taipei. Is it changing?

Slowly. In our institute there are 29 principal investigators and six of them are non-Taiwanese. Academia Sinica has a quota for international workers. They frequently talk about internationalising it more and some people definitely endorse that idea but there are also others who would like to keep it more oriented towards Taiwanese scientists. Taiwan is not as international as for example Singapore but it is more international than some other Asian countries.

Have you maintained strong links with Austrian scientists?

We closed our laboratory in Austria, but we are still finishing projects with former co-workers. Through websites and personal contacts I try to follow the events there and I am also keeping up with EMBO affairs. We visit regularly so we do not feel cut off by any means.

How big is your lab?

I run the lab with my husband Antonius and we work with six other people. Two of our postdoctoral researchers came with us from Vienna. The Taiwanese co-workers have been a big help with dealing with the language barrier. Now it is pretty smooth sailing.

What do you think is the strength of your lab?

In the last ten years, we have been pretty strong in carrying out genetic screening in *Arabidopsis* to identify the epigenetic factors involved in RNA-directed DNA methylation. Many of these factors were functionally uncharacterised before. We identified functions in this pathway for a number of previously unknown proteins and we found ways to set up transgenic systems that allowed us to get hold of these factors.

In hindsight, what were the major advantages of changing location?

It is stimulating to start working with coconut, a plant that is not typically used as a model system for research. We feel rejuvenated. Our laboratory is new, we have received the latest scientific equipment, and we are enjoying a different culture.

Coconut farm in Pingtung County, Southern Taiwan. The droppings from the ducks are used as fertilizer for the trees.

Skin, race and cancer: Making sense of the genetics

Dissimilarities in the susceptibility of individuals of different races to cancer are still not fully understood. Now a research team in Switzerland, with the support of the European Research Council, wants to probe deeper into the origins of SQUAMOUS CELL CARCINOMA, the second most prevalent form of malignant solid tumours in humans.

People of different racial origin have different predispositions to cancer of the skin. The incidence of all three types of skin cancer – deadly melanoma, basal cell carcinoma and squamous cell carcinoma – is substantially higher in Caucasians compared to East Asian and Black African people. While pigmentation can account for the different incidence, it does not explain the more aggressive behaviour of squamous cell carcinoma in Asian or Black African populations. Black Africans are also more susceptible to aggressive cancer of internal organs, for example the breast or prostate. The reasons for these differences in susceptibility are unclear.

Dissimilarities in cancer predisposition have been attributed to environmental factors, for example lifestyle, diet, or exposure to chemicals, but the genetic basis for such differences in humans is much less understood. Now a group of researchers led by Paolo Dotto at the University of Lausanne, Switzerland, want to take a closer look not only at genetic differences but also at changes in gene expression due to factors not immediately defined in an individual's DNA sequence, so-called epigenetic processes.

In particular, they will look at the susceptibility of individuals of different racial origins to squamous cell carcinoma. Squamous cell carcinoma, which is sometimes referred to as epidermoid carcinoma, is a type of malignant epithelial cell cancer. It shares cellular and architectural features of squamous cell differentiation that typically occur in the epidermis. One of the signature features of these tumours is the incredible diversity of cells that arise from elevated levels of cell differentiation. This may explain the resilience of such tumours to conventional cancer treatments like chemotherapy and novel targeted therapies including antibody drugs or small molecules that inhibit specific kinases.

"A high genetic risk for cancer can produce devastating consequences but scientific evidence for the molecular basis underlying the genetic risk factors of complex cancers is in many cases lacking," G. Paolo Dotto, Professor in the Department of Biochemistry at the University of Lausanne, Switzerland, remarked. "Many single nucleotide and copy number differences have been associated with predisposition to specific types of cancer but in most cases they result in only smaller increased risks of developing cancer."

The inability to account at the molecular level for genetic predisposition to cancer has led to the rise of the phrase "genetic dark matter," a symptom of the uncertainty and intractability of making sense of complex cancers at the level of genes alone. Dotto and colleagues want to use an approach that combines genomic and epigenetic analyses of cancer predisposition and apply this to the study of skin as an experimental and clinical system.

"Our first objective is to test if the hypothesis that different genetic and epigenetic factors are linked to different expression of genes and key regulatory factors in keratinocytes and dermal fibroblasts, specialized skin cells where changes linked to cancer take place," said Dotto. "Our second objective is to test if there are differences in the tumour-forming capabilities in these skin cells in individuals from different racial backgrounds."

Molecular signalling and Notch

Molecular signalling pathways play an essential role in the development of healthy skin. As in other tissues cancer can arise when these signalling pathways go awry. The Notch signal is vital for communication in skin cells and serves as a switch between the proliferation of epidermal cells and differentiation. When this control point is compromised it can lead to tumour development. The function of the Notch pathway depends a lot on where the signalling events take place. "While the function of several genes in the signalling network is under intense study, the possible role of genetic or epigenetic modifications of these genes in the predisposition to cancer is largely unexplored," Dotto said.

Attention has focused on the role of Notch signalling as a tumour suppressor in the epithelial compartment of the skin. In addition to pioneering work in this research area, Dotto and colleagues have now started to investigate the role of this pathway in the underlying mesenchyme, the loose connective tissue of mesodermal origin that provides a supporting scaffold to overlying epithelial cells. "In recent work in a mouse genetic model and clinically derived skin samples, we have shown that Notch signalling plays a role in the control of field cancerization," remarked Dotto. Epithelial tumours are usually thought to result from genetic changes in a discrete group of cells that originate from a single initial progenitor or mother cell. These changes take place immediately in the surroundings of normal cells. Field cancerization refers to cancer-promoting changes that take place in epithelial cells and surrounding stromal cells that occur in larger areas or fields. These larger target areas can be in the skin, oral cavity, lung, prostate or breast and expand as a consequence of aging. "These widespread changes help explain why cancer often occurs at multiple sites and in different locations and why after removal these tumours often reoccur".

Dotto and colleagues will be looking closely at how all these factors, genetic, epigenetic and location, play a role in squamous cell carcinoma. What they learn from skin cancer may also be relevant to cancer in other organs. A new Advanced Grant from the European Research Council will support the work.

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Paolo Dotto

VIDEO

How to get your paper published

http://youtu.be/XL8JsRgaWis

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Science live for Russian high-school students

A two-week Summer School in the Russian research centre Pushchino proved to be a life-changing event for some of the eighty high-school students in attendance. FYODOR KONDRASHOV, group leader at the Centre for Genomic Regulation in Barcelona, Spain, initiated the project two years ago to give young people a realistic experience of what it is like to do scientific research.

For EMBO Young Investigator Fyodor Kondrashov the summer of 2013 has been very eventful. Just a few weeks after receiving a starting grant from the European Research Council, he travelled to his home country Russia for a two-week summer school hosting 80 Russian high-schoolers aged 15–17. He took charge of this project almost single-handedly for the second time – a fulfilment of his life-long dream and an "extremely exhausting task."

The students participating in the "School of Molecular and Theoretical Biology" were accompanied by almost 60 faculty members. Most of these were graduate and postdoctoral students; a few group leaders also accepted the invitation to attend. Having genuine team leaders in the programme was an important part of the concept. "The idea is to make the kids participate in real science rather than just play like they are doing science," says Kondrashov. EMBO Installation Grantee Marcin Nowotny was on the faculty board as well as Long-Term Fellow Cajetan Neubauer from the California Institute of Technology in Pasadena, United States. Both came to Pushchino thanks to a small grant from the Howard Hughes Medical Institute.

Russia has a long tradition of extra-curricular activities at schools so it was not unusual that Fyodor began teaching junior colleagues while still a graduate student at the University of California at San Diego. Public engagement is a fantastic way for the scientists to gain important skills and to make a difference. "By the time the two weeks were over, we were completely exhausted. Yet it was an incredibly rewarding experience," concludes the evolutionary biologist.

The fourteen days in Pushchino were packed full with science. Every day, the students spent two hours in theoretical lectures; the remaining five or six hours were reserved for experiments and analyses at the bench – or the computer. Each group consisted of at most ten students and was guided by several scientists. Lectures and courses covered most of the modern life sciences, from embryology to paleontology and from bioinformatics to microbiology. The school was using the infrastructure of the research institutes in Pushchino, a science city two hours' drive south of Moscow.

Students collecting samples at the Oka River

© Doris Yee

Cajetan's group focused on environmental microbiology and regularly went on field trips to collect samples from the nearby river Oka. "I had some highly talented students from a variety of backgrounds," he says. Some of the attendees came from large cities such as St. Petersburg and Moscow, others from remote villages in Siberia. Their educational background was just as diverse. Whereas some had private school experience, others came from rather impoverished families. 17-year-old Grigory Khimulya from Sochi said: "The school was of the most important events in my life. It is hard to describe how enriching and exciting it was for me."

The school is organized and managed by the Dynasty Foundation, the largest private foundation in Russia supporting science and science education. In the future, Fyodor hopes to find additional sponsors and perhaps even organise one season of the school in Barcelona where he is currently working.

For more details please visit:
dynastybioschooleng.wordpress.com

Cajetan's group blog:
emicrobio.wordpress.com

On the last day of the school the students presented their research results to faculty

© Konstantin Gribov

VIDEO

Fyodor Kondrashov
Fyodor Kondrashov, EMBO Young Investigator and Group Leader at the Center for Genomic Regulation (CRG), talks about his science, how he benefitted from the programme and the highschool science teaching projects he is involved in.

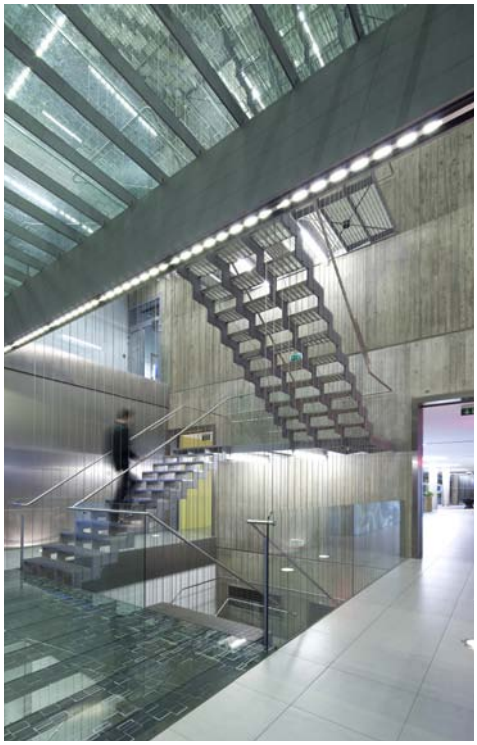
http://youtu.be/oqR6Q15NIZg

Impetus for the life sciences in the Czech Republic

The INSTITUTE OF MOLECULAR GENETICS OF THE ACADEMY OF SCIENCES OF THE CZECH REPUBLIC was founded as an independent research institute in 1962. As part of the new BIOCEV centre of excellence for biotechnology and biomedicine which is being built near Prague, it is building on its many scientific achievements and looking to start new collaborations.

Like many European countries, recent years have been challenging for the financial support of science in the Czech Republic. In spite of the constraints, The Institute of Molecular Genetics has continued to build on its many years of scientific progress.

More than 350 employees work at the Institute, including over 100 scientists, 100 PhD students and 30 undergraduates studying for diplomas. Many of the senior scientists also serve as university teachers. Twenty three research groups focus on molecular and cellular immunology, molecular genetics, functional genomics and bioinformatics, oncogenes, molecular biology of development, cell biology of the nucleus and cytoskeleton, structural biology and mechanisms of receptor signalling. Well-equipped core facilities support all of these activities (see Box 1).



© Institute of Molecular Genetics

The Institute of Biology of the Czechoslovak Academy of Sciences was established in 1953. It included the Department of Experimental Biology and Genetics, headed by Milan Hašek, one of the joint discoverers of immunological tolerance. In 1962, the Department became the independent Institute of Experimental Biology and Genetics of the Czechoslovak Academy of Science with Milan Hašek as its Director until 1970.

The nineteen sixties were notable for the institute – the "Czechoslovak immunogenetic school" was born, represented besides Hašek by such names as Pavol and Juraj Iványi and Jan Klein. An internationally renowned programme for retroviral research was also established under the leadership of Jan Svoboda.

In 1977, The Institute of Biology of the Czechoslovak Academy of Sciences was formally named the Institute of Molecular Genetics of the Czechoslovak Academy of Sciences (IMG), with Josef Říman as the Director. Subsequent years saw important scientific achievements including the joint discovery of reverse transcriptase (J. Říman), the discovery of virogeny (J. Svoboda), and the sequencing of one of the first viral genomes (V. Pačes).

Václav Hořejší has been the director since 2005. In 2007, the institute moved into a new building in the Prague-Krč campus of biomedical institutes of the Academy of Sciences. The institute also includes a modern animal facility, a conference hall with 300 seats (Milan Hašek Auditorium), a kindergarten for 20 children, and a sports facility. Several successful biotechnology spin-off companies have been established in recent years.

Strength through partnerships

The Institute of Molecular Genetics has recently been involved in a major project named BIOCEV (Biotechnology and Biomedicine Centre of the Academy of Sciences and Charles University in Vestec; www.biocev.eu/en). This is a joint project of six institutes of the Academy of Sciences of the Czech Republic and Charles University in Prague. The goal is to establish a new European Centre of Excellence in biomedicine and biotechnology in the village of Vestec which is located about 7 km from the present campus of the biomedical institutes of the Academy of Sciences. The building construction and equipment are being financed mainly from the European Regional Development Fund, which is providing approximately 80 million Euros for the project. The new center will host almost 600 people, including 200 students, in 54 research teams and five research programmes – functional genomics, cellular biology and virology, structural biology and protein engineering, biomaterials and tissue engineering, and development of therapeutic and diagnostic procedures. The building is scheduled to be completed by March 2015.

The research programmes have already started and the project should be a major boost for Czech biomedical research in the coming years.

More information is available at www.img.cas.cz

Box 1 | Core facilities and services at the institute

- Bioinformatics
- Genomics
- Animal house (mouse models)
- Cryobank
- Custom monoclonal antibody preparation
- Cell culture media preparation
- Flow cytometry
- Histology
- Information technologies
- Light and electron microscopy
- Transgenic unit (producing transgenic mice including gene knock-outs)
- X-ray irradiation

Table 1 | Research highlights

RESEARCH AREA	INVESTIGATORS	FOCUS	JOURNALS
Molecular genetics	**Jiří Forejt** *et al.*	Identification of Prdm9 as the first mammalian speciation gene responsible for the phenomenon of male hybrid sterility	*Science* 2009;**323**(5912):373 *PLoS Genet.* 2012;**8**(11):e1003044 *Proc Natl Acad Sci U S A* 2013;**110**(6):E468
Cell biology	**Vladimír Kořínek** *et al.*	Identification of novel regulators of Wnt signaling	*Dev Cell* 2006;**11**(2):203 *Nucleic Acids Res* 2009;**37**(9):3007 *Gastroenterology* 2013;**144**(2):381
Developmental biology	**Zbyněk Kozmik** *et al.*	Mechanisms of eye development	*Proc Natl Acad Sci U S A* 2008;**105**(26):8989 *Dev Biol* 2009;**334**(1):31
Cell biology	**David Staněk** *et al.*	Spliceosome assembly, dynamics of Cajal bodies formation	*J Cell Biol* 2010;**191**(1):7 *Mol Biol Cell* 2011; **22**(4):513
Cancer cell biology	**Libor Macůrek** *et al.*	Role of Wip1 phosphatase in the DNA damage response and predisposing to cancer	*J Cell Biol* 2013;**201**(4):511


EMBO Gold Medal winner Thijn Brummelkamp

Keynote lecture on Wnt signalling, stem cells and cancer

Meet the Speaker session

The EMBO Meeting – highlights

Thijn Brummelkamp was awarded the EMBO Gold Medal 2013 at *The EMBO Meeting* in Amsterdam, The Netherlands, on Sunday September 22. Brummelkamp received his award for work to accelerate the genetic analysis of human disease. In 2002, Brummelkamp developed an inexpensive method to permanently inactivate large numbers of genes by the use of RNA interference. This breakthrough involved the development of a new short hairpin RNA vector system (pSUPER) that directs the synthesis of small interfering RNAs in mammalian cells. Brummelkamp and his research group also investigate how viruses and bacteria make their ways into mammalian cells.

Thijn Brummelkamp received his PhD from Utrecht University in 2003 for his work at the Netherlands Cancer Institute (NKI). He did not pursue formal postdoctoral training but immediately accepted a position to establish his own research programme as a Whitehead Fellow at the prestigious Whitehead Institute for Biomedical Research, Massachusetts, Cambridge, United States. In 2011, he moved his laboratory to the NKI. He also holds an appointment as Adjunct Principal Investigator with the CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences.

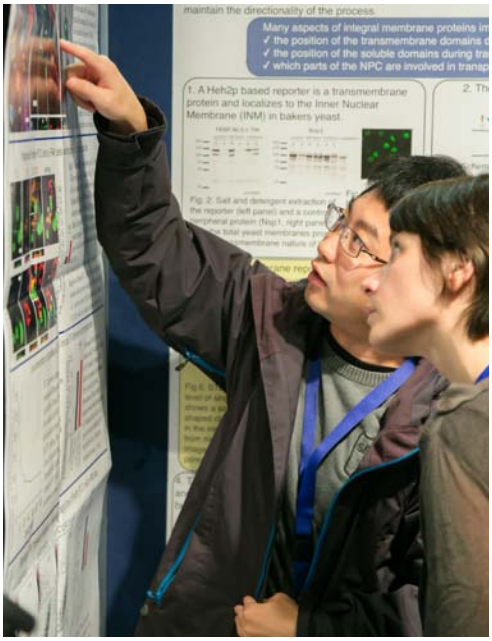
The *EMBO Meeting* 2013 included a wide range of talks from scientists from many scientific disciplines. In a keynote lecture, Hans Clevers, Professor of Molecular Genetics at the Hubrecht Institute, The Netherlands, and President of the Royal Netherlands Academy of Arts and Sciences, discussed the relationship between Wnt signaling, Lgr5 stem cells and cancer. In his talk, he

VIDEO

The EMBO Meeting – Focus on Hans Clevers

"It's up to us, to the scientists, to explain to all the parties involved what stem cells are and how to use safely." Hans Clevers talks to Thomas Lemberger, Chief Editor *Molecular Systems Biology* about the connection between stem cell and cancer research as well as their medical implications.

http://youtu.be/iKdoHLV9nag




Anne Glover


Michael Rosen

showed videos of stem cells in the intestine that illustrated how these self-renewing cells can give rise to all types of cells found in the intestine, including cancer cells. Clevers went on to explain that intestinal cancer is initiated by Wnt pathway-activating mutations in certain genes such as APC (adenomatous polyposis coli). Deletion of the APC gene in stem cells, but not in other cells of the villi, results in the formation of cancer tumours. This finding and others support the concept of cancer stem cells as the origin of cancer tumours.

The Louis-Jeantet Prize lecture took place on Monday September 23. This year there were three prize winners. Peter Hegemann, from the Humboldt University in Berlin, and Georg Nagel, from the University of Würzburg, Germany, discussed their contributions to the field of optogenetics, in particular how channelrhodopsin, a small algal photoreceptor, can be used for research applications. "Optogenetics is primarily an analytic instrument. But applications in the field of retinal prosthesis and deep brain stimulations are on the way and might be realized soon," said Hegemann speaking at the meeting.

The third prize winner, Sir Michael Stratton, Director of the Wellcome Trust Sanger Institute, explained how mutational processes in genes can lead to human cancer. In his lecture, Stratton explained how all cancers are caused by somatic mutations and he reviewed the mutational signatures found across different types of human cancer. Stratton currently heads the cancer genome project, an initiative that seeks to use the human genome sequence and high throughput techniques to discover disease mutations and help improve cancer diagnosis, treatment, and prevention. In 2009, Stratton and colleagues reported the first complete nucleotide sequences of cancer genomes from a lung tumour and a melanoma.

VIDEO

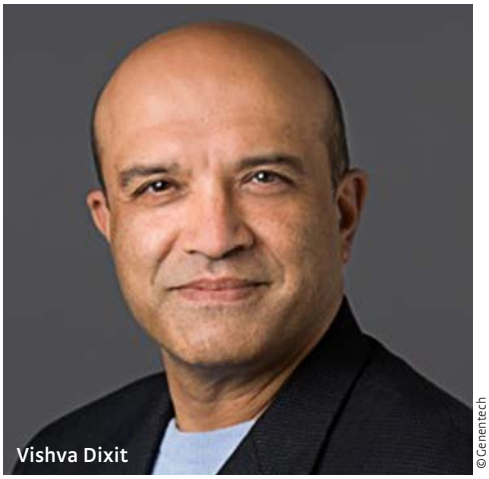
The EMBO Meeting – How to become a Group Leader / Principal Investigator

What does it take to become a Group Leader/ Principal Investigator? We asked three of the speakers, Cédric Blanpain, Carolyn Moores and Jaques Neefjes, for advice.

http://youtu.be/7zSNTlzbkqc

Exploring new territory

VISHVA DIXIT is Vice President of Physiological Chemistry at Genentech. In the 1990s, Dr. Dixit and colleagues made a series of discoveries at the University of Michigan that helped define the molecular events of programmed cell death. More recently, he has been looking at the links between molecular signaling, cancer and inflammation. At *The 5th EMBO Meeting* in Amsterdam, The Netherlands, he talked to Barry Whyte about his career in academic and industrial research.



Vishva Dixit

Let's go back to your formative years in Kenya. What influence did they have on you as a scientist?

We lived in a small town in Kenya. My parents were both physicians. They were in general practice and they ran a small clinic. It was incredibly busy. They would see very sick individuals. Many of them had infectious disease but they were effectively treated with antibiotics. And that always had an impression on me – the good work my parents were doing, and the ability of essentially reviving someone at death's door.

Did you think about medicine first as a career or science or a combination of both?

Well I would say it was a combination. My parents had bought me this series of books from *Time Life* on scientists and their work and that influenced me. I thought it would be fascinating to be a discoverer, an explorer, and that captivated my imagination.

What made you leave Kenya and go to the United States?

Well it was really about opportunities. I had finished medical school in Kenya. I had completed my internship and I wanted to do biomedical research. Unfortunately the facilities were not adequate for that. And that meant either going to Europe or the United States. My brother and sister had already settled in the United States so that made it easier.

What was the first research project you worked on there?

In the States I did a residency in pathology at Washington University in St. Louis. As part of that residency training I did my research with Bill Frazier in the Department of Biochemistry and we worked on thrombospondin, a protein involved in platelet aggregation.

And then you switched to cell death?

When I worked with Bill in St Louis the work on thrombospondin and extracellular matrix biology went reasonably well. I took a lot of that work with me to the University of Michigan. I started out as an assistant professor and my first grants were based on that work. We published papers. But it became evident to me that we were not the front-runners in the field. We were doing good work but we were not dominant, not painting on a larger canvas. I decided to throw caution to the winds and do something totally new. This was very risky since as an assistant professor in the United States you are not tenured. But you know nothing ventured, nothing gained.

And your discoveries in programmed cell death that took place in the 1990s?

The problem was how does one study cell death biochemically. You could induce cell death in many ways, but none at the time were biochemically amenable. What happened was that Shigekazu Nagata and Dave Goeddel had described members of the tumour necrosis factor receptor family – TNF receptor and FAS. If you engaged these receptors you got cell death. Now that was a biochemical handle. You could take a receptor and ask what was downstream as a way of illuminating the death pathway.

The results were really surprising? People were looking for ion channels, phosphorylation events.

I would say that probably the most important result was the realization that there was a protease involved. We came around to that in a very convoluted manner, but finally nailed it by using a virally encoded inhibitor of caspases.

This was a classic inhibitor experiment?

We could engage the death pathway by stimulating these receptors but what was downstream was a complete mystery. Around that time Bob Horowitz's team had identified Ced3 as a protease that was a component of the death pathway in the worm and this made us wonder whether an equivalent activity could exist in mammals, one responsible for death receptor-induced cell death. The use of a virally encoded caspase inhibitor was the key that unlocked a Pandora's box of riches.

And then you moved to Genentech in 1997?

It was really at the tail end of the heyday of apoptosis research that I moved to Genentech. I had exciting new responsibilities – at that time to form and run an oncology programme.

We hear a lot about the research culture of Genentech. It's very much a research driven environment. Can you tell us about the culture?

Research is given a very high premium. It's a very data driven organization and a very flat organization.

There clearly must be pressure to develop drugs. So how "free" is the research?

Yes, there are enormous pressures to develop drugs. At the end of the day that is what we are about. Making medicines is a highly competitive arena and we have to succeed in that. Our model for being a successful pharmaceutical company is just different. I won't say it is better or worse – it is just different. We believe a significant proportion of our resources should go to fundamental research.

Do you think it is a privilege to be a scientist? How do you see this?

I think it is an enormous privilege. It is essentially being paid to pursue one's hobby and it's an activity that you only find in enlightened societies. I think the quest for knowledge is a common human trait. We all want to know the unknown, but it's only in certain countries where one is afforded the luxury of being able to pursue curiosity.

And what advice would you give to a young scientist interested in working in industry or a university environment?

I would say that in the pharmaceutical industry it is very important to be a team player. You have to be able to play well with others in the sandbox. You have to realize that the creation of a drug is nothing short of a miracle and it requires the efforts of lots of people.

Are you excited by the future, for your science and science in general?

I think there is so much more to explore, so much more to find out – in terms of the pharmaceutical industry, in terms of medicines and human biology.

VIDEO

The EMBO Meeting – Focus on Vishva Dixit

http://youtu.be/FMmQnwK4_VQ

The Institute for Molecular Infection Biology at the University of Würzburg is 20

The INSTITUTE FOR MOLECULAR INFECTION BIOLOGY (IMIB) and the Research Center for Infectious Diseases at the University of Würzburg, Germany, celebrated their 20th anniversaries on the 28th of June.

©IMIB and ZINF

Hermann Bujard, Jörg Hacker and Jörg Vogel at the anniversary event

The IMIB and the Research Center for Infectious Diseases (Zentrum für Infektionsforschung or ZINF) were founded in 1993 as a means to facilitate the propagation of the then new molecular tools developed in different model pathogens to understand the basis for infection by bacteria, fungi, and parasites. While these molecular and cell-based approaches remain a central part of the institute there is now a focus on the application of new global approaches to understanding infectious diseases.

"The institute is increasingly investing in new discovery-based technologies to understand the infection process from a new viewpoint," current Director of the IMIB and EMBO Member Jörg Vogel stated. "For example, several of the groups are using deep sequencing to look into the many unexpected different roles that RNA molecules play in both infection and the immune response. We are also using global approaches to try to understand the molecular events involved in the epigenetic basis of gene regulation and how complex traits such as antibiotic resistance can evolve in a specific pathogen." He added: "In many cases, the institute is benefiting from new approaches brought in by the young investigators that allow us to answer these important and timely questions using different model pathogens."

The central role for young independent group leaders was a fundamental goal of IMIB and ZINF in 1993. "From the beginning we have placed a strong focus on the importance of young investigators in our laboratories. Our intention has been to give them the support they need to become independent early in their scientific career and to help them put in place research programmes that will stand the test of time," remarked EMBO Member Jörg Hacker, the founding director of IMIB and the first spokesperson for ZINF.

The anniversary event brought together many researchers from all over Europe and the rest of the world to reflect on the successes of the past and also to look to the future of infectious disease research. The programme included talks that provided an overview and different perspectives on current and future research on infection biology by Pascale Cossart, EMBO Member and Professor at the Institut Pasteur, France, and Michael Gilmore, the Sir William Osler Professor of Ophthalmology, Microbiology and Immunology at Harvard Medical School. EMBO Members Fritz Melchers and Werner Goebel also attended the meeting.

"The Institute for Molecular Infection Biology and the Zentrum für Infektionsforschung have achieved visibility and recognition for their scientific contributions to understand the mechanisms of infectious disease over the past 20 years," commented Pascale Cossart. "The expertise and commitment of its researchers and leadership team have helped to build a solid foundation to support infectious disease research in Europe. This will help, ultimately, in our global efforts to make new scientific discoveries and to improve the clinical understanding of infectious disease."

In her talk, Cossart emphasized that there are many interesting and in some cases crucial research options that institutions can either pursue or choose not to investigate. "My generation of scientists has made it possible to dissect the molecular processes associated with pathogens but the field is ready for other big discoveries provided that politicians and other decision makers are aware of the need to establish important links between scientific disciplines," said Cossart. "We must accept the fact that microbiology is no longer the field of Louis Pasteur or Robert Koch working alone with Petri dishes. What we need are new links with other disciplines including, for example, chemistry, ecology, veterinary science and nutrition. Infection biology requires significant investment in instruments, informatics and bioinformatics that will allow us to store and analyse large amounts of data."

The plenary lecture was given by John Mekalanos, Chair of the Department of Microbiology and Immunobiology, Harvard Medical School, who described some of molecular strategies used by bacteria to fight for superiority within a specific environmental niche.

Hermann Bujard, first chair of the Scientific Advisory Board of ZINF, and former EMBO Director, concluded: "It is very satisfying to see the progress that has taken place over the past 20 years at ZINF and the IMIB. Infectious disease research and its translation to 'the field' are essential if we are to make progress in improving public health across the world, a most important prerequisite for peaceful developments in numerous regions around the globe. Universities with their genuine responsibility for research and education are particularly suited to meet these challenges. The research programmes of ZINF and IMIB are excellent paradigms for innovative approaches in this crucial endeavour."

Pascale Cossart, Institut Pasteur

©IMIB and ZINF

Practical Courses

Metabolomics bioinformatics for life scientists
UK-Cambridge, 17–21 March

Advanced optical microscopy
UK-Plymouth, 2–12 April

Computational biology: Genomes to systems
CL-Puerto Varas, 3–9 April

Computational structural biology
UK-Hinxton, 7–11 April

Computational molecular evolution
GR-Heraklion, 5–14 May

Bioinformatics and genomes analyses
GR-Athens, 5–17 May

The structural characterization of macromolecular complexes
FR-Grenoble, 2–7 June

Non-coding RNAs: From discovery to function
IE-Galway, 7–13 June

Molecular genetics with fission yeast
FR-Paris, 30 June–11 July

3D Developmental imaging
PT-Oeiras, 4–12 July

Correlative light electron microscopy
UK-Bristol, 6–11 July

Solution and solid-state NMR of paramagnetic molecules
IT-Sesto Fiorentino, 13–19 July

Biomolecular simulation
FR-Paris, 20–27 July

Genotype to phenotype mapping of complex traits
UK-Hinxton, 28 July–1 August

Multidimensional NMR in structural biology
DE-Joachimsthal, 10–15 August

Light sheet microscopy
DE-Dresden, 18–29 August

Cryo-electron microscopy and 3D image processing
DE-Heidelberg, 31 August–9 September

Ubiquitin and related modifiers
IT-Alghero, 6–13 September

Protein expression, purification, and characterization (PEPC9)
DE-Hamburg, 8–16 September

Microscopy, modelling and biophysical methods
DE-Heidelberg, 8–20 September

Single-cell gene expression analysis
DE-Heidelberg, 19–25 September

Targeted proteomics: Experimental design and data analysis
ES-Barcelona,
28 September–3 October

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For a complete and up-to-date list of EMBO events please go to ***events.embo.org***

Workshops

Protein and lipid function in secretion and endocytosis
AT-Goldegg am See, 14–19 January

Signalling to and from endomembranes
DE-Hegne (Allensbach), 15–19 March

Mechanisms of neuronal remodelling
IL-Ein Gedi, 22–26 March

Stalked alpha-Proteobacteria and relatives: From genes to structure
DE-Ebsdorfergrund, 30 March–3 April

Recoding: Reprogramming genetic decoding
IE-Killarney, 13–18 May

Glycobiology and glycochemistry: Applications to human health and disease
PT-Lisbon, 24–28 May

Magnetic resonance for cellular structural biology
IT-Principina Terra (Grosseto), 1–6 June

Histone variants
FR-Strasbourg, 2–4 June

Cellular imaging of lipids
IT-Vico Equense, 2–6 June

Simultaneous profiling of RNA and protein using proximity ligation assay
UK-Chelmsford, 7 July

Intercellular communication in plant development and disease
FR-Bischoffsheim, 24–29 August

The regulation of aging and proteostasis
IL-Ma'ale Hachamisha, 7–12 September

Advances in protein–protein interaction analysis and modulation
FR-Hyères, 9–12 September

Current advances in membrane trafficking: Implications for polarity and diseases
CL-Puerto Natales, 9–14 September

Unraveling biological secrets by single-cell expression profiling
DE-Heidelberg, 25–26 September

Decoding neural circuit structure and function
TR-Istanbul, 26–28 September

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Conferences

The mighty *Daphnia*: Past, present and future
UK-Birmingham, 19–22 January

Visualizing biological data (VIZBI 2014)
DE-Heidelberg, 5–7 March

Human evolution in the genomic era: Origins, populations and phenotypes
UK-Leicester, 1–4 April

Telomeres, telomerase and disease
BE-Brussels, 30 April–4 May

Molecular biology of muscle development and regeneration
IT-Acaya (Lecce), 14–18 May

Lymphocyte signalling
IT-Bertinoro, 17–21 May

Cellular signalling and cancer therapy
HR-Cavtat, 23–27 May

Microtubules: Structure, regulation and functions
DE-Heidelberg, 28–31 May

Enzyme mechanisms by biological systems
UK-Manchester, 1–4 June

Gene transcription in yeast: From regulatory networks to mechanisms
ES-Sant Feliu de Guixols, 14–19 June

The molecular and developmental biology of *Drosophila*
GR-Kolymbari, 22–28 June

Microbiology after the genomics revolution (Genomes 2014)
FR-Paris, 24–27 June

Viruses of microbes: Structure and function, from molecules to communities
CH-Zurich, 14–18 July

Chemical biology
DE-Heidelberg, 20–23 August

Brain development and disorders
FR-Saint Raphaël, 5–8 September

The molecular and cellular basis of regeneration and tissue repair
ES-Sant Feliu de Guixols,
6–10 September

Interdisciplinary plant development
UK-Cambridge, 21–24 September

Innate lymphoid cells
FR-Paris, 29 September–1 October

Centrosomes and spindle pole bodies
PT-Lisbon, 30 September–3 October

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ESF | EMBO Symposia

Cell polarity and membrane trafficking
PL-Pułtusk, 10–15 May

Biology of plastids: Towards a blueprint for synthetic organelles
PL-Pułtusk, 21–26 June

Synthetic biology of antibiotic production
ES-Sant Feliu de Guixols,
30 August–4 September

Long regulatory RNAs
PL-Pułtusk, 13–18 September

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EMBO | EMBL Symposia

Translating diabetes
DE-Heidelberg, 30 April–3 May

Tumour microenvironment and signalling
DE-Heidelberg, 7–10 May

Molecular machines: Lessons from integrating structure, biophysics and chemistry
DE-Heidelberg, 18–21 May

Epithelia: The building blocks of multicellularity
DE-Heidelberg, 27–30 August

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DEADLINE 1 March 2014
ESF | EMBO SYMPOSIA
DEADLINE 1 October 2014

EMBO | FEBS Lecture Courses

Biophysics of channels and transporters
IT-Erice, 11–17 May

Nuclear proteomics
GR-Kos, 18–23 May

EMBO Global Activities Lecture Courses

Structural and biophysical methods for biological macromolecules in solution
BR-São Paulo, 19–26 January

Biology of bacterial non-coding RNAs
AR-Bernal, 4–9 March

High-throughput NGS applied to infectious diseases
TN-Tunis, 15–25 September

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Other EMBO events

EMBO Laboratory Management Courses
DE-Leimen, Various dates

FEBS | EMBO 2014
FR-Paris, 30 August–4 September

EMBO Members Meeting
DE-Heidelberg, 29–31 October

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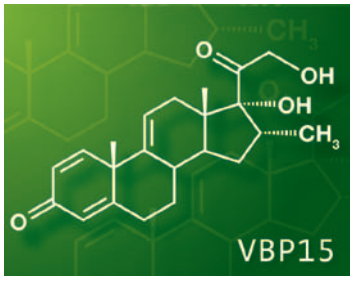
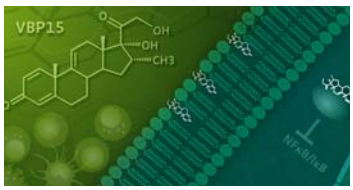
EMBO Molecular Medicine





RESEARCH ARTICLE

New muscular dystrophy treatment shows promise in early study

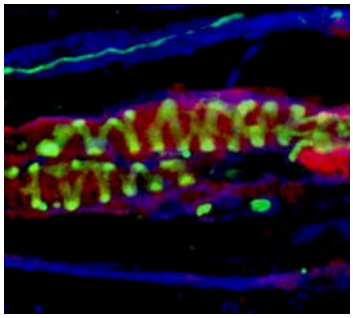
A preclinical study led by researchers in the United States revealed that a new oral drug shows early promise for the treatment of muscular dystrophy. The results show that VBP15 decreases inflammation in mice with symptoms similar to those found in patients with Duchenne muscular dystrophy. The authors found that the drug protects and strengthens muscle without the harsh side effects linked to current treatments with glucocorticoids such as prednisone.

"It is becoming increasingly clear that membrane integrity and repair are crucial factors in muscle, cardiovascular, neurodegenerative and airway disorders. The chemical properties of VBP15 also suggest potential for the treatment of other diseases," remarked Kanneboyina Nagaraju, DVM, PhD, the lead author of the study and a principal investigator in the Center for Genetic Medicine Research, Children's National Medical Center in Washington, DC.

The researchers observed that VBP15 inhibits the transcription factor NF-κB, a key cell-signaling molecule found in most animal cell types that plays a role in inflammation and tissue damage. The authors conclude that VBP15 merits further investigation for efficacy in clinical trials.

VBP15, a novel anti-inflammatory and membrane-stabilizer, improves muscular dystrophy without hormonal side effects
C.R. Heier, J.M. Damsker, Q. Yu et al.
Read the paper:
doi: 10.1002/emmm.201302621

THE EMBO JOURNAL



RESEARCH ARTICLE

Alzheimer's disease protein controls movement in mice

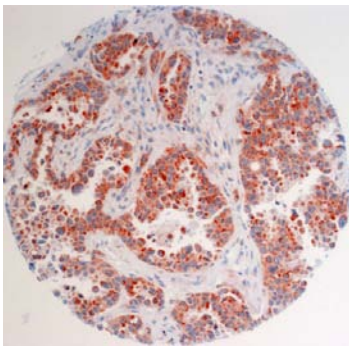
Researchers in Berlin and Munich, Germany, and Oxford, United Kingdom, have revealed that a protein well known for its role in Alzheimer's disease controls spindle development in muscle and leads to impaired movement in mice when the protein is absent or treated with inhibitors. The results suggest that drugs under development to target the beta-secretase-1 protein, which may be potential treatments for Alzheimer's disease, might produce unwanted side effects related to defective movement.

"Our results show that mice that lack Bace1 proteins or are treated with inhibitors of the enzyme have difficulties in coordination and walking and also show reduced muscle strength," remarked Carmen Birchmeier, one of the authors of the paper, Professor at the Max-Delbrück-Center for Molecular Medicine in Berlin, Germany, and an EMBO Member. "In addition, we were able to show that the combined activities of Bace1 and another protein, neuregulin-1 or Nrg1, are needed to sustain the muscle spindles in mice and to maintain motor coordination."

One unwanted side effect of the long-term inhibition of Bace1 might be the disruption of muscle spindle formation and impairment of movement. This finding is relevant to scientists looking for ways to develop drugs that target the Bace1 protein.

Bace1 and neuregulin-1 (Nrg1) cooperate to control formation and maintenance of muscle spindles
C. Cheret, M. Willem, F.R. Fricker et al.
Read the paper:
doi: 10.1038/emboj.2013.146

EMBO Molecular Medicine



RESEARCH ARTICLE

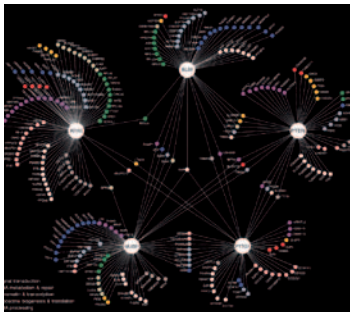
Alternative target for breast cancer drugs

Scientists have identified higher levels of a receptor protein found on the surface of human breast tumour cells that may serve as a new drug target for the treatment of breast cancer. The results show that elevated levels of the protein Ret, which is short for "Rearranged during transfection," are associated with a lower likelihood of survival for breast cancer patients in the years following surgery to remove tumours and cancerous tissue. The scientists examined tumour tissue microarrays of more than 100 breast cancer patients who had undergone surgery to remove their tumours. Antibodies were used to detect the levels of Ret in the samples. In other experiments, four different cancer cell lines were used and injected into mice to study the effects of Ret inhibitors on the progress and spread of the cancer.

"Our findings suggest that Ret kinase might be an attractive and novel alternative therapeutic target in selected groups of breast cancer patients," remarked Nancy Hynes, Professor at the Friedrich Miescher Institute for Biomedical Research and the University of Basel, Switzerland. "Initial experiments in mice that serve as model organisms for the study of breast cancer have revealed that specific inhibitors significantly block the spread of cancer and decrease the number of metastatic tumours found in the lungs."

Ret inhibition decreases growth and metastatic potential of estrogen receptor positive breast cancer cells
A. Gattelli, I. Nalvarte, A. Boulay et al.
Read the paper:
doi: 10.1002/emmm.201302625

molecular systems biology



RESEARCH ARTICLE

A negative genetic interaction map in isogenic cancer cell lines

A research team led by scientists at the University of Toronto, Canada, has defined a network of synthetic sick/lethal interactions with a set of query genes in a series of isogenic cancer cell lines. This study defined about 200 negative genetic interactions in the isogenic cancer cell line background. By mapping negative genetic interactions in a systematic fashion in isogenic cancer cell lines, the scientists revealed novel functions for several uncharacterized genes. The study demonstrated that differential essentiality profiles derived from isogenic cancer cell lines can be used to classify genetic dependencies in non-isogenic cancer cell lines.

Improved efforts are necessary to define the functional product of cancer mutations currently being revealed through large-scale sequencing efforts. Using genome-scale pooled shRNA screening technology, the researchers mapped negative genetic interactions across a set of isogenic cancer cell lines and confirmed hundreds of these interactions in orthogonal co-culture competition assays to generate a high-confidence genetic interaction network of differentially essential or differential essentiality genes. The work of the researchers suggests that many cancer vulnerabilities remain to be discovered through systematic derivation of a network of differentially essential genes in an isogenic cancer cell model.

A negative genetic interaction map in isogenic cancer cell lines reveals cancer cell vulnerabilities
F.J. Vizeacoumar, R. Arnold, F.S. Vizeacoumar et al.
Read the paper:
doi: 10.1038/msb.2013.54

MRC Cancer Cell Unit transfers to the University of Cambridge

As of last October, the former Cancer Cell Unit of the Medical Research Council (MRC) has become a new department within the University of Cambridge. The core funding and infrastructure support still come from the MRC.

The new structure – the so-called University Unit – is being more widely adopted by the MRC to better integrate its units into their host universities, enhance their research capacity, and offer new opportunities for both collaboration and funding. As part of the University of Cambridge, the new unit called the MRC Cancer Unit is also eligible for external funds from higher education institutes.

The centre, which is led by EMBO Member Ashok Venkitaraman, has become a leading institute for cancer research over the past decade. Today it consists of eight research programmes covering a range of areas and involving more than one hundred staff. Its overall focus is on understanding the molecular mechanisms that underlie early steps in the genesis of epithelial cancers, and translating this knowledge into clinical practice to improve cancer diagnosis and treatment, through the development of innovative enabling technologies.

A multidisciplinary network

The unit pursues a multidisciplinary approach, fostering collaboration not only between its internal research programmes but also with many external and commercial partners. This type of multi-disciplinary network has been particularly fruitful in the identification of chemical tools that modulate previously 'undruggable' cellular targets. The programme, led by Professor Ashok Venkitaraman, aims to improve understanding of the biological processes involved in the initiation of cancer, and also offers the tangible prospect of developing new anti-cancer agents.

An innovative approach integrating *in vivo* cancer models with 3D imaging, lineage tracing and computational biology has also been adopted in the programme led by Dr. Philip Jones. His group have been the first to use large-scale lineage tracing to quantify cell fate *in vivo*, utilising methods more commonly found in theoretical physics for data analysis. This research has revealed how all dividing cells constitute a self-maintaining population contributing equally to tissue maintenance, and showing how this homeostatic balance is perturbed during carcinogenesis, providing important insights into new avenues for therapy.

A recent recruit to the Unit is Dr. Christian Frezza, a former EMBO Long-Term Fellow. Frezza's programme combines biochemistry with the comprehensive analysis of small-molecule metabolites using the tools of systems biology to investigate the metabolic transformation that cancer cells undergo at an early stage in carcinogenesis, with the aim of developing new diagnostic and therapeutic tools.

Focus on translational biology

Other programmes in the unit focus on understanding cancers with a poor prognosis, including pancreatic, lung and oesophageal, and on the relationship between early invasion, metastasis and the tumour microenvironment, through studies on human tissues and genetically engineered mouse models. These laboratory studies have already triggered tangible clinical improvements, such as those for the early diagnosis and risk stratification of oesophageal cancer by Rebecca Fitzgerald.

Commenting on the strategic alliance between the University and MRC, Ashok Venkitaraman said, "This alliance will enhance the unit's ability to deliver on its research goals, and better coordinate our work with that of other institutions within the Cambridge Cancer Centre. The unit has already made several significant contributions to cancer research, and we look forward to continuing this work within the University whilst retaining our strong link with the Medical Research Council."

For more information visit
www.mrc-cu.cam.ac.uk

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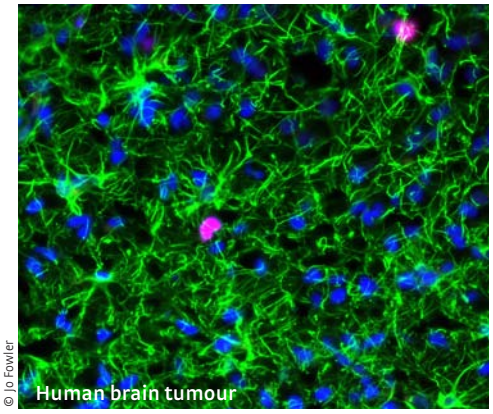
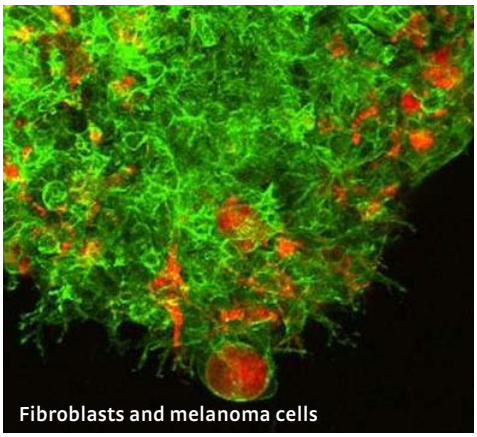

© Jo Fowler
Human brain tumour

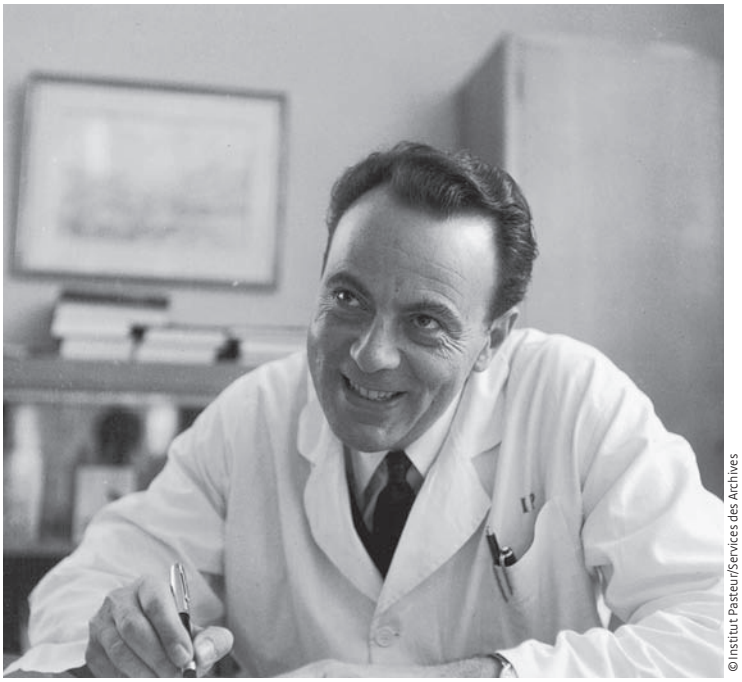

© Hutchison / MRC Research Centre
Professor Ashok Venkitaraman


© Julia Frede
Section of the mouse oesophagus


© Jacqui Shields
Fibroblasts and melanoma cells

OBITUARY

François Jacob 1920–2013



© Institut Pasteur/Services des Archives

François Jacob, one of the most influential scientists of 20th century molecular biology, died on April 19, 2013. His name will be remembered together with Jacques Monod and André Lwoff for unraveling the genetic control of enzyme and virus synthesis. These three scientific pioneers were jointly awarded the Nobel Prize in Physiology or Medicine in 1965. Beyond science, all three were heavily engaged in the fight against Nazi Germany during World War II: Monod and Lwoff in the Resistance and Jacob on the battlefield. In 1940, Jacob, a second-year medical student, joined de Gaulle's Free French Forces in England and participated in the entire Africa campaign. Shortly after the Normandy landing in June 1944, he was severely injured by an exploding bomb. He spent many months in hospital and never recovered completely.

Jacob had to abandon his early dream to become a surgeon because of his injuries. Nevertheless, he had the opportunity to begin research, as he recalls "in the right place at the right time." He joined Lwoff's laboratory at the Institut Pasteur in 1950 shortly after the discovery of prophage induction. Jacob started his research on the genetic analysis of lysogeny. He and Elie Wollman soon discovered a new phenomenon that they called "zygotic induction": crosses between a lysogenic male and a non-lysogenic female resulted in the induction of phage development, but not when the reciprocal cross was performed. This asymmetry in crosses suggested the existence of a cytoplasmic factor, a "repressor" that prevents phage induction. By analysing the conjugation process itself they showed that the male chromosome was injected into the female at a constant rate. This enabled them to map the order of genes and to demonstrate the circularity of the *Escherichia coli* chromosome.

In 1957, an exceptionally creative collaboration started between Jacques Monod and Jacob. They decided to use bacterial conjugation for a genetic analysis of the *E. coli* lactose system. Many mutants isolated and characterized by Monod were available and they were inserted in various combinations into male and female bacteria. The outcome of conjugation experiments between different mutants led to the model of negative regulation: a regulator gene produces a "repressor" that blocks enzyme synthesis. These experiments were crucial for the development of the messenger RNA concept and the operon model. They marked a turning point in how the mechanism of protein synthesis and its regulation were represented.

Jacob served on EMBO Council from 1963-1971. He was involved in many of the discussions that shaped the early direction of EMBO, including the decisions that led to the birth of the European Molecular Biology Laboratory. In his own words, the road to EMBL was 'more difficult than anticipated.' He remained a staunch supporter of EMBO and EMBL throughout his career.

Other major contributions in science included the replicon model, a paradigm for DNA replication, and Jacob's bright idea on the role of tinkering in evolution. His legacy was not limited to science. He was an exquisite and successful writer and his books were written in a highly personal and elegant style. He will be remembered as one of the most original intellects of his generation.

Agnes Ullmann

BOOK REVIEW

The Compatibility Gene

EMBO Young Investigator Daniel M. Davis has published a new popular science book entitled *The Compatibility Gene*. His book is about the genes of our immune system – our compatibility genes – and about the researchers who have pieced together the science he describes.

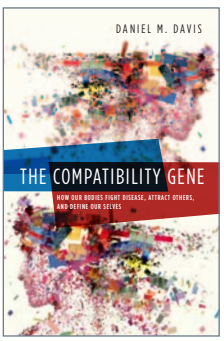
Daniel M. Davis's book is an account of how human beings fight off the illnesses and diseases that attack us on a daily basis. It is our compatibility genes that influence our susceptibility or resistance to multiple sclerosis, diabetes, arthritis and other diseases. They are also at the heart of our individuality. "This book is also about me trying to understand the differences between people and why our own uniqueness is important," says the author who is professor of immunology at the Manchester Collaborative Centre for Inflammation Research, United Kingdom.

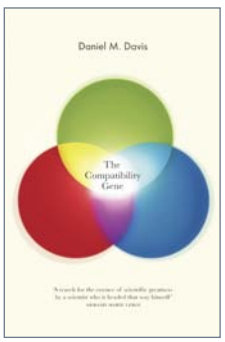
The Compatibility Gene takes readers on a journey spanning sixty years – from the beginnings of transplants and immunology leading to the edge of knowledge and current areas of research.

In parallel to the story about scientific discoveries, Davis shows that a great many people made these contributions. Many of them were strong personalities and some lived a turbulent life. Often one person did not appreciate another's approach. With warmth and in a light-handed way he writes about how the researchers have struggled to find the right answers and to understand the mechanisms that underlie our defences against diseases.

The book also discusses some of the medical and ethical issues that arise from our diversity in immune system genes. The final chapter of the book explores the role of the immune system and compatibility genes in pregnancy, brain plasticity and the selection of a mate.

"We built a shed at the bottom of my garden and I sat there writing intensely for one year and then on and off for another two years," says Davis. The result is an exciting science story that is also suitable for non-specialist readers.





Scientists must engage in creating dialogue

Biosciences for Farming in Africa is the latest project involving Christopher Leaver, an EMBO Member for more than 30 years, who has been committed to creating a dialogue with the public since he started his scientific career.

Christopher Leaver presenting a copy of B4FA essays to Kevin Urama, Executive Director of the African Technology Policy Studies Network

© B4FA

Today Christopher Leaver invests much of his time and energy to reach the public through science education and communication projects. Leaver is Emeritus Professor of Plant Science at the University of Oxford, former head of the Department of Plant Sciences at the University, and Chair of EMBO Council from 1996–1997. Biosciences for Farming in Africa (B4FA) is one of the many initiatives he engages in to address the global challenges of achieving food security and sustainability.

The plant biologist acts as a science adviser in the B4FA team and is involved in its work on a daily basis by providing advice, reviewing articles, and contributing to workshops and field visits in Africa. "Doing nothing is not an option," is a statement he often includes in his talks and presentations. He understands it as a call for action in the undernourished areas of East and West Africa. "I am very worried about the consequences of increasing population, from one to two billion over the next 40 years in Africa, the growing demands for food and the effects of plant diseases, pests and climate change on crop productivity," says Leaver.

A Fellowship scheme for African science journalists is just one project offered by B4FA, which is supported by the United States-based John Templeton Foundation. In the last year, Leaver has contributed to courses and given lectures in four-day workshops about modern methods of improving crop productivity in Ghana, Nigeria, Tanzania and Uganda. He emphasises the courses are not about teaching. His goal is to provide background information to journalists and to create dialogue. The decisions are entirely to be made by people in Africa.

Leaver believes scientists must engage in dialogue and debate: "I come from a rural background and tax payers in the United Kingdom supported my education and career from the moment I started school until I ended up as head of department at the University of Oxford." Since the development of modern molecular genetics and plant breeding – beginning with the so called Green Revolution – he has been committed to informing society and continues to do so by lecturing to students, the general public and by engagement with the media. He was a founding trustee of Sense about Science (senseaboutscience.org), a British charity that promotes the public understanding of science and contributes to the successful Science Media Centre in the United Kingdom – to name just a few. "My engagement arises from a long-standing belief in communicating the relevance of science to the many challenges we face for the next generation."

© Julia Vitullo-Martin B4FA

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Left: Professor Leaver extracting DNA with Nigerian journalist Ladidi Lucie Elukpo, one of the B4FA Fellows who works with Nigerian Guardian Newspapers. Right: Course participants visiting local farms and research stations.

More information on Biosciences for Farming in Africa is available at www.b4fa.org

ONLINE PETITION

Rules on animal research in Italy

Italian scientists publish an open letter to the European Commission to reverse new rules on animal research

Almost ten thousand Italian scientists have signed a petition addressed to the European Commissioner for the Environment, *Janez Potočnik,* and to a number of Italian legislators. The petition calls on politicians to defend the use of animals in biomedical research in Italy and was co-initiated by EMBO Members *Jacopo Meldolesi* and *Giacomo Rizzolatti.*

Last summer, the Italian parliament approved introducing extreme restrictions on the use of animals in research. The law now forbids xenotransplantation – a widely used method in which human tumour cells are implanted into mice to test cancer therapies – and bans the use of animals for studying drug abuse.

The petition can be found at: www.salvalasperimentazioneanimale.it/sperimentazione-animale/english-version/

New Single-Cell Genomics Centre in Hinxton

Scientists at the EMBL EUROPEAN BIOINFORMATICS INSTITUTE (EMBL-EBI) are exploring the DNA, RNA and epigenetic features of single cells to better understand biology and disease.

Scientists at EMBL-EBI and the Wellcome Trust Sanger Institute in Hinxton, United Kingdom, launched the Single Cell Genomics Centre (SCGC) earlier this year. The centre seeks to answer key biological questions by exploring cellular genetics at the highest resolution possible.

"The Single Cell Genomics Centre will stimulate the bioinformatics research needed for interpreting this new type of data," says EMBO Member Sarah Teichmann, who works at both institutes and is one of the six SCGC founders. "We are looking to establish the centre as a focal point for collaboration to accelerate the science, applications, methods and discoveries in single-cell genomics research."

Single-cell genomics enables researchers to identify differences between individual cells within developing tissues. Identifying and understanding differences between cell types and subpopulations is crucial to discover, for example, how cancer spreads or specialized cells – such as neurons – can be grown for use in regenerative medicine.

www.sanger.ac.uk/research/projects/singlecellcentre

Sarah Teichmann and Chris Ponting, two of the six founders of the Single Cell Genomics Centre

© EMBL PhotoLab | M. Schupp

Salvador Aznar Benitah wins The Metastasis Prize

The first winner of The Metastasis Prize from The Beug Foundation for Metastasis Research is SALVADOR AZNAR BENITAH from El Centre de Regulació Genòmica, Barcelona, Spain.

The Metastasis Prize is awarded to encourage research into new ways to impede the spread of cancer. Benitah will use the award to characterize a population of recently identified cells that may contribute to metastasis in patients with squamous cell carcinoma.

Further details are available at www.beugstiftung-metastase.org

50th anniversary at the University of Geneva

The Department of Molecular Biology at the University of Geneva is celebrating its 50th anniversary with a symposium in GENEVA, Switzerland, on JUNE 23, 2014.

The list of invited speakers includes *Werner Arber* (Nobel Prize 1978), *Gordon Hager, Jack Greenblatt, Bruce Alberts, Harry Noller, Erich Nigg* and *Susan Gasser,* all of whom have been affiliated with the department in the past.

For updates on the symposium, please visit: www.molbio.unige.ch

A new building for systems biology in Berlin

Berlin, already known for systems biology research and integration of different scientific disciplines, will soon become an even more attractive place for scientists from all over the world. The Berlin Institute for Medical Systems Biology or BIMSB, headed by EMBO Member NIKOLAUS RAJEWSKY, is a young branch of the Max Delbrück Center for Molecular Medicine (MDC) and will be moving to the centre of Berlin.

The new building will provide 5400 m^2 of laboratory and office space for up to 25 research groups, equally distributed between experimental and computational areas. The building will accommodate high-tech laboratories, flexible workspaces and communication spaces, allowing for innovative and interdisciplinary work as well as scientific exchange. The architectural design for the new building for BIMSB was selected through an open competition and will smoothly integrate into the new life science campus of the Humboldt University. It is located in close proximity to the Charité Hospital, the German Center for Rheumatology Research (DRFZ), and the Max Planck as well as Leibniz Institutes. The closeness of the new, interdisciplinary research building for BIMSB to the life sciences of the Humboldt University and other institutions was part of the university's successful 'Excellence concept' in 2012, where, Humboldt University, Charité Berlin (Medical University) and MDC partner to develop the "Integrative Research Institute for Life Sciences." The expansion of the MDC to the city centre is part of the innovation development strategy for life sciences in Berlin. Research and technologies of BIMSB will substantially contribute to the developments in systems medicine and the scientific agenda of the Berlin Institute for Health.

Currently, research groups at BIMSB are integrated into the scientific activities and the campus of the MDC in Berlin-Buch. Here, experimental, computational and high-end technological research contribute to the central themes of MDC research: cardiovascular and metabolic diseases, cancer, and diseases of the nervous system. Technology platforms at the institute offer state-of-the-art sequencing technologies as well as mass spectrometry with high capacities for quantitative genome, transcriptome, proteome and metabolome analysis. Data processing, analysis and integration are supported by high-performance computing capacities to facilitate functional analysis and mathematical modeling.

Research projects and publications are in many cases collaborative efforts amongst BIMSB and MDC research groups. They are integrated in national or European networks as well as international collaborations. Capacities and technology areas are expected to expand further with the recruitment of additional groups and the move to the new building.

Scientific progress

In such a dynamic, high-level scientific setting, scientific discoveries are almost inevitable: In the May edition of Nature Methods, for example, the flexible computational framework, microMUMMIE, was presented to identify regulatory microRNA binding sites (1). The group of Uwe Ohler, in collaboration with researchers from Duke University, published a computational approach to identify regulatory binding events by integrating sequence with cross-linking features from sophisticated experimental data. Another research highlight reflects the success of BIMSB in pursuing its scientific mission – 'to decipher the post-transcriptional regulatory code and to integrate it with major cellular regulatory mechanisms.' The laboratory of Nikolaus Rajewsky, in collaboration with the laboratory of Ferdinand le Noble and BIMSB research groups, combined biochemical, computational, and functional data to show that circular RNAs are a large class of animal RNAs that often have tissue and developmental stage-specific expression. Furthermore, they could show that circular RNAs can bind microRNAs, effectively interfering with microRNA-mediated regulation (2). They thus proposed that circular RNAs are likely a large class of post-transcriptional regulators. These findings, together with their extreme stability, make circular RNAs interesting candidates for biomarkers and therapeutic agents.

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The Berlin Institute for Medical Systems Biology

REFERENCES

1. *Nature Methods* **10,** 630–633 (2013) doi:10.1038/nmeth.2489
2. *Nature* **495,** 333–338 (21 March 2013) doi:10.1038/nature11928

VIDEO

Focus on Nikolaus Rajewsky
EMBO Member Nikolaus Rajewsky of the Berlin Institute for Medical Systems Biology talks about gene regulation, how gene sequencing is leading to personalized medicine and the passionate nature of scientists.

http://youtu.be/uL-cOyR0AiE

Mysteries of the unseen world

Researchers from the Biozentrum Basel headed by EMBO Member ERICH NIGG contributed movie sequences based on thousands of high-resolution electron microscopy images to a National Geographic film.

© Martin Oeggerli, supported by Kenneth N. Goldie, C-CINA, Biozentrum, University Basel

A high-precision image of a cat flea that in reality is not bigger than one millimetre.

The Basel team contributed barely five minutes to the 45-minute film *Mysteries of the Unseen World* – and yet it took them almost two years to develop the underlying technology. "We had to use a scanning electron microscope to image tiny organisms in IMAX quality, animated as movie sequences, in stereo and in colour – something that has never been done before," says professor Henning Stahlberg, head of the Center for Cellular Imaging and NanoAnalytics at the Biozentrum Basel. The results are short movie sequences that offer spectacular shots into the microcosm not visible to the naked eye. The film opened in IMAX cinemas this November.

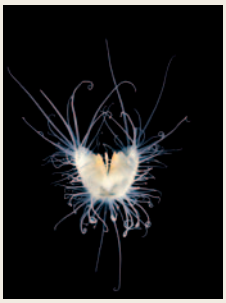
The movie follows people and animals, showing the micro- and nano-worlds around them. One scene in the movie follows a group of people walking a dog in the park. A zoom into the dog's fur shows how a tick bites him and begins to suck his blood. The journey continues into the blood stream, down to ever-smaller details, finally showing atoms. Another scene shows a breath-takingly real, gigantic cat flea that in reality is not bigger than one millimetre. Others show stunning high-precision images of even smaller insects, bacteria, viruses, and molecules.

National Geographic commissioned the film. To create the pictures, the National Geographic team initially approached the accomplished Swiss artist Martin Oeggerli, "International Photographer of the Year" in 2011 (International Photography Awards).

But even for him the project was a challenge. He approached Stahlberg's laboratory, which had the facility to host a one-tonne electron microscope needed to deliver the high-precision pictures. Colour had to be added electronically to the black and white pictures, a part that Oeggerli took care of. A five-minute-film contains roughly 14,000 images and the "micronaut", as the artist calls himself, normally needs up to 40 hours to add colour to one single picture. Refining the whole movie would be a lifelong task.

Based on a few hand-coloured pictures, a group of mathematicians and software engineers from the University of Basel developed a software tool that transfers colours from one picture to the next one, eventually adding colour to the entire movie sequence. "Now we are ready to use this worldwide unique combination of artistic skills, electron microscopy and computer software to visualise new stories and scientific findings," says Stahlberg. The team now wants to apply their movie technology to biological research topics to help make science more understandable to the general public.

http://movies.nationalgeographic.com/movies/mysteries-of-the-unseen-world/photos/



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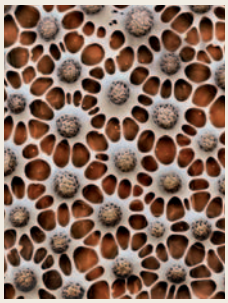

© M. Oeggerli

The EMBO Journal Cover Contest is back

Celebrating its 10th anniversary in 2014, this annual competition is organized by the editors of *The EMBO Journal* to select the best images for the front cover of the journal. Visit the website at covercontest.embo.org to find out how you can submit your pictures.

DEADLINE 20 December 2013

LEFT | **Best Cover Image 2012: *Portrait of a file clam* by Eric Röttinger**
RIGHT | **Best Cover Image 2012: *Superhydrophobic swimming beauty* by Martin Oeggerli**

Events

EMBO MEMBERS

Alzheimer's disease in Down syndrome: from molecules to cognition is the title of a meeting co-organized by EMBO Member **Victor Tybulewicz** at the **Wellcome Trust Genome Campus,** United Kingdom, from **27–29 March 2014.** Information & registration: https://registration.hinxton.wellcome.ac.uk/display_info.asp?id=378

EMBO Member **Harald von Boehmer** is one of the organizers of the ***Midwinter Conference 2014*** at the Olympic Congress Center in Seefeld, Austria, from **18–23 January 2014.** Conference homepage: www.seefeld.com/midwinter

EMBO Members **Giulio Superti-Furga** and **Denise Barlow** are co-organising the ***Austria EMBanniversary*** conference on **7–8 July 2014** in Aula der Wissenschaften in **Vienna,** Austria. The conference celebrates 50 years of EMBO and 40 years of EMBL. Full details at: www.cemm.oeaw.ac.at/index.php?id=6

Research opportunities

UNIVERSITY OF OXFORD

Weatherall Institute of Molecular Medicine, University of Oxford, is inviting expressions of interest for the prestigious **Chair of Molecular Medicine.** Please contact Professor **Douglas Higgs** at doug.higgs@imm.ox.ac.uk for further information.

INSTITUT CURIE

The **Department of Cell Biology** at the Institut Curie in Paris is offering **Group Leader positions** to "outstanding individuals interested in basic aspects of cell and tissue biology and in the mechanisms that govern normal and pathological cell function." Full details at http://umr144.curie.fr

A good read – Publications from the EMBO Community

EMBO MEMBERS, YOUNG INVESTIGATORS & FELLOWS

The microcephaly protein Asp regulates neuroepithelium morphogenesis by controlling the spatial distribution of myosin-II

Maria A. Rujano (EMBO Fellow) and colleagues

Nature Cell Biology | 6 October 2013
doi: 10.1038/ncb2858

Kinetic framework of spindle assembly checkpoint signaling

Daniel W. Gerlich (EMBO Young Investigator) and colleagues

Nature Cell Biology | 6 October 2013
doi:10.1038/ncb2842

Live visualization of chromatin dynamics with fluorescent TALEs

Yusuke Miyanari (EMBO Fellow), Maria-Elena Torres-Padilla (EMBO Young Investigator) and colleagues

Nature Structural & Molecular Biology
6 October 2013 | doi:10.1038/nsmb.2680

Equalization of odor representations by a network of electrically coupled inhibitory interneurons

Thomas Frank (EMBO Fellow) and colleagues

Nature Neuroscience | 29 September 2013
doi:10.1038/nn.3528

Temperature triggers immune evasion by *Neisseria meningitides*

Elisabeth Kugelberg (EMBO Fellow) and colleagues

Nature | 25 September 2013
doi: 10.1038/nature12616

Directional tissue migration through a self-generated chemokine gradient

Anton Khmelinskii (EMBO Fellow) and colleagues

Nature | 25 September 2013
doi: 10.1038/nature12635

Cycles in spatial and temporal chromosomal organization driven by the circadian clock

Lorena Aguilar-Arnal (EMBO Fellow), Paolo Sassone-Corsi (EMBO Member) and colleagues

Nature Structural & Molecular Biology
22 September 2013 | doi:10.1038/nsmb.2667

***Arabidopsis* meiotic crossover hot spots overlap with H2A.Z nucleosomes at gene promoters**

Kyuha Choi (EMBO Fellow) and colleagues

Nature Genetics | 22 September 2013
doi:10.1038/ng.2766

Reproducibility of high-throughput mRNA and small RNA sequencing across laboratories

Marc R Friedländer (EMBO Fellow) and colleagues

Nature Biotechnology | 15 September 2013
doi:10.1038/nbt.2702

Transcriptome and genome sequencing uncovers functional variation in humans

Marc R Friedländer (EMBO Fellow) and colleagues

Nature | 15 September 2013
doi:10.1038/nature12531

Telomeric RNA-DNA hybrids affect telomere-length dynamics and senescence

Sarah Luke-Glaser (EMBO Fellow) and colleagues

Nature Structural & Molecular Biology
8 September 2013 | doi:10.1038/nsmb.2662

The microprocessor controls the activity of mammalian retrotransposons

Sara Macias (EMBO Fellow) and colleagues

Nature Structural & Molecular Biology
1 September 2013 | doi:10.1038/nsmb.2658

Epigenetic and transcriptional signatures of stable versus plastic differentiation of proinflammatory gd T cell subsets

Bruno Silva-Santos (EMBO Young Investigator) and colleagues

Nature Immunology | 1 September 2013
10.1038/ni.2702

Molecular basis of tubulin transport within the cilium by IFT74 and IFT81

Esben Lorentzen (EMBO Young Investigator), Erich Nigg (EMBO Member) and colleagues

Science | 30 August 2013
doi:10.1126/science.1240985

Cerebral organoids model human brain development and microcephaly

Madeline A. Lancaster (EMBO Fellow), Josef M. Penninger (EMBO Member), Juergen A. Knoblich (EMBO Member) and colleagues

Nature | 28 August 2013
doi:10.1038/nature12517

A reversible gene trap collection empowers haploid genetics in human cells

Manuele Rebsamen (EMBO Fellow), Giulio Superti-Furga (EMBO Member)

Nature Methods | 25 August 2013
doi:10.1038/nmeth.2609

XMAP215 activity sets spindle length by controlling the total mass of spindle microtubules

Jonathon Howard (EMBO Member), Anthony A. Hyman (EMBO Member), Per O. Widlund (EMBO Fellow) and colleagues

Nature Cell Biology | 25 August 2013
doi:10.1038/ncb2834

The N-terminal acetylation of Sir3 stabilizes its binding to the nucleosome core particle

Fabrizio Martino (EMBO Fellow), Daniela Rhodes (EMBO Member) and colleagues

Nature Structural & Molecular Biology
11 August 2013 | doi:10.1038/nsmb.2641

Lineage-specific laminar organization of cortical GABAergic interneurons

Nathalie Dehorter (EMBO Fellow), Oscar Marín (EMBO Young Investigator) and colleagues

Nature Neuroscience | 11 August 2013
doi:10.1038/nn.3485

Dimeric WH2 domains in Vibrio VopF promote actin filament barbed-end uncapping and assisted elongation

Jozsef Orban (EMBO Short-Term Fellow) and colleagues

Nature Structural & Molecular Biology
4 August 2013 | doi:10.1038/nsmb.2639

Noncoding RNAs prevent spreading of a repressive histone mark

Marc Bühler (EMBO Young Investigator) and colleagues

Nature Structural & Molecular Biology
21 July 2013 | doi:10.1038/nsmb.2619

A two-step mechanism for epigenetic specification of centromere identity and function

Daniele Fachinetti (EMBO Fellow), Lars Jansen (EMBO Installation Grantee) and colleagues

Nature Cell Biology | 21 July 2013
doi:10.1038/ncb2805

The CRAPome: a contaminant repository for affinity purification–mass spectrometry data

Giulio Superti-Furga, (EMBO Member), Ruedi Aebersold (EMBO Member), Jacques Colinge (EMBO Fellow), Keiryn L Bennett (EMBO Fellow) and colleagues

Nature Methods | 7 July 2013
doi:10.1038/nmeth.2557

Dual mode operation of neuronal networks involved in left-right alternation

Julien Bouvier (EMBO Fellow) and colleagues

Nature | 30 June 2013
doi:10.1038/nature12286

Recalibrating *Equus* evolution using the genome sequence of an early Middle Pleistocene horse

Matteo Fumagalli (EMBO Fellow) and colleagues

Nature | 26 June 2013
doi:10.1038/nature12323

The species and organisms resources for fast and accurate identification of taxonomic names in text

Evangelos Pafilis (EMBO Short-Term Fellow) and colleagues

PLoS ONE | 18 June 2013
doi:10.1371/journal.pone.0065390

Atomic-resolution monitoring of protein maturation in live human cells by NMR

Lucia Banci (EMBO Member) and colleagues

Nature Chemical Biology | 3 March 2013
doi: 10.1038/nchembio.1202

Structural basis of tubulin tyrosination by tubulin tyrosine ligase

Michel O. Steinmetz (EMBO Member) and colleagues

Journal of Cell Biology | 28 January 2013
doi:10.1083/jcb.201211017

VIDEO

The EMBO Meeting – How to survive a PhD

A PhD can be a very rewarding but also daunting undertaking. We have asked participants at the PhD meets Postdoc Party at *The EMBO Meeting* 2013 for their advice on how best to survive a PhD.

http://youtu.be/PBBQ2blTQP4

VIDEO

Women in Science

As many women as men study towards PhDs in the life sciences. However, there are still noticeably less women in senior positions in academic scientific research. Why is this and what can be done? We asked several high-profile scientists, including Kai Simons and Susan Gasser at *The EMBO Meeting* 2013 in Amsterdam.

http://youtu.be/iUZqZ8aIzHk

EMBO Scientific Publications Poster Prize winners

Congratulations to the following winners:

THE EMBO JOURNAL

Andrew Kodani
University of California, San Francisco, USA

Centriolar satellites localize microcephaly proteins to the centrosome to control centriole duplication

Presented at The EMBO Meeting
Amsterdam, The Netherlands | 21–24 September 2013

Vladislava Chalei
University of Oxford, UK

DALI, a novel chromatin-associated lincRNA involved in controlling gene expression in neuronal cells

Presented at the EMBO | EMBL Symposia:
The Non-Coding Genome
Heidelberg, Germany | 9–12 October 2013

Quentin Defenouillere
Institut Pasteur, Paris, France

A Cdc-48-associated complex bound to 60S particles is required for the clearance of aberrant translation products

Presented at the EMBO Conference: Eukaryotic RNA turnover: From structural insights to diseases
Strasbourg, France | 21–24 April 2013

EMBO REPORTS

A. Kathrin Müller-Rischart
Ludwig Maximilians University Munich, Germany

The E3 ligase Parkin regulates a novel stress-protective pathway linking NF-kappaB signaling and mitochondrial integrity via linear ubiquitination

Presented at The EMBO Meeting
Amsterdam, The Netherlands | 21–24 September 2013

Isabel López de Silanes
Spanish National Cancer Center, Madrid, Spain

Identification of the subtelomeric sequence of the long non-coding RNA TERRA unveils its role at telomeres

Presented at the EMBO | EMBL Symposium:
The Non-Coding Genome
Heidelberg, Germany | 9–12 October 2013

MOLECULAR SYSTEMS BIOLOGY

Nicolas Battich and **Thomas Stöger**
University of Zurich, Switzerland

Large-scale image-based transcriptomics in thousands of single human cells at single-molecule resolution

Presented at The EMBO Meeting
Amsterdam, The Netherlands | 21–24 September 2013

EMBO MOLECULAR MEDICINE

Aurélie Ladang
University of Liege, France

Tumor initiation in the intestine requires the elongator acetylase complex

Presented at The EMBO Meeting
Amsterdam, The Netherlands | 21–24 September 2013

Editorial

Managing Editor Barry Whyte
Editor Yvonne Kaul
Print layout Uta Mackensen
Web version Aditya Kusuma Jati
E-newsletter Sandra Krahl, Katja Linssen

Awards of excellence

EMBO MEMBERS

2013 Nobel Prizes

EMBO Associate Members **Randy W. Schekman** and **James E. Rothman** won the 2013 Nobel Prize in Physiology or Medicine jointly with *Thomas C. Südhof* for their discoveries of machinery regulating vesicle traffic, a major transport system in our cells.

EMBO Member **Michael Levitt** was the winner of the Nobel Prize in Chemistry jointly with *Martin Karplus* and *Arieh Warshel* for the development of multiscale models for complex chemical systems.

2013 International Balzan Prize

Pascale Cossart of the Institute Pasteur in Paris is one of the winners of the 2013 International Balzan Prize, worth 750,000 Swiss francs, for her work on the molecular biology of pathogenic bacteria and their interaction with host cells. Speaking for the Balzan Foundation, *Peter Suter*, honorary vice president of the Swiss Academy of Medical Sciences, said, "Her research has provided very significant insights into the mechanisms underlying infectious diseases and how they might be combatted."

Max Rössler Prize

The 2013 Rössler Prize has been awarded to **Olivier Voinnet,** Professor of RNA Biology in the Department of Biology, ETH Zurich. Voinnet receives the 200,000 Swiss franc research prize for his groundbreaking discoveries in the field of molecular and cell biology.

2013 EMET Prize

Ben-Zion Shilo of the Weizmann Institute of Science and **Giora Simchen** of the Hebrew University of Jerusalem, Israel, received the 2013 EMET Prize in Genetics. The EMET Prize is an annual prize given for excellence in academic and professional achievements that have far reaching influence and significant contribution to society. The award is sponsored by the A.M.N. Foundation for the Advancement of Science, Art and Culture in Israel in cooperation with the Prime Minister of Israel.

Israel Prize

Nathan Nelson of the Tel Aviv University has been awarded the Israel Prize in the field of Life Sciences for the years 2012–2013. The Israel Prize is an award handed out by the State of Israel and is largely regarded as the state's highest honour. Nelson is an expert in biochemistry and molecular biology, with an international reputation in basic research into cell membrane molecular proteins and complexes.

American Society for Microbiology Lifetime Achievement Award

Julian Davies from the University of British Columbia, Canada, was awarded the 2013 American Society for Microbiology Lifetime Achievement Award. He was recognized for his pioneering work on antimicrobials and his leadership in the field of microbiology.

German National Academy of Sciences

Jörg Vogel of the University of Würzburg, Germany, has been elected to Leopoldina, the German National Academy of Sciences, and the American Academy of Microbiology this year.

Buchanan Medal

Douglas Higgs, head of the MRC Weatherall Institute of Molecular Medicine at Oxford University, has been named winner of the Buchanan Medal by the Royal Society. He received this medal for his outstanding work on the regulation of the human alpha-globin gene cluster and the role of the ATRX protein in genetic disease. The Buchanan Medal is awarded biennially for contributions to the medical sciences.

Royal Medal

Sir Walter Bodmer was one of three recipients of this year's Royal Medals from the Royal Society, in recognition of his seminal contributions to population genetics, gene mapping and understanding familial genetic disease. The Royal Medals, founded by King George IV in 1825, are an annual award recognising important contributions made in the fields of physical, biological and applied sciences.

US National Academy of Sciences

Edward De Robertis of the University of California, Los Angeles, was elected to the National Academy of Sciences in recognition of his distinguished and continuing achievements in basic research.

Human Genome Organization Council

Karen B. Avraham of the Tel Aviv University, Israel, and Huanming Yang of the Beijing Genomics Institute in China, were elected to the Human Genome Organization (HUGO) Council this year for the term 2013-2015.

Bernhard Rensch Lecture

Sarah Teichmann of the European Bioinformatics Institute and Wellcome Trust Sanger Institute Cambridge, United Kingdom, gave the Bernhard-Rensch-Lecture in Evolutionary Biology at the University of Münster, Germany, in June 2013.

European Research Council (ERC) Starting & Advanced Grants

Five EMBO Young Investigators and Installation Grantees have received 2013 ERC Starting Grants: **Ebru Erbay, Reto Gassmann, David Keays, Fyodor Kondrashov** and **Melina Schuh.**

For the full list of **EMBO Members** who received the 2013 ERC Advanced Grants please go to: http://erc.europa.eu/sites/default/files/document/file/erc_2013_adg_results_ls.pdf

EMBO STAFF

SPARC Innovator Award

The July 2013 SPARC Innovator Award recognizes creators of the San Francisco Declaration on Research Assessment (DORA). The list of awardees includes **Bernd Pulverer,** Head of Scientific Publications at EMBO. The prize is awarded by the US-based Scholarly Publishing and Academic Resources Coalition.

EMBO YOUNG INVESTIGATORS

Erik K. Fernström Prize

Tibor Harkany, Professor of Neurobiology at Karolinska Institutet, Sweden, has been awarded the 2013 Erik K. Fernström Prize for "important results that contribute to an in-depth understanding of the principles that control structure and function in nerve cells."

Royal Society Francis Crick Lecture

The Royal Wellcome Trust Sanger Institute Associate Faculty member, **Duncan Odom,** has been invited by the Royal Society to deliver the prestigious Francis Crick Lecture in 2014. The lecture is awarded each year to celebrate a biological sciences researcher, generally working in the field of genetics, at an early stage in their career.

2014 Colworth Medal

M. Madan Babu, MRC Laboratory of Molecular Biology in Cambridge, has been awarded the 2014 Colworth Medal by the Biochemical Society in recognition of his expertise in bioinformatics analysis of protein structure and gene networks. The medal is awarded annually to a biochemist under the age of 35 for outstanding research achievement.

Appointments

EMBO MEMBERS

Suzanne Cory, professor at the University of Melbourne, is the first woman elected as President of the Australian Academy of Science. She was also the first woman to be Director of the Walter and Eliza Hall Institute of Medical Research (1996–2009). Her research has had a major impact on the understanding of immunology and the development of cancer.

Jan-Michael Peters has been appointed Scientific Director of the Research Institute of Molecular Pathology (IMP) in Vienna, effective 1 July 2013. The German cell biologist has been leading a research group at the IMP since 1996. He took over the position from **Barry Dickson** who is leaving for Janelia Farm Research Campus in the United States.

As of September 2013, **Geneviève Almouzni** is director of the Institute Curie Research Centre. The specialist in epigenetics is the first woman since *Irène Joliot-Curie* to take over the management of the Institute Curie's research activities.

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Max D. **Cooper**

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Elaine **Fuchs**

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