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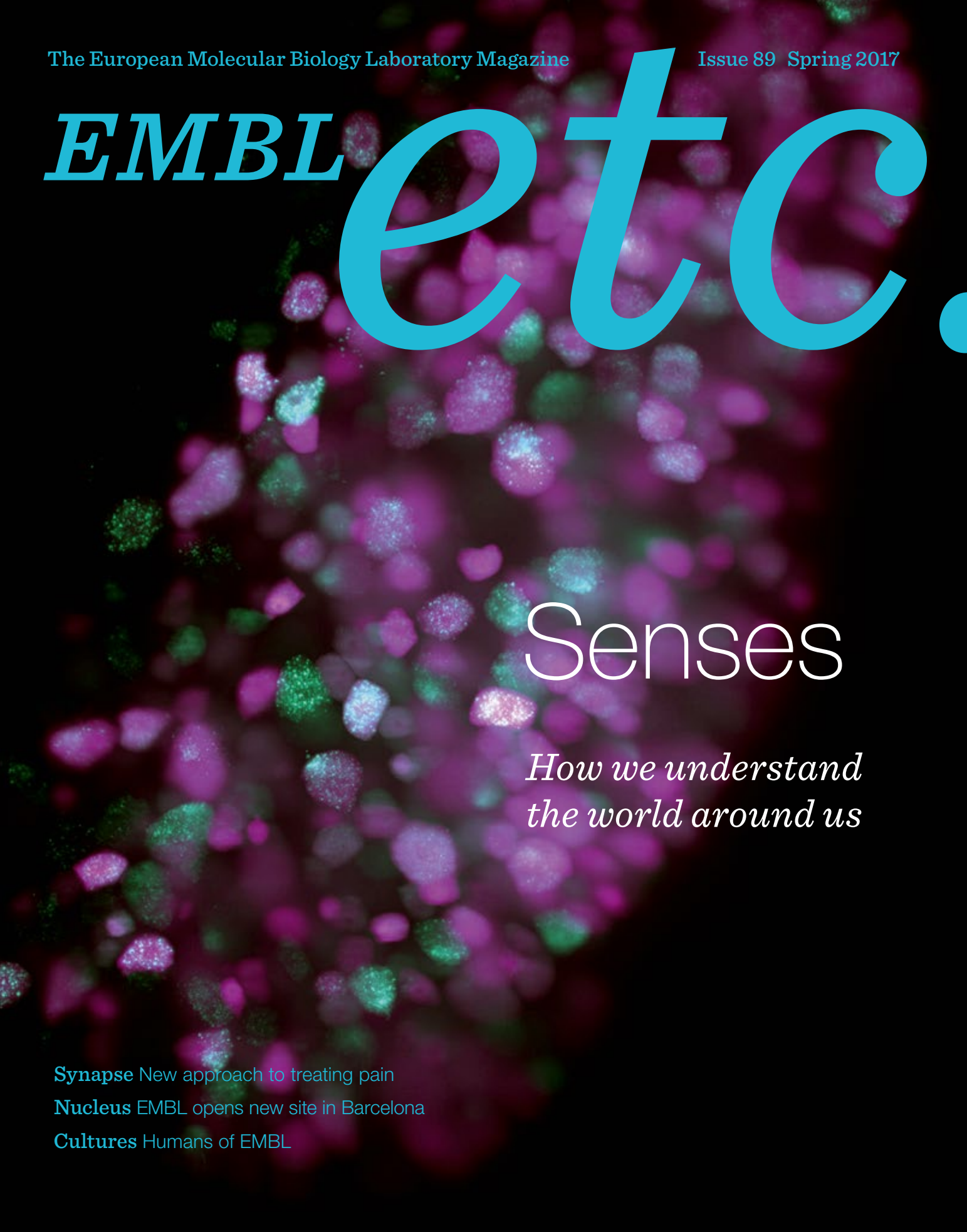
EMBL etc.



Senses

How we understand the world around us

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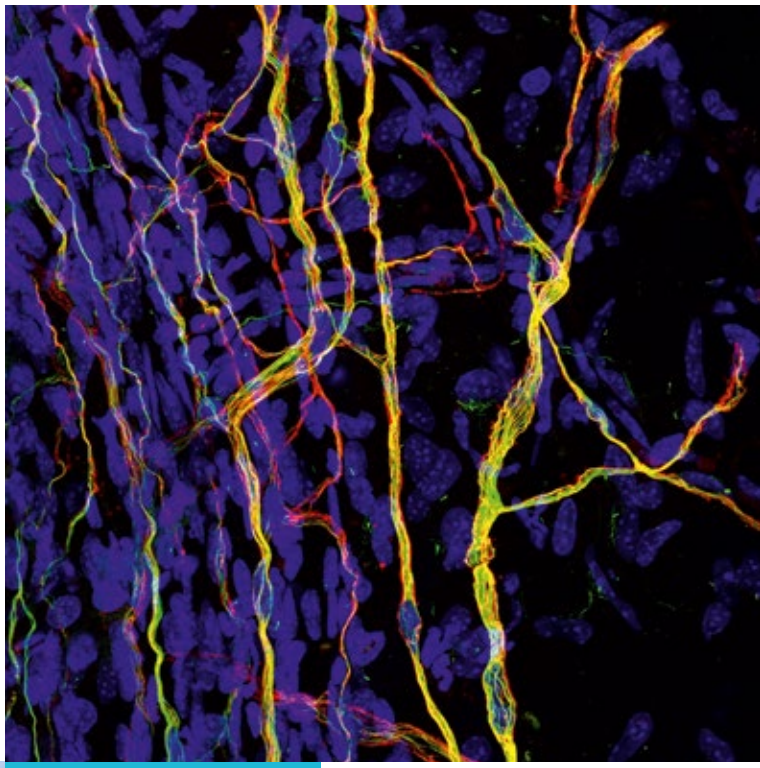

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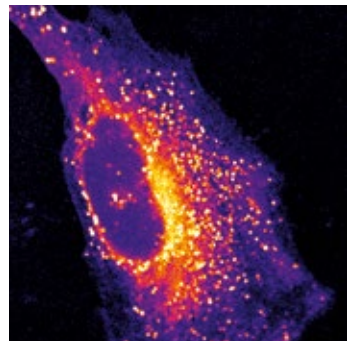

Cultures

EMBL community stories

PHOTO: EMBL/MARIETTA SCHUPP

Editorial

The human body is inundated with sensory information from our environment – when interpreted by our brains, it enables us to understand and interact with the universe around us. Whether it is the taste of a delicious fruit or the sense of dread as a spider crawls up your leg, we have known of the emotions invoked by sensory input for a very long time. Yet neuroscientists are just beginning to understand how your brain encodes and processes this information. Using new technologies and techniques, research at EMBL is presenting exciting opportunities to learn more – from indentifying potential new approaches to treating pain (page 6), to understanding how your housemate's genes could affect your health (page 12). Our cover story (page 18) – coming to our senses – highlights more exciting work from across the EMBL community, from how your internal state might affect how your eyes work, to hearing meaningful signals through the large amounts of data in modern life science studies. It is an exciting time for EMBL: the institute's sixth site has recently been launched in Barcelona (page 14) and we are also celebrating the 100th anniversary of EMBL's first Director-General John Kendrew's birthday (page 36). As always this edition also includes articles from the length and breadth of the EMBL community – from Humans of EMBL (page 38) to the amazing scientific adventures of EMBL alumni that have driven research projects hand-in-hand with development (page 24).

Adam Gristwood
Editor

Word to remember

Periaqueductal gray

Noun, pronunciation:
\ˈpir-ēˈak-wə-ˌdək-təl\ \ˈgrā\

A part of the brain, that governs quick-response survival mechanisms, such as fight or flight reactions.

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Faculty insights

Phil Avner and Cornelius Gross explain the refocusing of EMBL's Monterotondo site

We are currently honing our research focus on two of the most important fields of molecular research right now: neurobiology and epigenetics.

One of our goals is to understand more about how our senses work, at both the cellular and molecular levels. We want to understand how humans and other animals can adapt in such a flexible way to their environment: investigating what mechanisms, cells, and genes are involved, and also how disruptions in this adaptive capacity can lead to disease. There is much still to learn, but it is an incredibly exciting time. Researchers can now zoom in on the structure of individual neurons. They can study the biochemical mechanisms by which nerve cells work together in producing many thousands of types of protein and coordinating their activity. And they can learn more about how the billions of neurons in our brain are wired, allowing us to sense the world around us and interact with it.

Cornelius Gross, Deputy Head of EMBL Monterotondo

Coming to our senses

Some of our existing work in these areas has inspired this senses-themed edition of *EMBLetc.* Amongst stories featured from across the EMBL community, in this edition you can read how researchers at EMBL's Monterotondo site are investigating how we interact with our world. This work extends from neural mechanisms underlying touch sensation, to the molecular drivers of fear and anxiety, to the common principles that drive our neural system.

We also want to understand how genes and the environment interact to influence our health and behaviour. Through the study of epigenetics – chemical modifications to molecules that turn some genes off, while allowing others to be active – groups in our unit are investigating how our experiences physically alter the pattern of switches and change the workings of our brain cells. Stay tuned for more in a coming edition of the magazine.

European centre of excellence

Like all science at EMBL, our research goals involve bringing together great scientific minds from many different areas of expertise – structural biology, physics, genetics, and many more. Some of them are featured as 'Humans of EMBL' in this edition.

The interface between neuroscience and epigenetics is a natural focus area for our unit and will enable us to connect with the broad areas of expertise at EMBL and with partner institutes at the local, regional, national and international levels.

In recent years, progress in both neurobiology and epigenetics has been immense and there is great excitement about what we can achieve by studying their interface. Ultimately our goal is to take the laboratories here in Monterotondo to a new level of ambition, establishing a European centre of excellence for neurobiology and epigenetics.

Phil Avner, Head of EMBL Monterotondo

PHOTOS: HORST HAMANN

Study offers approach to treating pain

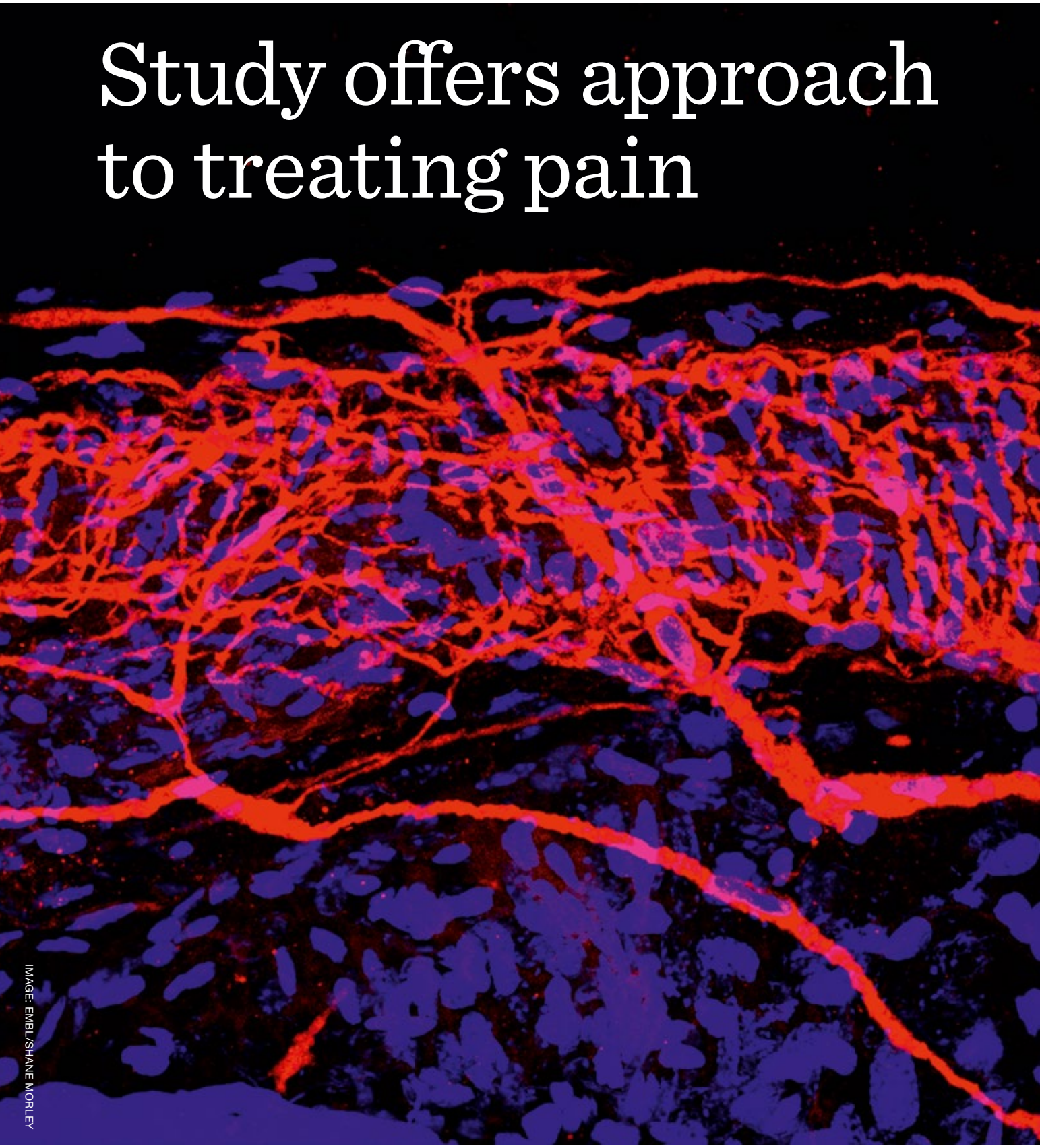
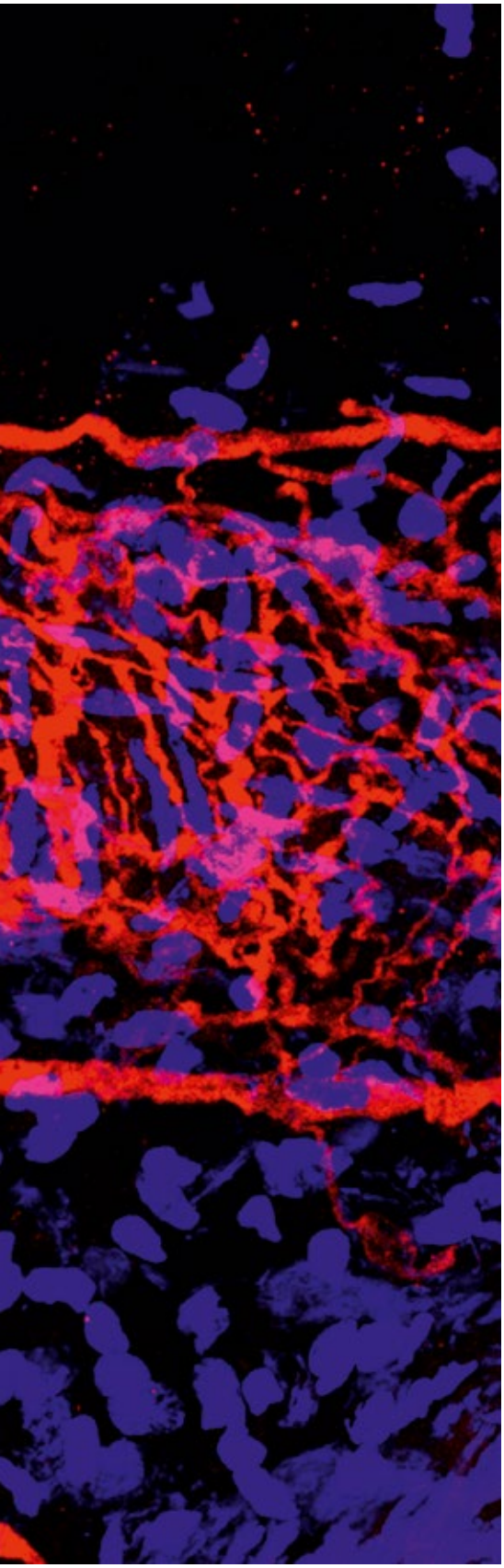


IMAGE: EMBL/SHANE MORLEY



Research on the effect of nerve cell stiffness on sensitivity to touch could lead to new painkillers

BY SONIA FURTADO NEVES

For many patients with chronic pain, any light touch – even just their clothes touching their skin – can be agony. Scientists at EMBL and the University of Tübingen have found a possible new avenue for producing painkillers that specifically treat this kind of pain. In a study published in *eLife*, they discovered how the stiffness of our nerve cells influences sensitivity to touch and pain.

Whether it's a light brush or a painful poke, when something touches you, receptors on the nerves under your skin sense it and carry that information to the brain. To be more precise, those receptors detect – and respond to – the bending of the nerve cell's membrane. The scientists discovered a molecule which, by influencing how stiff or bendy a nerve cell is, affects how sensitive a mouse is to touch and pain.

What they found

Paul Heppenstall and colleagues genetically engineered mice so that they could not produce a molecule called Atat1. They found that the nerve cells in the affected mice became more stiff, and they became insensitive to light touch and to mechanical pain. The Atat1 molecule is present in all cells. Scientists know that it modifies microtubules – tiny tubes that act as transport network and scaffolding inside cells – and that this happens in all cells, especially in nerve cells. So the team was surprised to find that the other senses seem not to be affected in the mice.

One difference that they found between nerve cells that detect touch and other cells is in how their microtubules are arranged. In sensory cells, they form a ring just below the cell membrane. In other cells, they don't. The scientists think that this ring probably fine-tunes how stiff or bendy a nerve cell's membrane is, influencing how sensitive that cell – and the animal in general – is to touch.

Why it's important

The nervous system and sense of touch are similar in mice and humans, so the results likely hold true for people too. And although problems in cell stiffness are unlikely to be at the root of most patients' hypersensitivity to touch, controlling how stiff nerve cells are could nevertheless be an effective way of treating that sensitivity.

"We're now looking for small molecules that interfere with this fine-tuning of cell stiffness, and which might one day be used to make painkillers specifically to treat this mechanical pain," says Heppenstall. "This is the first step in our sense of touch, so if we can stop the signal there, then we have a good chance of stopping everything which is downstream."

Morley SJ, Qi Y *et al. eLife*, published online 13 December 2016. DOI: 10.7554/eLife.20813

The group had previously visualised free nerve endings (seen in red) in the skin split into an incredible number of branches. Labelled in blue are the nuclei of the skin's cells

Neural connection keeps instincts in check

EMBL scientists identify the physical connection through which the prefrontal cortex inhibits instinctive behaviours

BY SONIA FURTADO NEVES

From fighting the urge to hit someone to resisting the temptation to run off stage instead of giving that public speech, we are often confronted with situations where we have to curb our instincts. Scientists at EMBL have traced exactly which neuronal projections prevent social animals like us from acting out such impulses. The study, published in *Nature Neuroscience*, could have implications for schizophrenia and mood disorders like depression.

"Instincts like fear and sex are important, but you don't want to be acting on them all the time," says Cornelius Gross, who led the work at EMBL. "We need to be able to dynamically control our instinctive behaviours, depending on the situation."

What they found

The driver of our instincts is the brainstem – the region at the very base of your brain, just above the spinal cord. Scientists have known for some time that another brain region, the prefrontal cortex, plays a role in keeping those instincts in check. But exactly how the prefrontal cortex puts a brake on the brainstem has remained unclear.

Now, Gross and colleagues have literally found the connection between prefrontal cortex and brainstem. The EMBL scientists teamed up with Tiago Branco's lab at the MRC Laboratory of Molecular Biology, and traced connections between neurons in a mouse brain. They discovered that the prefrontal cortex makes prominent connections directly to the brainstem.

Gross and colleagues went on to confirm that this physical connection was the brake that inhibits instinctive behaviour. They found that in mice that have been repeatedly defeated by another mouse – the murine equivalent to being bullied – this connection weakens, and the mice act more scared. The scientists found that they could elicit those same fearful behaviours in mice that had never been bullied, simply by using drugs to block the connection between prefrontal cortex and brainstem.

Why it's important

The scientists found that the connection from the prefrontal cortex is to a very specific region of the brainstem, called the periaqueductal grey (PAG), which is responsible for the acting out of our instincts. However, it doesn't affect the hypothalamus, the region that controls feelings and emotions. So the prefrontal cortex keeps behaviour in check, but doesn't affect the underlying instinctive feeling: it stops you from running off-stage, but doesn't abate the butterflies in your stomach.

Franklin TB *et al. Nature Neuroscience*, published online 9 January 2016.
DOI: 10.1038/nn.4470

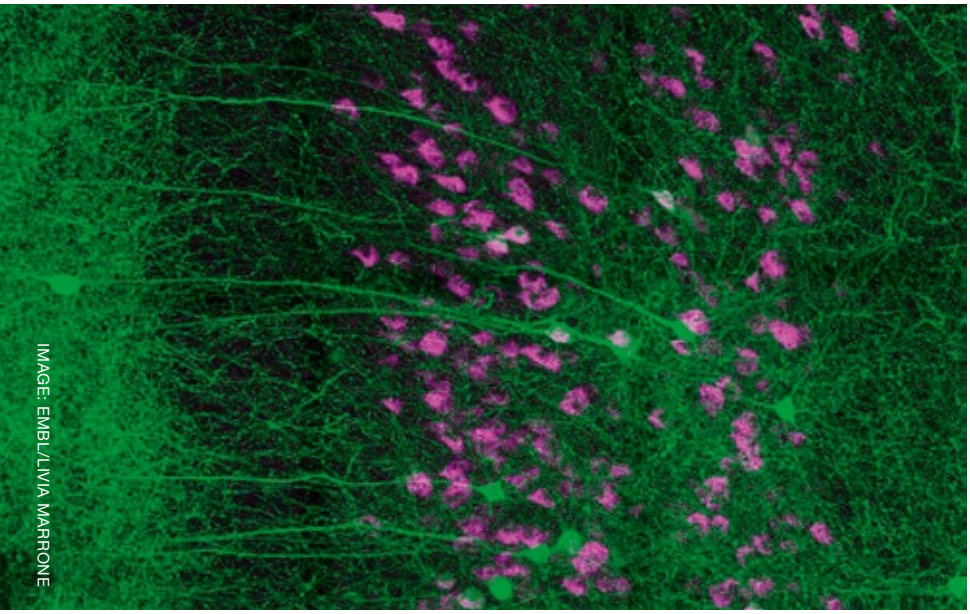


IMAGE: EMBL/LIVIA MARRONE

Prefrontal cortical neurons (purple) connect to the PAG in the brainstem and control instinctive behaviours

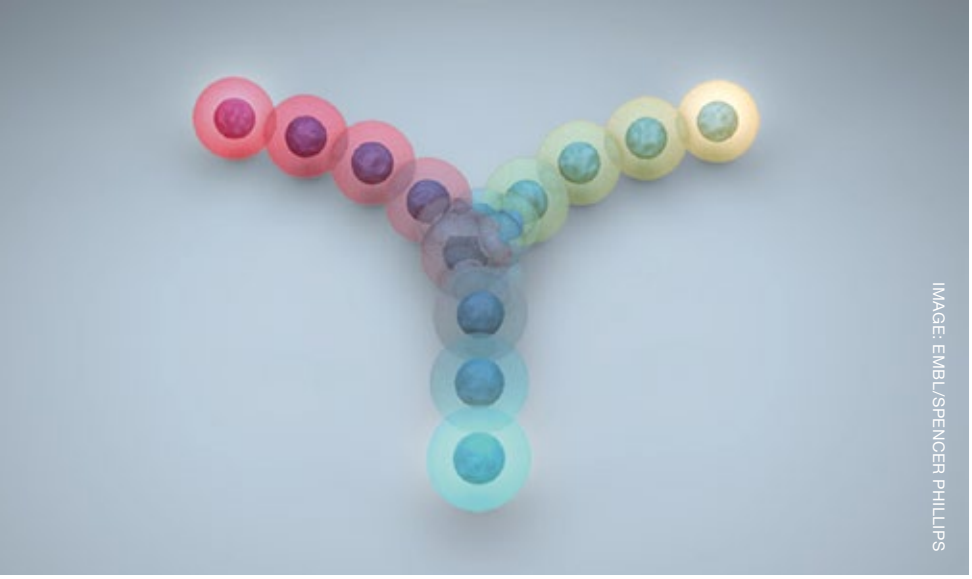


IMAGE: EMBL/SPENCER PHILLIPS

Researchers at EMBL-EBI and the Sanger Institute observed in detail how immature T cells develop into subtypes that fulfil different functions, with the aim of tackling infection. This is an artist's interpretation of the process

Fresh insight into how immune cells fight malaria

Secrets of immune system's response to malaria revealed by single-cell genomics

BY OANA STROE

The immune system is extremely complex. It responds to disease by developing many specific types of immune cells – some that fight and some that observe and remember. A joint study by EMBL, the Wellcome Trust Sanger Institute and QIMR Berghofer Medical Research Institute, Australia, has revealed for the first time how immature immune 'T' cells in mice choose which skill they will develop to fight malaria infection. Oliver Stegle, research group leader at EMBL-EBI and Sarah Teichmann, Head of Cellular Genetics at the Wellcome Trust Sanger Institute, explain.

What did you find?

Oliver: Using the latest single-cell genomics technology and machine learning methods, we uncovered the 'conversations' that are taking place amongst immune cells. We were able to model the way mouse immune cells respond to the malaria parasite. We can also see how they change over the course of the infection. That gives us a valuable tool for approaching many different biological questions, such as which genes to target in order to boost immunity to malaria.

The data also allowed us to identify tens or perhaps hundreds of genes within the T cells that may be involved in controlling antibody production during malaria infection. These genes could help researchers to develop new drugs to boost immunity to malaria and other infections. For example, one of the genes we found, Galectin 1, encouraged the development of a particular type of T cell when active.

Why does it matter?

Sarah: Activity in these genes may help the body, for example in curing an infection. But equally, it may allow cancerous cells to flourish. Researchers can use the principles and the computational methods we developed in future studies exploring these questions. An important next step for our collaboration will be to test many of the new gene targets we have identified. This will allow us to see if they respond to drugs that aim to boost immunity to malaria.

Lönnberg T *et al. Science Immunology*, published online 3 March 2017.
DOI: 10.1126/sciimmunol.aal2192

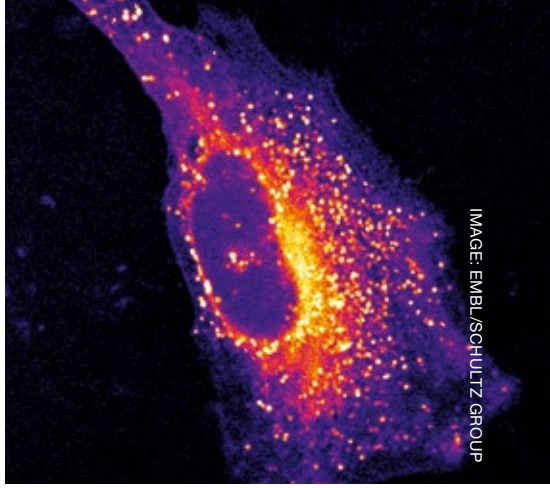
iNEXT up

A new call for service provision has opened at EMBL's site in Grenoble, based on the CrystalDirect technology and the MASSIF beamlines. Scientists from both the public and the private sectors with an interest in compound and fragment screening are invited to apply to the call, which is part of the European Commission-funded iNEXT project.

iNEXT brings together 23 European partners to provide free advice and services to European scientists in an effort to make tools and facilities for structural biology more widely accessible. Three EMBL sites bring tools to iNEXT: Grenoble – integrated crystallisation and data collection; Hamburg – macromolecular crystallography (MX) and small-angle X-ray scattering (SAXS) beamlines; and Heidelberg – advanced imaging technologies, including cryo-electron microscopy.

APPLY NOW:
INEXT-EU.ORG

Lipids in real time



A fluorescent chemical group reveals the position of lipids in the cell

A new technique developed at EMBL reveals the way fats interact with other molecules in cells

BY EDWARD DADSWELL

We know much less about the way fat molecules – or lipids – behave in cells than we do about other molecules like proteins. A new chemical biology technique developed at EMBL and reported in the journal *PNAS* may be about to change that, as study author Carsten Schultz explains.

What did you do?

We took lipid molecules and made three small modifications. First, we added a chemical group called a caging group that prevents the lipid from interacting with other molecules. The bond between this group and the lipid can be broken using a flash of light, allowing us to 'uncage' the lipid at a precise moment and leave it free to interact. Second, we added a chemical group that becomes extremely reactive when exposed to light of a certain wavelength. Another, higher energy, flash of light was used to activate this group, causing it to react with the nearest molecule – in this case attaching the lipid to whatever protein it was interacting with. Third, we added a chemical group that made the lipid easier to study, allowing us to either extract the lipid and its attached protein for analysis, or add a fluorescent group to reveal its position in the cell. With these modifications, we could identify which proteins a lipid was interacting with at a given point in time.

Why does it matter?

Our technique makes it possible to study lipids in a whole living cell on timescales of only a few seconds. This has not been done before, and is crucial because most lipids in a cell have very short lifetimes. We can also study the way lipids are transported and broken down within the cell. In principle the same technique could be used to study many types of small molecules in cells, including pharmaceuticals, so there's great potential for further research and beneficial applications.

Höglinger D *et al. PNAS*, published online 30 January 2017. DOI: 10.1073/pnas.1611096114

Genetic switches can change shape

EMBL scientists discover that common mutations can change the shape of gene promoters

BY SONIA FURTADO NEVES

Scientists in Eileen Furlong's and Oliver Stegle's labs at EMBL have revealed that genetic differences between individuals can affect the shape of sequences of DNA that turn genes on, known as promoters. The EMBL scientists also discovered that a promoter's shape – the area of genetic sequence that it controls – influences how much its output varies from cell to cell.

The switches that turn genes on and off can change shape, EMBL scientists have found

IMAGE: EMBL/TABEA RAUSCHER

Scientists have known for some time that promoters have a defined shape. 'Narrow' promoters turn genes on very precisely at a given position in the genome, while 'broad' promoters turn genes on in an area spanning several hundred bases. But until now, the functional differences between promoters with different shapes were unclear. The factors that determine these differences across individuals in a population were also a mystery.

Postdoc Ignacio Schor found that changes to single letters of genetic code often affect promoter shape. These single-letter mutations, called SNPs, are common. This explains why promoter shape for the same gene can vary dramatically from one individual to another. The

Structure of key system for TB infection

Researchers at EMBL, as part of a collaboration of European scientists, have revealed the overall architecture of an assembly of proteins known as Type VII secretion systems, found in a group of bacteria which cause diseases such as tuberculosis. "These results represent a big step forward in our understanding of how some of the deadliest pathogenic bacteria such as *Mycobacterium tuberculosis* function," says Head of EMBL's Hamburg site, Matthias Wilmanns.

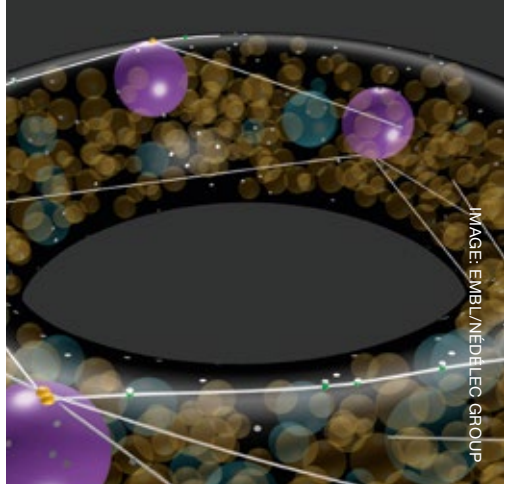
Beckham KSH *et al. Nature Microbiology*, published online 10 April 2017. DOI:10.1038/nmicrobiol.2017.47

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=9669

scientists also discovered that such SNPs, which alter promoter shape, frequently cause increased variability in promoter output between cells. These 'noisy' SNPs could have lethal effects, and hence are only tolerated in individuals whose genetic makeup also contains other SNPs that counteract this effect.

The same team has recently uncovered similar SNP interactions in another context. In that study, they pinpointed thousands of mutations that disrupt gene regulation during embryonic development.

Schor IE *et al. Nature Genetics*, 13 February 2017. DOI: 10.1038/ng.3791



A visualisation of the computer model shows nuclei (purple) with their attached microtubules (white lines) pulled by molecules of dynein (green)

Unlocking the secrets of nuclear movements

EMBL researchers develop a computer model to explore the movement of nuclei in a multinuclear cell

BY EDWARD DADSWELL

EMBL's François Nédélec believes computer modelling can play a key role in making sense of large amounts of biological data. A new study published in *Molecular Biology of the Cell* shows the power of this approach.

What did you do?

Based on the analysis of biological data obtained from different researchers, we constructed a computer model of the simple fungus *Ashbya gossypii*, which has cells containing many nuclei. Because the cells grow by elongating in one direction, it might be expected that the nuclei would simply move in straight lines in the same direction. However, the nuclei have protein strands called microtubules attached to them, which are pulled by dynein – a molecular motor. The nuclei can be observed making back and forth movements, and even exchanging places with one another. We wanted to know whether a system of dynein molecules pulling microtubules in random directions could explain this motion. Our model shows that it can.

Why does it matter?

This is the first time computer modelling has been used to explain the movement of multiple nuclei in a cell. We'd like to use the knowledge we've gained to tackle more complex problems, such as the way nuclei are positioned in human myotubes – elongated cells with multiple nuclei that are formed during muscle development. Improper positioning of the nuclei is associated with diseases such as dilated cardiomyopathy and muscular dystrophies.

Computer models have long been used to investigate problems in physics but are now increasingly important in our understanding of biological systems. They help us integrate large amounts of experimental data into a more manageable body of knowledge, allowing us to test whether our theories reflect the reality of what's happening in cells.

Gibeaux R *et al. Mol. Biol. Cell*, published online 11 January 2017. DOI: 10.1091/mbc.E16-11-0806

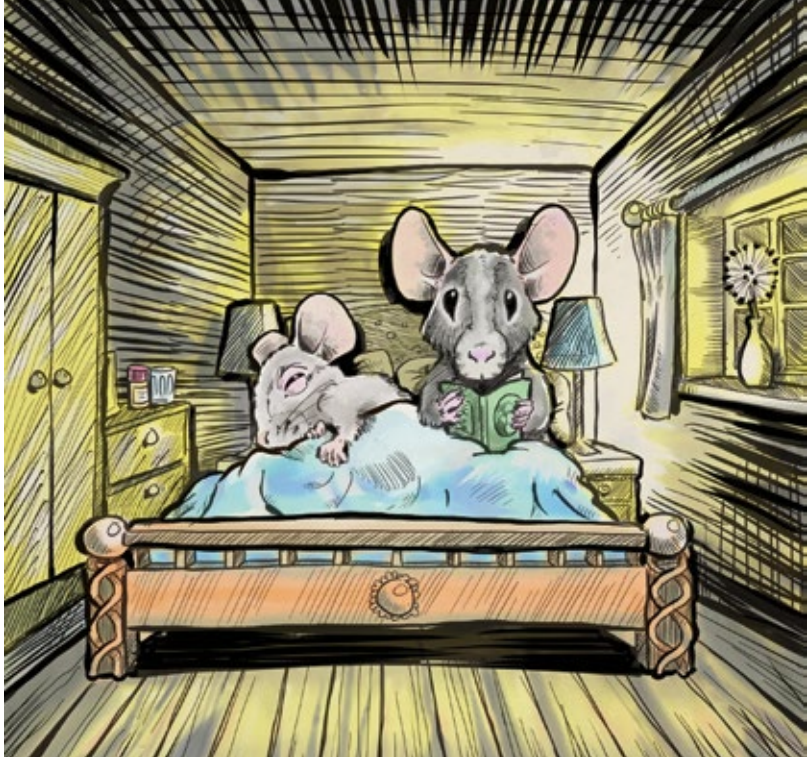


ILLUSTRATION: SPENCER PHILLIPS

An artist's interpretation of how a couple might experience 'social genetic effects'

How your housemate's genes could affect your health

Genetic makeup of social partners impacts health, healing and anxiety in mice

BY OANA STROE

Researchers at EMBL-EBI have shown that the health of individual mice is influenced by the genetic makeup of their partners. Their findings, published in *PLOS Genetics*, indicate that research into genetics and disease should include the genotypes both of individuals and their partners.

Control and influence

Most traits are genetically controlled to some extent. For example, sleep preferences have a genetic component. But nothing happens in isolation, so if your partner is a night owl and keeps you awake later than you'd like, their genotypes might be partly to blame.

"People influence your behaviour, health and wellbeing, and you influence theirs – this much we know already. What's been missing is recognition that there is a genetic basis for this," explains Amelie Baud of EMBL-EBI, who led the study. "If you're a researcher looking for links between genotypes and disease, it is very important to look not only at your patient but also at their social environment."

Research into 'social genetic effects' can help patients and doctors identify the best way to intervene when a patient's health is affected by their partner.

Birds of a feather

"Imagine you are a morning person and your partner is a night owl. So every night you end up going to sleep later than you'd like," explains Baud. "Now, say you develop an illness, but don't mention the sleep situation to your doctor because you don't know that it's important. Maybe your doctor doesn't ask you because she doesn't know it's relevant. But if research showed there was indeed a connection between your illness and the genes that control your partner's sleeping pattern, then your doctor could better probe your life habits and give useful advice. You and your night owl could then make the right change to ensure you get the sleep you need to heal. With this change, you would be mitigating the negative influence of the night owl's genotypes on your health."

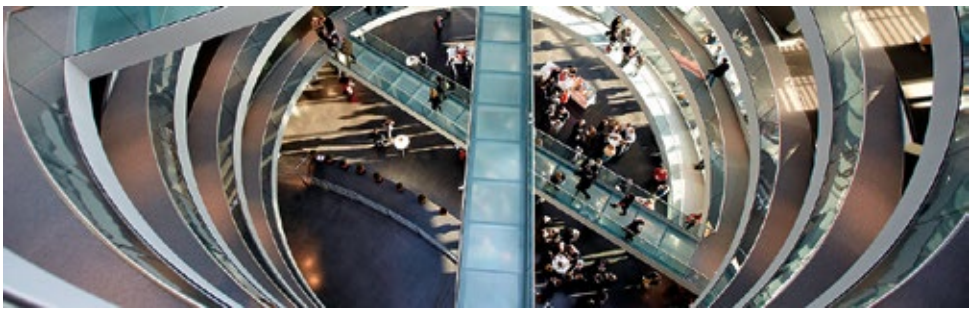
Further implications

Although today's study was carried out in mice living together, it provides food for thought about how individuals can be influenced by the genetic makeup of the people in their lives - and vice versa. "The methods and approaches we developed could certainly be applied to human studies," says Oliver Stegle of EMBL-EBI.

By studying social genetic effects, the researchers hope to learn more about the mechanisms whereby people influence one another.

Baud A *et al. PLOS Genetics,* published online 26 January 2017. DOI: 10.1371/journal.pgen.1006498

New industry initiatives



New EMBL and GSK collaboration

EMBL and GSK have signed a collaboration agreement to combine expertise, technologies, tools and data to create a better understanding of the efficacy and safety of candidate drugs. GSK will also provide funding for a joint EMBL-GSK postdoctoral programme and further collaborative research efforts. The alliance will initially run for five years and builds on successful scientific collaborations on EMBL's Heidelberg campus, where GSK's Cellzome site is located. By extending from target validation to drug discovery this new collaboration provides a continuum from Open Targets where GSK and EMBL-EBI have an ongoing collaboration.

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=9177

Sartorius joins EMBL's Corporate Partnership Programme

EMBL has strengthened its links with enterprise by welcoming Sartorius to the EMBL Advanced Training Centre Corporate Partnership Programme. Sartorius, a leading international pharmaceutical and laboratory equipment provider, employs close to 7000 people working at around 50 sites. Specifically, EMBL and Sartorius will collaborate in the provision of advanced training courses, conferences and workshops at EMBL. The company will also provide support to EMBL's science education programme by funding ten travel bursaries for teachers to attend international training courses run by EMBL's Learning Laboratory for the Life Sciences (ELLS) – and further collaboration is planned.

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=9185

EMBL-EBI welcomes new Industry Programme members

Three life science companies with global R&D programmes have recently joined the EMBL-EBI Industry Programme: AbbVie, Merck Sharp & Dohme (MSD) and Takeda, through Takeda Oncology, Boston, US.

"We are delighted to have new companies on board, and to further extend the international reach of our membership," says Dominic Clark, EMBL-EBI Industry Programme Manager. "I am excited about the diversity and impact these new members will bring to our growing US workshop programme."

As biology becomes more data-driven, pre-competitive collaborations, open-source software and informatics standards have become essential to improving efficiency and reducing costs for the world's bioindustries. EMBL-EBI's Industry Programme provides a forum for interaction and knowledge exchange for those working at the forefront of commercial bioinformatics.

"The neutral ground provided by our Industry Programme is the cornerstone of our mission to support industry R&D," says Rolf Apweiler, Director of EMBL-EBI. "We are very pleased to welcome AbbVie, MSD and Takeda to the programme, and look forward to fruitful collaborations and interaction."

EMBL opens new site in Barcelona

Spanish government and EMBL sign agreement for new site dedicated to tissue biology and disease modelling

BY SONIA FURTADO NEVES

At a ceremony in Barcelona on 10 April, EMBL and the Spanish government, represented by the Ministry of Economy, Industry and Competitiveness (MINECO), signed an agreement for a new EMBL site to be hosted in the city. Also present were the Catalan Government, represented by the Ministry of Business and Knowledge, and the Centre for Genomic Regulation (CRG), which have supported this initiative from the very beginning. EMBL Barcelona will be located on the campus of the Barcelona Biomedical Research Park (PRBB), and researchers at the site will explore how tissues and organs function and develop, and how preventing failures in those processes may help to tackle disease. Alongside cutting-edge research, the site will house state-of-the-art imaging facilities, making pioneering technologies available to scientists worldwide.

"This agreement to host EMBL in Barcelona is testament to the Spanish government's commitment to support excellent science and to capitalise on the rapid development of internationally competitive biomedical research," says Luis de Guindos, Spanish Minister of Economy, Industry and Competitiveness. "It reflects our ambition to place Spain at the forefront of research in the life sciences."

¡Hola collaboration!

Researchers at EMBL's new site will work in a highly collaborative, interdisciplinary and international environment, benefiting from the institute's long-lasting relationship with CRG, an international biomedical research institute based at the PRBB, and the close collaboration with other institutes on campus, as well as opportunities across EMBL sites and with other partners throughout Europe and beyond. "At CRG we've had a partnership with EMBL since 2006, and we've already made significant discoveries as a result of our collaboration," says Luis Serrano, Director of CRG. "This will continue in the future, and we will strengthen those links further now that EMBL will be physically present on site."

"This agreement to host EMBL in Barcelona is testament to the Spanish government's commitment to support excellent science"

"Hosting EMBL in Barcelona represents a landmark achievement in Catalonia's ambitious and successful R&D programme. The PRBB campus and the region host a vibrant community, conducting pioneering science, so this is the perfect setting for EMBL's new site," says Jordi Baiget, Minister of Business and Knowledge of the Catalan Government and President of the CRG Board of Trustees.

EMBL Barcelona will be the institute's sixth site and is expected to begin operations in autumn 2017.

PHOTO: IVAN PAULICK

Participants at the entrance of the PRBB auditorium, where the ceremony took place

Stories behind EMBL's Barcelona site

EMBL's directorate reflects on the work done to establish a new EMBL site in Barcelona

BY IAIN MATTAJ, EMBL DIRECTOR-GENERAL

Spain hosting an EMBL site has been on my mind almost from my first days as Director-General of EMBL. When I first visited the Ministry of Economy, Industry and Competitiveness (MINECO) in Madrid at the end of 2005, it was already very clear that they were keen to develop deeper links with us, up to and including hosting an EMBL site. From the beginning of the discussion, in 2011, there was a high level of support within EMBL's governing body, EMBL Council, for the idea of an EMBL site in Barcelona focusing on tissue biology and disease modelling. Within this area, there are many topics which are related and could act synergistically with our strategy and strengths in other areas, such as cell biology and biophysics, developmental biology, genome biology and bioinformatics. From the beginning the proposed focus felt right.

Distinctly complementary

The research in Barcelona will be both distinct from and complementary to that of the other parts of EMBL. It combines the development of new types of imaging – of large objects, and of imaging deeply into these objects with light microscopy – with research on the behaviour of groups of cells and the differentiation of individual tissues. The light sheet microscopy that was first developed at EMBL's Heidelberg site, for instance, complements the type of 3D imaging, optical projection tomography, which was developed in Barcelona. The partnership unit between EMBL and the Centre for Genomic Regulation (CRG) has built up a very strong background in computational biology, and the combination of quantitative imaging and >>

PHOTO: PRBB/FERRAN MATEO

>> computational modelling is an area of research in which we expect many biological and medical breakthroughs in the future.

"Spain hosting an EMBL site has been on my mind almost from my first days as Director General of EMBL"

There are a number of diseases and developmental problems that are caused not necessarily by individual cells, but by cells collectively not producing the right form for an organ or a tissue. A very simple example is type 1 diabetes, in which the immune system attacks and damages cells that normally produce insulin. Improved imaging of these cells in the pancreas, in conjunction with computational modelling of their mechanisms, contributes to a greater understanding of how this auto-immune attack affects the pancreas. Further, it could lend insight into how to treat type 1 diabetes patients.

Right place right time

Since we developed the idea of tissue biology being the focus at the Barcelona site, there has been an explosion of research on organoids, or very complex tissue culture systems that mimic organs such as parts of the intestine, parts of the kidney, or parts of the brain. These complex cell systems can be manipulated and imaged in ways that whole organisms are not amenable to.

Barcelona has very strong universities and scientific institutes with complementary expertise that we look forward to collaborating with. Our long-standing partner, CRG, for example, is one of the world's leading centres in fundamental biomedical sciences. In addition, next door to the EMBL Barcelona site in the Barcelona Biomedical Research Park is a research hospital, which will enable direct links to clinical science.

It is for all the above reasons that Barcelona seemed like the right place for a new EMBL site. The Spanish and Catalonian governments as well as CRG have been outstandingly supportive and cooperative in developing the detailed scientific plan for the site, working on a host site agreement and discussing space and infrastructure of the site. Working with them has really been a pleasure throughout this time, and I look forward to this continuing relationship as the site is set up.

PHOTO: PRBB/FERRAN MATEO

The Barcelona Biomedical Research Park will be home to EMBL's new site in the city

The internal structure of a mouse pancreas, imaged with a SPIM microscope like those that will be used at EMBL Barcelona

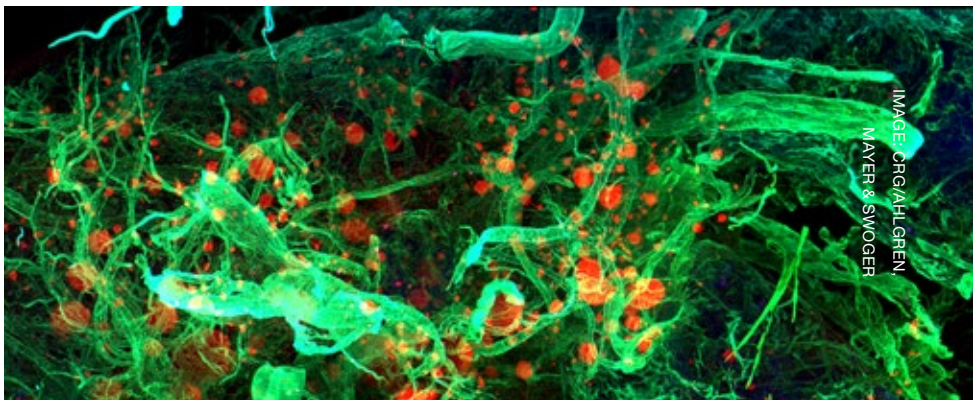


IMAGE: CRG/AHLGREN, MAYER & SWOGER

BY SILKE SCHUMACHER, DIRECTOR, INTERNATIONAL RELATIONS

There is a natural sense of connection between EMBL and Barcelona. The city, which was honoured as the first European Capital of Innovation in 2014, is a national hub of life science research and has long promoted alliances between research centres and universities. So it was with a great sense of excitement that we awaited the opening of EMBL's sixth site on 10 April.

A great adventure

Getting to this stage has been a fascinating journey. EMBL has not launched a new site for more than 15 years, when EMBL's Monterotondo site opened on the Italian National Research Council (CNR) campus. And there is no handbook detailing exactly how we go about setting up a new site – although perhaps now my team could write one. After more than a decade of complex – and often unpredictable – negotiations, we are now ready for the next chapter in this exciting adventure, which will eventually lead to the foundation of seven research groups and a core facility with a central focus: tissue biology.

Fortunately, in creating EMBL's Barcelona site we have had some well-established foundations to build on. The seeds of the new site were planted in 2006, when the Spanish government generously set up and funded an EMBL partnership at the Centre for Genomic Regulation (CRG) in Barcelona. The aim of the EMBL-CRG Systems Biology Partnership Unit was to bring together EMBL's expertise in computational biology with CRG capabilities in specific areas of genomics and proteomics to learn about key aspects of human health and disease.

The results have been tremendous. Research in the partnership covers a massive range of topics – from genetics to neuroscience, from the molecular to the cellular level. Initially headed by EMBL alumnus Luis Serrano, it has attracted several prestigious European Research Council grants, and in 2011 EMBL's Scientific Advisory Committee awarded it top marks as part of its general review of the EMBL partnership programme.

"Together, we can be proud of what we have achieved so far"

With the value of the cooperation between EMBL and CRG clear, the Spanish government declared its willingness to invest further and host a new EMBL site, while keeping the EMBL-CRG collaboration running (staff will be employed by CRG or EMBL). It was a clear demonstration of Spain's commitment to boosting excellent science and forming even closer links with EMBL. The site's specific focus on tissue biology ensures that the fundamental research focus of EMBL will complement the biomedical studies taking place on the PRBB campus.

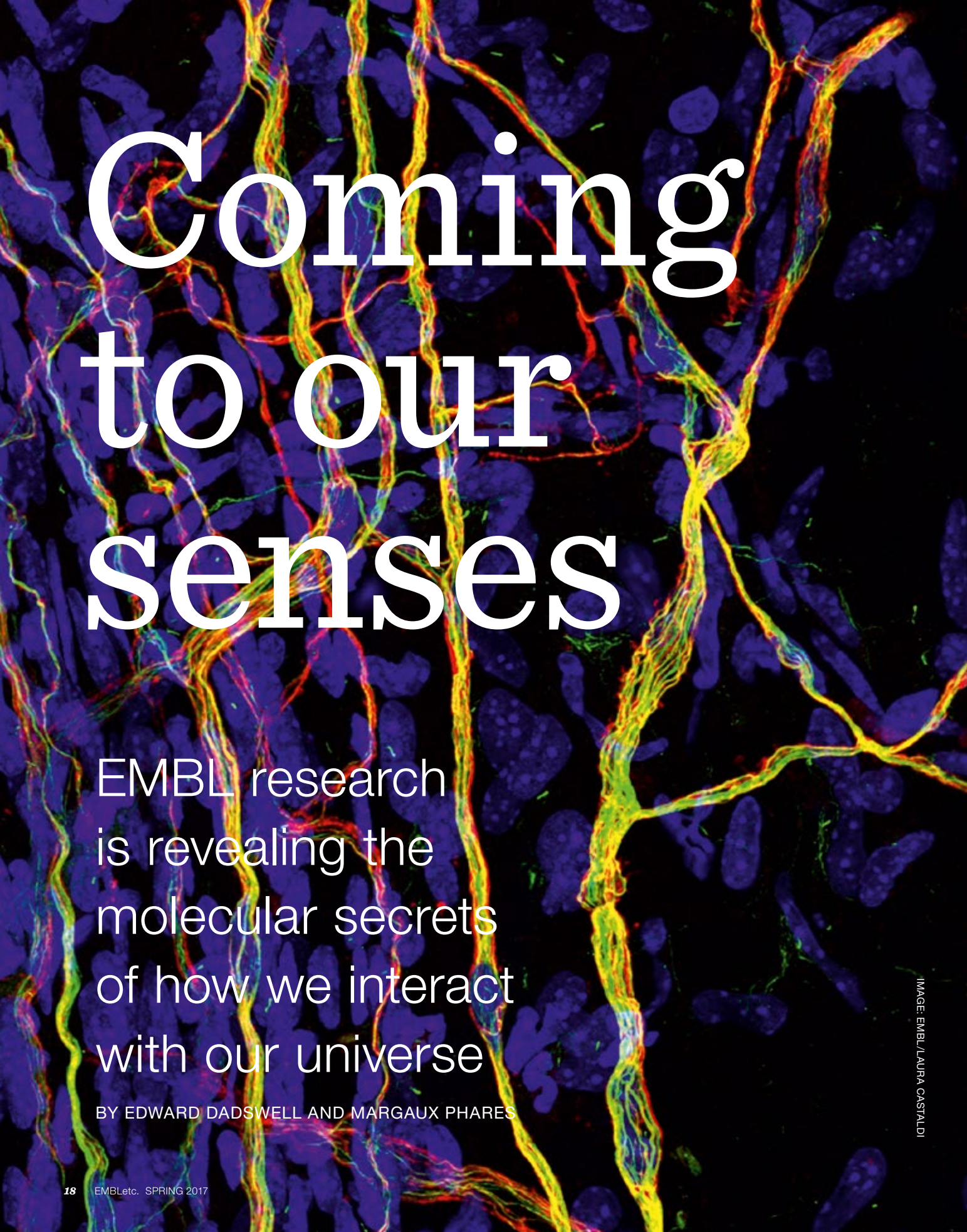
Detailed negotiations

One of the most important steps was the preparation of a host site agreement between EMBL and Spain. Such agreements ensure the site becomes part of EMBL's legal entity, providing comparable conditions to people working in other parts of EMBL. This required a lengthy negotiation process involving the government departments of foreign affairs, research, finance and social affairs. Negotiations began in parallel with the scientific plans being developed, discussed and approved by EMBL's Council – both took many years to complete. But on 23 December 2016 came the moment we had all been working so hard towards – the Spanish Council of Ministers finally approved the host site agreement.

Like other EMBL sites, EMBL's Barcelona site will be funded through a mix of EMBL Member State contributions and external funding obtained through competitive calls. And CRG has agreed to provide services such as access to CRG core facilities, IT and other services – with support from the Spanish government. This will facilitate close collaboration from the outset as the new site grows to its full size, beginning with the recruitment of a head of site to launch operations and recruit initial administrative and research staff. Multi-talented teams from across EMBL will provide further logistical and administrative support – from hiring staff to building and maintaining IT networks.

An exciting future

Meanwhile, the EMBL-CRG partnership will be converted from a remote to a local partnership. In turn, the partnership will also be made even broader, with a view to establishing collaborations not only between groups located in Barcelona, but across the whole of EMBL. Together, we can be proud of what we have achieved so far. I look forward to witnessing the ongoing development of EMBL's Barcelona site and the incredible results that will undoubtedly come from the research and service teams taking shape in the coming months and years.



Coming to our senses

EMBL research is revealing the molecular secrets of how we interact with our universe

BY EDWARD DADSWELL AND MARGAUX PHARES

IMAGE: EMBL/LAURA CASTALDI

What you see is how you feel

EMBL's Hiroki Asari investigates how our internal state can change the way our eyes work

Analogies can be useful things in science, but they can put a straitjacket on our thinking too. Hiroki Asari, a group leader at EMBL's Monterotondo site, is keen to escape from one analogy in particular: the idea that the eye is a camera. It's something we all learn at school. Light passes through the lens of the eye and falls on the layer of light-sensitive cells known as the retina. We're taught that the retina is like a roll of film or a digital sensor – it captures the pattern of light, which is then entirely processed in the brain.

Retinal reality

The reality is a little different. "The retina performs a lot of computations," explains Asari. "They're usually simple, like detecting motion or processing colours, while more complex computations – like face depiction or object recognition – happen in the brain. But I think the retina plays an important role in identifying certain elements of what we see."

This idea is not new, but Asari takes it a step further. "I believe these computations in the retina are affected by the internal states of our body. For example, when you see a cookie and you're feeling hungry, it looks attractive. But when you're full, it's less attractive. People assume that this kind of processing is happening in the brain. My hypothesis is that it's happening right at the very first stages of visual system processing – in other words, in the retina."

Where to look

Asari aims to investigate this theory in mice. He measures the activity of the retina and optic nerve to see how the retina responds to the same visual stimulus under different states, such as when the mouse is hungry or fed; running or standing still. This is done using a range of experimental neuroscience techniques. One is electrophysiology, in which very fine electrodes are inserted into nerve cells and used to measure the nerve impulses. Another is calcium imaging, in which microscopy equipment is used in combination with special dyes that fluoresce in the presence of calcium ions. These ions play an important role in the transmission of nerve signals, so Asari can use the technique to monitor the activity of individual nerve cells in real time.

PHOTO: EMBL/ALESSANDRO CICCARELLI

Hiroki Asari

His work at EMBL is only just starting, but Asari is clear about what he wants to achieve. He'd like to uncover common principles that can be applied to any neural system – starting with the retina – and create mathematical models to describe them. "It's like in physics, there are a few equations that can explain everything," he says. "Finding the same kind of equations in neural systems is the big goal of my research."

Silencing noise

Two EMBL researchers are exploring new ways to filter out noise and get to the data they need

Somehow, the multitudes of highly specialised cells in our bodies arise from just a single cell. It's a process that might seem far removed from the changes that occur in the body during a disease. But for John Marioni and Oliver Stegle, research group leaders at EMBL-EBI, one principle ties these processes together.

"In effect, we're trying to understand how cells make decisions," says Marioni. "During development, there's a process by which a cell decides to become a particular cell type. In a similar way, you can think of disease as a cell deciding to do something it shouldn't. If we can understand how cells make these decisions, we'll learn more about normal development and potentially gain deeper insight into what's going on in disease."

Silencing the cell cycle

To understand how these decisions are made, Marioni and Stegle use single-cell RNA sequencing, a technique that provides highly detailed information about the genes that are active in a cell. By studying the pattern of gene activity in many cells, they can identify different cell types. They can then start figuring out which genes are responsible for pushing a cell towards a particular fate.

Unfortunately there's a problem: noise. "When you say 'cell types', there's this notion that they're rather distinct, but in practice it's more of a continuum," Stegle explains. "There's variation between cells of different types, but also between cells of the same type. Sometimes that variation is biologically interesting, but often it's a source of noise in the data – obscuring the information you really care about."

Marioni and Stegle recently joined forces to tackle one source of noise in the data: the cell cycle. This is the repeating process in which cells copy their DNA and then divide to produce two daughter cells. As you might expect, a cell's gene activity is heavily influenced by where it is in the cell cycle. This is undoubtedly a biologically interesting process,

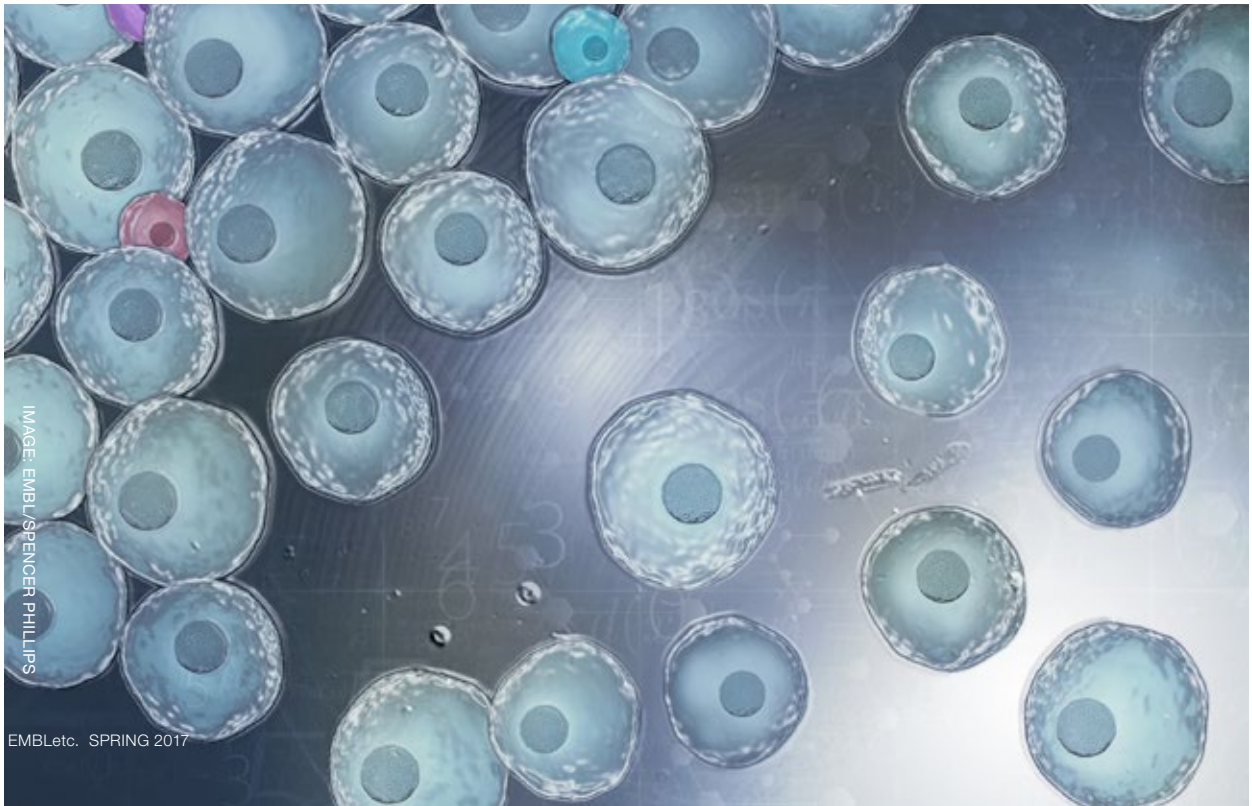


IMAGE: EMBL/SPENCER PHILLIPS

PHOTO: EMBL/ANA STROE

John Marioni

but it's not always the one that researchers like Marioni and Stegle are interested in. That's when it becomes noise.

To cut through the noise of the cell cycle, Stegle, Marioni, and their collaborators developed a new computational approach: the single-cell latent variable model (scLVM). By analysing a small number of key genes in the cell division process, they could classify each cell according to its stage in the cell cycle. They could then cancel out the effect of the cell cycle using sophisticated statistical methods in the scLVM. This makes it possible to infer 'corrected' gene-expression levels for a wider range of genes.

New directions

With this corrected gene expression data, the team were able to more accurately compare gene activity in different cells. The result: the detection of cells at different stages of differentiation towards an immune cell type called a T helper cell. This provides insight into basic biology and a potential avenue for disease research.

Developing methods to remove the effect of the cell cycle is just one important step towards obtaining high-quality data from single-cell sequencing.

"One of the limitations of our model is that you have to know the source of noise you're trying to remove," says Marioni. "The cell cycle is an important one, but there are others. The way we handle cells in the lab, for example, could increase the expression of stress-related genes. We want to take out the step where you decide in advance which noisy factors you want to remove."

"That will make a huge difference," Stegle adds, "allowing us to cut out noise and let the meaningful biological signals come through."

The method designed by Marioni and Stegle allows researchers to identify and correct for hidden differences between cells, creating order out of seeming chaos

"We're trying to understand how cells make decisions"

PHOTO: JON MOLD

Oliver Stegle

"This will let the meaningful biological signals come through"

IMAGE: EMBL/LIVIA MARRONE

Fathoming fear

EMBL's Cornelius Gross wants to understand fear responses and the brain circuitry that governs them

"When you're in a state of fear, there's this internal feeling, this sense of dread, this sense of threat, this sense of impending harm or doom," says Cornelius Gross, a group leader at EMBL's Monterotondo site. "That's the conscious state, but many things happen in your brain before you get to that point."

Exactly what happens before that point is what Gross and his team are trying to find out. They're interested in studying parts of the brain involved in states of fear and anxiety. Most of our conscious processing happens in the cortex – the layer of cells on the brain's surface, which is involved in some of our most complex activities. It helps us with things like social interaction, language, and memory. Fear states arise deeper in the brain, in regions like the amygdala, hypothalamus, and brainstem. These parts of the brain arose much earlier in our evolutionary history than the cortex, and are concerned primarily with instinctive behaviours and basic survival.

"Our current view is that information comes via your senses and goes to the hypothalamus, which is the most ancient part of your brain – the part you share with animals like worms and flies. We think the hypothalamus produces a state that can motivate you to take action – we're trying to figure out how that works," says Gross. "Then signals are passed to the brainstem, which contains motor neurons that run down to your spinal cord. The motor neurons make your muscles move to carry out your behavioural responses."

A brake on behaviour

Gross uses a range of techniques to investigate these processes in mice. One is calcium imaging, in which fluorescent molecules are used to reveal which neurons are firing in a living mouse while it's awake and engaged in various behaviours. Pharmacogenetics or optogenetics – in which a mouse's neurons can be controlled using either chemicals or light – are then used to block or activate specific neurons and determine how they control behaviour.

Recently Gross and his team have investigated defensive responses to social threats by observing the behaviour of a mouse when a more aggressive cagemate is introduced. "We've been able to block a specific region of the hypothalamus and

"You can think of fear as a sixth sense"

demonstrate that the animals then don't show avoidance or defensive behaviour," says Gross. "We've also shown that the cortex can inhibit the activity of these regions. Normally, that puts a brake on our behavioural responses, but in a stressful environment the brake can be gradually removed, allowing us to react more strongly when we perceive a threat. It's an important

way in which the brain regulates our behaviour according to experience."

Subconscious sensing

In all these processes, there's an intriguing mix of conscious and unconscious pathways. "When humans feel fear, this probably occurs when signals percolate up to the conscious realm from the hypothalamus, which is not directly conscious," explains Gross. "This is supported by findings from famous studies where people have suffered damage to their visual cortex and say they can't see anything, but when they've been shown snakes and other types of archetypal fear stimuli, there's been activation in the amygdala and other structures associated with fear – although they're not aware of it. You could almost think of that as a sixth sense. There's this conscious way that we experience the world, but the primary impulses are entirely unconscious. Both come from the same sensory organs, but drive our behaviour via different pathways."

PHOTO: EMBL

Cornelius Gross

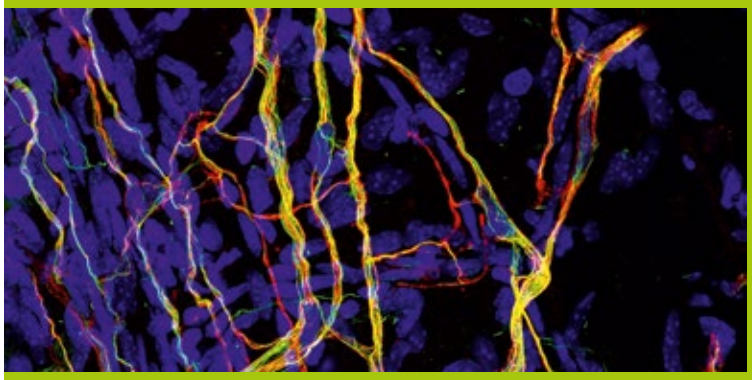


IMAGE: EMBL/LAURA CASTALDI

Keeping in touch

Paul Heppenstall's group at EMBL's Monterotondo site is combining behavioural and molecular biology studies to investigate the swarm of messages that buzzes through the nervous system when we experience touch.

FIND OUT MORE AT
NEWS.EMBL.DE/?p=9846

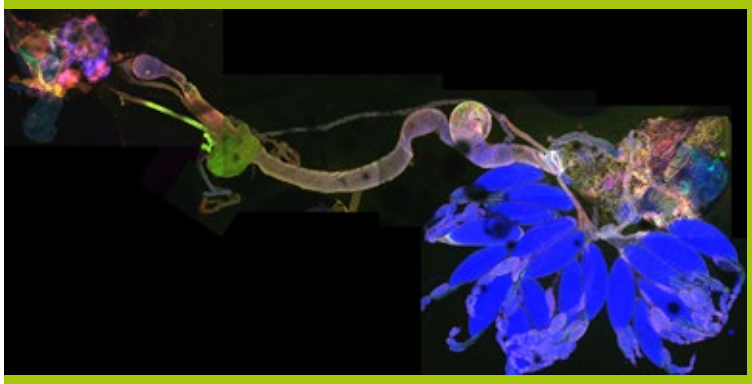


IMAGE: MAX PLANCK INSTITUTE OF NEUROBIOLOGY/LAURA LOSCHEK

Taste of temptation

As anyone who has been to a supermarket on an empty stomach can attest, being hungry can affect not just our mood but also the decisions we make. The same is true for fruit flies. EMBL alumna Ilona Grunwald-Kadow (1999-2002), a group leader at the Technical University of Munich, studies the chemosensory system – the senses of taste and smell. She wants to answer questions such as: why does food smell and taste better when you are hungry? How do animals choose the right food that their body needs? How does pregnancy influence our sense of taste and smell?

FIND OUT MORE AT
NEWS.EMBL.DE/?p=9848

Beyond science

EMBL Director-General Iain Mattaj and EMBL alumni explain how international collaborative science projects can also support peace and development worldwide

PHOTO: EMBL

In changing times, the voice of researchers needs to be loud and clear: diversity, internationality and collaboration works

BY IAIN MATTAJ

Take a walk around EMBL's sites and you will discover physicists, chemists, geneticists, computer scientists, crystallographers, mathematicians and experts from many other fields working together, united by a shared curiosity to solve the molecular mysteries of life. One striking aspect is the variety of intellectual backgrounds. Another is the astonishing range of nationalities – more than 80 different countries are represented in our workforce.

This diversity creates a fascinating environment and it is also crucial to our success as an organisation. Solving the most important puzzles in modern life science requires diverse teams of people contributing new perspectives and complementary expertise. Between different countries, researchers are often trained in highly disparate ways. It's extraordinarily enriching to move from one training environment to another and experience the variety of approaches that people of different nationalities use to answer questions.

This spirit of working together across borders is also reflected in numerous external partnerships and collaborations. One can see inspirational examples involving EMBL researchers: global genomics

projects, where international consortia bring teams of scientists from all over the world together to obtain and analyse the data needed to allow better fundamental and clinical interpretation of the genetic code. Or epic journeys such as the *Tara* Oceans expedition – a four-year voyage around the world to study microorganisms in the world's seas – that has enabled us to understand more about how some of the ocean's least understood creatures survive and thrive. By bringing together international teams diverse in discipline, language and culture we are able to tackle problems that do not respect national boundaries and whose solutions are important to every one of us.

Clear messages needed

Nevertheless, EMBL does not operate in a bubble. The science ecosystem which we are part of and rely on is dependent on the free international exchange of people, ideas and knowledge. In recent times, parts of the world have gone through striking changes in policy and politics. Sometimes, these changes can serve to make things more difficult for research, especially when freedom of movement of people is either threatened or undermined. As a community, scientists need to be part of the conversation – to show how solid reassurances and clear messages of support for our values can help to preserve and enhance the European and international research landscape.

Intergovernmental research organisations like EMBL, CERN and the European Space Agency were explicitly set up after World War II, when there was a lot of thought about how to promote peaceful interactions between countries. And there are countless inspiring stories of researchers who have made massive contributions to science against the odds – from Nobel laureate Sydney Brenner who left apartheid-era South Africa, to the construction of the phenomenal SESAME synchrotron recently launched in the Middle East. The common thread in these examples is that dialogue leads to progress. Scientists talk despite differences between nations, despite political tensions – and can inspire us to think differently about how we live and work together.

Prioritise dialogue

Shared problems that confront the world's nations – in healthcare, climate change, pandemic response, food security and many others – present massive challenges, but also opportunities to engage. The science community must also prioritise dialogue with society and policymakers; listening to public needs and concerns, while communicating the needs of our community. Dialogue is not always easy to establish and the conversations may be difficult, but we all stand to gain from having these conversations. Knowledge-based decision-making benefits every one of us.

"Knowledge-based decision making benefits every one of us"

Scientists must be part of the conversation

Achieving this depends upon exchange being exchange amongst equals. We need to show the world that diversity, internationality and collaboration across borders works. The rest will follow. EMBL's first director general, John Kendrew, described international activity as an important contributor to world peace. On the occasion of the 100th anniversary of his birth, his words seem as prescient today as they did more than forty years ago. Having the privilege of leading EMBL and seeing the benefits of internationality first-hand, gives me great confidence we will prevail.

PHOTO: ISABEL PALACIOS

EMBL alumna Isabel Palacios

Building labs with

Flies can do a lot for science, inside and outside the lab. EMBL alumna Isabel Palacios explains how

BY EDWARD DADSWELL

Isabel Palacios studies fruit flies. Not because she has any particular interest in flies themselves, but because they help her answer fundamental questions about animal development. Most animals start life as a single, roughly spherical cell. Somehow the symmetry of that cell gets lost and you end up with an animal that has a distinct head and tail, front and back. The curious thing is that even in that first cell – even before it's fertilised – microscopic cellular machinery is working to create subtle asymmetries that prepare the cell for development. Palacios, an EMBL alumna and group leader at the University of Cambridge, wants to understand how this happens.

But that's not the only ambition she has for her flies. As a founder of the DrosAfrica project, she believes the fruit fly, *Drosophila*, can play an important role in developing the research infrastructure of an entire continent, helping African scientists undertake high-impact projects and form collaborations around the world. The aim of the project is to teach scientists how to use the fly as a model system for studying human disease, ultimately creating an interconnected community of *Drosophila* researchers in Africa. This involves organising local workshops to train scientists, and providing basic equipment such as microscopes and antibodies.

A model for research

"People who don't know about the fly ask: 'How could it help with African research?'" says Palacios. "But actually there are a lot of questions you can answer." *Drosophila* has long been used in genetic studies and allows researchers to gain insight into many types of human disease, including cancer, diabetes, and neurodegenerative disorders such as Alzheimer's or Parkinson's. Flies can also be used in the study of host-pathogen interactions, including infection by viruses or *Plasmodium* – the organism that causes malaria. They therefore have a broad range of uses in basic biomedical research.

The other thing about fruit flies – as some of us have had the misfortune to discover outside the lab – is that they reproduce rapidly, without human assistance. This means you can produce adequate numbers at low cost, and very little specialist equipment is required to look after them. There are also many companies and university departments offering gene editing services for *Drosophila*, so it's easy, fast, and inexpensive to obtain flies with the genes you want to study. Palacios points out that the community is very open and willing to share, so if there's a particular type of fly that you'd like to research, there will often be someone in another part of the world who can send it to you, and the cost of shipping is very low. All these things make *Drosophila* an ideal organism to work with on a limited budget.

International science

Palacios compares the situation in Africa to that of Spain forty years ago, when the country underwent a period of rapid development. It was at this time that Antonio García-Bellido, a developmental biologist, began training a few *Drosophila* researchers who went on to train others, creating a large community of fly researchers in Spain. Some

also went abroad to start their own research groups. "Suddenly you could do competitive science using the fly, because it's very inexpensive and very easy to learn," says Palacios. "In terms of research, it helped put Spain in the international picture."

It was against this background that Palacios grew up. At the time, Madrid was the only university in Spain that offered any courses in molecular biology, so she initially enrolled for a general biology degree at the University of La Laguna in Tenerife. "But," she says, "any time they touched on a more cell biological aspect, that was what

flies

really interested me." After the first year, she decided to make the move to Madrid. "Financially, it was quite a stretch for my parents," she explains. "But once I was there, I loved it. I knew that this was what I wanted to do."

She went on to study for a PhD at EMBL in Heidelberg. "I applied thinking there's no way they'll invite me there, but they did, and then there's no way they'll offer me a place, but they did. I'd already started a PhD in Madrid, but my supervisor, Juan Ortín, said 'Take this chance, it's a really good one,' so that's where I went," she says, laughing. "Suddenly I was at one of the best molecular biology institutes in Europe! I couldn't believe my luck and I've been lucky ever since."

Building relationships

Palacios explains that the idea for DrosAfrica came from a chance meeting between one of her colleagues, Lucia Prieto Godino, and Sadiq Yusuf, a professor from Kampala International University (KIU) in Uganda. Godino and Yusuf decided to organise a workshop at KIU that would teach Yusuf and his students the skills needed to work with *Drosophila*. Palacios was invited to lead some of the sessions at the workshop. "It was clear that these scientists had a great desire for knowledge and wanted to do good research," she says, "but they didn't have the money or the facilities." Palacios and her colleagues realised that *Drosophila* could help these researchers – and others in Africa – achieve their goals.

Since then, they've organised several workshops in Uganda and Kenya, and more are planned in Nigeria, South Africa, and Egypt. Three years into the project, they're seeing attendees from the workshops setting up fly labs at their own institutions. They've had master's students successfully defend their theses on *Drosophila* and there are PhD students who will soon be doing the same. A network of scientists from several African countries is also developing. They've started organising their own workshops, and Palacios hopes they'll soon be running their labs and applying for grants independently.

"I find it the most satisfying project I have"

When I ask her about some of the difficulties she's faced with the project, she answers without hesitation. "The challenges are always time and funds. For most of us, this is not our main job and we also need to focus on the other aspects of being a scientist – publishing papers and getting grants," she explains. "But with DrosAfrica, what you put in and what you get out is a lot more balanced than it usually is in science. I find it the most satisfying project I have."

Palacios with participants of the 2013 DrosAfrica workshop at Kampala International University, Uganda

PHOTO: EMBL/ROSEMARY WILSON

EMBL alumna Zehra Sayers

SESAME: a light in the desert

EMBL alumna Zehra Sayers key driver of the Middle East's first synchrotron project

BY ROSEMARY WILSON

In the desert 30 km northwest of Jordan's capital Amman, a sparkling new light source will soon open for business. SESAME – the Middle East's first synchrotron – will enable researchers from across the region to explore the structural and chemical makeup of everything from metals to biological tissue. The first electrons were sent flying around the 133-metre ring in January and after 20 years of lobbying, training and construction work, SESAME is now gearing up to do great science.

EMBL alumna Zehra Sayers, a biophysicist who chairs SESAME's Scientific Advisory Committee has been a key driver of SESAME's development for much of the past two decades. Together with her colleagues, she has navigated and embraced engineering, scientific, economic and political challenges and opportunities that came part and parcel with delivering a multinational project of this scale in the Middle East. Now with much of the legwork done, Sayers is excited about the future of the project, both in terms of scientific importance and its potential to inspire future generations.

Sceptic to advocate

But Sayers, who worked at EMBL in Hamburg between 1986-98 and is now Professor at the Sabanci University in Istanbul, was not always a believer. "I had read about SESAME and initially I didn't believe it could happen," she says. "Firstly, I did not believe there were enough people doing synchrotron science in the region: who was going to use it? Secondly, I thought SESAME would use second-hand instruments from other synchrotrons and therefore be unsuitable for doing high-quality research."

While the initial ideas involved using an entire decommissioned synchrotron from Berlin called BESSY I, this soon developed to combine major components of BESSY I with a completely new 2.5 GeV storage ring. Having ignored their first attempts at rousing her interest, SESAME scientists tracked Sayers down in Hamburg, and convinced her she should play a key role in its realisation. "Dinner and a bottle of wine was all it took to convince me!" Sayers says. Over dinner they described the stunning specifications of the new storage ring and an established international training programme that was preparing scientists from the region with the skills needed to deliver SESAME. "Now I am a convert, and converts are the best advocates!" she adds, laughing.

Workers inside the future SESAME building set up the synchrotron ring that now accelerates particles to nearly the speed of light

Like EMBL, SESAME is an intergovernmental organisation that aims to serve its member states – currently Bahrain, Cyprus, Egypt, Israel, Iran, Jordan, Pakistan, the Palestinian Authority and Turkey – who make vital contributions at different levels. Particularly appealing to Sayers was the prospect of providing a facility that researchers returning to the region could use to continue their research. "There is a rich cultural heritage in the region and SESAME will be an important facility for studying material such as historical artefacts," says Sayers. Other research themes include the pharmaceutical potential of products produced from local herbs, and studies of the heavy metals present in the Yarmouk and Jordan rivers. Life sciences, materials science, physics and chemistry will all be catered for. "This has to work as a world-leading experimental facility," Sayers says. "If the science is great, many things will follow."

Truly international

Sayers and colleagues have been forced to confront many unexpected challenges: unprecedented snowfall caused the experimental hall roof to collapse, setting the project back by a year. And funding has remained an ever-present obstacle – five member states stepped forward with five million dollars each to finance the storage ring, only to have political events intervene: the Arab Spring long delayed Egypt formalising agreements, while Iran has been unable to transfer funds due to international sanctions.

Yet the sheer drive from scientists both in the region and internationally have helped to drive forward SESAME, which will open for business in May this year. The project secured support from observer countries including Italy, UK, USA and Germany, as well as the European Union through CERN, whose engineers have helped to oversee the construction. Moreover, many recruited into SESAME's training program have now moved back to Jordan to help construct and run the facility after spending time learning their craft at other synchrotrons around the world. "First we needed to train people, then we needed to make sure we had a good machine – now it's about the science," says Sayers. "We have a user community of more than 200 researchers who are eager to work with us."

Safe place for science

And Sayers points to an exciting future ahead. "With all the social and political unrest going on around us, things in the world of science are clearer," she says. "Science creates another sense of community, regardless of nationality or religion. In the long run I hope SESAME will be useful for building a better future for the region. From my own experience working at Sabanci University, where we are relatively protected from the political upheaval going on in Turkey – I experience a sense of sanity when I am there. I hope that SESAME can provide a similar environment for many others: a safe place where we can produce high-quality work, leave other worries to one side and just talk science. That is what I am striving for."

Building bioinformatics capacity in Africa

EMBL alumna Nicola Mulder reflects on her pan-African bioinformatics project and its impact on young scientists

BY ANNIKA DUDA

Africa exceeds every continent on Earth in genetic diversity. Many African nations need to build a critical mass of people with the science and technology skills to study this diversity comprehensively – and EMBL alumna Nicola Mulder is on the case.

As head of the computational group at the University of Cape Town, Mulder has driven the development of H3ABioNet: a pan-African bioinformatics network that aims to build capacity for genomics research, and to train the next generation of computational biologists. She wants to empower African scientists to carry out data analysis locally, so they can act on their findings quickly.

Strong research foundations

"Many African countries battle serious health challenges, including neglected tropical diseases, malaria, and the spread of HIV," Mulder explains. The H3ABioNet project, a pan-African bioinformatics network for Human Heredity and Health in Africa, aims to boost genomics research and enhance understanding of the molecular basis of disease. It connects 32 research groups across 14 African countries.

"We are building a solid reference dataset for the African population that could help many countries move a bit more towards precision medicine," she adds. "African research institutions are generating a lot of data from multiple sites

EMBL alumna Nicola Mulder

PHOTO: EMBL

and fields of study, but historically most send this data overseas for analysis. We want to turn off this mentality and empower scientists closest to experiments to interpret and analyse their own data."

Essential infrastructure

H3ABioNet is building African data infrastructure and access, research partnerships and scientific skills. It promotes training programmes, workshops and fellowships in countries including Mali, Nigeria, Tanzania and South Africa.
"All researchers working with high-throughput biology can benefit from learning statistics and programming," explains Mulder, who was a team leader at EMBL-EBI – a global leader in computational biology research – for more than eight years. "It is not always necessary to be a bioinformatics expert, but if you know certain parameters you are better placed to determine the tweaks that can help you to explore your data.

More than 40 workshops have taken place since the initiative was launched in 2012, providing training opportunities to more than 600 researchers. The network has also funded more than 20 fellowships for researchers to learn new skills and is branching out into e-learning. "We also need to train people from across the science and technology spectrum," adds Mulder. "For instance, bioinformatics engineers develop essential algorithms, build infrastructure, find solutions to data storage challenges and support other researchers in analysing data."

Persistence: essential to science

Reflecting on the hurdles she has leapt, Mulder smiles: "I do not know where to start!"

Skills, funding shortages, limited computer equipment and low Internet coverage top the list. "We literally tested every single online platform for communication that has ever been made", she says. And the H3ABioNet journey is not without its diplomatic hurdles: political sanctions in Sudan, border politics, persuading a widely distributed research community of the initiative's worth. Yet after dusting themselves off and developing an informal network, Mulder's consortium was eventually awarded grant funding for five years. The network provides an infrastructure backbone for the Human Heredity and Health in Africa (H3Africa) Initiative, a partnership between the NIH, the African Society of Human Genetics and the Wellcome Trust to study determinants of genetic diseases with the aim of improving the health of African populations.

"It is about finding that niche area where Africa can take the lead"

Data-driven science

From the start, Mulder's team was stunned by the sheer appetite for bioinformatics training across Africa. "Within one hour of our first call for courses, we had more than 100 applications," Mulder says. "It surprised me how desperately this had been needed, for so long. In the past five years we've managed to build a large group of young and enthusiastic people and have witnessed the emergence of a new generation of African leaders in bioinformatics."

Courses, often developed together with the H3Africa consortium, are heavily oversubscribed. To keep the programme sustainable in the long term, the project trains local trainers, as well as providing logistical support for scientific institutions to develop bioinformatics degree courses.

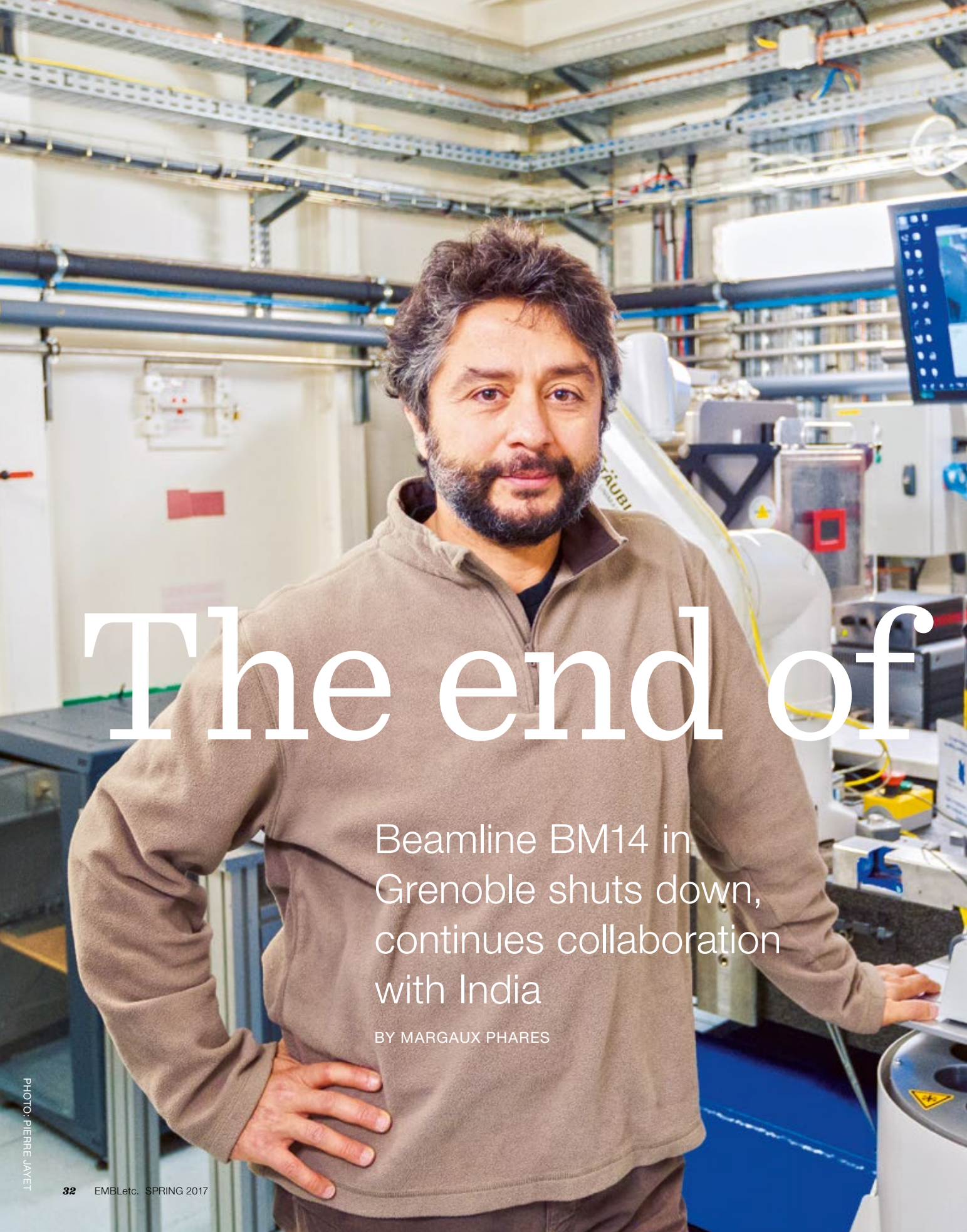
"Previously isolated bioinformatics groups distributed over the continent are now regularly meeting like-minded people from other countries. Our network helps them to feel part of something bigger," explains Mulder. "There has been a demonstrable, positive impact of this approach. Some institutions have leveraged funding and we have seen a fresh confidence amongst bioinformatics researchers in African countries to apply for grants together and develop collaborative research projects."

Keeping the EMBL connection

Mulder retains a firm connection to EMBL as a member of the ELIXIR, InterPro and Training Programme scientific advisory boards. "The connection to ELIXIR has been very useful," Mulder says. "ELIXIR is building research infrastructures and that is what we are doing in Africa. I have been able to learn from ELIXIR and they are able to learn from my experiences here."

Previously, Mulder was responsible for developing bioinformatics data resources at EMBL-EBI, which benefit scientists throughout the world. After leaving EMBL, she returned to the research scene at the University of Cape Town, where she first recognised the acute need for training while organising a national training programme.

"Building bioinformatics capacity in Africa remains a big challenge," Mulder remarks. "However, bioinformatics is one of the cheapest sciences you can do – you don't need to buy expensive lab equipment; all you need is data and someone to work with it on a computer. The success of the H3ABioNet initiative shows that just because you have limited resources doesn't mean you will fall behind in a field: rather, it is about finding that niche area where Africa can take the lead."



The end of

Beamline BM14 in Grenoble shuts down, continues collaboration with India

BY MARGAUX PHARES

PHOTO: PIERRE JAYET

an era

"Take your time," Hassan Belrhali tells me as I rush to finish my lunch. It's 2 pm in EMBL's Grenoble site canteen and most people have already left to get back to work. The soft-spoken scientist sits across from me, patiently. But when we start to talk about his work with Beamline 14, his voice quickens. In excited tones Belrhali shares stories of the beamline and the science it helped make possible at the European Synchrotron Radiation Facility (ESRF).

Between 2010 and 2016, a fruitful collaboration between EMBL, the ESRF and the Regional Centre for Biotechnology (RCB) based in New Delhi, India allowed hundreds of Indian scientists to access the resources and services offered by EMBL and ESRF and to further their research at a pace that wouldn't have been possible otherwise. But, like other beamlines at the ESRF, BM14's time is drawing to a close. My lunch finally eaten, I follow Belrhali to the synchrotron to learn more about the legacy of both the instrument and the collaboration it supported.

A pair of bright green double doors signals the entrance to Belrhali's office, which is decorated with both the EU and Indian flags and a sign that reads, 'Welcome to BM14, an ESRF-EMBL-India MX MAD Beamline.'

Hassan Belrhali at BM14

MX is short for 'macromolecular crystallography', the study of determining the 3D structure of large molecules. MAD, on the other hand, stands for 'multiple anomalous dispersion', a technique that lets scientists determine 3D structural details of a molecule by comparing its diffraction patterns at different wavelengths. In 2006, Belrhali and Amit Sharma, from the International Centre for Genetic Engineering and Biotechnology in India, used a similar technique at BM14 to elucidate the structure of a molecule that lets a malaria parasite enter and infect human red blood cells.

Formalising the partnership

The results of their study were instrumental in further understanding malaria. In an effort to let others benefit from the same resources they had access to, Belrhali and Sharma decided to create a formal partnership with ESRF and EMBL. Their idea was to allow the whole Indian scientific community to access the powerful tools from BM14 and take their experiments to the next level.

Most Indian users run experiments on a 'home source,' which uses the same principles as X-ray machines in hospitals: an electron beam fires at a piece of metal, exciting the atoms which then emit X-rays as they relax down to their 'ground state'. Just as Belrhali and Sharma had found during their work on malaria, biological crystals often diffract poorly at in-house sources. Determining 3D structures became very challenging. As more users grew frustrated with their resources, Belrhali tells me, "the natural evolution was that they gained access to BM14."

Into the synchrotron

From the outside, the ESRF facility is so big that it is easy to forget that it is ring-shaped. On the inside it is even more impressive: Belrhali and >>

PHOTO: PIERRE JAYET

Hassan focuses on the control screen of BM14 to make sure that the experiment is running according to plan

>> I stand above the large outer ring of the synchrotron and a labyrinthine corridor of 43 beamlines radiating from the main ring. Below our feet, the electron beam hurtles through the 850-metre circumference at nearly the speed of light, just like it does 24 hours a day. Behind us, a scientist idly whizzes past us on a scooter.

The ESRF creates X-rays by accelerating electrons around the huge ring layered with magnets. The magnets control the speed and direction of the electrons; whenever they accelerate electrons around the ring they also generate X-rays that are fired off tangentially. At each of those points a beamline channels those X-rays and uses them for a particular experiment.

EMBL and ESRF manage seven beamlines together and make them available to around 2500 structural biology users each year. Every day they enable the elucidation of new structures for biological macromolecules, but also technical advancements to make crystallography experiments more efficient.

Slowing down

Some scientists joke that when you've seen one beamline, you've seen them all. At a glance, they look alike. But in fact, each beamline runs different experiments, is run by a different scientist and specialises in different techniques. BM14, or Bending Magnet 14, is a dedicated crystallography beamline for macromolecules; it is run in collaboration by the RCB, ESRF and EMBL and was one of the first beamlines to use the MAD technique on biological material. It is also one of the last beamlines where things are still run by hand.

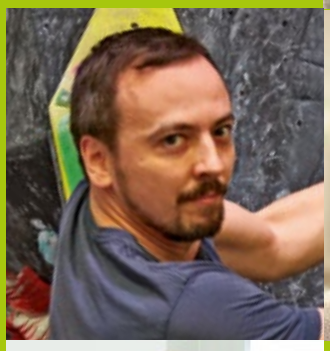
"It's the end of an era. But the collaboration is not over yet"

"BM14 is like an old taxi with lots of charm. An experiment is like the landscape – with BM14, you have time to immerse yourself in it," Belrhali says. "New beamlines are like new taxis – fast and shiny. But in the end, both can get you to your destination." Technological improvements in beamline technology have allowed experiments to run autonomously, remotely and with better resolution. It is these beamlines that are in higher demand, and BM14 is in the process of being shut down to make way for them.

The impact of BM14 on Indian research and the development of structural biology in India is considerable. Between 2010 and 2016, 58 groups from 34 institutes visited BM14. Here, hundreds of experiments took place and 418 papers were published. Belrhali is considering a second career as a teacher, in order to continue sharing his passion with students and spreading the best practices on the most advanced technologies. "BM14 was a fantastic place to train new students and enable experiments that were near impossible in India!" he exclaims. "It's the end of an era. But the collaboration is not over yet."

Building upon the very fruitful collaborative relationship that BM14 enabled, EMBL and India are looking to identify and encourage new, long-term cooperative activities of mutual benefit in fields of common interest.

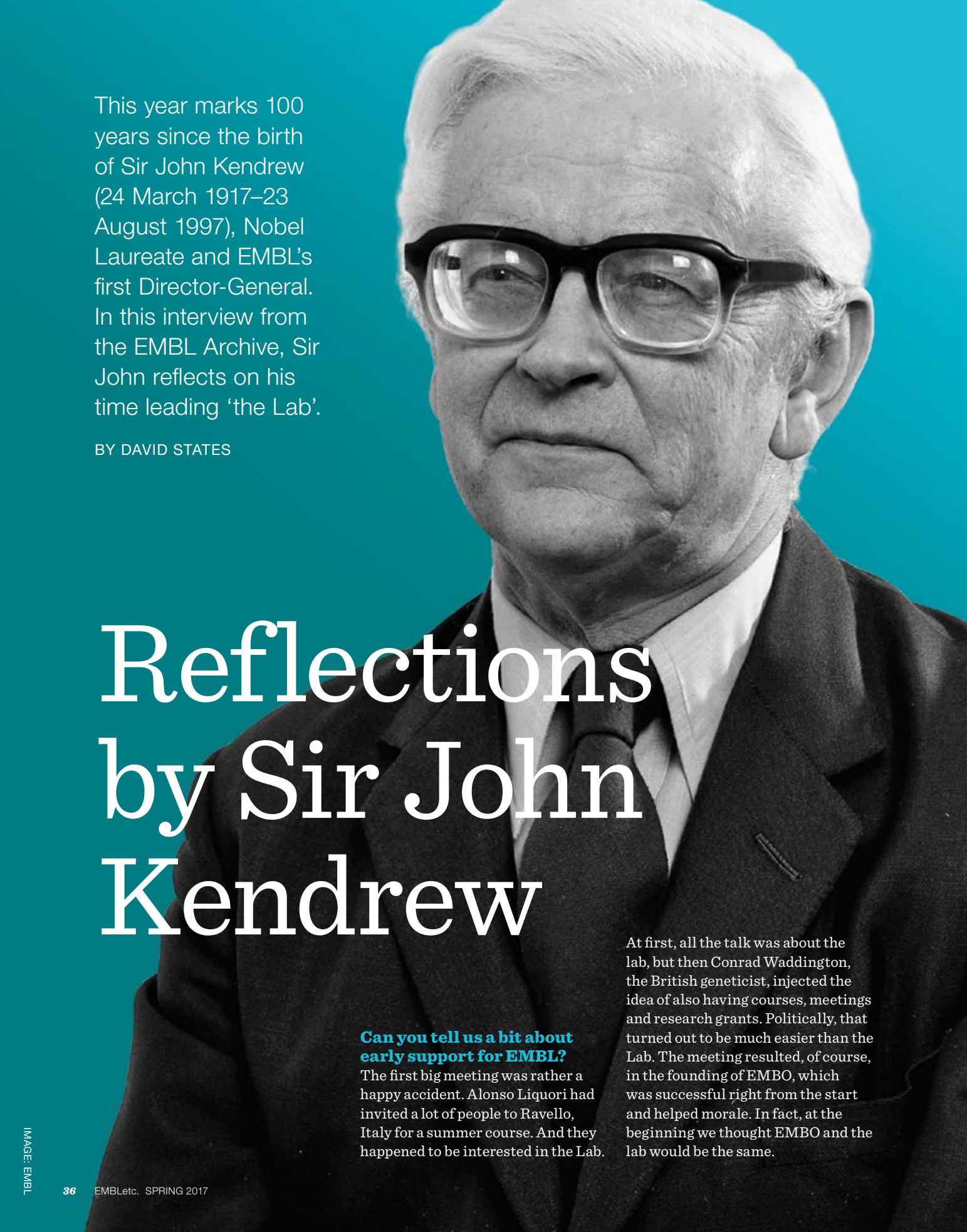
Cultures



This year marks 100 years since the birth of Sir John Kendrew (24 March 1917–23 August 1997), Nobel Laureate and EMBL's first Director-General. In this interview from the EMBL Archive, Sir John reflects on his time leading 'the Lab'.

BY DAVID STATES

Reflections by Sir John Kendrew



Can you tell us a bit about early support for EMBL?

The first big meeting was rather a happy accident. Alonso Liquori had invited a lot of people to Ravello, Italy for a summer course. And they happened to be interested in the Lab. At first, all the talk was about the lab, but then Conrad Waddington, the British geneticist, injected the idea of also having courses, meetings and research grants. Politically, that turned out to be much easier than the Lab. The meeting resulted, of course, in the founding of EMBO, which was successful right from the start and helped morale. In fact, at the beginning we thought EMBO and the lab would be the same.

IMAGE: EMBL

"Personally, I believe that international activity is very important in building world peace. And science has always been the most developed international activity that there is. It is as simple as that"

CERN, the international physics lab, and the UK's Laboratory of Molecular Biology seem to have had a large influence on the design of EMBL.

The internationalism of CERN was, of course, a major influence, We felt creating the right atmosphere and building a critical mass of biologists in a wide range of fields could best be done at a European level. CERN, of course, had a big machine. You couldn't do that nationally. That was a big political advantage. The trouble with biology was that there was no big machine. It was only in the late '60s that large machines came into play with molecular biology – the synchrotron facility, for example. By then we argued for at least 50 per cent instrumentation. But we always wanted to incorporate some instrumentation at the EMBL. Of course, the UK Laboratory of Molecular Biology was a major influence – after all, I had worked there for many years and one of the advantages we had at Cambridge, for example, was that at first we were in the physics department with lots of big shops. In the early days of protein crystallography, almost all of the equipment was made in the laboratory.

What were the scientific strengths of the early EMBL?

We were very strong in instrumentation, so things like EM (electron microscopy) at Heidelberg and crystallography at Grenoble and Hamburg were going to do well. Incidentally, the Hamburg outstation was really a bit of personal generosity on the part of Ken Holmes and Gerd Rosenbaum. This was also the time when molecular cell biology was getting off the ground, a rather obvious area. One very important article was by Ari Helenius and Kai Simons on how viruses get into cells. The paper was turned down at first – the editor said it wasn't "interesting" [he laughs], but it turned out to be one of the most interesting papers in the field.

When EMBL started, you had no facilities. How did you convince scientists to come?

A lot of senior people played with the idea, but for one reason or other didn't come. It was easier to get young people because they didn't have such entrenched positions. We looked for excellence and promise. We took a strong position with our Council that we were not going to have national quotas. We had our Council in all the countries, and good friends in America, like Paul Doty and Jim Watson.

Any personal reflections on the time you worked at EMBL?

Well, it was the most interesting 20 years of my life. You see, starting something from zero presents a rather unusual opportunity. You have so much freedom to be creative. Personally, I believe that international activity is very important in building world peace. And science has always been the most developed international activity that there is. It is as simple as that.

This interview was first published in EMBL 20 Years On: 1974–1994, *a report issued to celebrate the Laboratory's 20th anniversary.*

Celebrating Sir John Kendrew's 100th birthday

24 March

Pensioners' Annual Coffee at EMBL in Heidelberg, for EMBL alumni to share stories about John Kendrew. Sir John would have turned 100 on this day.

21 July

The 10th John Kendrew Award ceremony at EMBL in Heidelberg (see page 46 to find out who won this year's award).

16-17 November

Conference at EMBL in Heidelberg: "Revolutions in Structural Biology: Celebrating the 100th Anniversary of Sir John Kendrew". The meeting explores how methodological developments in structural biology have dramatically advanced the field, and includes a special event on Sir John's legacy for EMBL alumni. Abstract deadline: 24 August. Registration deadline: 5 October.

EMBL.DE/EVENTS

Humans of EMBL

People across EMBL's sites reflect on the ways they perceive their world

BY EDWARD DADSWELL

I discovered bouldering about seven or eight years ago; I can't remember when exactly. It's like if you're asked when you first met a friend – usually you don't remember, it just happened at some point. Unlike regular climbing, in bouldering you have no ropes, no security whatsoever. The routes typically are shorter but more intense in terms of the movements you make and the muscles that are engaged. Touch is very important because often you can't see beyond an overhang, or you can't turn your head to look at your hand. You have to just extend your arm and feel if there is something to grasp. If there is, it's the best feeling in the world at that moment!

Bouldering fascinates me because it's a mental as well as a physical challenge: you have to figure out how you go from down here to up there. You have a theoretical plan in your head, but when you're on the wall it rarely works out in the easy way you imagine at the beginning. In a way, it's like working in science: projects often turn out to be more complicated than you thought, so you have to be ready to adapt and try new strategies. When I climb a route I'm really focused on climbing that route; all other thoughts are off the list at that moment. It frees you from all the things that are bothering you because you're just focused on getting the job done: the job in this case being to go from here to there.

Christian Arnold

Bioinformatician, EMBL's Heidelberg site

PHOTO: EMBL/MARIETTA SCHUPP

PHOTO: EMBL/ANNE-FLORE LALOË

PHOTO: COURTESY OF JIM SAWITSKE

We're quite a small site over here, almost like a family. I enjoy baking, and I often make things for the lab and the institute. When you do that, everyone's happy. Having some cookies or sweets at four o'clock in the afternoon often helps, I think. People relax and spend some time in the kitchen and talk to each other. I think that's important for our science and our sense of community here. It makes you feel supported.

Being so close to Rome is amazing. I love the architecture, with all the old buildings and monuments. It seems like every time you turn a corner you see a fountain that's been there for about a thousand years! I remember the first time I saw St Peter's Basilica. It was before I started my PhD and I was there with my family. It was very hot. It's overwhelming to stand in the plaza and feel how incredible it is that someone built this. Some people get used to living here and passing things like St Peter's or the Colosseum every day – I don't think I could ever get used to that.

Emmy Tsang

PhD Student,
EMBL's Monterotondo site

When I was doing my PhD in Oregon, I had a huge pear tree in my yard. The pears would fall on the roof of my house every night and keep me awake. I tried fermenting them to make perry, but it was a year before it was ready and most of it was bad. I thought, "This was a disaster, I don't want to do this anymore," but I had friends who made beer and they suggested I make beer instead. I wasn't convinced, but I tried it and it turned out great! I've now been brewing award-winning beer for more than twenty years, and in 2011 I achieved National ranking as a judge at beer competitions. I also oversee exams for people aiming to qualify as beer judges, and in the space of two months I'm doing that in Spain, Italy, Israel, and Poland. When people hear you're a beer judge they think: "Great! You get free beer!" but it's actually a lot of work. The exam you have to pass is amazingly hard – other than getting my PhD, it's probably the hardest exam I've ever taken.

Brewing is like science at home, and I approach it the same way. I have a notebook that I write up my beers in, because if I make a fantastic beer I want to be able to recreate it. Some of my recipes I've made fifteen times, and I'm always trying to perfect them just a little more.

Jim Sawitzke

Head of Genome Engineering Services,
EMBL's Monterotondo site

PHOTO: EMBL/MARIETTA SCHUPP

I grew up in France, in a place just south of Paris called the Vallée de Chevreuse. When I was a kid, maybe five years old, my father's sister lived with us for a while. She was studying pharmacy, and to learn things by heart she would tell them to me, so I ended up learning them as well. At the time you could buy a series of booklets that each came with a model of a human bone, so you could put together a whole skeleton. She was buying this for me and I liked it a lot. Since then I've been interested in science. Now I study the way DNA is packed up and organised in cells.

One of the high points of research is when you do an experiment and it works, but 99% of your time is failed experiments. That's why I like to do other activities outside work such as taking part in the cooking club at EMBL, because you get something out of it right away. People tell you that they like what you made, that they are happy. It's also a relaxed way to meet new people. I've always enjoyed cooking. My family is from Iran so my mother makes a lot of Persian food, which I really like. The other day I was walking in the street and suddenly I smelt a Persian dish. I thought, "I haven't eaten this in ages!" Just by the smell, you can really recognise it. It's a popular dish called Ghormeh Sabzi which has a lot of fresh herbs in, so there's this special taste of the herbs and the meat together – it's not like anything else.

I've been here more than seven years, but I'm leaving EMBL in a few months and going back to France to start my own lab. I'm really excited.

Yad Ghavi-Helm

Research Staff Scientist, EMBL's Heidelberg site

Painting, singing, and dancing are all things that I love. In painting you can take a thought or an emotion and capture it on a piece of paper; in singing you can put it into your voice; in dancing you can shape it using your body's momentum. Then you can catch it for a moment – it's like a snapshot of your life that you can share with others.

When I do microscopy or spectroscopy, I make observations and sometimes even small details can reveal something really fascinating about nature's intelligence. When you paint you try to do the same thing: to observe details and ask why they happen and what's behind them. In both fields I'm thinking, "How can I help people see the beauty that I see?", "How can I make it clear?" Science and art go hand in hand with me, although it's not obvious. I'm happy that I have an opportunity to combine them.

Arina Rybina

EMBL Interdisciplinary Postdoc, EMBL's Heidelberg site


PHOTO: EMBL/MARIETTA SCHUPP

PHOTO: COURTESY OF NEIL DEAR

My work involves altering the genetic makeup of mice to help us understand human diseases. When I'm at home, I like DIY. I like repairing things, building things, laying floors. I even like things like rewiring. Most of all, I like knocking down walls! I like the fact that something's better at the end than it was when you started. A few years ago I went on a plastering course. I actually find plastering more difficult than what I do at work. When I'm doing gene editing I'm meticulous but I don't have to be super-quick. In plastering, you have to be both. You get about fifteen minutes before the plaster sets, so fifteen minutes to cover the wall and get it completely flat. You can iron out a few things later on but not much, so you've got to be fast. I'm not great at it but I love it when it works. Whatever I do, I'm always aiming for perfection.

Neil Dear

Head of Transgenic Facility, EMBL's Monterotondo site

Three years ago I cycled from Strasbourg to Istanbul. I did it at the end of my master's degree because I knew once I started work I wouldn't get the chance. Nobody around me was really motivated to train, so I decided to go on my own. I didn't want to wait because otherwise I might wait forever. I also think when you're alone you're much more open to meeting other people, and people want to talk with you because they have a kind of curiosity about what you're doing.

I took my flute on the journey – along with my bike, it's one of the two things I need wherever I go. I played it just for myself or for people who asked me. It was good to have it with me and to have music whenever I wanted.

It was a crazy feeling when I arrived in Istanbul, to think I did it by myself – I just pushed on the pedals and came here. I was taking a picture in front of Istanbul's most famous building, Hagia Sophia, and this guy came up to me and wanted to sell me a boat trip on the Bosphorus. He asked where I'd come from with my bike and I said from France. He told me he didn't believe me, so I said: "You believe whatever you want – I know what I've done!"

Anne-Sophie Humm

Research Technician, EMBL's Grenoble site

PHOTO: EMBL/FRANCK FELISAZ

Helke Hillebrand at EMBL's 2016 graduation ceremony

Degrees of excellence

We catch up with Helke Hillebrand, on leaving EMBL after nine years as Academic Coordinator and Dean of Graduate Studies

BY ADAM GRISTWOOD

What is special about being a fellow at EMBL?

There are now more than 550 fellows at EMBL, including around 250 postdocs, 200 PhD students as well as many undergraduates and interns – it's a big ship, and it is growing. The combination of mentoring and support for early independence on EMBL's fellowship programmes presents a fabulous opportunity for early career scientists to make their mark. The range of expertise at EMBL – in biology, chemistry, computer science, mathematics, medicine and more – enables fellows to include a great range of dimensions in their research projects. Throughout my time at EMBL, my goal has been to develop the programmes in ways that enable fellows to explore science at its best, to take advantage of the many opportunities available to them and to be fully informed when planning their next career steps. It is important that fellows feel thoroughly empowered to employ their talents to the fullest.

What have you learned during your time at EMBL?

My role developed significantly during my time here: I began as Dean of Graduate Studies and went on to become responsible for all internal training activities at EMBL. Meeting the diverse needs of a huge variety of stakeholders was a great challenge, one that provided me with a constant source of inspiration. The experiences and skill set I developed throughout my career before EMBL prepared me well for this role and I greatly enjoyed adding a dimension of strategic planning for tertiary education across Europe, as well as building up EMBL's Internal Training Team. I further improved my leadership skills and I was fortunate to work with an outstanding team and great colleagues within the EMBL

"EMBL was a very special time in my life, and my advice to all who are here, present and future: carpe diem!"

International Centre for Advanced Training (EICAT) and across all EMBL sites. The people are what make EMBL great and I have learned a lot from the different worlds I have worked so closely with during my time here. Our team is a bit like a connector – in touch with everybody at the institute, linking people across departments, sites and countries. It is something I have enjoyed tremendously.

What do you regard as your biggest achievement while at EMBL?

There are so many fulfilling things that spring to my mind. But if I have to pick two, they would be: working with EMBL's administration to include fellows in social and pension benefit schemes and the development of the EMBL Interdisciplinary Postdoc Programme (EIPOD). The EIPOD programme embodies the EMBL spirit: enabling young researchers to work between groups and units on highly collaborative and interdisciplinary projects. Behind the scenes, my team worked very hard in growing this, driving two successful applications for co-funding from the European Commission's Marie Skłodowska-Curie initiative. Our most recent application, in 2014, sits firmly in my mind: we worked day and night for many weeks to develop a very innovative proposal. It was worth it: the Commission graded the application very highly and we secured funding for EIPOD postdocs for the next five years. It includes scope not only for interdisciplinary projects for postdocs between groups and units at EMBL, but also for fellows to collaborate with external partners in industry and academia. With this award, we were also able to appoint a dedicated career development advisor.

What are your best memories of EMBL?

I had a lot of personal high points at EMBL. In particular, my role has involved mentoring and coaching, one of the aspects I find most rewarding. The positive feedback I have received from students and supervisors over the years made me realise that our team was making a difference at EMBL. Another highlight was the evolution of the graduation ceremonies for our PhD students. Each year the event marks the culmination of many years of blood, sweat, tears and success that ultimately result in a highly respected doctorate. Every single ceremony had its own memorable touch with a terrific atmosphere in the auditorium, proud parents in attendance, personal stories told and celebrations carrying on until the early hours. Hearing what alumni have gone on to achieve after leaving EMBL is another highlight – it is great when people check in and let me know the incredible adventures they have been on after leaving EMBL. Finally, I have also had my best 'cloning' experience here at EMBL – my daughter Charlotte. It was a great experience to combine parenthood with my EMBL role and I think EMBL was the perfect place to do that. I have very few regrets from my time here, but perhaps the main one is that I still can't speak proper Italian, despite many coffees, lunches and other events with Italian colleagues!

And what now?

The finer details of my new role are yet to be defined – in many respects it is an open book, much like when I started at EMBL. As Director of the Graduate Academy at the University of Heidelberg, I will be working with all of the 12 diverse faculties. I look forward to staying in close contact with colleagues at EMBL – I am not going far! – and seeing the lab continuing to develop. EMBL was a very special time in my life, and my advice to all who are here, present and future: carpe diem!

PHOTO: UNIVERSITY OF COPENHAGEN

Janet Thornton receiving her honorary doctorate from the dean of the University of Copenhagen, Ulla Wewer

Awards & Honours

Dame Janet Thornton, senior researcher and former director of EMBL-EBI, has received an honorary doctorate from the University of Copenhagen in recognition of her influence on the development of bioinformatics in Denmark and globally. Dame Janet received the award at the University's annual reception, which was attended by the Queen of Denmark.

EMBL Director **Matthias Hentze** received the 2016 Heidelberg Molecular Life Sciences Investigator Award in December last year. The €100 000 prize is awarded to outstanding scientists who are actively engaged in life science research in Heidelberg.

Martin Beck and **Jonas Ries** have both been awarded a European Research Council (ERC) consolidator grant. The ERC celebrated its 10-year anniversary in March. Visit news.embl.de/tag/futures for more on the work of EMBL's many ERC grantees.

Welcome to EMBL

We meet two new EMBL group leaders; Robert Prevedel and Wojciech Galej

BY ADAM GRISTWOOD AND MARGAUX PHARES

Both Robert Prevedel and Wojciech Galej recently joined EMBL. While the two new group leaders have different research focuses, they are both looking at the small but complex worlds of molecular life. At EMBL's Heidelberg site, Prevedel is developing deep-tissue microscopy so that scientists can peer deep inside living organisms and better understand how they work. And from his lab overlooking the Chartreuse Mountains at EMBL's Grenoble site, Galej will use state-of-the-art methods in structural biology and biochemistry to investigate the structure of large RNA-protein complexes.

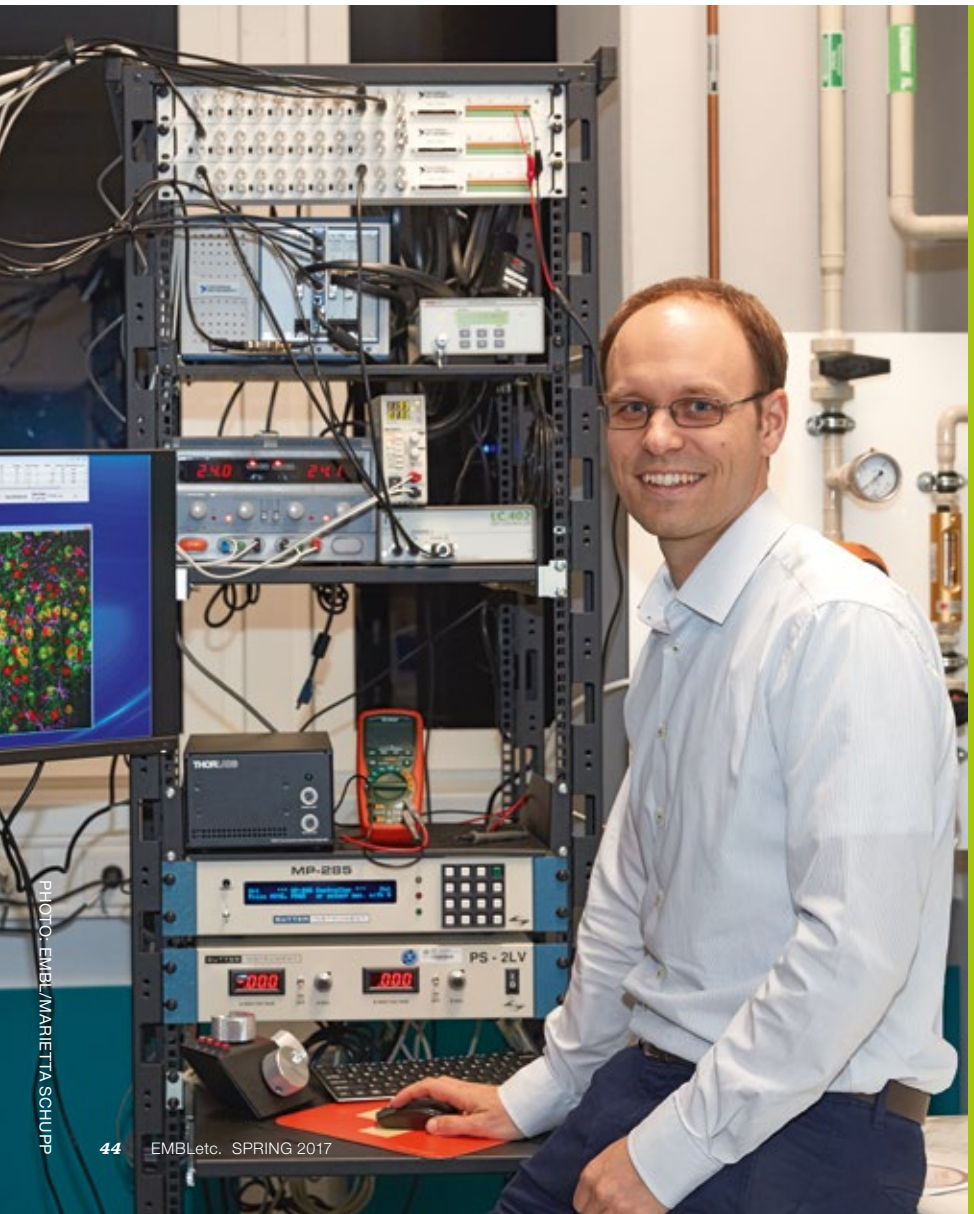


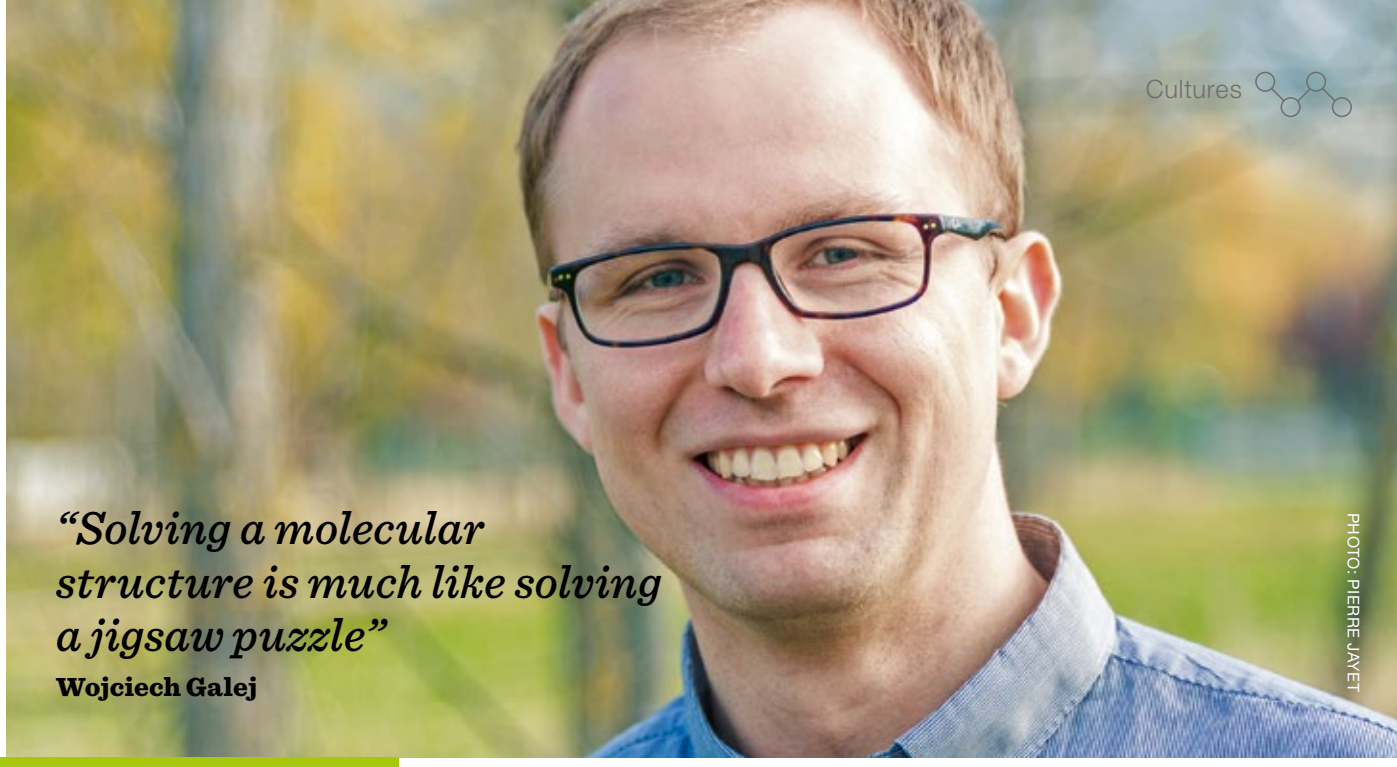
PHOTO: EMBL/MARIETTA SCHUPP

"I moved into biological imaging because I love light!"

Robert Prevedel

Optical telescopes allow us to see many light-years away, yet we struggle to see within matter right here at our fingertips. Our atmosphere is almost transparent, but when light interacts with thick biological tissue, light scattering leads to blurry, low-resolution images. You can see this effect if you put a flashlight against the palm of your hand – you cannot see through it, but you see a glow.

My group uses a range of techniques to try to overcome this problem, including multi-photon microscopy, adaptive optics, computational imaging and optical engineering – technologies that can enable us to see deep inside living tissues without the blur. Adaptive optics, for instance, enables us to bend light



"Solving a molecular structure is much like solving a jigsaw puzzle"

Wojciech Galej

PHOTO: PIERRE JAYET

rays so that they come together at a single point to create a perfect focus – something that, for example, enables the imaging of individual cells or neurons deep in the brain.

Impact of imaging

I moved into biological imaging because I love light! During my postdoc I started a project using quantum imaging: we generated single photon states to probe very simple biological samples with higher resolution – in our case we imaged onion skin. It worked well, but it was merely a proof of principle: I realised we cannot take these ideas and build a practical microscope at the moment. Biological imaging, however, is a field where my work could have a much more immediate impact. The connection of research to society has always been important to me: the microscopes developed by my team play a small, but hopefully important role in understanding questions of great relevance.

FULL INTERVIEW ONLINE:
NEWS.EMBL.DE/?p=8356

The structure of biological molecules plays a major role in determining their function. My group uses structural biology methods to study the molecular bricks that, when assembled, form the basis of one of the most complex yet fundamental cellular machines: the spliceosome.

The first step of gene expression is a process called transcription. Eukaryotic genes are transcribed into pre-messenger RNA. This pre-mRNA is punctuated by regions that code for proteins – exons – and regions that do not code for proteins – introns. The spliceosome acts like a molecular editor: it cuts out the introns and pieces the exons back together. This process creates a molecular blueprint for making a protein.

Switching focus

I was quite a keen experimentalist as a youngster, and I had a little chemistry lab at home. Initially this was more of a hobby than something I saw turning into a career. But while I was initially intending to pursue a career in medicine – like my father and my brother – these early experiments and some inspiring teachers I met along the way had a profound impact on me. I switched my focus to experimental science. It's been a challenging and very rewarding career path, and I have never looked back!

Joy of discovery

In every structural biology experiment there is that moment of seeing your structure for the first time. It is an amazing feeling to be the only person in the world to know something that others don't. I have to confess that sometimes I like to prolong that moment by not telling my colleagues straight away!

The process of solving a molecular structure is much like solving a jigsaw puzzle. The only difference is that while we know what the pieces look like, we don't really know the final image we are aiming to put together – and the pieces often don't fit together perfectly. So sometimes we need to extrapolate and be creative to understand what the protein looks like and investigate its function.

FULL INTERVIEW ONLINE:
NEWS.EMBL.DE/?p=9048

Alumni

For the future

PHOTO: EMBL

This edition of EMBLetc features how alumni are changing the life science landscape globally (page 26). We share the outcome of the 28th Alumni Association board meeting (right) and interview one board member about his transition from science to business and from Europe to the US (page 48). We also announce this year's winners of the John Kendrew and Lennart Philipson Awards (below) – please mark your diaries to join us at the ceremony on EMBL Lab Day, 21 July. Finally, 2017 marks 100 years since the birth of Sir John Kendrew, EMBL's first Director-General (24 March 1917–23 August 1997) – see page 37.

Mehrnoosh Rayner
Head of Alumni Relations

For a full list of 2017 alumni events, see the back page of this edition.

Alumni award winners chosen

At the recent Alumni board meeting in Monterotondo the John Kendrew and Lennart Philipson Award winners for 2017 were announced.
And the winners are...

John Kendrew Award winner 2017:

Philipp Keller (Heidelberg 2005-2010)

Former EMBL Cell Biology and Biophysics PhD student, Philipp Keller (2005-2010), has been selected as this year's John Kendrew Young Scientist Award winner for ground-breaking work on light-sheet microscopy and computational technologies that allow whole-animal imaging. Much of the image analysis software and microscope blueprints developed by Philipp and his team are now in the public domain, and the work has granted him an outstanding record of publications in high ranking journals (40 in the past seven years). Philipp, now group leader at the Janelia Research Campus of the Howard Hughes Medical Institute, studies early brain development and function. He has co-organised several conference series that have strengthened bonds between EMBL and Janelia Research Campus, and participates in philanthropic activities for children's science education.

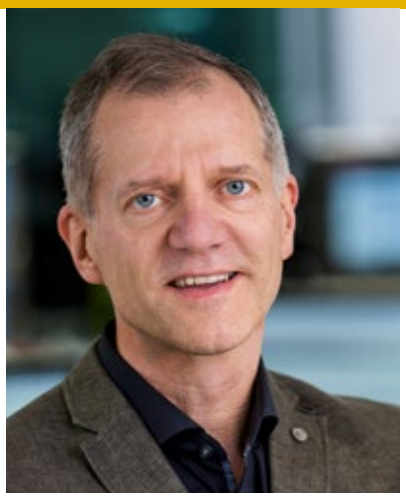
28th EMBL Alumni Association board meeting

On 27 January, staff and alumni gathered at EMBL Monterotondo for the 28th Alumni Association Board Meeting followed by a drinks reception.

L-R: Jamie Hackett, Des Higgins and Cornelius Gross

Key decisions included the selection of award winners (see below) and the recruitment of an EMBL Alumni Volunteer Officer to harness the increasing number of alumni willing to support EMBL with their time and expertise.

Matthias Hentze, EMBL Director, presented an update of EMBL activities and Phil Avner, Head of EMBL Monterotondo, thanked alumni for their help in strengthening the site's support base with scientists and institutes throughout Italy.



Lennart Philipson Award winner 2017: Matthias Mann (Heidelberg 1992-1998)

A former group leader in EMBL's Biochemical Instrumentation Programme, Matthias has been a pioneer in the field of proteomics. His contributions include the 'peptide sequence tag' approach which allows proteins to be computationally identified by the fragment spectra, methods for analysing proteins after extracting them from 2D gels, and nanoelectrospray techniques which allow minute quantities of protein to be sequenced. Since 2005 Matthias has been director of the Department of Proteomics and Signal Transduction at the Max Planck Institute for Biochemistry in Munich where his group develops and applies methods of mass spectrometry based proteomics in a variety of biological areas. He is also programme director of the clinical proteomics group of the Novo Nordisk Foundation Center for Protein Research at the University of Copenhagen.

EMBL.DE/ABOUTUS/ALUMNI/ALUMNI-AWARDS/INDEX.HTML

Alumni obituaries

We are sad to announce that the following Alumni have recently passed away

Riccardo Cortese (Heidelberg 1979-1990)

Tobias Doerks (Heidelberg 1998-2014)

Katrin Eichelbaum (Heidelberg 2008-2013)

Bernd Fischer (Heidelberg and EMBL-EBI 2008-2014)

Jörg Langowski (Grenoble 1985-1994)

Konrad Müller (Heidelberg 1975-1995)

Anna Tramontano (Heidelberg 1988-1991)

FULL ARTICLES ONLINE: EMBL.ORG/ALUMNI/OBITUARIES

Pathways:

Life science investment

A PhD doesn't always mean a life in the lab. EMBL alumnus Joep Muijrers talks about making the transition from science into business

BY EDWARD DADSWELL

"I came out of the lab and all of a sudden I was responsible for business development," says Joep Muijrers. Muijrers is a former PhD student at EMBL's Heidelberg site and now an investor in life science companies. "You find yourself in the middle of it and you learn as you go."

Jumping into a situation and teaching yourself what you need is something that many scientists will be familiar with. It's easy to think of science and business as separate worlds, but Muijrers points to many skills that are common to both. The people who are most successful in making the transition, he says, are those who are "very open-minded. Who understand that there's a lot

of things they don't know yet, and who don't mind a challenge." And in business, as in science, you have to put in the hours – "but there's no way I would need to tell anyone at EMBL that!"

"There's a lot of collective expertise in the alumni network"

Muijrers came to EMBL in 1997. The subject of his thesis was ET recombination – a method for editing specific sections of DNA. It was more efficient than other techniques available at the time and made it possible to work with longer DNA sequences. In 2000, a group of four – including Muijrers and his supervisor Francis Stewart – founded EMBL spinoff Gene Bridges, a company focused on DNA recombineering. Muijrers became Director of Business Development.

PHOTO: LIFE SCIENCES PARTNERS

EMBL alumnus Joep Muijrers

Taking things forward

Eager to increase his financial knowledge, Muijrers moved to an investment bank and now works at Life Sciences Partners (LSP). LSP is one of the largest investment groups that specialises in medical innovation companies. The company manages funds for a mix of private individuals and larger institutions. Muijrers' area of expertise is investing in listed companies. He recently moved to LSP's offices in Boston, US. The Boston area, he says, is an exceptional place for biological research. "Europe is a very good area for innovative science and there are some very good companies there," he explains. "But arguably there are not that many places like Boston as an ecosystem for life sciences and biotech. I haven't been here a long time but what I've seen so far is quite amazing."

His life now may be very different to that of a PhD student in Heidelberg, but Muijrers is clear about what he's gained from his time at EMBL. "It's much easier to have a background in molecular biology," he says, "rather than trying to master molecular biology as an economist." Having worked in research himself, Muijrers says he's also better able to understand the companies he's looking to invest in. "Any company I see will tell me everything is great. Everything is going to plan. Their science is fantastic and their products are fantastic – yeah, right! It never happens that way and that's something you know if you've spent some time in a lab."

Giving back

Muijrers' broad experience was also one of the reasons he was keen to get involved in the EMBL Alumni Association. He's spent the last five years as a board member, and played a major role in securing sponsorship for EMBL's 40th Anniversary Reunion in 2014. "I felt, if you really enjoyed your time so much at EMBL and feel you can add something that might be of value, then why not?" he tells me. Muijrers knows it's not always easy for scientists to make contact with investors. This is one of the reasons he's planning a new industry event at EMBL, starting in 2018. He's also happy to talk to EMBL alumni and make introductions where he can. He emphasises that it's a two-way street: as an investor, he benefits from the contacts he's made via the alumni network. "There's a lot of collective expertise there," he says, "and anyone is invited to tap into that."

PHOTO: EMBL

EMBL in pictures

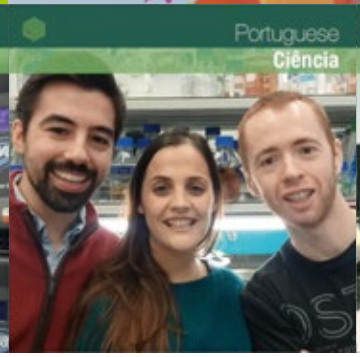
2017 got off to a snowy start in Heidelberg

PHOTO: EMBL-EBI

The annual European Learning Laboratory for the Life Sciences Insight Lecture was delivered by EMBL-EBI Director Ewan Birney to nearly 100 schoolchildren in Hinxton (and streamed to more worldwide)

PHOTO: ROBERT SLOWLEY

Researcher Amelie Baud marks her birthplace on EMBL-EBI's world map. Pink dots represent the places where staff members were born, while yellow dots mark the places they've lived for more than six months – online version coming soon!



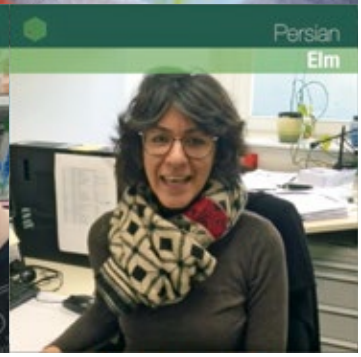


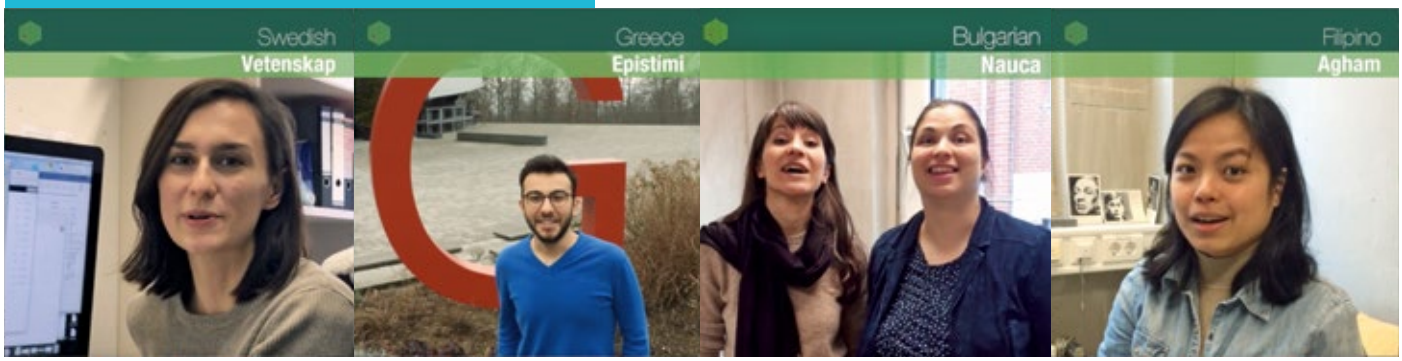
PHOTO: WÜRTH GROUP

Business and science - inspiring each other: thanks to the Würth Group for hosting some of our young scientists for a two-day symposium with Würth scientists

Congratulations to the newly-graduated EMBL PhD class of 2016

PHOTO: EMBL

Learning languages: EMBLers shared how they say 'science' with the world, to celebrate our international diversity



Events

May
18

EMBL Heidelberg
Karlstorbahnhof Heidelberg
EMBL Science Movie Night:
The Matrix

June
9

EMBL Hamburg
EMBL Forum Lecture:
Do microbes control the mind? Issues in brain, gut and microbiota research
Maureen O'Malley,
University of Bordeaux

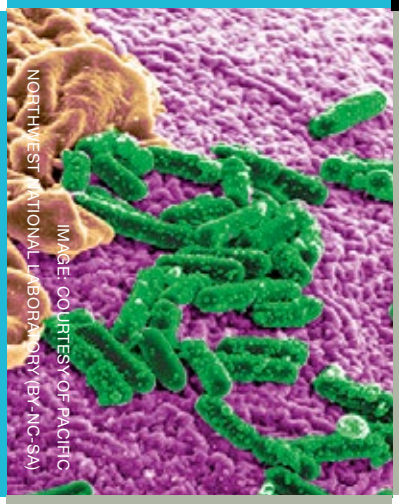


IMAGE: COURTESY OF PACIFIC NORTHWEST NATIONAL LABORATORY (BY-NC-SA)

June
12-23

EMBL Monterotondo
Summer in Science:
International Summer School for students

July
3-7

EMBL-EBI Hinxton
BioExcel Summer School:
Foundation Skills for HPC in Computational Biomolecular Research

July
21

EMBL Heidelberg
Lab Day

September
13-16

EMBL Heidelberg
EMBO | EMBL Symposium:
The Non-Coding Genome

Upcoming meetings
Alumni

22 May
EMBL in the UK, Oxford University

9 June
EMBL in France, Institut Européen de Chimie Biologie, Bordeaux

9 June
EMBL in Australia, Garvan Institute of Medical Research, Sydney

21 July
Alumni Board Meeting, EMBL Heidelberg

21 July
Alumni Awards @ Lab Day, EMBL Heidelberg

29 September
EMBL in Norway, Oslo University

3-5 November
EMBL in the USA, Beauport Hotel, Gloucester, MA

VIEW THE COMPLETE LIST OF EVENTS ONLINE: EMBL.ORG/EVENTS