

The European Molecular Biology Laboratory Magazine

Issue 94 Winter 2019/20

EMBL

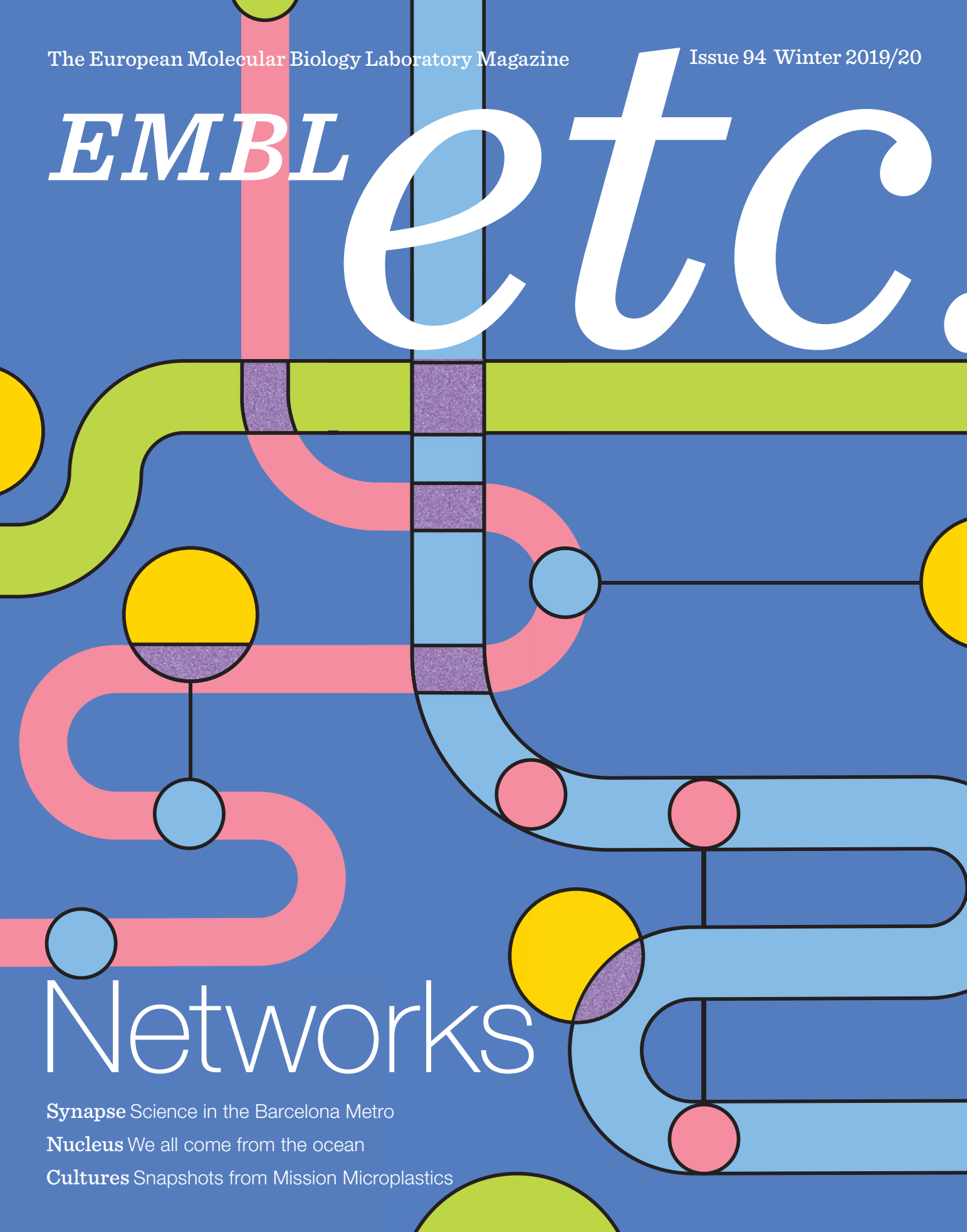
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Networks

Synapse Science in the Barcelona Metro

Nucleus We all come from the ocean

Cultures Snapshots from Mission Microplastics



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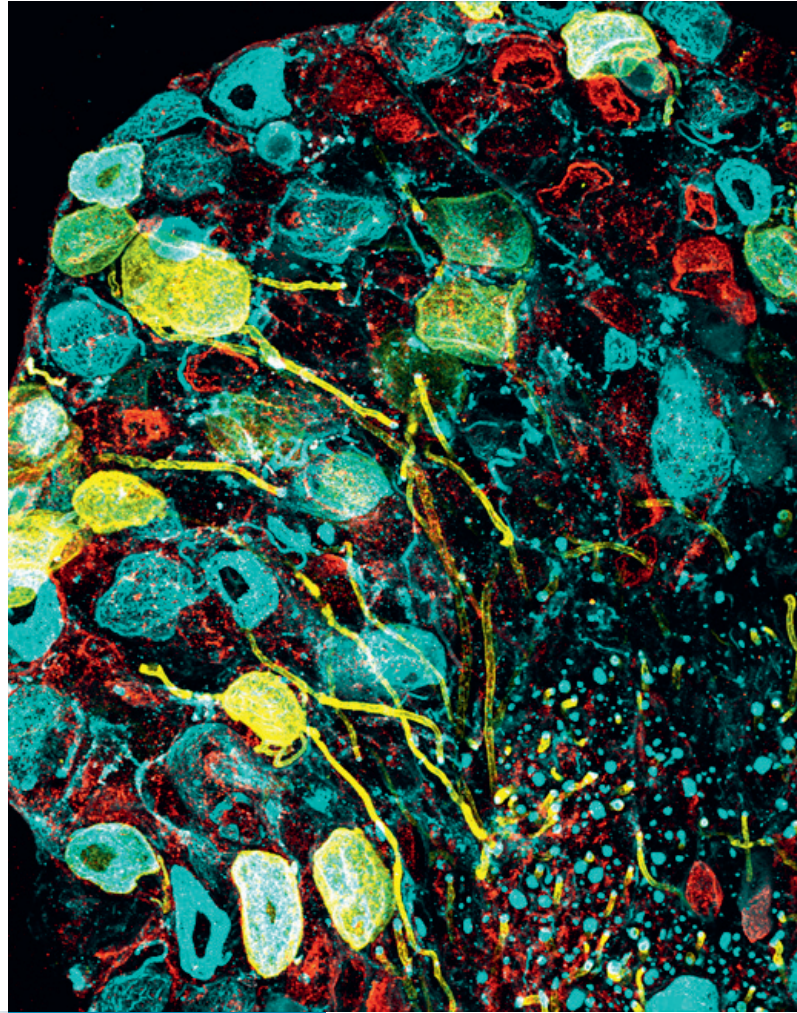


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We all come from the ocean

Eric Karsenti's dream of combining his loves of biology and sailing set in motion the Tara Oceans expedition



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Editorial

Research in biology reveals a multitude of networks. In this issue, we explore the elaborate networks of neurons that make up the brain and nervous system (p. 14), and report on a new microscope, developed at EMBL, that scientists hope to use in studying the dynamics of neuronal networks (p. 7). At EMBL-EBI, scientists are investigating the network of cells and messenger molecules that make up the immune system, which could lead to improved forms of immunotherapy for the treatment of cancer (p. 8).

Networks are vital to the collaborative nature of EMBL research. Eric Karsenti, the EMBL scientist behind the Tara Oceans expedition, discusses the network of collaborators that made his dream possible (p. 20). We report on the first results of an inter-institutional collaboration at the Centre for Structural Systems Biology (CSSB) in Hamburg (p. 10), and on new funding for the EMBL | Stanford Life Science Alliance (p. 11).

This year has also been an opportunity to celebrate EMBL's network of sites. With EMBL Rome marking its 20th anniversary in July (p. 32), the first two heads of EMBL Rome discuss some of the challenges of the site's first years (pp. 34–37). EMBL-EBI had its 25th anniversary celebrations in September (p. 30), and we report on the origins of that site, set up at the time another great network was starting to show its power: the internet (p. 26).

At her inauguration symposium in October, EMBL Director General Edith Heard emphasised the importance of EMBL's network of collaborators and its alumni community (p. 38). We continue this theme as we report on the first EMBL World Alumni Day (p. 42), and highlight EMBL's network of supporters, the Friends of EMBL (p. 47).

We hope this is an issue you will want to share with your network.

Edward Dadswell
Editor

Word to remember Chromatin

Noun

Pronunciation:
/'krɒsmətɪn/

To fit inside your cells, your DNA has to be coiled up and packaged with various proteins. This complex of DNA and protein is called chromatin.

The 3D arrangement of chromatin is thought to play a role in regulating gene expression, although the significance of this role has recently been questioned by EMBL's Furlong group (p. 9). The Noh group is studying the link between changes in chromatin and neurodevelopmental disorders (p. 17).

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Drosophila embryo showing expression patterns of three enhancers that partially overlap, imaged with confocal fluorescence microscopy.

Transcriptional hubs confer phenotypic robustness

Enhancers in *Drosophila* embryos gather to preserve phenotypes under stressful conditions

BY JOSH TAPLEY

As an embryo develops from a group of cells, precise patterns of gene expression determine how these cells differentiate into various types. These patterns are controlled by regions of DNA called enhancers, which are bound by molecules known as transcription factors.

Scientists from the Crocker group have previously shown that multiple sections of DNA that contain enhancers for the same gene can gather to form a microenvironment within the cell's nucleus – a transcriptional ‘hub’. These hubs are enriched for enhancers and transcription factors, providing a mechanism to keep the expression of their corresponding gene more consistent and more resistant to the failure of a single enhancer.

When scientists deleted one enhancer from its original location and inserted it into a different chromosome of the *Drosophila melanogaster* genome, it was able to find its way to the same hub. Their results show that these adaptable transcriptional hubs help preserve the phenotype of an organ developing under environmental stress.

The researchers removed an enhancer connected to the production of hooks known as trichomes on the epidermis of fly larvae. Under normal conditions, no defects were observed, but under the stress of high temperature, embryos developed abnormally low numbers of trichomes.

The researchers then moved the enhancer region to a different chromosome. Despite the high

temperature, the embryos developed enough trichomes. The region of DNA containing the enhancer had moved to the same hub as the original gene, reinforcing gene expression and preserving the phenotype.

This research provides insight into how embryos are robust to environmental and genetic stresses through cooperative interactions across the genome. Researchers must now ask how this robustness occurs in living embryos. How do these hubs form? What are the necessary components and conditions? This system opens avenues to explore fundamental questions related to gene expression, evolution, and development.

Tsai, A, Alves, MRP, Crocker, J. *eLife*, 11 July 2019. DOI: 10.7554/eLife.45325

MEG3 kissing loops essential for tumour suppression

EMBL scientists reveal the complex structure of a cancer-preventing molecule

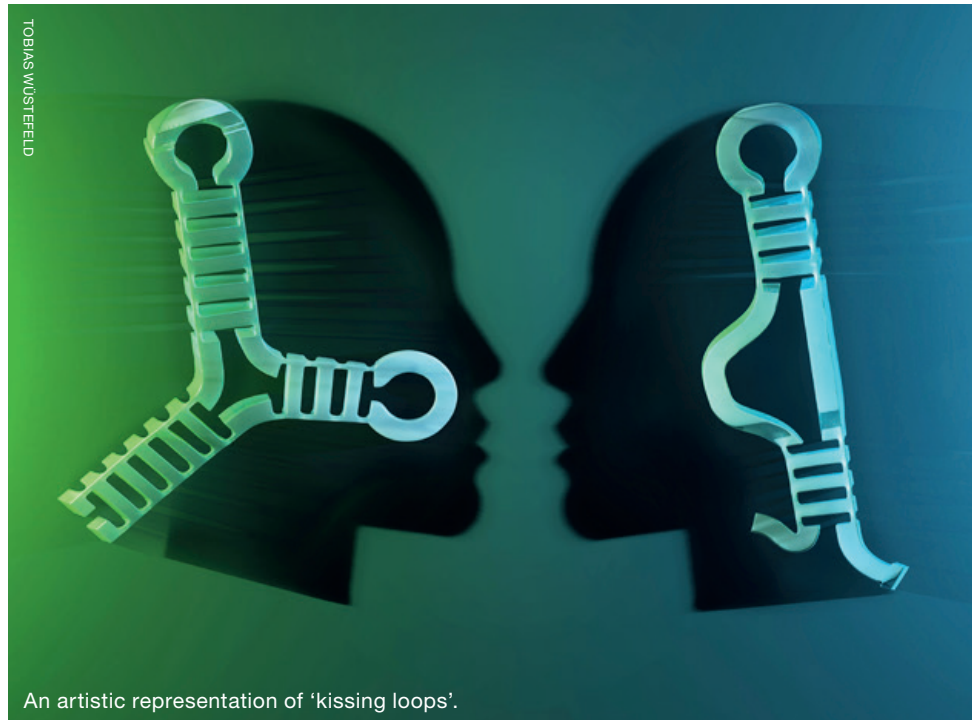
BY DOREEN FEIKE

Human cells – like those of many other organisms – have developed mechanisms to protect us from cancer. Healthy cells produce a suite of molecules that stop harmful mutations from accumulating. Researchers in the Marcia group at EMBL Grenoble have discovered that the cancer-preventing molecule MEG3 adopts a complex three-dimensional structure to fulfil its function. The group systematically removed and modified the building blocks of MEG3 to find out which of them are essential for its functionality. This

way, the researchers discovered two elements that are more important than others for the molecule's function as a tumour suppressor. These elements form hairpin structures that biologists call 'kissing loops'. When these kissing loops were disrupted by manipulating the building blocks

of MEG3, the tumour suppression function of MEG3 was also disrupted. The results of this study could help to advance diagnosis and treatment of certain types of cancer.

Uroda, T *et al.* *Molecular Cell*, 20 August 2019. DOI: 10.1016/j.molcel.2019.07.025



An artistic representation of 'kissing loops'.

A tRNA modifier at work

Cryo-EM reveals the structure of a piece of cellular machinery with important medical implications

BY CELLA CARR

All living cells employ ribosomes and transfer RNA (tRNA) molecules to decode messenger RNA sequences and translate the genetic information into correctly

assembled and functional proteins. It's crucial to produce these proteins at the right speed to avoid protein misfolding and aggregation within cells. The modification of tRNA molecules by specialised enzymes is one way to regulate the production speed to the correct pace.

Scientists from the Müller and Kosinski groups and collaborators have managed to catch a crucial component of the tRNA modification machinery at work. Using cryo-electron microscopy, they determined the structure

of a large protein complex called Elongator.

Mutations in the six subunits of Elongator are associated with the onset of human diseases, including obesity, asthma, intellectual disability, Rolandic epilepsy, and cancer. Thus, its potential as a drug target is ripe for exploration. These results provide insight into one of the key mechanisms in ribosome-mediated protein synthesis.

Dauden, MI *et al.* *Science Advances*, 10 July 2019. DOI: 10.1126/sciadv.aaw2326



Breaking the bottleneck in imaging data collection

Scientists develop software tools for automated acquisition of electron microscopy data

BY CELLA CARR

There's a growing demand for high-throughput data acquisition in structural and cell biology research. Developments in microscopy hardware and computing performance have increased the speed and quality of transmission electron microscopy (TEM) but, until now, scientists had to manually select the features to be imaged, and identify their precise coordinates. This is a time-consuming task that creates a bottleneck in data acquisition.

Martin Schorb, Application Engineer in EMBL's Electron Microscopy Core Facility, and colleagues have developed software tools – SerialEM and py-EM – that allow automated acquisition of electron microscopy data. Users no longer need to define discrete positions on an object for data acquisition. Instead, they define whole target objects, such as cells or distinct tissue features, and the tools create automated feedback TEM workflows for these objects.

The software opens up new possibilities for TEM applications, and significantly increases throughput in structural analyses of molecular complexes using cryo-electron microscopy.

Schorb, M *et al.* *Nature Methods*, 13 May 2019. DOI: 10.1038/s41592-019-0396-9

New 3D microscope

A newly developed 3D microscope visualises fast biological processes better than ever

BY MATHIAS JÄGER

Capturing fast processes in high resolution and in 3D is a challenge in biology. EMBL's Hufnagel and Prevedel groups have developed a new light-field microscopy system that creates up to 200 3D images per second.

To demonstrate the capabilities of the new technique, the team studied the beating heart and blood flow in medaka – Japanese rice fish – in real time. The images showed for the first time how individual blood cells move through the two heart chambers. The technology can be used to research heart defects, showing how genetic backgrounds or mutations affect the dynamics of heartbeats.

This illustration, based on real data, shows the heart of a Japanese rice fish. The green and blue laser beams demonstrate how the newly developed 3D imaging microscope is scanning the heart.

The study on the medaka heart was only the first test. The scientists are looking forward to using the microscope to study the activity and dynamics of neuronal cell populations in these animals, and anticipate that future developments will make it an attractive tool to study the dynamics within small neuronal networks.

Wagner, N, Norlin, N *et al.* *Nature Methods*, 29 April 2019. DOI: 10.1038/s41592-019-0393-z

TOBIAS WÜSTEFELD

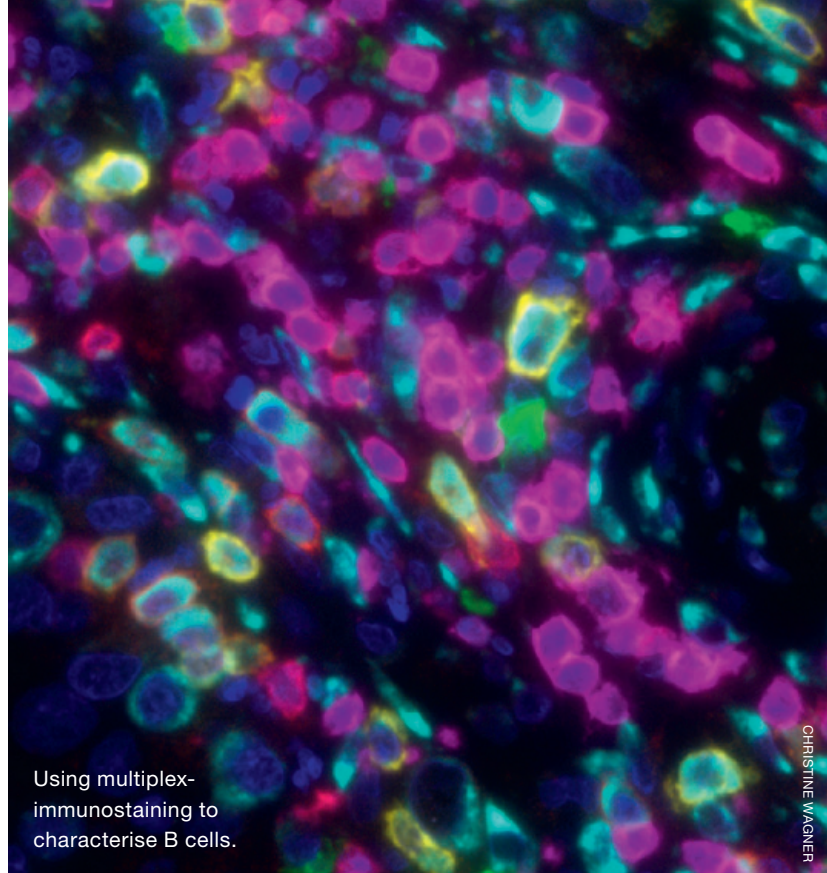
B cells linked to immunotherapy

Researchers find evidence that B cells may be more important in immunotherapy than previously thought

BY OANA STROE

Immunotherapy is a form of cancer treatment that uses the body's own immune system to recognise and fight the disease. It comes in a variety of forms, including cancer vaccines, targeted antibodies or tumour-infecting viruses. Only some cancer patients currently benefit from this kind of therapy.

Researchers at EMBL-EBI and the Medical University of Vienna have found that B cells might play an important role in immunotherapy for a particularly aggressive form of skin cancer called melanoma. Currently, immunotherapies for melanoma focus on T cells, but the results



Using multiplex-immunostaining to characterise B cells.

CHRISTINE WAGNER

suggest that B cells could provide an interesting research avenue.

B cells play a critical role in triggering melanoma-associated inflammation. A type of white blood cell, they can produce antibodies along with several important messenger molecules. The

researchers found that, in the case of melanoma, B cells direct T cells to the tumour via the secretion of such distinct messenger molecules.

Griss, J *et al. Nature Communications*, 13 September 2019. DOI: 10.1038/s41467-019-12160-2

Understanding molecular mechanisms of ageing

Researchers use epigenetic clock to identify gene linked to ageing in humans

BY OANA STROE

Researchers at EMBL's European Bioinformatics Institute (EMBL-EBI), the Babraham Institute and collaborators have used the epigenetic clock to explore the molecular mechanisms that may drive ageing in humans. The epigenetic clock is a mathematical

model that predicts an organism's biological age – a measure of how well it's functioning on a molecular level – by measuring DNA methylation levels in different sites across the genome.

The researchers examined different datasets – many of them publicly available – of people with developmental disorders, to see whether there were any associations between specific genes and an acceleration of biological age. They found that individuals with a mutation in gene *NSD1* had an

accelerated biological age according to the epigenetic clock, meaning they were ageing faster at a molecular level.

By comparing biological age with chronological age in different tissues, scientists can gain insights into how ageing is linked to cancer, obesity, Alzheimer's disease and other conditions.

Martín-Herranz, DE *et al. Genome Biology*, 14 August 2019. DOI: 10.1186/s13059-019-1753-9

Rearranging chromosomes

Does rearranging chromosomes affect their function? EMBL scientists reveal uncoupling of 3D chromatin organisation and gene expression

BY IRIS KRUIJEN

Molecular biologists long thought that domains in the genome's 3D organisation control how genes are expressed. However, after studying highly rearranged mutant chromosomes in the fruit fly, researchers at EMBL are now questioning the generality of this dogma. Their findings reveal an

uncoupling between the 3D genome organisation – also called chromatin topology – and gene expression.

Our chromosomes are compartmentalised into domains. Regulatory regions of the DNA that control gene expression – so-called enhancers – are often located in the same chromatin domains (called topologically associated domains)

as their target genes. To date, there are a number of interesting examples where domains restrict the activity of enhancers to only the genes within their domain.

The researchers found that changes in chromatin domains were not predictive of changes in gene expression. This means that, besides domains, there must be other mechanisms that control the specificity of interactions between enhancers and their target genes.

Ghavi-Helm, Y, Jankowski, A, Meiers, S *et al. Nature Genetics*, 15 July 2019. DOI: 10.1038/s41588-019-0462-3

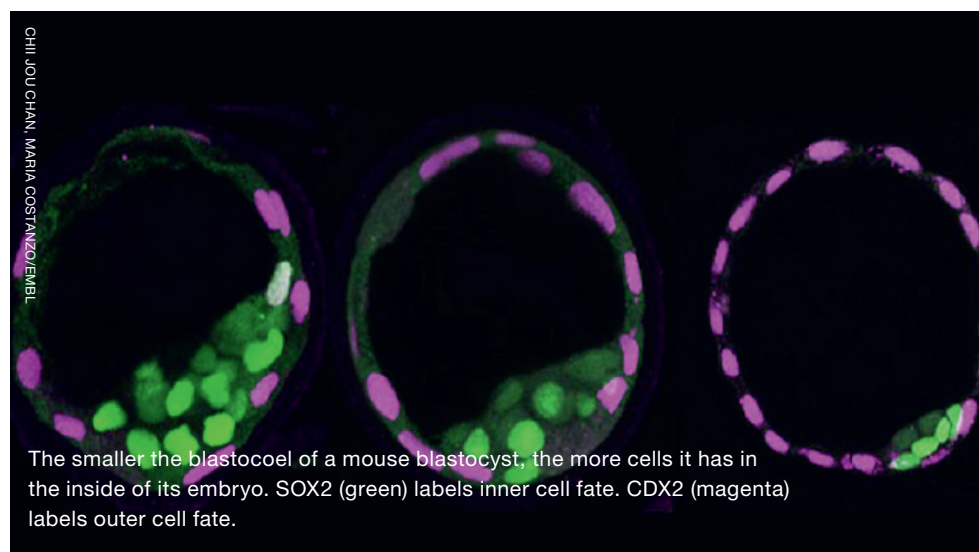
Hydraulic force shapes mammalian embryos

EMBL researchers uncover new role of fluid pressure in controlling embryo size and cell fate

BY JOSH TAPLEY

Fluid pressure in the blastocoel of an early mouse embryo plays an important role in controlling the embryo's size and determining the fate of its cells, according to researchers from EMBL and Harvard University.

As the fluid pressure increases, it causes increased mechanical stress in the surrounding trophoblast cells. This triggers an active recruitment of junctional proteins to seal the junctions between adjacent cells. This mechanosensing mechanism allows the blastocyst to continue to grow.



However, when the cellular tension reaches a critical threshold, these proteins can no longer maintain adhesion between cells during cell division. Fluid begins to leak through the junctions in a process known as 'blastocyst collapse'. This pressure decrease causes the junctions to seal again and the whole

process is repeated. Thus the size of a mature blastocyst oscillates about a certain point – a process described by a theoretical model developed in collaboration with physicists from Harvard.

Chan, CJ *et al. Nature*, 12 June 2019. DOI: 10.1038/s41586-019-1309-x

First results from CSSB

EMBL scientists collaborate to develop new protocol for screening membrane protein stability

BY FABIAN OSWALD

Six research groups, including two from EMBL Hamburg, have developed a protocol that will simplify the process of solubilising integral membrane proteins

(IMPs). The protocol allows the identification of suitable conditions for membrane proteins during purification, and is the first result of a collaboration at the Centre for Structural Systems Biology (CSSB) in Hamburg.

EMBL team leader Maria Garcia Alai and collaborators showed that it's possible to measure the stability and solubility of IMPs by diluting them into different detergents. The result was a protocol that allows the identification of suitable conditions for membrane proteins during purification.

Kotov, V *et al. Scientific Reports*, 17 July 2019. DOI: 10.1038/s41598-019-46686-8

Sex and diet affect proteotype

Scientists from EMBL Heidelberg have discovered that the collection of proteins in an animal cell – called the proteome – is substantially affected by both the animal's sex and its diet

BY MATHIAS JÄGER

Researchers from EMBL and collaborators have analysed 11 large public datasets containing detailed information on proteotypes in humans and mice, as well as on their diet and genetic status. The study showed that a higher than expected proportion – around 12% – of proteotype variation is determined by both sex and diet.

This study provides a major stepping stone in understanding which cellular alterations in an individual with a disease can potentially be reversed by lifestyle changes. Understanding individual proteomes could provide a basis for personalised treatments for humans in the future.

Romanov, N *et al. Cell*, 25 April 2019. DOI: 10.1016/j.cell.2019.03.015

Paving the way for new flu drugs

Snapshots of the flu virus replication machine in action

BY MATHIAS JÄGER

Using X-ray crystallography and cryo-electron microscopy, researchers from the Cusack group at EMBL Grenoble have, for the first time, observed different functional states of the influenza virus polymerase as it is actively transcribing genomic RNA into mRNA.

As the viral polymerase is essential for the replication of the flu virus, it is a prime target for the development of anti-influenza drugs. These results provide valuable information for developing the next generation of these drugs. The advantage of drugs that stop the polymerase functioning is that the virus is less likely to mutate in a way that would render the drug useless.

Kouba, T, Drncová, P, Cusack, S. *Nature Structural & Molecular Biology*, 3 June 2019. DOI: 10.1038/s41594-019-0232-z



The students and organisers of the 2019 EMBL Lautenschläger Summer School.

MARILETTA SCHUPPE/EMBL

Dieter Schwarz Foundation supports Life Science Alliance

Facing the challenges of the 21st century together

BY MATHIAS JÄGER

Representatives from the Dieter Schwarz Foundation have announced funding to EMBL to support its collaborative effort with Stanford University School of Medicine, called the EMBL | Stanford Life Science Alliance. With this funding, the Alliance will work to create interdisciplinary, cross-border scientific cooperation that aims to address scientific opportunities and challenges in the fields of genomics, computational biology, biological imaging, and structural biology.

The Alliance will promote inter-institutional collaboration with a joint postdoctoral fellowship programme and a researcher exchange programme. In addition, joint events will help bring together the wider life science community to encourage networking and the sharing of new ideas.

“The Alliance builds on a number of longstanding collaborations,” says EMBL Director General Edith Heard. “Being able to tap into two world-leading institutions that are doing biological research and that have extensive networks provides a great opportunity to bring together researchers from different fields. The Alliance will also support and promote the global exchange of knowledge and technology.”

EMBL Lautenschläger Summer School success

Visualising life in an interdisciplinary research environment

BY CELLA CARR

The EMBL Lautenschläger Summer School was established to inspire students from fields such as physics, maths, engineering and computer science to pursue interdisciplinary research in the life sciences. The inaugural programme ran from 15–26 July at EMBL Heidelberg, with 20 students from 18 countries, including 13 EMBL member states. The summer school is made possible thanks to a substantial gift from the Manfred Lautenschläger-Stiftung and further generous donations.

Practical sessions during the two-week programme included building compound microscopes and writing

code to extract information from a large dataset of images. The workshops were complemented by lectures and talks by EMBL group leaders, postdocs, and PhD students.

“The students’ engagement and interest in biology were reflected in the deep and challenging questions they asked during the lectures,” says EMBL group leader Aissam Ikmi, one of the summer school’s organisers. “I have no doubt that this initiation into experimental biology will make them more confident about considering a career in biological research. We feel the summer school has been a complete success.”

Science as art in the Barcelona Metro



The mural commemorating the 500th anniversary of the death of Leonardo da Vinci. Ciutadella|Vila Olímpica station, Barcelona.

JAMES SHARPE/EMBL

Striking mural commemorating Leonardo da Vinci brings a touch of inspiration to the daily commute

BY CELLA CARR

“The noblest pleasure is the joy of understanding.” So said Leonardo da Vinci over 500 years ago. Earlier this year, travellers on the Barcelona Metro could experience something of that pleasure in the Ciutadella | Vila Olímpica station, thanks to an art–science initiative of the Barcelona Biomedical Research Park (PRBB).

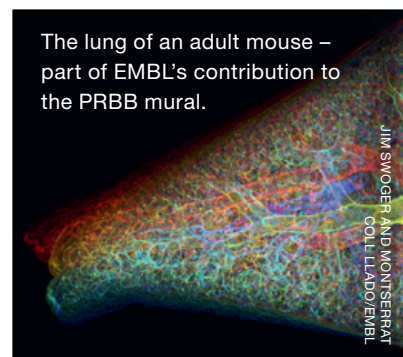
For three months, the station walls were transformed by a mural depicting human biology in all its colourful glory, spanning the scale from macro to micro. Research at EMBL Barcelona – on tissue and organ development – sits somewhere in the middle of this scale, and was represented by captivating images produced at EMBL’s Mesoscopic Imaging Facility.

A glimpse of art and science

Carla Manzanás, Liaison Officer at EMBL Barcelona, explains the background to the exhibition: “This year marks the 500th anniversary of the death of Leonardo da Vinci, and the institutes in the PRBB wanted to do something to commemorate this – to somehow bring together the scientific and artistic parts of da Vinci’s work with what we do here.”

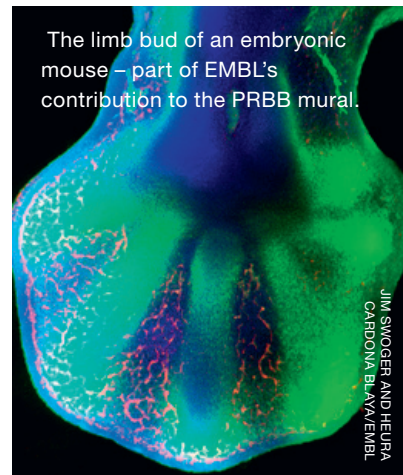
EMBL Barcelona is one of six independent research institutes housed in the PRBB, an architecturally impressive building with an enviable seafront location. It arouses the curiosity of passers-by, but many have no idea what goes on behind the façade of wood and glass. “One of the objectives of the exhibition was to explain what we do in this building,” says Manzanás.

The lung of an adult mouse – part of EMBL’s contribution to the PRBB mural.



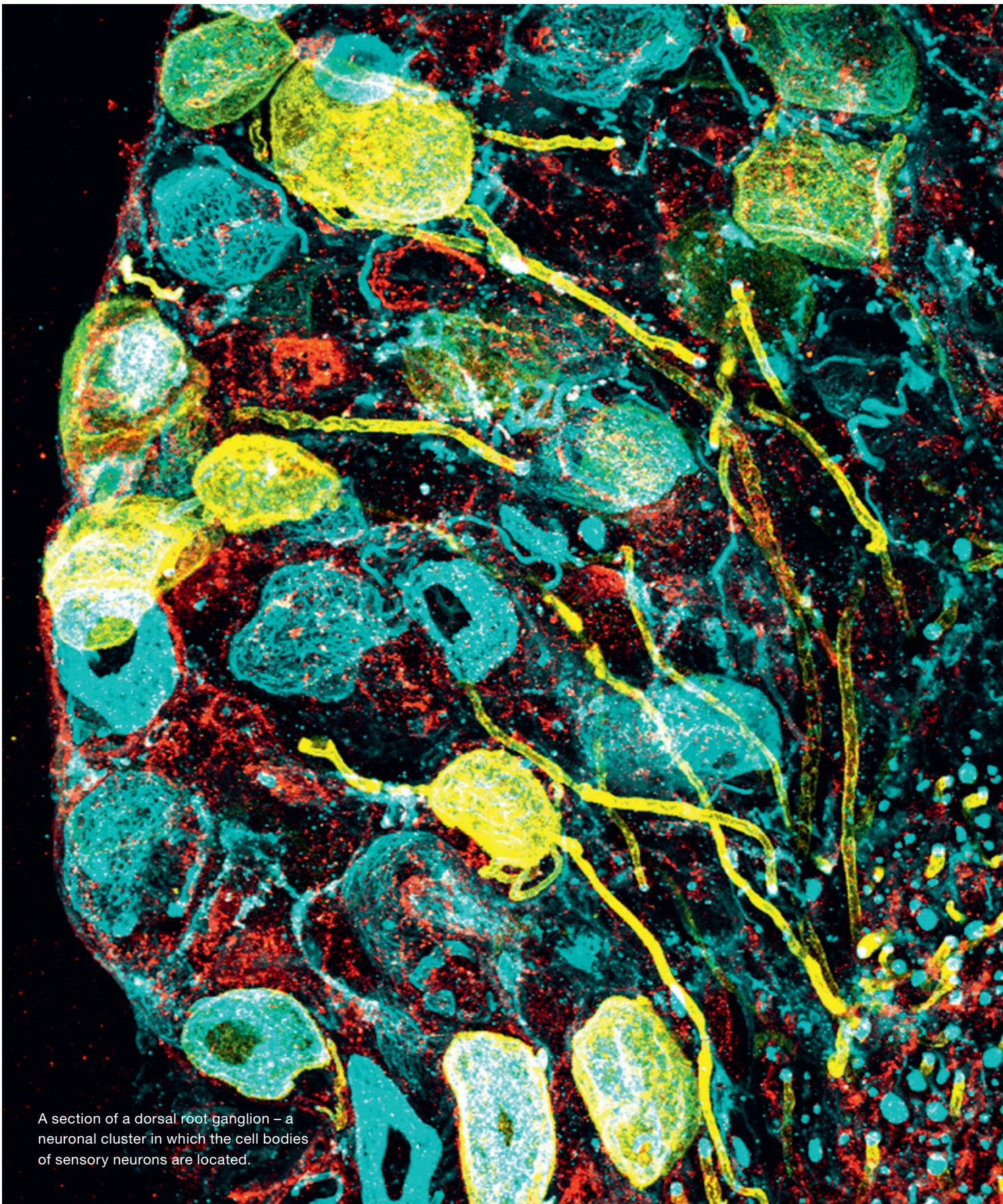
JIM SWOGER AND MONTSERRAT COLL LLADÓ/EMBL

The limb bud of an embryonic mouse – part of EMBL’s contribution to the PRBB mural.



JIM SWOGER AND HEURA CARDONA BLAYA/EMBL

The mural combined images from the life sciences and biomedicine with illustrations from da Vinci and text in Catalan, Spanish and English. “The idea was to have as little text as possible, because if you’re on your way to or from work, you don’t want to stop and read,” says Manzanás. “But just a sentence and an image glimpsed on the way past can make you think.”



A section of a dorsal root ganglion – a neuronal cluster in which the cell bodies of sensory neurons are located.



Neural pathways

Exploring the diverse routes by which EMBL scientists are driving forward neurobiology

BY CELLA CARR

Making sense of the human experience has long been a quest of philosophers and scientists. How do we perceive the world around us? Why do we behave in a certain way in response to a stimulus? How do our neurons organise themselves into circuits and networks to keep our internal supercomputers running at maximum efficiency – and what happens when a bug gets into the operating system? These questions are typical of the conundrums exercising the minds of neurobiologists at EMBL.

Computer brain

“The brain is just too complex!” says Hiroki Asari, group leader at EMBL Rome. He smiles now at the recollection of his “undergrad naivety” as a physics and maths student: “I had this idea that I could simulate the brain using a computer. That was a big motivation for getting into neurobiology.”

Asari was nearing the end of his PhD in systems neuroscience at Cold Spring Harbor Laboratory in the US when a realisation triggered a shift in his focus and methodology: his computer work alone – modelling how the brain processes sound – couldn’t tell him what was actually going on inside the brain. He decided to switch from the auditory to the visual system, to >>

CHIARA MORELLI/EMBL

“When you look at neurons under the microscope, you can’t but fall in love”

explore how the retina converts light signals into electrical neuronal signals – the first stage of sensory processing. “Unless we understand this, we can’t understand the brain,” he says.

Asari now complements his computational work with experimental approaches in the lab, to study how the retina works *in vivo*. “We’re trying to answer a couple of big questions,” he says. “What kinds of signals are the eyes sending to the brain, and how are those signals affected by different internal or behavioural states? If you’re hungry, for example, a cookie looks a lot more attractive than if you’re not.”

Anastasiia Vlasiuk, PhD student in the Asari group, recording the visual responses of an isolated retina.

Mouse brain

Working with mouse models, Asari uses fluorescent proteins to study visual responses to a light stimulus. These proteins – delivered to the neurons via an injected virus – make it possible to tell whether a neuron is active or not. If it’s active, it shines.

But we humans are not mouse-brained. Can Asari’s work tell us anything relevant about our own neural function? “I believe so,” he says. “The organisation of the retinal circuitry is fairly preserved across species, among mammals especially. So we think our basic findings in mice can be applied to humans by understanding the principles underlying neural circuit functions. This is where a computational approach is very useful – we can try to build a model to generalise the function of the retina across different species.”

Threat and response

Cornelius Gross, Asari’s colleague and fellow group leader at EMBL Rome, is also looking to mice to help unravel some of the mysteries of the human condition. His interest lies in behaviour, and in understanding the subtle differences between individuals in how mice – and people – respond to certain stimuli.

“I’ve always been interested in behaviours associated with defence, fear and anxiety – I want to understand how our neural circuits encode and control these behaviours,” says Gross. He’s focusing on the hypothalamus – an old part of the brain, in evolutionary terms – which is associated with some fundamental behaviours, including fear.

As it turns out, there’s not just a single fear circuit in the brain that determines how we respond to threatening stimuli. The *type* of threat matters. Gross has studied two fundamental types of fear: fear of predators, and fear as a response to social threats, such as bullying or aggression. “We found that there are two separate, independent pathways for handling these two types of threat. Even if the final outputs – the fear responses – are the same, they’re encoded by two dedicated circuits in the hypothalamus,” he says. This hadn’t been shown before.

Another finding to emerge from Gross’s work is that there’s also an encoding of space, or territory, when it comes to social interactions. Mice are naturally territorial, and it seems that their awareness of being in a safe place versus being in a threatening place is linked to their neuronal activity. “In other words,” Gross explains, “a place in the brain that was considered to be only social and instinctive



MARIETTA SCHUPPIENIEL



suddenly becomes much more sophisticated – it has a map of your world, of your territory.”

Eat me

A smaller but no less fascinating part of the work in Gross’s lab focuses on microglia. These are cells that are born not in the brain but in the yolk sac – a membrane connected to the embryo in early development. They then migrate into the brain, where – as shown by *in vivo* imaging – they’re continuously moving around. But what are they doing?

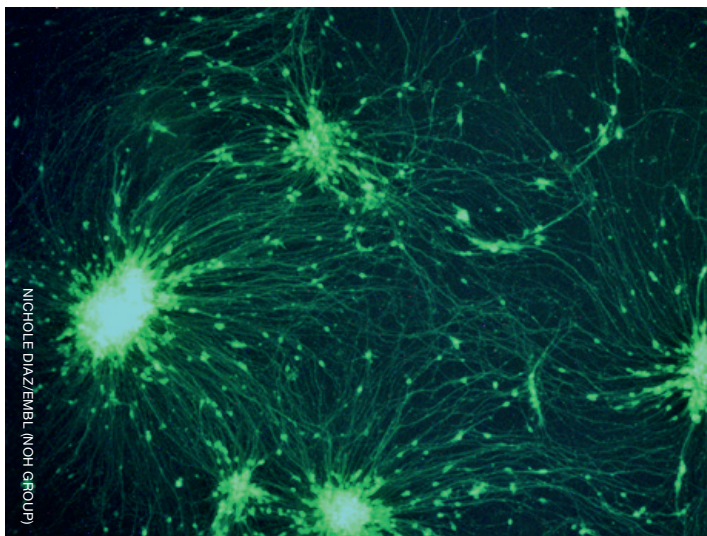
“We don’t really know,” says Gross. “This is a field that’s in its infancy.” What he does know is that during the early period of brain development, when most of the neural connectivity is formed, neurons actively send out signals to microglia. “These microglia have been described as phagocytic: they eat things,” Gross continues. This led him to a hypothesis: the microglia eat synapses – the connections between neurons – that need to be removed for some reason.

Gross and his team subsequently discovered that microglia don’t eat synapses. Not exactly. Rather, they seem to ‘nibble’ parts of synapses and neurons. It’s not yet clear what this nibbling does, but it may promote new contacts between neurons. Also unclear is what determines which neurons get nibbled. “What’s the ‘eat me’ signal?” Gross wonders. “That’s what we want to find out next.”

Beneath the surface

EMBL Rome is a hub for EMBL’s neurobiology research, but scientists at other EMBL sites are also active in the field. Kyung-Min Noh – a group leader at EMBL Heidelberg – broke the mould when she decided to become a scientist, in a family more inclined towards the arts. It’s perhaps unsurprising, then, that it was aesthetics that first lured her into the field of neurobiology. “When you look at neurons under the microscope, you can’t but fall in love,” she says. “They’re beautiful.”

However, Noh soon began to look beyond the morphology of the neuron, to what was going on in the nucleus while neurological pathways were being developed in the brain. She found there was a link between neurodevelopmental disorders and chromatin – the mass of DNA



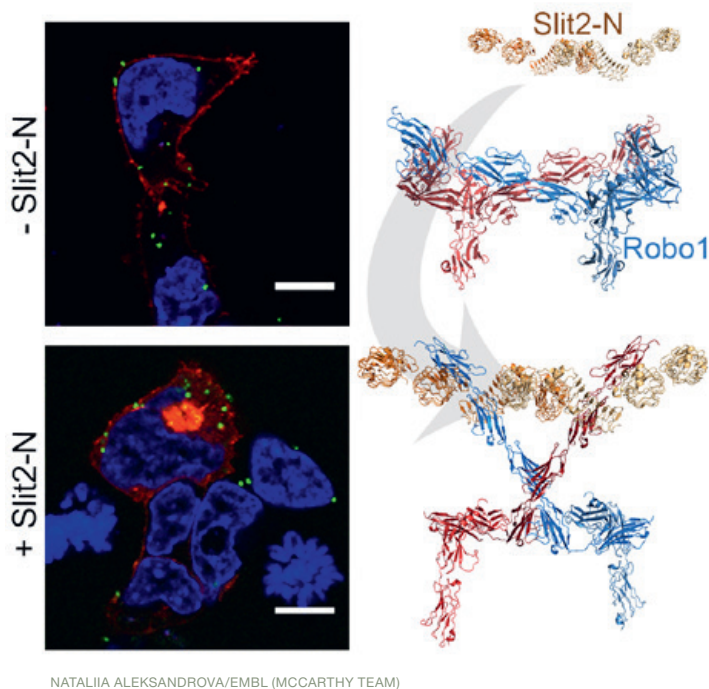
and proteins in the cell nucleus, which plays a role in gene expression. “In the lab, we’re trying to understand how this works mechanistically – the molecular mechanisms that link genetic mutations and changes in gene expression to changes in the chromatin,” she says.

On individuality

One aspect of the research carried out in Noh’s lab focuses on mutations in people with autism spectrum disorders: “We know the genetic mutations happen in the chromatin. They’re all under the umbrella of autism spectrum disorders, but individually they’re very different. We’re trying to understand the differences between these individual molecules, which present behaviourally as autism spectrum disorders. What exactly is happening inside the cells?”

To find out, Noh uses the CRISPR gene editing tool to introduce mutations into mouse cells or human induced pluripotent stem (iPS) cells – cells that are generated from adult cells and can differentiate into many different cell types. She collaborates with fellow Heidelberg group leaders Judith Zaugg and Christoph Müller, working with Zaugg’s group on genomic sequencing and bioinformatic analysis, and with Müller’s group to understand the molecular structure of the chromatin-associated protein complex. “This collaborative effort means that we can apply the state of the art to all aspects of the work,” says Noh. >>

Green fluorescent protein-expressing human neurons generated from induced pluripotent stem cells.



NATALIIA ALEKSANDROVA/EMBL (MCCARTHY TEAM)

How proteins signal

Andrew McCarthy, a team leader at EMBL Grenoble, is also interested in molecular structures in the context of neurobiology. Specifically, he wants to uncover the underlying mechanism of the Slit and Roundabout (Slit–Robo) cell signalling pathway – essentially, how signals from outside a cell are transmitted to the inside. “These are two proteins. Slit is secreted by specialised glial cells in the nervous system, and Robo is the cognate receptor in the neuronal cell membrane. They interact with each other – they ‘talk’ to each other – and we’re trying to figure out how they signal once they interact,” McCarthy says.

These proteins are expressed in the early stages of embryonic development, when

In the presence of Slit2, Robo1 on the cell surface undergoes a conformation change from the inactive closed state, observed here by electron microscopy, to an open activated form, as shown on the right.

the neural networks are being laid down – connecting the eyes and the muscles to the brain, for example, for the visual and motor systems. “A lot of these developmental processes are very dynamic,” says McCarthy, “so the proteins are sensing their environment rapidly, and cells infer how to grow or retract in different areas.”

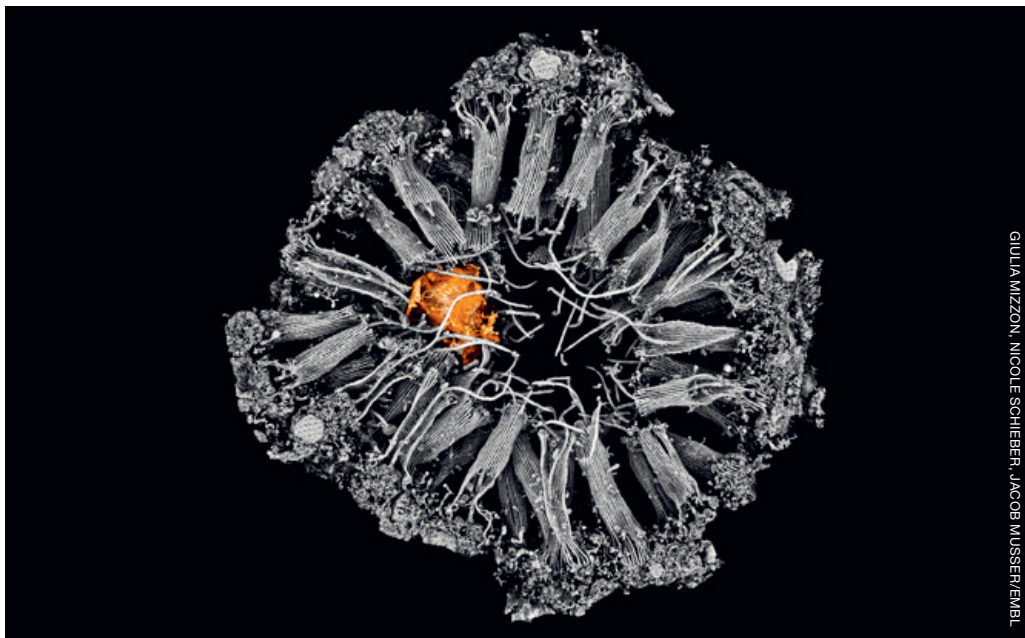
Many cancers and other diseases have been linked to these developmental proteins. “Not just Slit and Roundabout,” McCarthy adds. “There’s a whole plethora of them.” The link is particularly strong in the case of metastatic cancer cells because such proteins can inform cells to migrate and react to their environment. If unregulated, the proteins can induce primary tumour cells to break away and move to other parts of the body.

These are difficult proteins to work with in the lab. “They’re large, very flexible, and hard to handle,” says McCarthy. But technological developments are making things easier. Improvements in the beamlines at the European Synchrotron Radiation Facility (ESRF), with which EMBL Grenoble has close ties, mean that data can be collected faster, and from smaller crystals. McCarthy would also like to take advantage of developments in electron and light microscopy. “We know what these proteins look like – roughly. Now we need to see them in context, moving to or from the cell surface.”

Origin and evolution

With these scientists following their curiosity down diverse lines of inquiry, our knowledge about the most complex system in the human body is ever increasing. Yet there remains a great mystery to be solved: how did neurons and nervous systems evolve? This is the question that intrigues EMBL Heidelberg group leader Detlev Arendt.

“Humans have always wanted to know where we come from”



GIULIA MIZZON, NICOLE SCHIEBER, JACOBI MUSSEY/EMBL

A choanocyte chamber of the sponge *Spongilla lacustris*, with a neuroid cell (orange) nestled within it.

“Humans have always wanted to know where we come from, and this is what we’d like to find out,” Arendt says. “We want to trace evolutionary paths towards neurons and nervous systems. So we look at animals that are more remote on the animal tree – animals with simple versions of a nervous system, or those that don’t have a nervous system because they branched off earlier.”

Looking to the ocean for answers

Landlocked Heidelberg, hundreds of kilometres from the ocean, is an unlikely location for a marine biology lab. Yet Arendt’s lab is full of tanks in which a variety of marine species reside in water from the North Sea. These include sponges, molluscs, and the marine worm *Platynereis dumerilii* – a relative of the earthworm, with a typical rope-ladder-like nervous system. But what can we learn from these species?

Arendt explains: “We’re interested in ancestors, and this famous urbilaterian – the last common ancestor of all animals with bilateral symmetry. So we’re working on a lot of informative species to try to reconstruct that animal by comparison. If a trait – be it a gene, a cell type, or a body part – exists in many species using shared information, it’s likely that this feature existed in the last common ancestor.”

Arendt and collaborators Yannick Schwab, Anna Kreshuk and Christian Tischer at EMBL Heidelberg – who share his enthusiasm for neurobiology – recently made a fascinating discovery in sponges – our most remote cousins in the animal kingdom. Although they don’t have a nervous system, sponges have a lot of the same proteins found at the synapses – the connections between neurons – in other animals. The scientists wanted to find out what these synaptic proteins were doing, and in the course of their investigations they discovered two cell types highly enriched in synaptic proteins: a migratory cell type with a lot of extensions – similar to a neuron’s axons – that contacts cells in the choanocyte chamber, which acts as a water pump, bringing oxygen and nutrients into the sponge. Their next step is to investigate where precisely the proteins are located in the cells, and how they function in cellular communication.

EMBL-flavoured neurobiology

Neurobiology research at EMBL continues to take shape in interesting directions, and Cornelius Gross is emphatic that EMBL has something unique to offer in this sphere. “EMBL is great at genomics and gene expression, it’s great at imaging, and it’s great at structural biology. Neurobiology at EMBL should take advantage of those features. That’s the vision – a kind of EMBL-flavoured neurobiology.”

We all come from the ocean

Eric Karsenti's dream of combining his loves of biology and sailing set in motion the Tara Oceans expedition



Tara docked in the harbour in Hamburg.

MASSIMO DEL PRETE/EMBL



BY FABIAN OSWALD

The camera team wanders around the quay, looking for the right angles to capture the boat. In the meantime, two French school classes are receiving a guided tour with scientific demonstrations. The French ambassador and consul appear, escorted by five bodyguards, and an elderly sailboat enthusiast walks by and insists to be let on board to greet the captain. Shortly afterwards, a rubber dinghy enters the harbour, bringing back some of the *Tara* crew who set out earlier to take samples from the river Elbe. It is a sunny morning in June and the *Tara* schooner is docked at the *Sandtorhafen*: Hamburg's historic harbour.

Amid all the movement, EMBL scientist Eric Karsenti appears at the quay and is immediately drawn on board. He is greeted with hugs and *les bises* by the crew. After a few minutes he vanishes below deck to take a look around the boat – the one that took him on the expedition he dreamed of for so long. Later in the morning, he finds a quiet corner to sit and talk to me about his connections with science, the ocean, and the origins of the *Tara* Oceans expedition.

The call to adventure

“For part of my childhood I was raised close to the sea, by the English Channel. I have always been attracted to it,” says Karsenti. “I think the ocean represents a kind of dream for everyone, a dream of the time of expeditions, of exploring the world. When you're sailing on it, you live differently. Time disappears. It's like being in the desert, but at the same time it's so full of life that you cannot see. It's a special feeling. And, in the end, we all come from the ocean. It's where life started and where life became complex.”

Karsenti started sailing at the age of twelve. “Then I got the bug and I have never stopped since,” he says, laughing. At eighteen, he went to a sailing school and then became a sailing teacher in Brittany, France. He pursued this career for ten years, while studying and earning his PhD. He then stopped sailing



MASSIMO DEL PRETE/EMBL

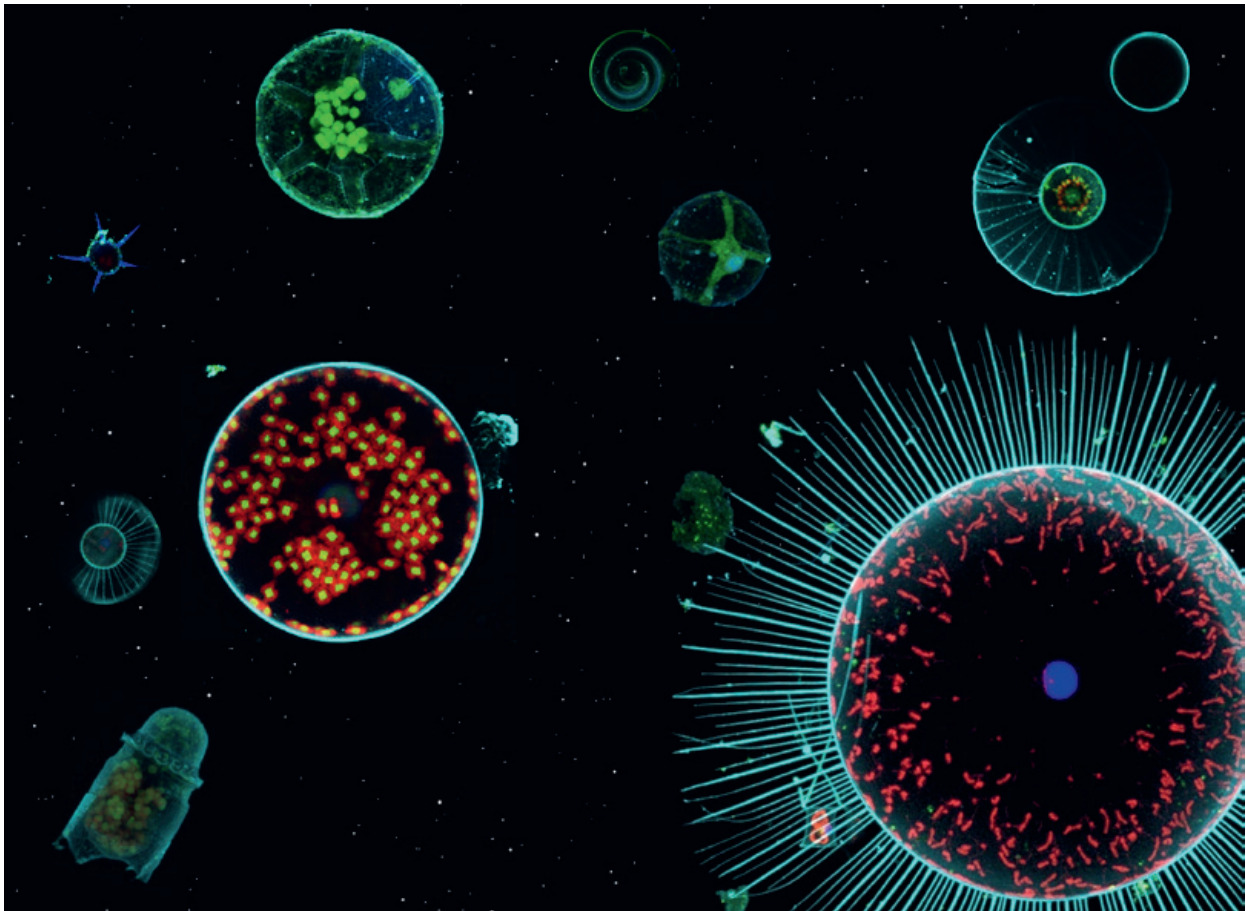
professionally to focus on his scientific career. Soon, the bug would call him back to the sea.

Eric Karsenti discusses *Tara* at the stopover in Hamburg.

While he was the head of EMBL's Cell Biology and Biophysics Unit, Karsenti read Darwin's book *The Voyage of the Beagle*, and was fascinated by the story it told. “It's a mixture of adventure and science. It was kind of magic. And, because I sail myself, I could imagine very well what Darwin went through. I thought it would be great to do a modern expedition. The dream was to have a sailing boat going around the world and talking about life, evolution, cell biology and what we're doing at EMBL.” Karsenti wanted to popularise the life sciences using a sailing expedition with extensive media coverage. However, there were some obstacles in the way.

“We had no boat, no money, no TV producer,” Karsenti says, with a grin. “After some >>

“I think the ocean represents a kind of dream for everyone”



LUCA SANTANGELI/EMBL

Diverse examples of plankton collected during the Tara Oceans expedition.

time I thought: ‘Well, the only way to make this work is to do a proper scientific expedition.’ So I started to talk to friends, like Christian Sardet.”

Karsenti and Sardet – now Emeritus Research Director at the Observatoire Océanologique de Villefranche-sur-Mer – came up with the idea of starting an expedition focusing on plankton biodiversity. Another friend of Karsenti’s, French sailor and single-handed racer Michel Desjoyeaux, knew the crew of a boat called *Tara*, which at the time was on an expedition drifting in the Arctic ice. A manager working with Desjoyeaux, Didier Velayoudon, put Karsenti in contact with Romain Troublé and Étienne Bourgois, who were running *Tara*. “And that’s how the whole thing started,” says Karsenti.

Shaping a common goal

Karsenti realised that his goals and the goals of the *Tara* crew were very complementary. *Tara* was lacking long-term commitment from the scientific community. “So, when

we started to work together, to develop a strong programme, this went very well: we all wanted something very similar,” says Karsenti.

Although they now had a boat, Karsenti’s dream still faced various challenges before it could become a reality. The first was to develop a scientific project that would be suited to *Tara*’s size. “Nobody had really worked from a scientific point of view on the global ecosystem, which is what we wanted to do,” says Karsenti. This took about two years to put together. “We had meetings every three months to discuss how to take samples, how to analyse a sample and how to generate models.”

Karsenti explains that the key to success while designing the scientific project was the collective effort. This led to another challenge. “The second challenge was to get all the different scientists to understand that they should really work together, not for themselves

but for a common goal, and that they would get more out of it if they worked together than if they worked individually on a small topic. You need a huge collaboration because there are so many different kinds of knowledge needed. That's what CERN did for physics, and I think the power of EMBL is to do the same thing for biology."

The third challenge was working with the media. "The *Tara* crew were extremely good at getting journalists. But we had to tell the media that things would work, even though we weren't sure at all that they would. That was very difficult for me, because as a scientist I was not trained to do this. That is against our culture."

The fourth and final challenge was to raise the money for the expedition. Together with Troublé and the other scientists, this took Karsenti three years of very hard work.

A more than accomplished dream

Finally, the *Tara* Oceans expedition became reality, followed by *Tara Méditerranée*, the *Tara Pacific* expedition, and now Mission Microplastics. Looking back, Karsenti considers his dream more than accomplished. "We did so much more than I thought we would

"We did so much more than I thought we would do"

do. I think this is now a very important project for the whole of humanity, because for the first time it may allow us to understand ocean ecosystems. I'm very happy. I've started to withdraw a little from the whole thing because I'm not so young any more. And it seems to be working extremely well without me. So that is even nicer, because it means I did a good job."

Karsenti will keep in touch with *Tara*, and will continue to work on conceptual parts of the project, especially in coordinating the efforts of the institutions involved. However, he doesn't want to be active in the day-to-day running of the project any more, as he wants to spend more time with his family. Once again, he shows a knack for combining the most important things in his life: he plans to take them sailing.



(Left to right) Matthias Wilmanns, Head of EMBL Hamburg; Anne-Marie Descôtes, French ambassador to Germany; Romain Troublé, Director of the *Tara* Ocean Foundation; Edith Heard, EMBL Director General; and Eric Karsenti, EMBL group leader and initiator of the *Tara* Oceans expedition, on board *Tara*.

Tara expeditions

Exploring the world's oceans

Tara expeditions are scientific voyages that probe the molecular diversity of the world's oceans and seas.

The data collected by the Tara schooner are stored in public data archives, such as the ones managed by EMBL's European Bioinformatics Institute (EMBL-EBI). The data are freely available to researchers all over the world.

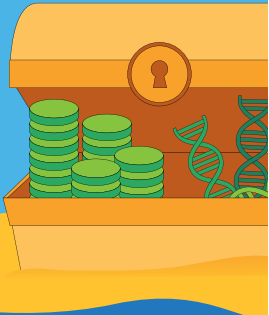
A treasure trove of data

11 535
gigabytes

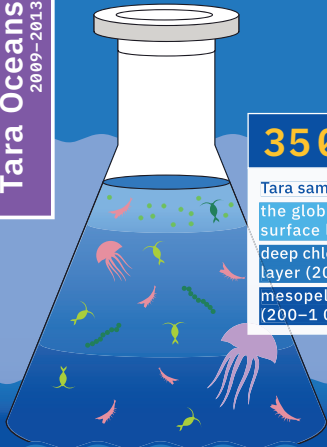
The size of Tara datasets freely available through the European Nucleotide Archive as of 2019

7 012
datasets

155 million genes



Tara Oceans 2009–2013



35 000 samples

Tara sampled plankton from:
the global ocean surface layer (0–10 m)
deep chlorophyll maximum layer (20–100 m)
mesopelagic layer (200–1 000 m)



140 000 km
distance sailed from Lorient over 38 months

120 crew and scientists

40 nations globally

210 stations visited

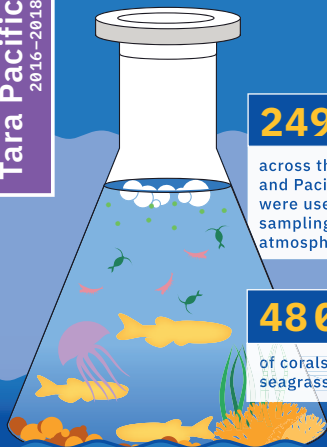
30%
molecular

SAMPLES COLLECTED

50%
imaging

20%
biogeochemical

Tara Pacific 2016–2018



249 sites

across the Atlantic and Pacific Oceans were used for sampling the ocean-atmosphere interface

48 000 samples

of corals, fish, plankton, seagrass, and sediments



110 000 km
distance sailed from Lorient over 29 months

180 crew and scientists

32 islands visited

110 coral reef ecosystems studied

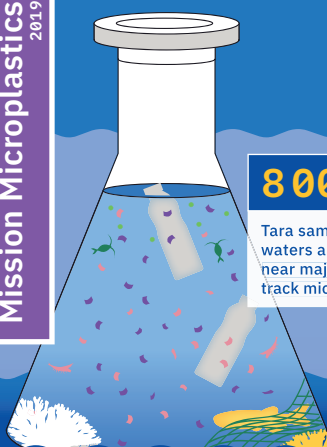
50%
molecular

SAMPLES COLLECTED

30%
imaging

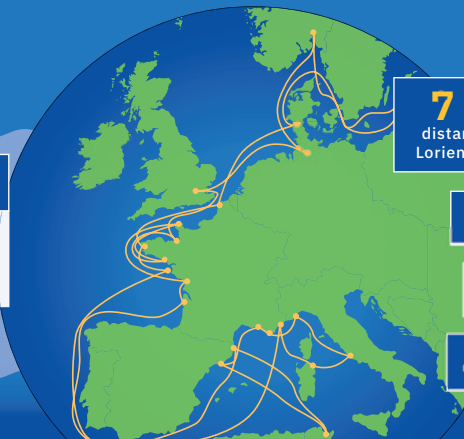
20%
biogeochemical

Mission Microplastics 2019



8 000 samples

Tara sampled surface waters and marine litter near major port cities, to track microplastic pollution



7 500 km
distance sailed from Lorient over 6 months

10 European rivers

5 sites along each river

40 crew and scientists

40%
molecular

SAMPLES COLLECTED

20%
imaging

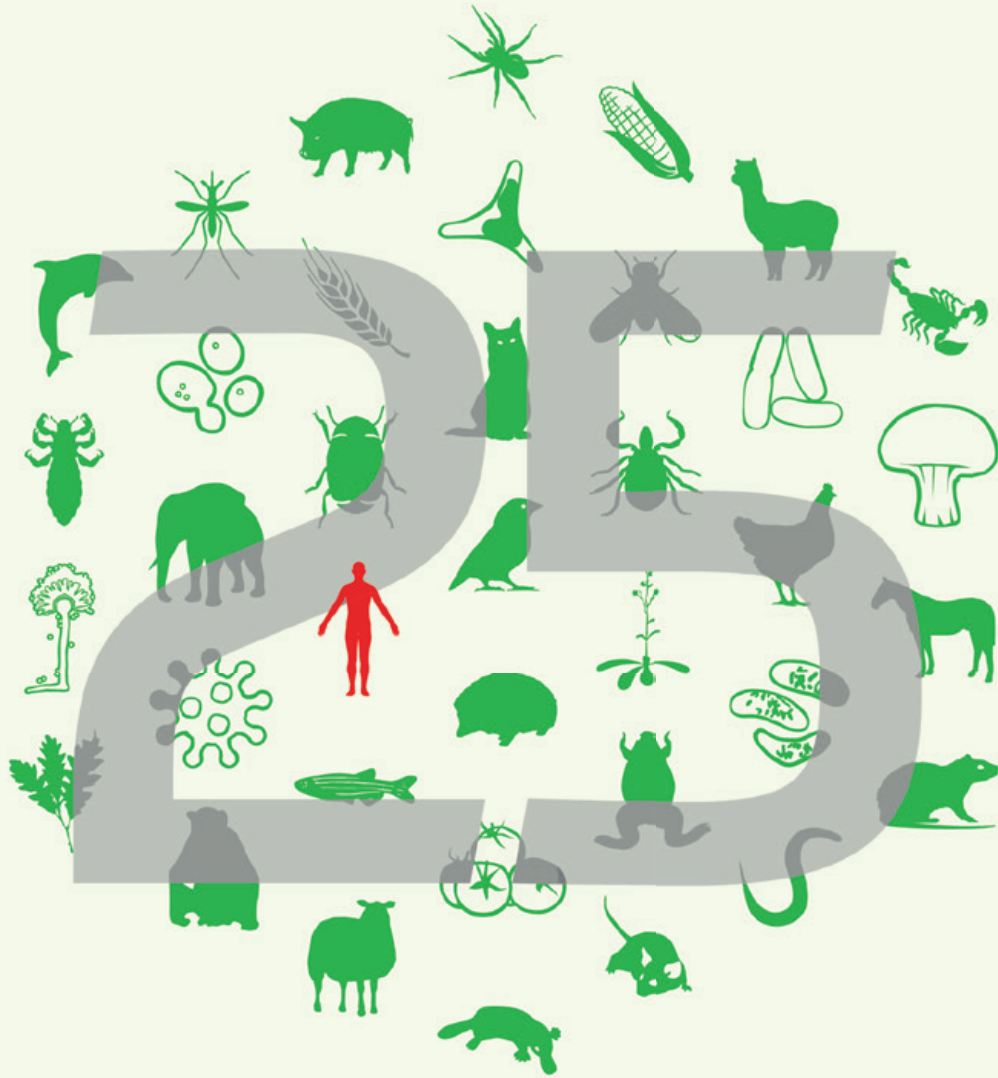
40%
biogeochemical

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SPENCER PHILLIPS/EMBL

25 years of EMBL-EBI

EMBL-EBI celebrated its 25th anniversary
on 1 September

BY OANA STROE

Cast your mind back to 1994. It was the year Brazil won the World Cup after a penalty shoot-out with Italy, and the hit TV series *Friends* debuted on NBC. In the world of technology, Amazon and Yahoo had just been set up and the first commercial web browser, Netscape Navigator, was launched. The internet, previously used mostly by scientists and scholars, was beginning to look like the next big thing.

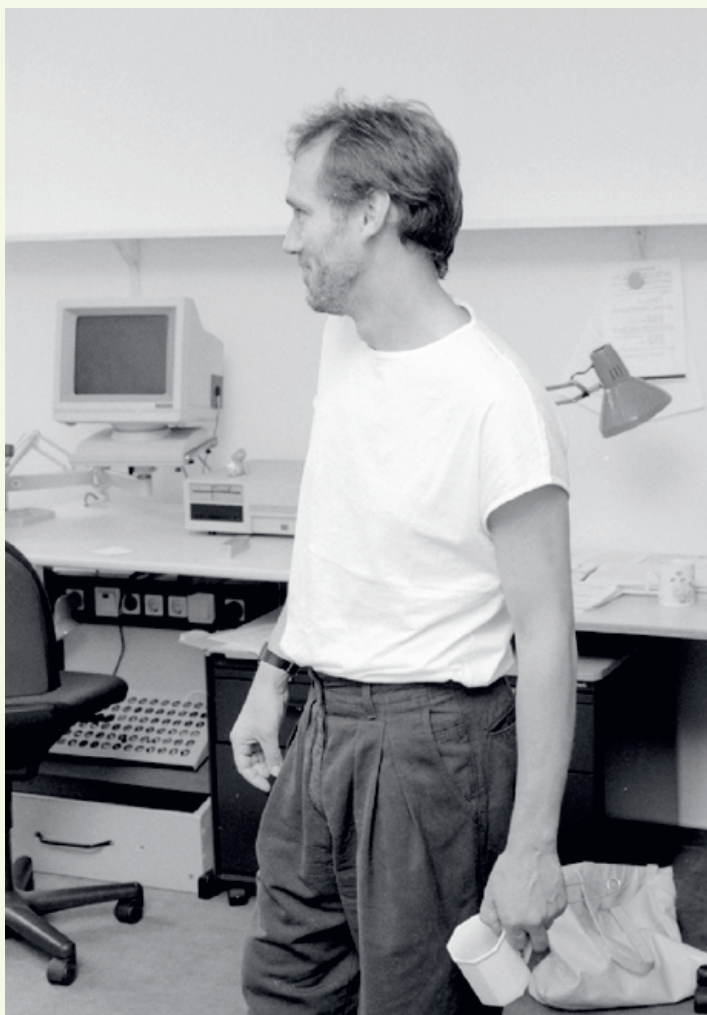
In September 1994, a small group of researchers from EMBL Heidelberg travelled to a remote campus in the Cambridgeshire countryside to set up a home for the growing volumes of biological data being generated around the world: the European Bioinformatics Institute (EMBL-EBI).

“The idea for EMBL-EBI was born in the mind of Graham Cameron, who ran the EMBL Data Library,” explains Rolf Apweiler, Director of EMBL-EBI. “He believed sequencing would be transformative for biology, but only as long as there was a place that would archive, analyse and annotate the sequences, and – most importantly – make them publicly available.”

Humble beginnings

Today, EMBL-EBI’s two buildings accommodate around 800 employees from over 60 countries, but back in 1994, things were very different.

“EMBL-EBI was a couple of Portakabins and a hole in the ground that Graham Cameron very proudly gave us a tour of,” recalls Claire O’Donovan, Head of Metabolomics. “What’s funny is that today we still have Portakabins



EMBL

on site, but only because the institute is growing so fast that we often have to use them for staff overspill.”

And it’s not just the number of people that is on the rise. Maria Martin, who joined EMBL-EBI as a database developer in 1996 and now runs the Protein Function Development team, reflects on how much the data volumes have changed. “Back then, Swiss-Prot – today >>

Graham Cameron developed the concept for EMBL’s European Bioinformatics Institute.

“EMBL-EBI was a couple of Portakabins and a hole in the ground”



EMBL-EBI Main Building under construction.

part of UniProt – had about 80,000 entries. We thought this was a lot and were wondering how to handle the amount of data coming in from collaborators. Nowadays we have over 150 million protein sequences, and growing.”

All about the data

In 1994, the two data resources for EMBL-EBI were the EMBL Nucleotide Data Bank – now the European Nucleotide Archive – and Swiss-Prot. Alongside these, there was also a small research group and a huge sense of excitement for what was to come.

“We’re just scratching the surface of what we can do with the web”

Over time, the volume and diversity of data increased significantly. “In the late ’90s, the microarray revolution started at Stanford,” explains Alvis Brazma, Head of Molecular Atlas Services. “I remember that industry was particularly interested in the topic. In fact, ArrayExpress was one of the first data resources set up with industry contributions.”

These days, genomics, single-cell sequencing, metagenomics and imaging data are just some of the many data types EMBL-EBI resources accommodate. “We have always been very good at pre-empting the next big thing and adapting to it,” says Brazma.

A computing revolution

As data volumes grew, so did the demand for infrastructure. The first computer room consisted of only a few racks. When the time came to expand, it sparked a big debate.

Mark Green, former Head of Administration, recalls: “The table tennis room was quite a large social area, so we thought it would be a

terrible waste to convert it into a computer room, as it would take us years to fill it with kit. In the end, we bit the bullet and converted it. Within 18 months, the place was rammed full of kit and we were running out of space yet again. Soon after, we set up a data centre on campus. Now, we have three data centres plus cloud storage, which is constantly on the rise.”

Another technical milestone was setting up the first web servers for EMBL-EBI data resources in the late 1990s: the early days of the internet. “There were lots of problems with connectivity back then, so getting data from the United States required special traffic permissions,” recalls Rodrigo Lopez, Head of Web Production.

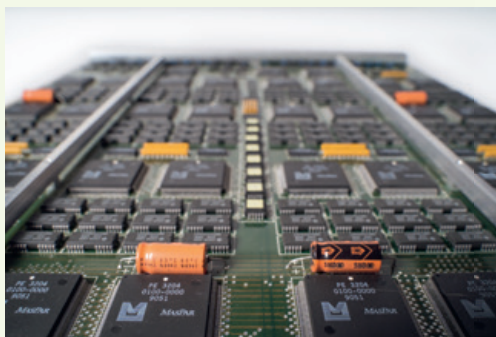
“From the beginning, the internet was all about search,” Lopez continues. “And all of a sudden, you didn’t have to go to the library, sit in a queue or wait for books. You simply sat at your desk and connected to the network. It was a huge shift in how science worked.

“We used to have these crazy coding competitions to see who wrote more code, and we would count lines and mistakes to determine the winner.

We had a hell of a good time back then: we were writing code, we were developing methods, we were doing science. It was all cutting edge and there was an amazing atmosphere. Even today I think we’re just scratching the surface of what we can do with the web.”

Hole-in-the-Wall Gang

So what about the people who made all these things happen? “Before I joined EMBL in Heidelberg, I had been told that EMBL was a bit like the Hole-in-the-Wall Gang – they didn’t follow rules, they made their own. And I discovered that EMBL-EBI was a bit like the Hole-in-the-Wall Gang’s Hole-in-the-Wall Gang,” says Mark Green.



“It felt more like a group of friends working together; a young institute where everybody was a colleague and we had regular international cuisine parties,” recalls Maria Martin.

As the institute grew, it became impossible to know everybody. But, to this day, teams work together closely through ‘glue projects’, ensuring that data are interoperable. Knowledge exchange and collaboration within and outside EMBL-EBI are pillars of open data and open science.

Looking to the future

Much has changed in 25 years, but some things remain the same. EMBL-EBI is still collecting, analysing and opening up data for its users. It just happens at a much wider, more diverse scale. In the past, data were used mainly by bioinformaticians, but they now power discoveries in human health and disease, precision medicine, agri-tech, biodiversity and beyond.

So, what’s next? “The big unknown now is the functional part,” says Rolf Apweiler. “We know only a small number of the functions of genes, transcripts and proteins, but we need to work out their full characterisation. Sequencing only scratches the surface. The functional question is a much bigger one and will take a very, very long time to answer. But when we crack it, it may allow us to do things we can now only dream of.”

Left: MasPar facilitated a significant increase in the number of sequence similarity searches that could be done in a given timeframe.

Right: EMBL-EBI’s first router, which allowed the institute to launch its first web servers.

Celebrating 25 years

EMBL-EBI held a day of celebrations to mark its 25th anniversary

BY OANA STROE

On 6 September, EMBL-EBI celebrated 25 years of activity: a quarter of a century during which bioinformatics moved from being a niche discipline with an unpronounceable name, to playing a central role in the life

sciences. To mark the milestone, EMBL-EBI organised a day-long event for staff, with talks on the history and future of the field, as well as fun activities and games to open up bioinformatics to non-specialists.



EMBL-EBI leadership, past and present: (back row, left to right) Paul Flicek, Associate Director of EMBL-EBI Services; Rolf Apweiler, Director of EMBL-EBI; Edith Heard, EMBL Director General; Ewan Birney, Director of EMBL-EBI; Graham Cameron, Director Emeritus of EMBL-EBI; (front row, left to right) Jo McEntyre, Associate Director of EMBL-EBI Services; Michael Ashburner, Director Emeritus of EMBL-EBI; Janet Thornton, Director Emeritus of EMBL-EBI.

Buon compleanno!

Celebrating 20 years of EMBL Rome

Friends old and new mark the occasion in style

BY CELLA CARR

Members of the EMBL community and friends gathered in Rome on 8 July to celebrate a special anniversary: EMBL Rome's 20th. Phil Avner, Head of EMBL Rome, welcomed EMBL Director General Edith Heard and other guests to the event. The beautiful summer's

day provided the perfect backdrop for elegant al fresco dining, relaxed mingling, and an assortment of games. It was an occasion to reflect with pride on the achievements of the past 20 years, and to look forward to the planned refurbishment of the EMBL Rome site, and to more great science in the coming years.



EMBL Rome group leaders Jamie Hackett (left) and Santiago Rompani (centre) talk to guests.

MASSIMO DEL PRETE/EMBL



Lunch and talks were followed by an afternoon of fun in the garden.

MASSIMO DEL PRETE/EMBL



Phil Avner, Head of EMBL Rome, with photographer Horst Hamann, who joined the anniversary event.

MASSIMO DEL PRETE/EMBL



Villa Livia on Via Appia Antica in Rome is ready for the celebrations.

MASSIMO DEL PRETE/EMBL



Guests enjoyed various games, including pool and darts.

MASSIMO DEL PRETE/EMBL



After aperitivi by the pool, presentations of group posters by EMBL Rome scientists, and a buffet dinner in the courtyard, it was time for Phil Avner, Head of EMBL Rome, to cut the anniversary cake.

MASSIMO DEL PRETE/EMBL



Edith Heard, EMBL Director General, at the reception.

MASSIMO DEL PRETE/EMBL

From rodents to roadsters

Klaus Rajewsky, Head of EMBL Rome 1996–2001 (then known as the EMBL Mouse Biology Programme), recalls the pioneering spirit of the site's first years

BY JOSH TAPLEY

The EMBL Rome story, for me, starts with Fotis Kafatos. I was giving a seminar at the ZMBH (Heidelberg University's centre for molecular biology) about conditional gene targeting, which my lab was developing in a big way. Fotis, then EMBL Director General, attended the seminar and we met afterwards. That evening he asked whether I would like to lead the new EMBL site for mouse biology that they were thinking of setting up just north of Rome, in Monterotondo.

At the time, I was slowly approaching the retirement age in Germany. I still had a while, but time goes by quickly and I had seen from my father, who was also a scientist, that retirement can be a difficult thing. I promised myself that I would do my best to avoid a similar situation, so I took the job. It was an opportunity for real adventure and it was in an area of research that I was deeply passionate about.

The plans began to take shape, and in 1996 I got my contract. I would spend half my time in Monterotondo and the other half in Cologne at the Institute for Genetics, where I had my lab. I was extremely lucky to rent a fantastic apartment in Via Flaminia, right next to the Piazza del Popolo. In the morning I would drive out to Monterotondo, along the Tiberina,

against the incoming Roman commuter traffic, and in the evening I would drive home against them as they were leaving the city. It was wonderful!

When we first started out, there wasn't much to work with. There was a portion of a relatively small research facility available to us on the Monterotondo campus and, of course, there was Glauco Tocchini-Valentini, then Director of the Genetic Engineering Target Project at the Italian National Research Council (CNR). Glauco had a long connection with EMBL and was heavily involved in the founding of the European Mutant Mouse Archive (EMMA). He was really a key figure in setting the whole thing up and he became a good friend.

We had a very limited budget and, to start with, we had only two research groups. The real pioneer was Walter Witke, now a professor at the University of Bonn. Walter was my main local partner initially. He was recruited before the space in Monterotondo was ready, so he was initially put up in a lab at EMBL Heidelberg. Then one day the trucks arrived, packed up his lab, and off they went to Rome.

Then came my staff scientist, Ulrich Kalinke – now Executive Director of TWINCORE in Hannover – and others followed. At the time,



Klaus Rajewsky.

EMBL

Ulrich was in possession of an old Porsche. It came from a time before power steering, so it could be a real effort to drive but well worth it. It wasn't exactly suitable for his everyday life, and he had another car that he used most of the time. The agreement was that whenever I came to Rome, I would use his Porsche to drive out to Monterotondo and back. Driving this wonderful Porsche through Rome and its surroundings was quite something!

During my time in Monterotondo, we grew to four research groups. Walter's and my own, then the groups of José Luis de la Pompa and Claus Nerlov. Our greatest challenge was putting our site on the map. We were a tiny venture compared to other institutions, and getting noticed was no small feat. In 2000 – just one year after we'd officially opened and three years after we'd started building the place up from scratch – we had our first evaluation. Thanks to a lot of hard work, and a little miracle, we were evaluated as 'outstanding'. That was a great boost: from then, the site really began to grow into what it is today.

Working at EMBL introduced me to a whole new community of people. I was surrounded by

“The site in Monterotondo became a place I loved”

top scientists from many different nations and vastly different areas of research, and I learned many new things. The site in Monterotondo became a place I loved. I think we all had a good time there and thoroughly enjoyed working in the labs.

In 2001, I left. The site's future development was still somewhat uncertain, and I happened to receive an offer from Harvard University. So, off I went to Harvard Medical School. I was followed as Head of the Mouse Biology Programme by Nadia Rosenthal.

Since then, I've watched from afar as EMBL Rome has developed. I've been able to come back a few times, I've given a lecture here, and one of my former postdocs, Manolis Pasparakis, even came here as a group leader. It has definitely grown, but much of it still feels familiar.



Nadia Rosenthal.

EMBL

Fallingwater filled with mice

Nadia Rosenthal, Head of EMBL Rome 2001–2012 (initially known as the EMBL Mouse Biology Programme; later as EMBL Monterotondo), describes how she built EMBL Rome’s mouse house

BY EDWARD DADSWELL AND ANNE-FLORE LALOË

When I first came to Monterotondo in 2000 I was interviewing alongside a group of prominent scientists. All the hopefuls had to present our proposals in front of each other, so it was pretty stressful. I’ll never forget the moment later that evening when Fotis Kafatos, then EMBL Director General, took me

aside and said, “You got the job and you have twenty-four hours to make a decision whether you take it!”

At that time, the site in Monterotondo had intermittent internet and only 12 staff members. The European Mutant Mouse Archive (EMMA) was next door, and EMBL’s

mice were kept in a rented room there. The first few years were pretty tough, with a tight budget and no facilities of our own for doing mouse biology. I knew a lot of people at The Jackson Laboratory in the US, where I now work, who used Thoren, a company in Pennsylvania, to develop individually ventilated mouse cages. I ordered 25 of those cages, and that meant we could use our laboratories – which had not been set up with any special air-handling system – to do work on mouse biology.

All of that was challenging, especially when I was trying to recruit new group leaders, so I had to use my powers of persuasion to get several fantastic people to work there. One of the early people we hired was Cornelius Gross, now Deputy Head of EMBL Rome, and that was just the first of a spectacular run of scientists. Another was José Gonzales, whom I'd worked with at Harvard, who joined us to help set up the mouse house.

When I came for my interview, I was shown plans for a new mouse house that would be added to the existing building. Later I was told that we couldn't use that design because the renovations would cost too much, and it would be better to start from scratch. But when I spoke to the site manager, Emilio Mattoccia, who was hired by the Italian National Research Council (CNR) to run the whole campus, he said the Town had decided that no further building could happen on site, because we were in the floodplain of the Tiber and there were also concerns over seismic activity.

By that point, I couldn't see how we were going to have a mouse facility and a mouse biology programme if we couldn't build a mouse house! So I had to get creative.

One night, as I was lying awake wondering what I was going to do, I started thinking about how the site was configured. Our research building had a depressed loading bay with a ramp to make the basement accessible to delivery vans. It suddenly occurred to me that we could cantilever the facility out over the loading bay, rather than pour a new foundation. The next day I told Emilio that I wanted to build something

“I feel very proud that we made it work”

like Frank Lloyd Wright's Fallingwater over the back loading bay and fill it with mice.

Emilio thought this was very clever, and we started to work out how many posts we would need to hold the whole thing up. As long as the posts were far enough apart, he discovered, it would not be considered a new construction by the Town. So we designed the entire mouse house to be an extension of the existing facility, not exceeding the loading bay perimeter.

Then Emilio's genius came in. He found a company in Parma that made prefabricated operating theatres for hospitals, with constant temperature, pressure, and humidity, which is exactly what you need for a mouse house. It was like Lego: we ordered these units and clicked them together with a shell around them, with all the machinery to handle the air above them. The whole construction could be approved by the Town as a request for new equipment, and we were able to finish the construction of our mouse house for under €3 million.

The new facility was up and running by 2004 and as far as I know it's never broken down. I feel very proud that we made it work. After that, I began lobbying to make the site in Monterotondo a new EMBL Unit, which was soon made official. By the time I left in 2012, our mouse house was full and our staff of 80 scientists included a healthy number of students and postdocs. We had an international network of collaborators and a world-class reputation in mouse-based biomedical research. I have great memories of my time there, and I still believe the EMBL model for running a scientific institute is the best I've ever experienced.

With thanks to EMBL Archivist Anne-Flore Laloë, who carried out the oral history interview on which this text is based.

Edith's inauguration

Edith Heard is inaugurated as EMBL Director General

(Below) Edith Heard, EMBL Director General, and Patrick Cramer, Chair of the EMBL Council, listen to the talks.

On 17 October, representatives from the EMBL member states, EMBL faculty, and other distinguished guests gathered for the inauguration of EMBL Director General Edith Heard. The inauguration symposium, 'EMBL: A vision for European Life Sciences', was held in the historic Alte Aula at Heidelberg University. Speakers included ministerial representatives from all countries that host EMBL sites, as well as from Lithuania – the most recent member

state to join EMBL.

Speaking at the symposium, Edith described the importance of EMBL's network of collaborators and its alumni community, who have spread the EMBL model to many institutions across Europe and around the world. "I have often described coming to EMBL as coming home," she said, "because I had already heard so much about EMBL from some of EMBL's greatest advocates: its alumni."



The inauguration was held in Heidelberg University's Alte Aula; a site of academic celebrations for more than 130 years.



The inauguration symposium was followed by a gala dinner at the Palais Prinz Carl restaurant in Heidelberg.



EMBL Director General Edith Heard.



DIRK HANSEN/TERRITORY

Gert Hansen (second from left) presents the Hansen Family Award to EMBL Director General Edith Heard (centre), along with members of the Heard group: Antonia Hauth (left), François Dossin (second from right), and Yuvia Perez (right).

Awards & honours

Group leader **Miki Ebisuya** has received the 1st Jun Ashida Award for Brilliant Female Researchers. The award, presented by the Japan Science and Technology Agency, commends female researchers working on outstanding research that contributes to a sustainable future society.

Holly Giles, a PhD student in the Huber group, has been awarded an Add-on Fellowship for Interdisciplinary Life Science by the Joachim Herz Foundation. The grant, of up to €12,500 to be spent over a period of two years, supports young scientists to undertake professional training, attend conferences, finance research stays, and participate in

fellowship meetings and other events organised by the Joachim Herz Foundation.

On 28 October, EMBL Director General **Edith Heard** received the Hansen Family Award from the Bayer Science & Education Foundation, for groundbreaking insights in the field of epigenetics and its role in basic medical research.

On 3 December, **Edith Heard** gave the Karl Friedrich Bonhoeffer Lecture and was awarded a medal and a prize of €5,000 in honour of her scientific achievements.

Sissy Kalayil, postdoctoral fellow in the Cusack group, has been awarded

the Young Talent France 2019 L'Oréal-UNESCO Prize for Women in Science.

In October, **Michael Knopp** received a postdoctoral fellowship from the Swedish Research Council to join the Typas group.

EMBO Director **Maria Leptin** has been awarded a Doctor Honoris Causa by EPFL, Lausanne, Switzerland.

Sumana Sharma, postdoctoral fellow in the Petsalaki group, has been awarded a Sir Henry Wellcome Postdoctoral Fellowship.

Snapshots from Mission Microplastics

Highlights from *Tara's* stopovers around Europe

For six months this year, the *Tara* research vessel travelled around the coastlines of Europe, stopping at various locations along the way so the team of scientists on board could collect water samples from the estuaries of 10 major rivers. The aims of this operation, called Mission Microplastics, were to learn about the sources of microplastic pollution, how these tiny particles of plastic behave when they disperse into the ocean, and how they affect marine life.

Tara's journey included stopovers in London, Hamburg, Rome, Marseille, and Barcelona, with EMBL scientists participating in various public outreach activities, press conferences, and events for the scientific community.



Families meet the crew of *Tara* in Hamburg.

MASSIMO DEL PRETE/EMBL

Tara in London at dusk.



PHIL MYNNOIT



JORDI CASANAS



MASSIMO DEL PRETE/EMBL

Edith Heard, EMBL Director General, and James Sharpe, Head of EMBL Barcelona, were among the guests at a special reception on board *Tara* during the stopover in Barcelona.



VINCENT LOMBARDO

Romain Troublé, Executive Director of the Tara Ocean Foundation, and Edith Heard, EMBL Director General, speak at the scientific conference 'On the waves of science' during the stopover in Rome.

EMBL alumni and friends gather in the Marseille sunshine for a tour aboard *Tara* as part of the EMBL in France event.

Alumni

An international network



This year, more than ever, has been a fantastic opportunity to celebrate EMBL's global alumni network. In July, we held our first ever EMBL World Alumni Day (p. 46), with alumni joining us in Heidelberg and connecting online from around the world. October saw the official inauguration of

EMBL Director General Edith Heard, who took the opportunity to praise EMBL's alumni community for spreading the EMBL model to other institutions, giving her a sense that she knew EMBL even before she arrived here (p. 38).

The great work our alumni do in sharing the EMBL spirit is particularly evident at our 'EMBL in' events, where

alumni connect with local scientific communities in countries worldwide. This year, we held events in seven countries (p. 42), with our events in France and Spain coinciding with stops made by the *Tara* research vessel during its Mission Microplastics voyage (p. 40).

Alumni also joined us for two significant anniversaries this year: EMBL Rome's 20th (p. 32) and EMBL-EBI's 25th (p. 30). In our article on the history of EMBL-EBI (p. 26), alumnus Mark Green shares some memories from the 20 years he spent there, while alumni Klaus Rajewsky (p. 34) and Nadia Rosenthal (p. 36) describe their experiences of building EMBL's site in Italy.

We're already looking forward to our next World Alumni Day on 17 July, along with many other events in the coming year (see back cover and online).

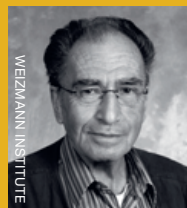
Mehrnoosh Rayner
Head of Alumni Relations

In memory...

...of colleagues and good friends we have lost in 2019.
Our thoughts are with them and their loved ones.



Giovanni Morrone
d. 26 Jan, aged 63
Was: Professor of Biochemistry, University of Catanzaro Magna Graecia, Catanzaro, Italy
EMBL: Visiting Scientist, Genome Biology Unit, 1985–1989



Talmon Arad
d. 5 Apr, aged 80
Was: Retired scientist; previously at the Weizmann Institute of Science, Rehovot, Israel
EMBL: Research Technician, Structural and Computational Biology Unit, 1976–1984



Suzanne Eaton
d. 2 Jul, aged 59
Was: Professor, Biotechnology Center (BIOTEC), TU Dresden, Germany
EMBL: Staff Scientist, Cell Biology and Biophysics Unit, 1993–2001



Bernd-Uwe Jahn
d. 7 Aug, aged 75
Was: Retired; Ministerialrat a.D.
EMBL: Administrative Director, 2001–2009



Heidi Dvinge
d. 20 Sep, aged 42
Was: Professor, University of Wisconsin–Madison, USA
EMBL: PhD student, EMBL-EBI, 2006–2010



Chica Schaller
d. 27 Oct, aged 82
Was: Founder and member of the Board of Directors of the Chica and Heinz Schaller Foundation
EMBL: Staff Scientist, Cell Biology and Biophysics Unit, 1975–1979

EMBL in...

EMBL alumni and scientists around the world come together to collaborate and share ideas

‘EMBL in’ events are an interdisciplinary forum where members of the EMBL community expand their knowledge and networks, learn about others’ research, and reflect on their own work. The events are open to current staff, alumni, and scientists of all disciplines. The aim is to share what’s happening at EMBL with communities in our member states, ensuring that as many people as possible have access to the opportunities and resources that EMBL provides. This year, we hosted events in Italy, the UK, Australia, France, Spain, Sweden, and the USA. For the first time, one of our events – EMBL in Italy – was held on site at a company, thanks to alumnus Alfredo Nicosia,

co-founder of Nouscom. This led to job offers for three participants from EMBL Rome.

As ever, the role of alumni in shaping our vibrant events programme has been vital. We’re grateful to all who have volunteered their time to co-organise or host an event, travelling at their own expense, which allows us to keep these events free of charge. Thank you to everyone who has added to the debate as an attendee – we hope to see you again at an ‘EMBL in’ event soon!

 **ALUMNI EVENTS:**
[BIT.LY/embl-94-alumni-events](https://bit.ly/embl-94-alumni-events)

EMBL in Italy



EMBL in Italy participants on site at biotechnology companies Nouscom and ReiThera, just outside Rome.

Phil Avner, Head of EMBL Rome; co-organiser: “It’s really important for us to link EMBL in with the whole panorama of science in Italy. This year’s event, organised in association with the biotechnology

companies Nouscom and ReiThera, was a further important step in this direction. It allowed many of our students – often for the first time – to visit and experience a biotechnology company. Hopefully it will provide

us in the future with new avenues for improving and completing our careers advice to the students on campus and elsewhere at EMBL.”

Mariano Maffei, EMBL alumnus and Senior Research Scientist at Takis Biotech, Rome; participant: “EMBL alumni meetings have been of paramount importance for my career. During the past few years they have allowed me to build up a strong network within the Italian scientific academic community, and to meet prominent researchers from the pharma and biotech worlds. Most importantly, it is through these events that I was able to get my current job after leaving EMBL. I strongly recommend that PhD students and postdocs attend them. Don’t be shy!”

EMBL in the UK

Max Gutierrez, EMBL alumnus and Senior Group Leader at the Francis Crick Institute, London; co-organiser: “I really enjoyed organising the event at the Crick. It was nice to see so many familiar faces and to stay in contact with the Alumni Association. I always feel very close to EMBL, both personally and scientifically, and I will always support EMBL endeavours to promote the highest quality of science in Europe and around the world. I’m very happy that the relationship between the Crick and EMBL is growing!”

Silvia Santos, EMBL alumna and Group Leader at the Francis Crick Institute, London; co-organiser: “I often say I became the scientist I am today during my PhD at EMBL. It’s



EMBL in the UK co-organisers Max Gutierrez and Silvia Santos at the Francis Crick Institute, London.

exciting to have now established my own lab in a scientific home that is so much in line with the EMBL ethos. EMBL and the Crick have recently become partner institutes, and share pretty much the same vision: science without borders, fostering a multicultural, multidisciplinary,

and highly collaborative research environment. Importantly, both institutes are committed to providing excellent training to early career group leaders, many of whom go on to establish labs all around the world.”

EMBL in Australia



EMBL in Australia participants, QIMR Berghofer Medical Research Institute, Brisbane.

Frank Gannon, EMBO and EMBL alumnus and Director of the QIMR Berghofer Medical Research Institute, Brisbane; co-organiser:

“I can say that the EMBL ethos is unchanged: EMBL is unchanged in the fantastic training it provides for scientists at every stage. It’s

unchanged in the sense that it gives back to the member states excellent people who come highly trained from an institute with cutting-edge equipment. So, although the buildings are new and the people are different, it’s really the same model that reflects why EMBL was set up in the first place.

“I’d gone to the alumni meeting in Sydney two years ago, and I recognised the need for people who are new to EMBL Australia to get to know the alumni. The overall aim is to try to raise the consciousness around EMBL and build an internal network of people that will hopefully yield something positive.”

EMBL in France

Juan Reguera, EMBL alumnus and Group Leader at AFMB Inserm, Marseille; co-organiser: “The *Tara* expedition was scheduled to stop in Marseille in September. At the same time, we wanted to do an EMBL alumni event to bring together people from all over France and beyond, to start networking. All these things connected in Marseille, where I had just started my group. Stephen Cusack, Head of EMBL Grenoble, called and asked me if I would be willing to help organise the event, and I saw the opportunity to bring together EMBL alumni working in diverse subject areas in this very nice set-up.



EMBL in France participants taking a boat tour of the Frioul Islands in Marseille.

“Even if our scientific subjects are very diverse, there are links between different fields. These links emerge at these interdisciplinary meetings. You listen to talks on a diverse range

of subjects, and realise there may be opportunities for future scientific collaborations.”

EMBL in Spain



EMBL in Spain participants, Barcelona Biomedical Research Park (PRBB).

Teresa Sardón, EMBL alumna and Business Unit Manager and Senior Researcher at Anaxomics Biotech, Barcelona; speaker: “For me, EMBL is an example of the highest standards to which research should aim: enough resources, a collaborative environment, access to high-level seminars, and contact with passionate scientists. After working there, you know how

science can be made enjoyable, and you try to adjust other scientific environments to the same high standards.

“I think it’s important to go abroad to do research, to learn different ways of working, different techniques, and to develop scientifically. It will help to open your mind and build your network.”

Marco Milán, EMBL alumnus and Group Leader at the Institute for Research in Biomedicine (IRB) Barcelona; co-organiser: “After being at EMBL for a relatively long time, you gain two important things: the first is networking skills – the capacity to meet a lot of people from different countries or different parts of your own country – and the second is exposure to a wide variety of scientific fields and topics.

“In life, you have to be especially thankful to those people and institutions that have greatly contributed to your training towards becoming an independent scientist. EMBL played a fundamental role in my development in this regard.”

EMBL in Sweden

Johanna Höög, EMBL alumna and Associate Professor at the University of Gothenburg; co-organiser: “EMBL is the best place I’ve ever worked, both in terms of the science produced and in terms of being a fantastic employer. For me, arranging the event gave me a reason to reconnect and form new bonds with other EMBL alumni in Sweden, which was great. I hope the participants got to know more about what kind of research is done at EMBL, and that they will try to spend some time there in the future.

“Sweden is a country with a small population but large investments

in science. Our small but very good research community would benefit from increased international exchange. I consider EMBL the best research institute in Europe for gaining insight into new methods and groundbreaking research. It should be one of our top destinations for an international PhD or postdoc, or for starting PIs.”

EMBL in Sweden participants, University of Gothenburg.



EMBL in the USA



Industry panel discussion at the EMBL in the USA event at Stanford University. (Left to right) **Jürgen Bauer**, Deputy Managing Director of EMBL’s technology transfer partner, EMBLEM; **Lars Steinmetz**, EMBL senior scientist and Director of the EMBL | Stanford Life Science Alliance; **Gitte Neubauer**, EMBL alumna and co-founder of Cellzome; **Oliver Hanisch**, co-founder and Managing Partner at German Silicon Valley Innovators; **Fay Christodoulou**, EMBL alumna and co-founder and Chief Scientific Officer at Miroculus; and **Patrick Baeuerle**, EMBL alumnus and Executive Partner at MPM Capital.

Georgios Skiniotis, EMBL alumnus and Professor of Molecular and Cellular Physiology and

Structural Biology at Stanford University; speaker: “EMBL is a very special place. I can say that,

having experienced different types of universities and institutions. It pulls together a very diverse mix of scientists. At EMBL, you interact closely with people from other programmes. Whether you’re in developmental biology, structural biology or some other discipline, there’s always a connection – there’s always crosstalk.”

Lars Steinmetz, EMBL senior scientist and Director of the EMBL | Stanford Life Science Alliance; co-organiser: “Stanford is at the heart of innovation in Silicon Valley, and a lot of our EMBL alumni in the US are entrepreneurs. So this is an opportunity to think about projects and collaborations at a level where industry can get involved – to take innovations from the lab to the market. This is ultimately one of the major ways that we can bring the benefits of science to society.”



A range of activities took place online, at EMBL Heidelberg, and around the world. (Top left) EMBL alumnus Angus Lamond, master of ceremonies for EMBL World Alumni Day, with Mehrnoosh Rayner, Head of Alumni Relations.

EMBL World Alumni Day

A worldwide celebration of EMBL's alumni community

BY TOM FURNIVAL-ADAMS

The first annual EMBL World Alumni Day took place on 19 July 2019, both online and at events hosted by alumni in locations worldwide. It was a special opportunity to connect the global alumni community with EMBL. Speakers, performers, and alumni came together at EMBL Heidelberg to celebrate the 20th anniversary of the EMBL Alumni Association, in an event that was streamed live around the world. Alumni shared inspiring stories on social media using the hashtag #EMBLalumni, explaining how their time at EMBL has shaped their lives and careers.

Edith Heard, EMBL Director General, introduced herself to EMBL alumni and friends, and addressed the key role of alumni in EMBL's future plans. EMBL World Alumni Day will continue to be used as a platform to

share new developments at EMBL with the alumni community, and to gain valuable input and feedback.

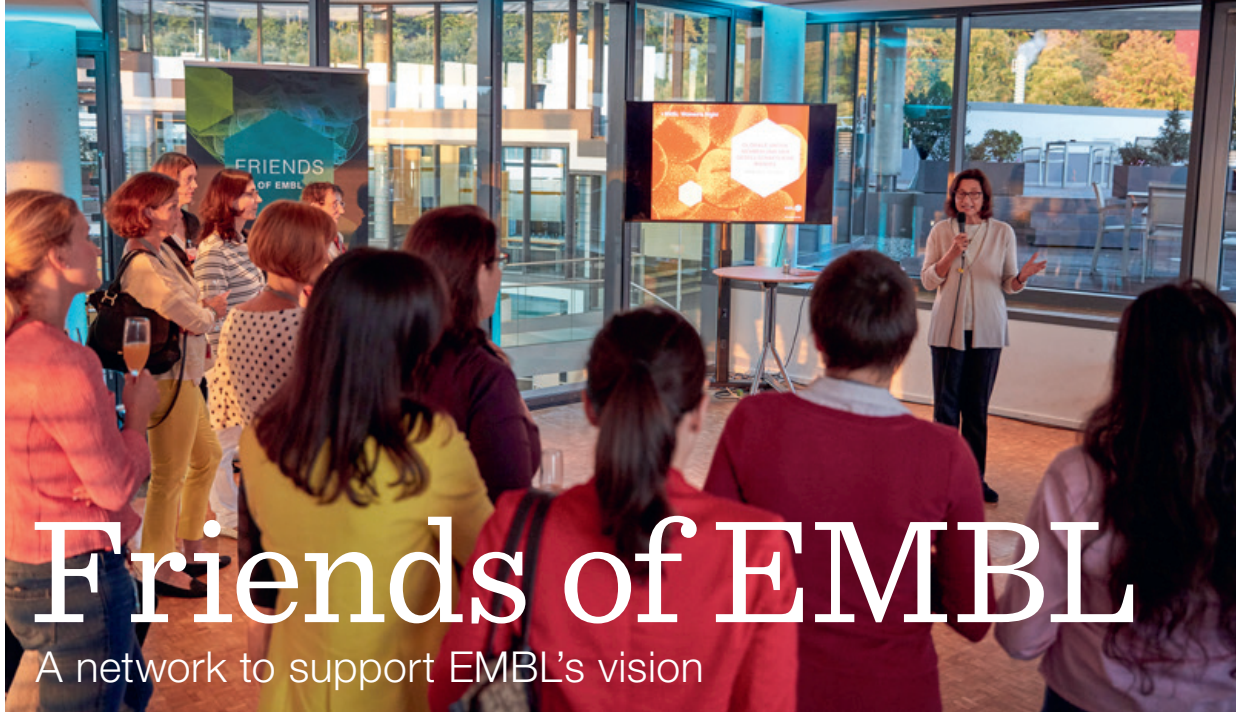
Help us make 2020 even bigger

We're already planning for World Alumni Day 2020, which will take place on 17 July. We want to make the next World Alumni Day even bigger and better, so your input will be crucial. You can get involved as a host, participant, video contributor, or social media ambassador. Contact us at alumni@embl.org to share your ideas and help make World Alumni Day a fittingly fun, collaborative, colourful, and impactful celebration of the incredible people who have made – and continue to make – EMBL what it is.

 WATCH THE FULL EVENT:
[BIT.LY/embl-94-wad2019](https://bit.ly/embl-94-wad2019)



MARIETTA SCHUPP/EMBL



Friends of EMBL

A network to support EMBL's vision

EMBL Women's Night, run by the Friends of EMBL.

BY BARBARA SOLICH

The Friends of EMBL programme has its origins in 2014, when EMBL celebrated its 40th anniversary. As EMBL alumni, research partners, local and international collaborators, and science enthusiasts congratulated EMBL on this milestone, many of them asked how they could support EMBL's research and other activities. The Friends of EMBL programme was therefore set up for all those – whether individual supporters or companies – who wish to contribute to EMBL's endeavours to unravel the mysteries of life and shape a better future.

Ever since, the Friends of EMBL have been among EMBL's closest supporters. Their annual membership donations have significantly contributed to many

EMBL initiatives, including biodiversity research, a microscopy project for schools, career development support for PhD students, and the advancement of women in science. The Friends of EMBL support EMBL for the benefit of society.

Members of the Friends of EMBL network meet regularly at inspiring events at EMBL Heidelberg, to hear about recent EMBL research and to meet fellow supporters and EMBL scientists. We're delighted to welcome new Friends and keen to expand our network further, also geographically. If you're interested in joining or learning more about our vibrant community, please contact the Friends of EMBL at friends@embl.de or visit embl.org/friends.

COURTESY OF J. FELDMANN



“EMBL is a leading institution of socially relevant cutting-edge research, based on international and

interdisciplinary teams, with a governance that ensures constant review and innovation and provides outstanding young scientists with an excellent working platform.”
Dr John Feldmann, Friend of EMBL

COURTESY OF M. SCHÜßLER



“I like EMBL because of the dedicated scientific work and the way they let us participate – through lectures

and events in the most pleasant surroundings and a warm and hospitable atmosphere!”
Dr Manfred Schüßler, Friend of EMBL

SPARKASSE HEIDELBERG



“Sparkasse Heidelberg has always been committed to sustainability, economic growth, as well as to social

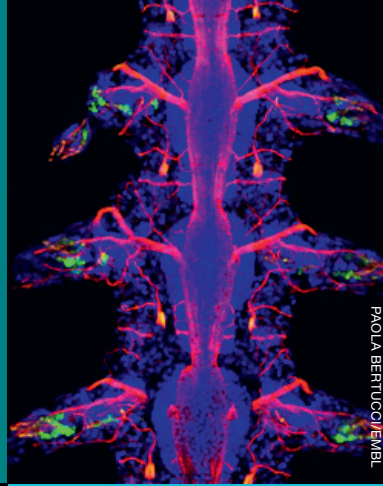
development and quality of life for the citizens of the region. We have been close supporters of the local research institutions, and are very happy to be Business Friends of EMBL.”

Rainer Arens, CEO of Sparkasse Heidelberg, Business Friend of EMBL

Events

February
10–12

La Pedrera, Barcelona
EMBL-IBEC Winter
Conference:
Engineering Multicellular
Systems



PAOLA BERTUCCI/EMBL

Upcoming meetings
Alumni

31 January
**Alumni Association
board meeting and drinks
reception, EMBL Barcelona**

20 March
**EMBL Retirees' Afternoon,
EMBL Heidelberg**

7–8 May
EMBL in Italy, IIT, Genoa

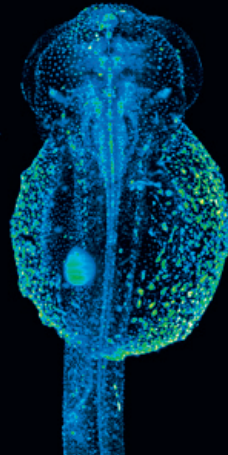
18 May
**EMBL in the UK, University
of Dundee**

8–9 June
**Edith Heard Symposium,
Collège de France, Paris**

17 July
EMBL World Alumni Day

March
1–4

EMBL Heidelberg
EMBO | EMBL Symposium:
The Organism and its
Environment



DIMITRI KROMM, LEONIE ADELWANN, COLIN LISCHIK/EMBL,
COS, HEIDELBERG UNIVERSITY

March
15–20

EMBL Heidelberg
EMBO Practical Course:
FISHing for RNAs: Classical to
Single Molecule Approaches

March–April
29–1

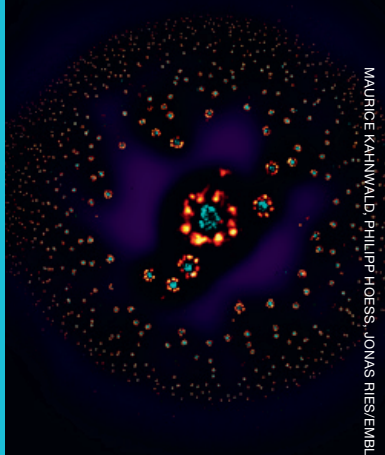
EMBL Heidelberg
EMBO | EMBL Symposium:
The Four-Dimensional Genome

April
20–22

EMBL-EBI
EMBL Conference:
2nd European Network Biology
Conference: From Networks to
Modelling

April
20–27

EMBL Heidelberg
EMBO Practical Course:
Microbial Metagenomics:
A 360° Approach



MAURICE KAHNVAALD, PHILIPP HOESS, JONAS RIES/EMBL

April
23–24

EMBL-EBI
EMBL Course:
Advanced Network Analysis
and Visualisation in Cytoscape



VIEW THE COMPLETE
LIST OF EVENTS ONLINE:
embl.org/events