

# Annual Report

embl.org European Molecular Biology Laboratory



A metamorphosing sea anemone planula larva developing tentacle buds. The nuclei of the organism's cells are shown in green and the actin cytoskeleton in blue.

Anniek Stokkermans/EMBL

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Cover image: Single plane illumination microscopy image of a portion of a chemically cleared adult mouse lung, taken at the newly opened Mesoscopic Imaging Facility at EMBL Barcelona. Structures are shown with colour encoding depth. Jim Swoger/EMBL; Greetje Vande Velde/KU Leuven





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## Foreword

This Annual Report marks a transition period for EMBL, as Iain Mattaj passes the baton to me as Director General. It is an opportunity to reflect on EMBL's most recent successes as well as the highlights of the past 14 years, made possible thanks to Iain's leadership (p. 4). These include the establishment of EMBL Barcelona, the construction of new buildings across many of EMBL's sites, and the welcoming of eight new member states into the EMBL family. With these achievements, EMBL has grown tremendously.

Alongside EMBL's growth, the skills and collaborative attitudes of people working at EMBL have been nurtured. Since starting as Director General in January 2019, I have already gained a sense of people's energy, enthusiasm and creativity. This motivation to perform and support excellent fundamental research gives me assurance as I begin my first year as EMBL Director General.

I have always looked to EMBL as a model for excellent fundamental life sciences research, and the research highlights that have emerged from EMBL in 2018 are no exception (p. 6). What also strikes me about EMBL's achievements in 2018 are the efforts being taken to bring together science and society through numerous outreach initiatives. This includes European Researchers' Night (p. 40), an event that invited local communities to interact with and learn about EMBL's research near two EMBL sites. It is this ever-increasing awareness of our vital link with society that brings further value to our member states.

As we look forward, I am keen to build on these successes by working with everyone in the EMBL community to further foster exceptional science, along with positive and productive working environments, across EMBL's six sites.

Edith Heard, FRS Director General



Iain Mattaj and Edith Heard.

## **Farewell** Iain Mattaj

### Celebrating EMBL's achievements under Iain's leadership

EMBL has flourished under Iain Mattaj's leadership. Here is a selection of achievements from the past 14 years, from across EMBL's sites, Europe and the wider world



"Excellent science has always been Iain's guiding principle and the foundation for all institutional decisions. His vision and thoroughness earned him great trust with EMBL staff."

Silke Schumacher Director of International Relations



"Iain's academic excellence has enriched EMBL's work and reputation for many years. His outstanding communication skills and leadership qualities have enabled so much." Patrick Cramer Chair of EMBL Council



"I love EMBL and I have huge respect for Iain and all that he's done over these years. He's been a fantastic force for EMBL, for European science and, through that, world science."

Paul Nurse Chair of the Scientific Advisory Committee





#### EMBL SITE ADVANCES

#### EMBL BARCELONA • Establishment and opening of EMBL Barcelona 2017

EMBL-EBI • Extension of the EMBL-EBI

- building 2007 Construction of the South
- Building 2013
- EMBL GRENOBLE · Construction of the Carl-Ivar Brändén Building on the European Photon and
- Neutron (EPN) campus to house the Partnership for Structural Biology 2006
- EMBL HAMBURG
- Construction of three synchrotron beamlines as part of the synchrotron radiation source PETRA III 2009

- · Construction of the Centre for Structural Systems Biology building on the Deutsches Elektronen-Synchrotron (DESY) campus 2017
- EMBL HEIDELBERG Construction of:

• Building 13 2009 Advanced Training

- Centre 2010 • Building 14 2018 • EMBL Imaging Centre
- completion in 2021

EMBL ROME • Funds raised for the renovation of Building 21 **2018** 

#### **NEW MEMBER STATES**

• Iceland 2005 • Croatia 2006 Luxembourg 2007 • Czech Republic 2014 • Malta 2016 • Hungary 2017 • Slovakia 2018 Montenegro 2018

#### **NEW PARTNERSHIPS**

- Partnership in Systems Biology with the Centre for Genomic Regulation 2006
- Nordic EMBL Partnership for Molecular Medicine 2007
- EMBL Australia Partnership Laboratory 2010
- Wellcome Sanger Institute 2012

#### NEW ASSOCIATE MEMBER STATES

- Australia 2008
- Argentina 2014
- EMBL-Hubrecht Partnership for Stem Cell and Tissue Biology **2016**
- Hungarian Center of Excellence for Molecular Medicine-EMBL Partnership 2018

## Research highlights

EMBL performs fundamental research in molecular biology

#### EMBL BARCELONA

The Sharpe group analysed computational evidence that Turing systems can be much more flexible than previously thought, expanding Alan Turing's 1952 theory of morphogenesis. The researchers suggest that the structure of feedback between a network's components is what determines its fundamental properties. The Sharpe group then collaborated with the Bristol Robotics Laboratory and the Centre for Genomic Regulation and applied its research to robotics. By programming swarms of tiny robots with instructions on how to interact only with their neighbours, the group imitated the growth of biological forms.

Diego X et al. (2018) Key features of Turing systems are determined purely by network technology. *Physical Review X* 8(2):021071. doi: 10.1103/PhysRevX.8.021071 Slavkov I, Carrillo-Zapata D et al. (2018) Morphogenesis in robot swarms. Science Robotics 3(25):eaau9178. doi: 10.1126/scirobotics.aau9178

Synthetic biology aims to create synthetic tissues that can help us understand natural development mechanisms. The first step towards creating synthetic tissue is controlling cellular pattern formation. Scientists led by Miki Ebisuya have shown, through a combination of synthetic and theoretical biology, that a reconstituted Nodal-Lefty network in mammalian cells spontaneously gives rise to a reactiondiffusion pattern.

Sekine R et al. (2018) Synthetic mammalian pattern formation driven by differential diffusivity of Nodal and Lefty. Nature Communications 9:5456. doi: 10.1038/s41467-018-07847-x



#### EMBL-EBI

Scientists in the Stegle and Marioni groups, in collaboration with scientists at the Babraham Institute and the University of Edinburgh, have developed the first single-cell analysis method that allows simultaneous analysis of the nucleosome, methylation and transcription sequencing (scNMTseq). ScNMT-seq allows researchers to analyse differences between single cells that could play key roles in both the early stages of life and the first stages of diseases such as cancer.

Clark SJ et al. (2018) scNMT-seq enables joint profiling of chromatin accessibility DNA methylation and transcription in single cells. Nature Communications 9:781. doi: 10.1038/ s41467-018-03149-4

Cancer is caused by mutations transforming normal cells into cancerous ones. Mutations arise when aberrant DNA is not repaired correctly, and this process is greatly accelerated when DNA repair pathways are compromised. By studying DNA mismatch repair deficiency in Caenorhabditis elegans and human cancers, the Gerstung group, with researchers at the University of Dundee and the Wellcome Sanger Institute, has begun to understand the footprints of these mutational processes.

Meier B, Volkova NV et al. (2018) Mutational signatures of DNA mismatch repair deficiency in C. elegans and human cancers. Genome Research 28(5):666-675. doi: 10.1101/gr.226845.117



The Gerstung group demonstrate that experiments using C. elegans are a key resource for understanding human cancer.

Scientists from the CRyPTIC consortium, including members of the Iqbal group, have shown for the first time that DNA-based diagnostics for tuberculosis (TB) are sufficiently accurate to replace traditional tests for detecting susceptibility to the four first-line drugs. The number of drug-resistant TB cases is rising, making it complicated to identify the right treatment for each patient. By sequencing TB bacteria from patients, clinicians can predict which anti-TB drugs offer the best treatment options.

CRyPTIC Consortium and the 100,000 Genomes Project (2018) Prediction of susceptibility to first-line tuberculosis drugs by DNA sequencing. The New England Journal of Medicine 379:1403–1415. doi: 10.1056/NEJMoa1800474

Scientists from the Beltrao group, collaborating with the Typas group in Heidelberg, have computed the impact of nearly all possible amino acid and nucleotide variants in the reference genomes of humans, yeast and Escherichia coli. This resource allows scientists to rely on computational predictions for how variations in genes will present themselves, before carrying out costly experiments.

Wagih O et al. (2018) A resource of variant effect predictions of single nucleotide variants in model organisms. Molecular Systems Biology 14:e8430. doi: 10.15252/msb.20188430

#### EMBL GRENOBLE

drug, weakening the drug's effect.

The Cusack group has worked with scientists at Japanese pharmaceutical company Shionogi to assess potential drug resistance to their new flu medicine, Xofluza, which targets a key viral enzyme called the endonuclease. The EMBL scientists determined crystal structures of the drug bound to normal and mutated forms of the endonuclease. The mutation led only to a small structural change, but this change resulted in reduced contact with the

Omoto S et al. (2018) Characterization of influenza virus variants induced by treatment with the endonuclease inhibitor baloxavir marboxil. Scientific Reports 8:9633. doi: 10.1038/ s41598-018-27890-4





Mutations at the amino acid shown in orange lead to reduced susceptibility to the new flu medicine, Xofluza.



The Panne group reveal how cellular signalling controls chromatin modification.

Signals from cellular receptors lead to chromatin modifications and changes in gene expression. For example, gene activation is typically associated with chromatin acetylation. To reveal the underlying mechanism, researchers led by former EMBL group leader Daniel Panne studied p300, an enzyme that transfers acetyl groups. They found that transcription factor dimerisation activates p300, thus revealing the molecular mechanism and how cellular signalling controls this process.

Ortega E et al. (2018) Transcription factor dimerization activates the p300 acetvltransferase. Nature 562:538-544. doi: 10.1038/ s41586-018-0621-1

To respond rapidly to microbial infection, the immune system uses pattern recognition receptors to detect pathogens. Receptors are activated and signals are sent via adaptor proteins. The Cusack group, in collaboration with other teams, has combined X-ray crystallography, solid-state nuclear magnetic resonance spectroscopy and high-resolution cryo-electron microscopy to determine the atomic structure of filaments of adaptor proteins and reveal the intermolecular interactions that stabilise the assembly.

Pellegrini E et al. (2018) RIP2 filament formation is required for NOD2 dependent NF-KB signalling. Nature Communications 9:4043. doi: 10.1038/s41467-018-06451-3

#### EMBL HAMBURG

Clathrin-mediated endocytosis is essential for protein retrieval and receptor recycling. Adaptor proteins assemble together with clathrin through interactions with specific lipids on the plasma membrane, but the precise mechanism of this assembly is unknown. Scientists led by Maria Garcia Alai and Rob Meijers have used mass spectrometry and X-ray crystal structures to propose a phospholipid-driven mechanism that could govern this process and explain why it differs between humans and fungi.

Garcia Alai MM, Heidemann J et al. (2018) Epsin and Sla2 form assemblies through phospholipid interfaces. Nature Communications 9:328. doi: 10.1038/s41467-017-02443-x

During spinal cord development, neurons have to project axons across the body's midline to coordinate movements between its left and right sides. By determining the 3D structures, scientists from the Meijers and Svergun groups, in collaboration with Peking University, have discovered how the protein Netrin-1, which guides axons towards the midline, links up with the protein Draxin, which drives axons to gather into bundles, to form a bridge between axons.

Liu Y, Bohmick T et al. (2018) Structural basis for Draxin-modulated axon guidance and fasciculation by Netrin-1 through DCC. Neuron 97(6):1261–1267. doi: 10.1016/j.neuron.2018.02.010

#### EMBL HEIDELBERG

#### Cell Biology and Biophysics

A cell neatly packages more than two metres of DNA into compact chromosomes during cell division. Researchers from Delft University and the Häring group have managed to film the action of the central protein complex in this process for the first time. They witnessed - in real time - how a single condensin complex reels DNA into loops.

Ganji M et al. (2018) Real-time imaging of DNA loop extrusion by condensin. Science 360(6384):102-105. doi: 10.1126/science aar7831



A condensin protein complex creates a loop in DNA.



A 3D rendering of the dual spindle, shown in green, attached to kinetochore proteins, shown in orange, during an embryo's first cell division.

Group leader Jonas Ries led research, in collaboration with Marko Kaksonen and François Nédélec, to image sites on yeast cell membranes where cells 'eat' nutrients and other molecules by endocytosis. They discovered different proteins gathering in precise shapes on the membrane. These proteins act as templates to recruit actin molecules, which pull the membrane inwards to surround external molecules before they are brought into the cell.

Mund M et al. (2018) Systematic nanoscale analysis of endocytosis links efficient vesicle formation to patterned actin nucleation. Cell 174(4):884-896. doi: 10.1016/j. cell.2018.06.032

It was thought that during an embryo's first cell division, one spindle was responsible for segregating the embryo's chromosomes into two cells. Research led by the Ellenberg group now shows that in mice, there are two spindles keeping each parent's genetic information apart throughout the first cell division. The group has also developed a 4D computer model for real-time tracking of proteins during mitosis. Users of this public resource can now choose any combination of mitotic proteins and see where and with which other proteins they work during cell division.

Cai Y. Hossain J et al. (2018) Experimental and computational framework for a dynamic protein atlas of human cell division. Nature 561:411-415. doi: 10.1038/ s41586-018-0518-z

Reichmann J et al. (2018) Dual-spindle formation in zygotes keeps parental genomes apart in early mammalian embryos. Science 361(6398):189-193. doi: 10.1126/science. aar7462

### **Developmental Biology**

Researchers led by Stefano De Renzis have guided the shaping of tissues using optogenetics - thereby controlling protein activity with light. They reconstructed epithelial folding: a fundamental process during embryo development that eventually gives rise to internal tissues like muscles. They also showed that these processes could be prevented in fruit fly embryos by stiffening cell surfaces, thereby making it impossible for them to bend inwards and shape organs.

Izquierdo E et al. (2018) Guided morphogenesis through optogenetic activation of Rho signalling during early Drosophila embryogenesis. Nature Communications 9:2366. doi: 10.1038/s41467-018-04754-z Krueger D, Tardivo P et al. (2018) Downregulation of basal myosin-II is required for cell shape changes and tissue invagination. The EMBO Journal 37(23):e100170. doi: 10.15252/embj.2018100170

Cells activate specific genes in a rhythmic manner during early development, causing waves of activation to sweep through an embryo. Scientists from the Aulehla and Merten groups have now shown that the difference in rhythm between two specific sets of waves is key for the formation of new segments in mouse embryos.

Sonnen KF et al. (2018) Modulation of phase shift between Wnt and Notch signaling oscillations controls mesoderm segmentation. Cell 172(5):1079-1090. doi: 10.1016/j.cell.2018.01.026

#### **Directors' Research**

By interacting with nucleic acids (DNA and RNA), proteins create complexes that regulate cell behaviour. To understand how these complexes regulate cell function, they must be isolated from nucleic acids. Claudio Asencio, a researcher in the Hentze group, has developed a new method, called Complex Capture (2C), that simplifies the extraction of complexes by using silica-based extraction columns commonly used in labs to purify nucleic acids.

Asencio C et al. (2018) Silica-based solid-phase extraction of cross-linked nucleic acid-bound proteins. Life Science Alliance 1(3):e201800088. doi: 10.26508/lsa.201800088



Artistic rendering of the elution of an RNA-protein complex from a silica matrix spin column during the final step of the 2C method.



#### **Genome Biology**

In collaboration with researchers at the University of Washington, the Furlong group has shown that single-cell measurements of chromatin accessibility can be used to deduce a cell's identity and developmental stage. The group demonstrated this genome-wide in almost 30 000 cells. The data uncovered a new potential lineage and reveal new insights into the control elements that regulate embryogenesis. This method will help researchers to uncover lineage trajectories and their regulation during embryonic development.

Cusanovich DA, Reddington JP, Garfield DA et al. (2018) The cis-regulatory dynamics of embryonic development at single-cell resolution. Nature 555:538-542. doi: 10.1038/nature25981

Arrows representing information that gives rise to different cell types emanate out of chromatin.

About 1% of patients diagnosed with autism spectrum disorder and intellectual disability have a mutation in a gene called SETD5. Scientists led by EMBL group leader Kyung-Min Noh and Gaia Novarino, of IST Austria, discovered what happens on a molecular level when SETD5 is mutated in cell cultures and in mice, and how this affects the chromatin environment and the mice's behaviour, respectively.

Deliu E, Arecco N, Morandell J, Dotter CP et al. (2018) Haploinsufficiency of the intellectual disability gene SETD5 disturbs developmental gene expression and cognition. Nature Neuroscience 21:1717-1727. doi: 10.1038/s41593-018-0266-2

The Typas, Bork and Patil groups and the Zeller team have profiled direct interactions between marketed drugs and individual gut bacteria. The study revealed that one in four non-antibiotic drugs inhibits the growth of abundant commensal gut bacteria. These drugs have antibiotic-like side effects and may promote antibiotic resistance. The researchers also developed new scientific recipes for growing gut bacteria in defined media, to facilitate mechanistic studies on microbiome-environment interactions.

Maier L, Pruteanu M et al. (2018) Extensive impact of non-antibiotic drugs on human gut bacteria. *Nature* 555:623–628. doi: 10.1038/nature25979 Tramontano M, Andrejev S et al. (2018) Nutritional preferences of human gut bacteria reveal their metabolic idiosyncrasies. Nature Microbiology 3:514-522. doi: 10.1038/ s41564-018-0123-9

### Structural and Computational Biology

The Bork group and researchers from the University of Tartu conducted the first global study of bacteria and fungi in soil. The team found that bacterial diversity in soil is lower if there are relatively more fungi around. They also discovered a strong positive correlation between the number of antibiotic-resistance genes in bacteria and the amount of fungi in the same sample.

Bahram M, Hildebrand F et al. (2018) Structure and function of the global topsoil microbiome. Nature 560:233-237. doi: 10.1038/s41586-018-0386-6

When transferred between bacteria, transposons - genetic elements that can switch locations in the genome autonomously - can carry antibioticresistance genes within them. Scientists in the Barabas group have provided the first crystal structure of a protein-DNA machine that inserts the transposons into recipient bacteria. The scientists also developed molecules and provided a proof of principle for blocking a transposon's movement.

Rubio-Cosials A et al. (2018) Transposase-DNA complex structures reveal mechanisms for conjugative transposition of antibiotic resistance. Cell 173(1):208-220. doi: 10.1016/j. cell.2018.02.032

Growing and dividing cells need large amounts of protein to build new tissue. To create the components required for protein synthesis, the cell first activates enzymes, such as Pol III, to read DNA. A study led by group leader Christoph Müller showed how Pol III begins to unwind and read DNA so quickly: it has all the necessary tools for its job built in and doesn't have to wait for help from other molecules.

Vorländer MK et al. (2018) Molecular mechanism of promoter opening by RNA polymerase III. Nature 553:295-300. doi: 10.1038/nature25440



Global warfare between bacteria and fungi in soil.

#### EMBL ROME

The Lancrin group and researchers at the Wellcome Sanger Institute have described a possible method to explain how blood stem cells are produced from cells in vascular walls. In the lab, they saw two cell fates compete with each other in a stem cell. If one key transcription factor is down-regulated, the transition to one cell type is accelerated. This could describe what is happening inside the naturally occurring 'undecided' cells lining our blood vessels.

Bergiers I et al. (2018) Single-cell transcriptomics reveals a new dynamical function of transcription factors during embryonic hematopoiesis. eLife 7:e29312. doi: 10.7554/eLife.29312

Scientists in the Heppenstall group have identified a population of nerve cells in the skin of mice, which are also responsible for the pain felt by patients with neuropathic pain. They developed a light-sensitive chemical that selectively binds to this type of nerve cell. When the affected skin area is first injected with the chemical and then illuminated with nearinfrared light, the targeted nerve cells retract from the skin's surface and pain is relieved. The team developed a similar method to combat itching using a chemical that binds only to the nerve cells that cause itching.

Dhandapani R et al. (2018) Control of mechanical pain hypersensitivity in mice through ligand-targeted photoablation of TrkB-positive sensory neurons. Nature Communications 9:1640. doi: 10.1038/s41467-018-04049-3

Nocchi L et al. (2018) Interleukin-31-mediated photoablation of pruritogenic epidermal neurons reduces itchassociated behaviours in mice. Nature Biomedical Engineering 3:114-125. doi: 10.1038/s41551-018-0328-5



Multiple synapse heads send out filopodia, shown in green, converging on a microglial cell, shown in red.

Microglia are part of the central nervous system's active immune defence and help guide healthy brain development. Researchers in the Gross group showed, for the first time, that microglia prune neuronal synaptic connections during early circuit refinement. In collaboration with the Schwab team in Heidelberg, they discovered that this pruning makes the synaptic connections stronger, rather than weaker.

Weinhard L et al. (2018) Microglia remodel synapses by presynaptic trogocytosis and spine head filopodia induction. Nature Communications 9:1228. doi: 10.1038/s41467-018-03566-5

### **Research in numbers**

Scientific publications and active research grants in 2018



#### **AWARD-WINNING RESEARCH**

Simon Fromm, Tanmay Bharat,

Sachse group

Paper of the Year 2018

#### **ERC GRANT SUCCESS RATE**



EMBL has the second highest success rate for receiving ERC

37% of ERC grant applications from compared with an average of 13%

\* Between 2007 and 2017

## **Group leader** profiles

Meet some of EMBL's curious scientists who lead fundamental research



#### Anna Kreshuk

EMBL Heidelberg Mathematics is aesthetically beautiful, but it was a bit too theoretical for me. I decided to do a PhD in computer science, focusing on machine-learning methods that could be applied to the life sciences. There were times when I couldn't see the road ahead, but you just have to keep going: the view will open when you turn the corner. In my group, we will develop machine-learning methods and tools for analysis of biological images, so biologists can extract information from images automatically. It's quite abstract, but it can be used for so many things!

#### Santiago Rompani

**EMBL** Rome I was fascinated by the concept of neuroscience as a way of fully understanding what it means to be human. Humans are very visual creatures: so much of our brain has evolved to process visual information and is tied into how we see the world. The visual thalamus, which receives direct input from the eye, had been thought of as a very simple relay nucleus, just passing on information to the visual cortex. However, we found that it is much more sophisticated than that. I believe understanding this at the level of brain circuitry will really help us understand the fundamental computations that make us human.



My group will help biologists get precise information from their images by developing analysis tools that blend mathematical models and computer vision algorithms. We're all working on very specific research projects, but it's important to keep sight of the bigger picture. The way I see it, all scientists are working together to help understand our world. I'm hoping to find enthusiastic PhD students and postdoctoral fellows who are excited about working at the intersection of biology, computer science and mathematics. This type of interdisciplinary work isn't an easy career path, so ambition and a strong motivation are key!

### Sagar Bhogaraju

**EMBL** Grenoble

In my lab, we're trying to understand a family of proteins known as melanoma antigens - proteins expressed by certain tumours, which can trigger an immune response. I also try to read a lot around my field, attend a talk on a different subject, or maybe once in a while go to a conference that doesn't focus only on my research topic. It's important to keep an open mind. At EMBL, I find it quite amazing to work with extraordinary people right next to me, to have lunch with them and talk about the latest technologies and developments. It's an enriching experience.



#### Miki Ebisuya

#### **EMBL** Barcelona

Since I was a child, I've really liked science. At university, I learned to make a hypothesis, try the experiment, repeat it and then fail! Only once in a while do we succeed, but I really enjoy this process. In my lab, we alter the genetics of cells to recreate and understand what happens during animal development. We've built artificial gene circuits, where genes are inserted into the genome of cells. Creating these gene circuits is really difficult, and in almost all cases it fails. I want researchers in my lab who don't give up - even if they fail a hundred times.



## **Services**

EMBL offers vital services to scientists

#### **Bioinformatics services**

EMBL-EBI is a global hub for open biological data resources and tools. These data resources are freely available to researchers around the world and enable efficient and innovative research in the life sciences. Daily requests to EMBL-EBI's data resource websites rose to 64 million in 2018, and at the close of the year, EMBL-EBI had more than 200 petabytes of data storage capacity, compared to 155 at the end of 2017. In 2018, EMBL-EBI launched several new data resources and tools, and released many added-value datasets originating from landmark global collaborations.

In response to the increasing accessibility of singlecell sequencing technology, EMBL-EBI launched the Single Cell Expression Atlas, which hosts and processes single-cell RNA sequencing data for a range of species. The service, a part of EMBL-EBI's Expression Atlas, enables scientists to search multiple experiments to see how a gene is expressed in individual cells. The service is expected to grow as data generation activities for the Human Cell Atlas ramp up.

In collaboration with The Jackson Laboratory, EMBL-EBI launched the first open research portal for patient-derived xenograft (PDX) models, called PDX Finder. The resource is hosted at EMBL-EBI and catalogues PDX models from numerous international repositories, including EuroPDX. PDX mouse models are used increasingly to study how cancers in

individual patients will react to tested drugs. The initial release of PDX Finder contained over 1900 models from multiple repositories, spanning cancers of the digestive system, respiratory tract, skin, breast, urinary system and more.

EMBL-EBI and partners have also launched the updated PhenoMeNal website, a portal for large-scale metabolomics analysis. The project, funded by the Horizon 2020 programme, uses innovative methods to help researchers with little or no programming experience to understand the drivers of health, ageing and disease through metabolomics.

EBI Metagenomics has changed its name to MGnify and has implemented a series of improvements. MGnify is a free resource for the analysis, archiving and browsing of all types of microbiome-derived sequence data. Over the past two years, MGnify has increased the number of datasets analysed tenfold. It contains data from collaborative projects such as Tara Oceans, Ocean Sampling Day, American and British Gut. and METASOIL.

In a major collaboration with EMBL-EBI and other partners, the Wellcome Sanger Institute announced it will sequence the genomes of 66 000 UK species. The project, known as the Darwin Tree of Life, is part of the wider Earth BioGenome Project, which aims to drive solutions for preserving biodiversity and sustaining human societies.

### **EMBL-EBI** services in numbers

EMBL-EBI's open databases, tools and software can be accessed by anyone worldwide

#### DATA GROWTH BY EMBL-EBI SERVICE



#### USAGE OF EMBL-EBI WEBSITES





EMBL-EBI launches the Single Cell Expression Atlas.

Europe PMC, the discovery platform for life sciences literature based at EMBL-EBI, now includes preprint abstracts alongside peer-reviewed content in its search results. The change aims to make science reported in preprints readily discoverable. At the end of 2018, almost 60 000 preprint abstracts were available in Europe PMC. EMBL-EBI's involvement in the Global Alliance for Genomics and Health (GA4GH) deepened in 2018, with several EMBL-EBI tools added to the GA4GH Suite, which aims to facilitate responsible international genomics data sharing. Among other benefits, these tools provide a secure protocol for researchers to access data and enable access to reference genomic sequences.

#### Structural biology services

EMBL provides infrastructure for structural biologists from all over Europe at the European Synchrotron Radiation Facility (ESRF) in Grenoble and Deutsches Elektronen-Synchrotron (DESY) in Hamburg. At both EMBL Grenoble and EMBL Hamburg, the synchrotron beamlines for macromolecular crystallography and smallangle X-ray scattering are complemented by advanced facilities for the preparation, characterisation and crystallisation of biological samples. Computational resources and EMBL-developed software packages for the analysis of structural data are also available. Through these integrated resources and facilities, EMBL offers access to services, expertise and user training across the entire structural biology workflow.

SERVICES

#### EMBL GRENOBLE

As part of the bilateral EMBL-ESRF Joint Structural Biology Group, EMBL and ESRF scientists and engineers have now automated most instruments on the macromolecular crystallography and small-angle X-ray scattering beamlines at the ESRF. One recent joint success was the full automation of the process of protein structure determination. This was achieved by combining the world's first fully automated protein crystallography beamline, MASSIF, with CrystalDirect, the robot developed by EMBL scientists that automates crystal harvesting (p. 31). This full automation is increasingly in demand from academics involved in EU-funded access programmes such as iNEXT and from the pharmaceutical industry.

The ESRF Extremely Brilliant Source upgrade has been underway since December 2018, and user operations will recommence in August 2020. In anticipation of this much-improved X-ray source, EMBL and the ESRF have launched new collaborative projects to develop instruments and methods necessary for the study of ever-smaller samples at microsecond resolution.

Alongside X-ray crystallography, cryo-electron microscopy (cryo-EM) is increasingly becoming a standard approach for structural biologists to obtain structures of large macromolecular complexes at



A 3D reconstruction of the atomic structure of an adenovirus fibre and its receptor, solved using ESRF's Titan Krios cryo-electron microscope.

atomic resolution. The ESRF, EMBL and the Institut de Biologie Structurale started their first full year of user service for the Titan Krios cryo-electron microscope. Funded largely by the ESRF, the microscope is operated by a team of three scientists – one from each institute – who are on hand to support users. To screen samples prior to imaging by the Titan Krios, EMBL installed a 200 KeV Glacios microscope with a direct detector at the end of 2018. The new facility is open to scientists from the ESRF's 22 partner nations and to the partner institutes' researchers, with access granted through a peer-review system on the basis of scientific merit. The cryo-EM facilities on the European Photon and Neutron (EPN) campus will continue to run throughout the ESRF shutdown.

#### EMBL HAMBURG

In February 2018, EMBL Hamburg welcomed Maria Garcia Alai as head of the Sample Preparation and Characterisation Facility (p. 29). With state-of-the-art biosensors and a synchrotron on site, the facility is one of the best equipped in Europe. It provides a range of services for structural biology research, from sample preparation and quality control, to biophysical techniques for determining protein structures, how proteins assemble, and how they interact with cell membranes.

In 2018, EMBL Hamburg played a key role in an international collaboration that developed a new, simplified method for taking snapshot movies of the motions of biomolecules. The 'hit-and-return' method is much faster than conventional time-resolved X-ray crystallography, which requires several hours of data collection to produce a single structural snapshot. Using the 'hit-and-return' method, many snapshots can be recorded in a single experimental session and then assembled into a time-lapse sequence. The method was developed by researchers from the Center for Free-Electron Laser Science and the Centre for Ultrafast Imaging in Hamburg, the University of Toronto in Canada, and ETH Zurich in Switzerland. The method was used with intense micro-focused X-ray beams from beamline P14 at EMBL Hamburg and beamline P11 at DESY to study an important enzyme for the breakdown of man-made pollutants. It is now being implemented as a standard sample environment for the new time-resolved macromolecular crystallography endstation on EMBL's beamline P14 at the PETRA III synchrotron at DESY. The efficiency of this new method means that many more researchers will have the opportunity to carry out timeresolved crystallography studies.



The sample environment on the new endstation on beamline P14 at EMBL Hamburg helps to decipher a biomolecule's structure and dynamics.

### Structural biology services in numbers

EMBL Grenoble<sup>\*</sup> and EMBL Hamburg services in 2018



#### **COMPUTATIONAL FACILITIES**



Computational facilities and software packages for data analysis 15 570 users

### Core Facilities, IT Services and imaging facilities

**Core Facilities** 

EMBL's Core Facilities offer scientists at EMBL and in its member states access to state-of-the-art equipment and expert support, enabling them to achieve their research goals. The services offered develop flexibly according to changing demands in the scientific community, and they are often developed in close collaboration with industry partners. The services currently cover the following areas: advanced light microscopy, chemical biology, electron microscopy, flow cytometry, genomics, metabolomics, protein expression and purification, and proteomics. These services are provided by experts who also share their knowledge with the broader scientific community. In 2018, a total of 422 scientists from EMBL member states visited or used the Core Facilities as external users. EU funding programmes iNEXT and CORBEL funded seven and three users. respectively, to visit and use the Core Facilities. In addition, four users received funding from the Christian Boulin Fellowship. This fund was established in memory of the late Christian Boulin, former Director of Core Facilities and Services, who made the Core Facilities accessible to external researchers.

The Advanced Light Microscopy Facility (ALMF) specialises in state-of-the-art light microscopy equipment and image processing tools to visualise all kinds of samples, ranging from the nanometre to the millimetre scale. The facility has installed a new inverted light-sheet microscope, which allows 3D time-lapse imaging of extremely sensitive samples such as early mouse embryos at the pre-implantation stage. The facility also significantly increased its capacity in confocal microscopy in response to requests by its users. A new STORM-based

super-resolution microscope equipped with computer-controlled microfluidics allows onstage staining of samples for highly multiplexed imaging techniques such as DNA-paint. The ALMF, in collaboration with the Genomics Core Facility (GeneCore), created a new service integrating the analysis of fluorescence microscopy images with single-cell transcriptome analysis.

The Electron Microscopy Core Facility (EMCF) makes the tools, equipment and expertise available to visualise samples, such as subcellular structures, at the ultrastructural level. The EMCF has developed transmission electron microscopy workflows that recognise features of interest within a sample before automatically acquiring new images. Implemented on two microscopes, the tools enable high-throughput acquisition of images to screen a sample relatively quickly for phenotypes. The tool can also drive the acquisition of serial tomograms for 3D reconstruction of subcellular features. The facility has increased its capacity in 3D electron microscopy by installing a second focused ion beam scanning electron microscope. In a collaboration with the ALMF, the EMCF has further developed automated correlative light-electron microscopy to allow the automatic correlative analyses of several tens of cells in one experiment.

The Flow Cytometry Core Facility analyses and categorises the physical and chemical characteristics of different cells within a sample. In 2018, the facility introduced a new service in flow cytometry of safety level 2 samples. It also supports several single-cell sequencing approaches in close cooperation with GeneCore.



A virtual slice through a chemically cleared embryonic mouse limb bud taken at the Mesoscopic Imaging Facility at EMBL Barcelona. Vasculature is shown in red, nuclei are shown in blue, and the expression of Sox9 is shown in green.

GeneCore prepares, sequences and analyses genomic data to allow the referencing, identification and further analysis of biological samples from organisms ranging from bacteria to humans. GeneCore has further improved its services in single-cell transcriptomics by establishing the 10X chromium technology. The facility also offers a service for direct eukaryotic mRNA sequencing.

The Protein Expression and Purification Core Facility advises and assists users with experiments related to protein expression, purification and biophysical characterisation. The facility has acquired a new PEAQ-ITC calorimeter, which has a higher sensitivity and is more user-friendly than the older ITC200

instrument. Consequently, users can now operate the calorimeter independently after having received training provided by the facility.

The Proteomics Core Facility provides the infrastructure needed to identify and characterise proteins. In 2018, the facility acquired another Fusion Lumos mass spectrometer, which allows deeper and faster proteome analyses and thus increases the facility's capacity and possibilities to develop new services. Together with members of the Beck group, the facility has developed cross-linking mass spectrometry as a new service.

## **Team leader** profiles

Meet some of EMBL's curious team leaders who head the scientific services

#### IT Services

EMBL's IT infrastructure is designed to support data-driven science. IT virtualisation and cloud technologies are vital for providing large-scale IT services that are robust, scalable, flexible and cost-effective. In 2018, IT Services upgraded the cloud-based graphics processing unit power to support the increasingly strong demand for specialised computing capacity, accelerating machine learning in areas such as large-scale image data analysis. In November, Rupert Lück, Head of IT at EMBL Heidelberg, was selected as one of 11 Executive Board members of the European Open Science Cloud, which aims to provide access to all outputs of publicly funded research in Europe by 2020. Lück will represent EMBL, as supported by EIROforum, in the expert group, which will assist the European Commission in the first phase of development of the service.

#### Imaging facilities

In 2018, the new Mesoscopic Imaging Facility opened at EMBL Barcelona, providing scientists with access to world-class microscopy and modelling technologies designed for studying tissues. The facility, together with the EMCF and ALMF in Heidelberg, is being used as part of the EU-funded CORBEL project.

At EMBL Heidelberg, construction began on the new EMBL Imaging Centre, which is scheduled to begin operations in 2021. The centre will offer access to the latest light and electron microscopy technologies, along with data analysis facilities and expert support. Technology developers, biological application specialists and microscope users will work together in the creative hub to further develop imaging technology prototypes. Close collaborative links with industry will be maintained to facilitate the global transfer and amplification of technology development.



#### Sarah Butcher

EMBL-EBI | Software Development and Operations I started as a wet-lab biologist who was frustrated by computers and ended up launching the bioinformatics service at Imperial College London. I'd like to use my experience to help bridge the gap between the people who develop and maintain EMBL-EBI data resources and the researchers who use them. As someone who has sat in all areas, I'd like to think I can assist communications on all sides.

#### Maria Garcia Alai

EMBL Hamburg | Sample Preparation and Characterisation Facility My team and I provide high-throughput crystallisation experiments to help users determine the biophysical characterisation of proteins. Some of the users that come to the facility in Hamburg are not structural biologists, so we provide them with support and supervision. Some scientists prefer to have a big question and answer that. I like to see what the puzzle looks like in the end, too, but the truth is I have so much fun with the methodology.

#### Jim Swoger

EMBL Barcelona | Mesoscopic Imaging Facility I've worked in international labs and institutes in Heidelberg, Edinburgh and now Barcelona, where I'm head of the new Mesoscopic Imaging Facility. We focus on intermediate-size samples that are large enough to be observed with the naked eye, but small enough that you need an instrument to see them properly. The immediate goal is to get the facility running at full capacity, but I would also like to create a network of imaging facilities for studying biology.





## Technology

EMBL actively engages in technology development, transfer and industry relations

Scientists at EMBL often seek innovative ways to answer biological questions, frequently developing new technologies and methods as part of the process. Imaging methods have consistently been a key area of innovation and development at EMBL, and 2018 was no exception.

EMBL's technology transfer arm, EMBLEM, manages the process of translating EMBL's fundamental research into practical applications, making the discoveries, technologies and methods developed at EMBL available for the broader scientific community and for commercial partners. This includes identifying and protecting intellectual property, facilitating the establishment of EMBL spin-off companies, developing collaborative research agreements, licensing technologies to third parties, and marketing and contracting scientific consultancy services.

In 2018, the Hentze group began a research collaboration with SolMic Research GmbH to investigate the modes of action of natural extracts used for medical applications, particularly in traditional Chinese medicine. The enhanced RNA Interactome Capture method developed by the Hentze group will be applied to SolMic Research's extracts to elucidate the molecular mechanisms involved in their action.

Building on their existing relationships, EMBL and GSK signed an agreement to initiate five new research collaborations at GSK's Cellzome site on the EMBL Heidelberg campus. These include collaborations

with the Hentze, Merten, Müller and Zaugg groups and the Pepperkok team. All five collaborations aim to enhance understanding of disease and drug mechanisms by applying EMBL technologies to disease-related challenges. Judith Zaugg began a collaboration with GSK with the aim of understanding the molecular mechanisms behind the regulation of certain cells within the immune system, thus providing insights into the autoimmune processes involved in various diseases. Rainer Pepperkok and colleagues imaged human lung tissue to study the mechanisms regulating inflammation and infectionmediated damage. They aim to develop predictive biomarkers for chronic obstructive pulmonary disease by understanding variations in patient response to infection.

John Marioni, group leader at EMBL-EBI, began a collaboration with biologics research and development company MedImmune on the use of single-cell RNA sequencing, including cell typespecific signal detection and comparison of different cell types, to study respiratory disease. Also at EMBL-EBI, building on a long-standing relationship with Oxford Nanopore Technologies, Ewan Birney and Robert Finn began another research project to work on the development of novel sequence analysis tools. EMBL-EBI group leader Pedro Beltrao entered into a collaboration with Roche to develop new computational approaches to reconstruct specific signalling networks and enable the prediction of cell type-specific targets.

At EMBL Grenoble, the Márquez team extended its collaboration with Merck Serono on the development of automated pipelines for drug design based on the CrystalDirect and CRIMS technologies developed at EMBL by José Márguez, Florent Cipriani and colleagues. Through this collaboration, Merck Serono and EMBL aim to support the company's





Human lung tissue imaged as part of a collaborative project between the Pepperkok team and GSK.

drug discovery process by evaluating the EMBL ligand screening pipelines based on the CrystalDirect technology. The goal of the extension is to validate workflows for high-throughput crystallography developed throughout the initial phase of the collaboration, for specific drug discovery projects (p. 23).

Open Targets was established in 2014 to address one of the most pressing problems in the pharmaceutical industry, namely the high failure rate in drug development. In 2018, Open Targets welcomed two more pharmaceutical companies, Celgene and Sanofi. The initiative fully exploits genomic and other omics data and produces data and informatics techniques that implicate targets to support data-driven decisionmaking and hypothesis generation, which can lead to higher success rates in drug development. Open Targets has established a portfolio of more than 50 interlinked projects in oncology, immunology and inflammation, and respiratory and neurodegenerative disease. Targets are being evaluated in-house by the industry partners, with key findings impacting the inflammatory bowel disease, respiratory and oncology programmes. Open Targets makes its

results available to the public and the initiative is becoming the pre-eminent centre for human drug target validation. Continuing EMBL-EBI's highly successful work on Open Targets, which involves more than 20 of the 44 EMBL-EBI groups and teams, in 2018 the partnership was opened up to all EMBL sites, including experimental as well as computational groups. Calls for proposals for Open Targets projects are now shared across EMBL.

The Corporate Partnership Programme continues its work to promote advanced training collaborations and community-building initiatives that position EMBL as a platform for connecting industry and academia. In 2018, the programme welcomed four global leaders in healthcare delivery and biomedical research as new members. Single-cell profiling and omics technology



EMBL staff and representatives of the Corporate Partnership Programme connect at the Corporate Partnership Programme event.

### **EMBLEM** in numbers

EMBLEM's technology transfer figures in 2018

## €11 287 000 38 disclosed 365 License and collaboration agreements concluded

and analysis company 10x Genomics, and biomedical research product developer and manufacturer Miltenyi Biotec joined the programme as Corporate Partners. Joining at the Associate Partner level in 2018 were Roche Diagnostics, a leader in delivering personalised healthcare and providing in vitro diagnostics, and Promega, a leader providing more than 4000 products in the fields of genomics, protein analysis and expression, cellular analysis, drug discovery and genetics.

The EMBL-EBI Industry Programme is a subscriptionbased programme for major companies that make significant use of the data and resources provided by EMBL-EBI as a core part of their research and

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development. The 25 member companies represent primarily the pharmaceutical sector but also the agri-food and consumer goods industries. In 2018, Daiichi Sankyo joined the Industry Programme, increasing the critical mass of companies from which to leverage activities in Japan. A key area of the Industry Programme's activity is delivering knowledge exchange workshops for industry partners, EMBL-EBI and other leading academic institutes. In 2018, 12 successful workshops were delivered, representing both technical and more therapeutically focused topics, such as machine learning in drug discovery and precision medicine, cancer systems biology, and pharmacokinetics prediction and design for biologics.

## **Training and** outreach

EMBL trains scientists, students and visitors at all levels

### Internal training

EMBL's PhD and postdoctoral research programmes provide world-class training for scientists within a collaborative and interdisciplinary environment. At any given time, EMBL hosts more than 500 PhD and postdoctoral researchers.

The EMBL International PhD Programme, established in 1983, continues to attract science graduates from around the globe. Currently 45 nationalities are represented. The programme supports students in gaining early independence through a combination of dedicated mentoring and creative freedom. In 2018, 58 new PhD students were admitted to the programme, including the first intake of students at EMBL Barcelona.

The 20th annual EMBL PhD Symposium took place in Heidelberg in November 2018 and was the largest to date. The theme, 'Game Changers: Taking Life Sciences to the Next Level', celebrated revolutionary ideas in molecular life sciences. Speakers included Nobel Laureates Stefan Hell and Christiane Nüsslein-Volhard.

The EMBL Interdisciplinary Postdoctoral Programme (EIPOD), currently in its third generation (EI3POD), provides training and career development opportunities for young researchers. Co-funded by the EU's Marie Skłodowska-Curie Actions, the

programme supports interdisciplinary research projects that span multiple groups and units at EMBL, and may also involve industry or inter-institutional collaborations. The EI3POD programme is characterised by ongoing innovation and development in the training it offers. In 2018, EMBL hosted 76 EIPOD fellows, of whom 21 are involved in cross-site collaborations.

In September 2018, 20 EMBL postdocs participated in the week-long EIPOD Corporate Summer School, which showcased research developments in industry. A series of talks highlighted various research avenues in industry, including in the pharmaceutical and healthcare sectors, giving a flavour of the research and collaboration opportunities available to researchers beyond academia, as well as the challenges faced by the life sciences industry.

In 2018, an in-house EMBO Lab Leadership course was offered for the first time at EMBL, to train postdocs in leadership and management skills. Another new offering is the Postdoctoral Management module, through which postdocs can record all training and career development activities completed during their time at EMBL. A training certificate containing this information can then be generated to support job applications as postdocs transition to their next career stage.

### Internal training in numbers

Number of EMBL PhD students and postdocs in 2018



#### **POSTDOCTORAL PROGRAMMES**



### External training

EMBL's Course and Conference programme for 2018 covered a diverse range of topics, bringing together experts to share new ideas and techniques, foster collaborations, and develop strategies to drive future research. The Advanced Training Centre in Heidelberg was the hub for the programme, hosting 25 of EMBL's 26 conferences and 31 courses. EMBL-EBI ran 25 bioinformatics courses, and EMBO practical courses also took place in Heidelberg and at the Hamburg and Grenoble sites. New themes featured in the 2018 programme included DNA replication, tissue self-organisation, imaging mouse development and systems genetics.

Among the conferences that took place in Heidelberg, three attracted an especially large number of delegates: 'Transcription and Chromatin', 'Organoids: Modelling Organ Development and Disease in 3D Culture', and 'The Complex Life of RNA'. Each brought together approximately 400 experts, postdocs and students to disseminate and discuss the latest advances in these fields.



Postdoctoral fellows participating in the Corporate Summer School.

### External training in numbers

EMBL's courses, conferences and scientific visitors in 2018



of scientific visitors rated their stay at EMBL as 'extremely useful'\*

76%

of participants were from EMBL member and associate member states

#### **CONFERENCES**

26

EMBL sites

75%

of conferences rated as 'excellent' by the



97%

of participants would recommend the conference to their

86%

visit to their colleague\*

\* Between October 2015 and January 2019



Robot avatars join EMBL-EBI training programmes, allowing remote participation.

A novel development in EMBL-EBI Training in 2018 was the use of robot avatars in bioinformatics training. With the help of small robots, two students on the genomic medicine master's programme who were new mothers were able to participate in course activities remotely, enabling them to continue their training while caring for their babies. As part of RItrain, the Research Infrastructure Training Programme, EMBL-EBI also hosted a workshop on equality, diversity and inclusion, and issued calls for knowledge-exchange visits for managers of research infrastructures.

The first research secondments via the international CABANA project, which aims to build bioinformatics capacity in Latin America, began at EMBL-EBI in 2018. The first off-site workshop, a train-the-trainer event, took place in Bogotá, Colombia, in November, and the use of webinars and e-learning tutorials was piloted

as part of a new master's course at the University of the Andes, Colombia. In October 2018, the first formal educational qualification in biocuration was launched at the University of Cambridge, UK, in collaboration with EMBL-EBI.

In addition to courses and conferences, EMBL promotes scientific excellence through its Scientific Visitor Programme. The programme provides opportunities for visiting scientists and students to benefit from new technologies and state-of-the-art equipment in EMBL laboratories and Core Facilities, and to establish collaborations with laboratories and group leaders across all EMBL sites. In 2018, scientific visitors participated in five successful flashtalk sessions that brought together visiting scientists from all EMBL sites. Feedback from visitors regarding their time at EMBL is consistently positive (p. 37).

#### Outreach, communications and education

Public engagement and outreach are an important part of EMBL's remit. Together, the Strategy and Communications team, the European Learning Laboratory for the Life Sciences (ELLS), EMBL's Science and Society Programme and the newly inaugurated EMBL Archive seek to inspire and educate people in clear and engaging ways.

EMBL organised and participated in an array of outreach events in 2018. As part of the international Pint of Science festival, EMBL scientists discussed their research with the public at events in Cambridge, Grenoble, Hamburg and Heidelberg city centres. An exhibition of artworks inspired by structural biology took place in Cambridge, following a two-year outreach project run by EMBL-EBI's Protein Data Bank in Europe (PDBe), known as PDB Art, which involved local schools and art societies. Scientists from EMBL Grenoble conducted outreach activities at Fête de la Science, a festival to promote science awareness and engagement among the general public. In Barcelona, EMBL scientists marked the International Day of Women and Girls in Science by discussing the importance of curiosity with a group of six-year-olds at Eulàlia Bota Primary School and participated in the Barcelona Biomedical Research Park (PRBB) Open Day.

EMBL also welcomed visitor groups onto its campuses. In Hamburg, students from Tel Aviv, Israel, chose to explore EMBL's structural biology facilities on the DESY campus, attending lectures and

receiving hands-on training. In Rome, enthusiastic high-school students attended seminars and practical laboratory sessions run by EMBL scientists as part of the two-week Summer in Science programme organised by the non-profit organisation Adamas Scienza. As part of EMBL's visitor programme for adult education, 23 groups comprising more than 500 visitors were welcomed onto the Heidelberg campus.

In 2018, ELLS, EMBL's educational programme, reached more than 200 high-school teachers and 2100 students, and engaged with 2000 members of the general public. In addition to welcoming 16 school groups to EMBL Heidelberg, ELLS organised two practical courses in molecular biology for European science teachers. One of the training workshops, on 'Genes, Research and Disease', was organised in collaboration with the Ministry for Education and Employment of Malta, the University of Malta, and the Esplora Interactive Science Centre in Malta.

Together with EMBL group leader Robert Prevedel and colleagues, ELLS set up a series of workshops entitled 'From Nature to Technology - Microscopes in Action'. Within these workshops, students aged 14-15 from the Internationale Gesamtschule Heidelberg learned to build a fluorescence microscope. The project culminated in a poster session that was covered by the local press. The project was kindly supported by generous donations from a regional foundation and from the Zukunft Metropolregion Rhein-Neckar e.V. ELLS also successfully applied to the European

Commission to organise European Researchers' Night on 27 September 2018, coordinated by EMBL and involving activities in both Heidelberg and Mannheim. The aim of the event was to bring together science and society and to attract young people to pursue research careers. Together with nine organisations spanning research, education, communication and the arts, the event offered a vibrant collection of 148 activities for thousands of visitors. Two members from the EMBL Teens programme, run by the Friends of EMBL, joined numerous activities and shared their impressions with many followers on the EMBL Instagram page. EMBL-EBI also participated in European Researchers' Night as a project partner of LifeLab, a collection of events coordinated by the Wellcome Genome Campus Public Engagement Team.

Engagement with local, national and international press was ongoing throughout 2018, with EMBL's research covered by major news outlets such as The Economist, national newspapers in all of EMBL's host countries, and radio and television appearances in the UK, Germany and Brazil. The importance of engaging with the press was exemplified in November 2018, when the story emerged that twins had been born in China whose genomes had been edited using CRISPR technology. EMBL responded with an explanation of what CRISPR is, how it can be used, and why strong regulation is needed for any research involving gene editing in humans.

The 2018 EMBL Science and Society conference, 'Infectious Diseases: Past, Present, and Future', explored topics including antimicrobial resistance, biosecurity, diseases of poverty, and public perceptions and misconceptions regarding vaccines.

In July, the EMBL Archive was inaugurated, making EMBL's rich scientific and institutional history accessible through documents and artefacts. Other outreach activities during the year included two EMBL Science Movie Nights, organised by the Friends of EMBL (p. 43), in which EMBL scientists dissected the plots of Contagion and The Martian to excise any scientific inaccuracies, improbabilities, or pure Hollywood fantasy.



A flash mob engages visitors as part of the European Researchers' Night.



The Benefit Gala in October raised generous support for the new 'Summer School for Undergraduates – Talents teach Talents'.

#### **Private support**

EMBL is grateful for all the generous support given by its supporters and sponsors, both anonymous and named. The Friends of EMBL is a fundraising initiative through which members of the public can provide annual donations to support EMBL researchers in their quest to unravel the mysteries of life. Generous donations by members of the Friends of EMBL were raised to support the Steinmetz Cardiomyopathy Fund and to provide further funding for the EMBL International PhD Programme. Local entrepreneur Manfred Lautenschläger was awarded an honorary membership of the Friends of EMBL in recognition of his long-standing support. Initial funding for the EMBL Lautenschläger Summer School, 'Talents teach Talents', was raised by a Benefit Gala in October, hosted at EMBL Heidelberg, with some 170 guests representing business, private funders and foundations and academia. Inspired by this, the Manfred Lautenschläger Stiftung gave a substantial gift, enabling the Summer School to run for five years.

The second European Conference of Life Science Funders and Foundations took place in Heidelberg in April. The event brought together a diverse group of stakeholders – from private investors and policymakers to entrepreneurial scientists - to explore potential opportunities for collaboration across borders and between organisations. Together, they considered how cutting-edge scientific and technological resources could be used most effectively to tackle some of the major challenges facing humanity.



A highlight of the Benefit Gala was a panel discussion with predoctoral fellows.

# Integrating life sciences

EMBL fosters collaboration among international scientific communities in Europe and around the world

#### Member state relations

As Europe's only intergovernmental organisation dedicated to research in the life sciences, EMBL plays a leading role in shaping science policy and strategy. EMBL fosters international relations in the spheres of science and politics in Europe and worldwide among its member states, with a broad range of funders, policymakers and scientific collaborators.

EMBL actively engages in strengthening relations with its member states. Within this mission, an EMBL delegation headed by the Director of International Relations visited the Collège de France in Paris to foster closer cooperation with the institute and with the French research community more broadly. This was formalised by the signing of a Memorandum of Understanding. The first EMBL-Consiglio Nazionale delle Ricerche steering committee meeting took place in Rome to discuss key issues regarding the renovation of EMBL premises in Italy. Other key engagements pursued by EMBL included a lunch with German parliamentarians, which was co-organised by the Humboldt Foundation, and participation in a conference dedicated to research and innovation in Israel, organised under the auspices of the Israeli Prime Minister. EMBL's Director General and Director of International Relations also visited Australia. where they met representatives of government and academia and group leaders in the EMBL Partner

Laboratory Network. This was followed by a visit from the EMBL Partner Laboratory Network in Australia to EMBL Heidelberg to attend a dedicated scientific symposium organised to foster collaboration among group leaders.

EMBL hosted a number of other visits from key scientific and political representatives. In January and February 2018, member of the House of Lords Stephen Green and British politician Vince Cable visited EMBL-EBI to learn more about the research and services undertaken at the Wellcome Genome Campus. In the latter part of 2018, Christian Luft, State Secretary at the German Federal Ministry of Education and Research, gave an address at the farewell event for EMBL Director General Iain Mattaj. Luft emphasised the fundamental importance of cooperation and networking across national borders in seeking innovative solutions to global challenges. Following the signing of a Memorandum of Understanding for scientific collaboration between EMBL and the University of Montenegro, a group of students from the University of Montenegro visited EMBL Heidelberg to learn about research and training opportunities at EMBL. In November, the leadership of Luxembourg Institute of Health and the Integrated Biobank of Luxembourg visited EMBL Heidelberg to nurture opportunities for future collaboration,

and an agreement was signed to provide financial support for cooperation between EMBL and researchers in Luxembourg.

Collaborative links were also celebrated between EMBL, the Czech Republic and other key partners in the field of microbiome research in 2018 with the launch of the BIOCEV project under the twinning instrument of the EU Research and Innovation

EMBL Sites

Member States

New Member States

Associate Member States



programme Horizon 2020. This programme fosters scientific excellence and innovation in research at the Faculty of Science of Charles University in Prague. The Horizon 2020 grant will facilitate knowledge transfer and training of Czech researchers in genomics. These collaborations follow on from the recently concluded trio of three-year twinning projects between EMBL and the Central European Institute of Technology in Brno.

EMBL welcomed two new member states in 2018: Slovakia in January and Montenegro in May. Their accession brings the total number of EMBL member states at the end of 2018 to 25, underscoring EMBL's commitment to promoting European life sciences research and strengthening collaboration within the research community. As member states, Slovakia and Montenegro will have access to EMBL's state-ofthe-art facilities and services, and each country can nominate two delegates to EMBL Council.

Lithuania has been an EMBL prospect member state since 2015, and its request to join EMBL as a full member was endorsed by EMBL Council in July 2018. Lithuania is now going through the national ratification process. In preparation for Poland's accession as a member state, the Nencki Institute

of Experimental Biology in Warsaw hosted a twoday conference in June, entitled 'Polish Science Towards EMBL', which was co-organised by the Polish Ministry of Science and Higher Education. EMBL's Director General, Director of International Relations and faculty members attended the event, which presented the wide range of opportunities offered by EMBL to the Polish scientific community. EMBL is also a strategic partner in an initiative funded by the Foundation for Polish Science that aims to establish a centre of excellence in neural plasticity and brain disorders - BRAINCITY - at the Nencki Institute. BRAINCITY's goal is to understand the mechanisms behind conditions such as autism, schizophrenia and Alzheimer's disease, and to develop new diagnostic and therapeutic methods.



The Nordic EMBL Partnership directors visit EMBL Heidelberg. From left to right: Agata Pernus Voigt, Plamena Markova, Janna Saarela, Mark Daly, Edith Heard, Iain Mattaj, Poul Nissen, Oliver Billker and Silke Schumacher.

#### **EMBL** partnerships

Through its partnerships with institutes and research organisations in member and associate member states, EMBL is at the heart of a network of centres of excellence in the life sciences. As part of this, EMBL renewed and extended its partnership with the Wellcome Sanger Institute. This mutually beneficial arrangement fosters close collaboration between EMBL-EBI and the Wellcome Sanger Institute. The Centre for Molecular Medicine Norway (NCMM) hosted the ninth annual meeting of the Nordic EMBL Partnership for Molecular Medicine in Oslo, Norway. The meeting brought together researchers at all levels from the four nodes of the network and from EMBL. New directors were appointed for three of the four partner institutes: Mark Daly at Institute for Molecular Medicine Finland (FIMM), Oliver Billker at the Laboratory for Molecular Infection Medicine Sweden (MIMS), and Janna Saarela at NCMM. Poul Nissen of the Danish Research Institute of Translational Neuroscience (DANDRITE) was chosen as the new speaker for the Nordic Partnership. The new directors visited EMBL to meet EMBL Director General Iain Mattaj and to discuss ideas for strengthening the partnership. Also in 2018, the Molecular Medicine Partnership Unit (MMPU), a joint venture between EMBL and the Medical Faculty of the University of Heidelberg, appointed Jan Korbel as Co-Director alongside Andreas Kulozik and Matthias Hentze. Helmut Dosch, Director at DESY, also visited EMBL Heidelberg in September to discuss ongoing collaboration opportunities with EMBL, particularly with EMBL Hamburg.

In addition to strengthening existing partnerships, EMBL fostered a new partnership with the Hungarian Centre of Excellence for Molecular Medicine (HCEMM). The HCEMM is newly established by the Biological Research Centre of the Hungarian Academy of Sciences, the University of Szeged and Semmelweis University, and is co-funded by the Hungarian Government and the European Commission through a Horizon 2020 Teaming grant.

#### Further broadening horizons

EMBL seeks to promote integration of the life sciences through cooperation with countries beyond its current membership base. In April 2018, the Slovenian State Secretary for Research visited EMBL to discuss potential collaborations. This was followed by a reciprocal visit to Slovenia by the EMBL Director of International Relations in November, to further explore joint areas of interest. Another focal country for EMBL's relationship-building efforts in 2018 was Estonia, where the opportunities offered by EMBL membership were presented to the Estonian life sciences community and key decision-makers.

### EU relations

EMBL maintains a strong relationship with the European Commission and regularly engages on European science policy issues, thereby contributing to the future direction of European Framework Programmes. This close collaboration is based on a Memorandum of Understanding and is implemented through biennial work plans that address areas of common interest and key challenges.

In line with this activity, EMBL provided input to key members of the European Parliament and the European Commission regarding the next EU Framework Programme for Research and Innovation, Horizon Europe. EMBL also published a paper setting out its vision for the next Framework Programme, and EMBL leadership and senior scientists took part in key EU conferences addressing the future of research. EMBL hosted the 64th plenary meeting of the Scientific Council, the governing body of the European Research Council (ERC), which was followed by a workshop discussing the position of life sciences research in the ERC.

#### EIROforum

EIROforum is a consortium of eight of Europe's largest intergovernmental research organisations. Its mission is to promote quality and impact in European research across a broad range of scientific disciplines. EIROforum also plays an important role in informing European science policy, and supports and facilitates international cooperation.

During the time when EMBL was chairing EIROforum, from July 2017 to June 2018, EIROforum signed a new Work Plan with the European Commission for the period 2018-2020. EIROforum also submitted a paper to the European Commission on simplifying the administrative rules and procedures of the future EU Framework Programme. EMBL Director General Iain Mattaj delivered a keynote address at the Bulgarian EU Presidency Flagship Conference on 'Research Infrastructures Beyond 2020'. He emphasised that, while collaboration with industry is indeed gaining momentum, the missions of providing scientific services and performing basic research lie at the heart of research infrastructures. EIROforum organisations also met with representatives of the Austrian EU Presidency to convey their views on the future of the EU Framework Programme. In addition, EIROforum, through its Chair, addressed a large audience during the International Conference for Research Infrastructures and reflected on the important role that intergovernmental research organisations play in setting global and European research policy agenda.

#### European research infrastructures

With its extensive experience in managing distributed life sciences research infrastructures, EMBL has been closely involved in the development of Biological and Medical Sciences projects on the European Strategy Forum on Research Infrastructures (ESFRI) roadmap. In particular, EMBL played a leading role in coordinating the preparatory phases of the Euro-BioImaging and ELIXIR projects.

ELIXIR, the ESFRI research infrastructure for biological data, which coordinates bioinformatics services across its member states, continued its successful operations throughout 2018. In December, ELIXIR celebrated its fifth anniversary and the launch of a new scientific programme. Since its inception, ELIXIR has grown to encompass 22 countries and now reports on its progress in the ELIXIR 2018 Annual Report.

In 2018, following a two-year evaluation process, ESFRI granted Euro-BioImaging the Landmark status of 'European Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences'. This status is recognised by the European Commission as a benchmark for quality, and it endorses Euro-BioImaging as the leading research infrastructure supporting imaging research across Europe. Euro-BioImaging aims to break down the barriers associated with biological and biomedical imaging by providing scientists with open access to imaging technologies, resources and expertise.

The Euro-BioImaging Preparatory Phase II project concluded successfully in 2018, paving the way for Euro-BioImaging to become a European Research Infrastructure Consortium (ERIC). An ERIC becomes a legal entity when the ERIC statutes are signed by all its member states. Its principal task is to establish and operate new or existing research infrastructures on a non-profit basis.

Euro-BioImaging began collaborating with two international partners – Australia and India – in December 2015 as part of the EU-funded Global BioImaging project, and by 2018, membership had increased to ten international partners. This international network facilitates the exchange of best practices and technological advances in imaging. As part of this, three key Global BioImaging events took place in Sydney, Australia, in September 2018. An 'Exchange of Experience' workshop brought together imaging infrastructure managers, directors, technical staff, scientists, decision-makers and funders to discuss quality issues in imaging infrastructures and the long-term sustainability of the Global BioImaging network. This was followed by two training courses on management and operation of imaging facilities, and on image data management and analysis.

## Honours and awards

#### HONOURS



#### **Ewan Birney**

Director of EMBL-EBI, Joint Head of EMBL-EBI Research and Senior Scientist

- Commander of the Order of the **British Empire** Sovereign of the United Kingdom
- Council Member UK Research and Innovation -Biotechnology and Biological Sciences Research Council

#### HONOURS & AWARDS

#### Peer Bork

Bork | Head of Unit, Senior Scientist and EMBL Heidelberg Strategic Head of Bioinformatics

- Heinz P. R. Seeliger Prize Seeliger Foundation
- Honorary Professorship Fudan University, China
- Elected Member Academia Europaea

#### **Matthias Hentze**

Hentze | Director and Co-Director of MMPU

- Ilse und Helmut Wachter Prize Ilse und Helmut Wachter Foundation
- International Honorary Member American Academy of Arts and Sciences





#### **AWARDS**



Alexandrov | Team Leader • Chica and Heinz Schaller **Research Award** Chica and Heinz

Jan Korbel

Senior Scientist

Korbel | Group Leader and

Cancer Research

Cancer Researcher Award

The Pezcoller Foundation -

European Association for

Schaller Foundation

 Otto Schmeil Prize Heidelberger Akademie der Wissenschaften

 Open Science Fellow Wikimedia Germany, Stifterverband and

**Tobias Wenzel** Merten and Bork | Postdoctoral Fellow Volkswagen Foundation



#### **Janet Thornton**

Jan Ellenberg

Senior Scientist

Leopoldina

• Member

Ellenberg | Head of Unit and

Academy of Sciences

Thornton | Group Leader and Senior Scientist

- Vice President for Life Sciences
- European Research Council's Scientific Council

#### Malvika Sharan Gibson | Computational Biologist

 Community Service Award (Joint Award) The Carpentries

 Mozilla Open Leader Mozilla Foundation





## Mikhail Savitski Savitski | Team Leader and Head

- of Proteomics Core Facility
  - One of the Top 40 Under 40 Power List The Analytical Scientist



Svergun | Joint Head of Research Infrastructures, Group Leader and

International Union of Crystallography Commission



#### Honours & awards won in 2018





**Robin Diekmann** Ries | Postdoctoral Fellow Tycho Jæger Prize Norwegian Physical Society

Toby Hodges Zeller | Bioinformatics Community **Project Manager** 

• Community Service Award (Joint Award) The Carpentries

Lisa Maier Typas | Postdoctoral Fellow Postdoctoral Award for **Young Scientists** Robert Koch Foundation and German Societies for Hygiene and Microbiology, Immunology

and Virology

Lars Velten Steinmetz | Research Staff Scientist













## Alumni

EMBL connects researchers around the world

EMBL's alumni number more than 8300 and are a valuable asset to EMBL's member states and the wider international scientific community. From sharing expertise to helping facilitate collaborations with their new institutions and countries, the alumni community embodies EMBL's spirit. To aid alumni in their continued success, EMBL created the position of Alumni Volunteer Officer. In the first year of this role, more 'EMBL in...' events were organised and held in Finland, Italy, Spain and the UK. The events empower alumni across the world to connect and network, enabling them to meet and share ideas with the life sciences community in a passionate and interdisciplinary environment. This year, the organisers of the first 'EMBL in Norway' event, Gareth Griffiths and Rein Aasland, received the Volunteer of the Year award from the Council for Advancement and Support of Education.

Each year, the EMBL Alumni Association celebrates the achievements of EMBL alumni with the John Kendrew and Lennart Philipson awards. Nils Gehlenborg was the 2018 recipient of the John Kendrew Young Scientist Award, which recognises excellence in science and science communication. Gehlenborg uses computer science to build tools and visual interfaces that enable researchers to efficiently interact with biomedical data. Now Assistant Professor of Biomedical Informatics at Harvard Medical School, he develops tools to visualise various types of data from large-scale cancer genomics studies such as The Cancer Genome Atlas. The Lennart Philipson Award recognises outstanding contributions to translational research and technology development. In 2018, this award went to Raffaele De Francesco for his revolutionary work on the Hepatitis C virus. De Francesco's work enabled Hepatitis C to become the first case in the history of medicine in which a chronic viral infection was cured with direct antiviral agents.

In 2018, alumnus Jacques Dubochet donated an official replica of his Nobel Prize medal to EMBL. Visitors and staff can view the medal in the EMBL Archive. In the accompanying note, he wrote:

"I am pleased to offer this copy of my Nobel medal to EMBL in testimony of my great thankfulness to an institution that, in my view, would deserve to be the laureate of the Prize."



Participants at the EMBL in the UK event.

## Administration

#### EMBL supports staff to thrive

EMBL Administration supports staff across all six EMBL sites. It establishes and maintains the processes, procedures and systems necessary to facilitate the pursuit of EMBL's missions within a cooperative and flexible culture that fosters equality and diversity. In 2018, a dedicated Council Working Group worked closely with EMBL management and representatives of the Staff Association to evaluate working conditions at EMBL. The Working Group recommended a number of changes to staff members' terms and conditions of employment across a range of areas, from parental leave to insurance, and these came into effect on 1 January 2019. The Working Group concluded that the terms and conditions of employment enable EMBL to attract and retain highly qualified staff.

In November, members of Human Resources and the Staff Association presented the newly published 'Guidelines on Flexible Working Arrangements' at all EMBL sites. EMBL recognises the many benefits of flexible working for employees and the organisation, and flexible working arrangements came into effect across EMBL at the beginning of 2019.



Rachel Curran, the new Head of Administration and Operations at EMBL-EBI.

In August, EMBL-EBI welcomed Rachel Curran as the new Head of Administration and Operations. A neuroscientist by training, Rachel will manage administrative functions such as finance and human resources, as well as overseeing facilities and strategic operational projects.

At EMBL Heidelberg, the construction of Building 14 was completed, providing a new home for the Staff Association, Facility Management, the Ombuds Office and the EMBL Archive. The building also has two videoconferencing rooms; a family room that can be used by EMBL staff members with children; and a large multipurpose space for exercise classes, courses, clubs, and use by the Kinderhaus. The space that was formerly occupied by Facility Management is being refurbished to become an extension of the existing animal facility.

#### **EMBL** Aid

Supported by the Staff Association, the EMBL Aid group organised a variety of fundraising events and initiatives throughout 2018, including a secret valentine fundraiser, bake and burger sales, tombolas, and sales of the EMBL calendar. The group also provided four consignments of donated clothes to the Caritasverband in Heidelberg, and assisted local refugees by taking photographs for job applications. All these efforts were facilitated by various teams and individuals across EMBL, including the Photolab, the Photo Club, Reception, Finance, the Hausmeister team and the Staff Association committee. In 2018, donations continued for the EMBL charity Aid for Labs, which sends laboratory equipment to institutions in need around the world. Other charities receiving donations included the Asylarbeitskreis, Child Care Project, Schifferkinderheim, Waldpiraten and Kinderplanet.



Building 14 houses the Staff Association, Facility Management, the Ombuds Office and the EMBL Archive.

## Personnel statistics

EMBL hires talented people from around the world

#### **PERSONNEL CATEGORIES IN 2018**



#### STAFF NATIONALITIES IN 2018



#### STAFF CLASSIFICATION IN 2018



#### **SCIENTIFIC VISITORS IN 2018**





#### VISITORS' NATIONALITIES in 2018



## Total 1 784

In full-time equivalent (FTE)

	I.	
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	I.	
	l	

Research Scientific services Scientific or technical support Training and outreach Administrative support General support

173 EMBL-EBI **Core Facilities and Scientific Services** Structural and Computational Biology Cell Biology and Biophysics Genome Biology EMBL Rome Developmental Biology Directors' Research **EMBL** Hamburg EMBL Grenoble EMBL Barcelona

472

25

EMBL member and associate member states EMBL prospect member states Non-member states

## Total 684

EMBL 2018 ANNUAL REPORT

## **Financial report**

EMBL's financial figures for 2018







\* Includes additional contributions from the UK Government for the Technical Hub and European Data Centre on the EMBL-EBI campus and from the German Government for the EMBL Heidelberg Imaging Centre

\*\* Includes ELIXIR member state contributions

\*\*\* Includes income from donations and operational entities such as contributions from EMBO, course and conference fees, canteen and cafeteria, guesthouses, etc.

#### Member state contributions

	x €1,000	%
Ordinary contribution	ns	
Austria	2,353	2.3
Belgium	2,884	2.8
Croatia	292	0.3
Czech Republic	989	0.9
Denmark	1,895	1.8
Finland	1,406	1.4
France	15,879	15.2
Germany	21,584	20.7
Greece	1,302	1.2
Hungary	258	0.2
Iceland	73	0.1
Ireland	1,125	1.1
Israel	1,645	1.6
Italy	11,787	11.3
Luxembourg	208	0.2
Malta	36	< 0.1
Montenegro	7	< 0.1
Netherlands	5,039	4.8
Norway	2,999	2.9
Portugal	1,197	1.1
Slovakia	156	0.1
Spain	7,778	7.4
Sweden	3,290	3.1
Switzerland	4,113	3.9
United Kingdom	16,233	15.6
	104.528	100

	x €1,000
Currency adjustment	
for Sterling adjustments	(1,240)
Entry fees	
Hungary	124
Slovakia	100
Montenegro	4
	228
	220
Associate member	
state contributions	
Australia	3,208

state contributions	
Australia	3,208
Argentina	695
	3,903

7,809

1,883

#### Additional contributions United Kingdom Germany 9.692

## **Reviews of scientific** and service units

### EMBL Core Facilities and IT Services review

The EMBL Core Facilities and IT Services were reviewed on 6-8 March 2018 by a panel of 17 international experts, including two members of the Scientific Advisory Committee (SAC). The review was chaired by Kai Johnsson, Max Planck Institute for Medical Research, Heidelberg, SAC Chair Paul Nurse and EMBL Director General Elect Edith Heard attended the review as observers.

#### **Evaluation summary**

The mission of the EMBL Core Facilities and IT Services is to support research groups at EMBL and, where capacity permits, scientists at institutions from EMBL's member states. It was the opinion of the review panel that both the Core Facilities and the IT Services perform exceptionally well and have a fundamental impact on research at EMBL and on European life sciences in general.

EMBL currently has eight Core Facilities, offering services in genomics, flow cytometry, advanced light microscopy, electron microscopy, chemical biology, protein expression and purification, proteomics and metabolomics. The panel rated the overall performance and the quality of the services offered by the facilities as outstanding. The Core Facilities and their leadership were congratulated on how they responded to major challenges over the last review period, including the turnover of three Core Facility Heads. Furthermore, a new facility - in metabolomics was successfully established, addressing a major need within EMBL.

The review panel also commended the facilities' efforts in developing new methods and workflows to help fulfil user needs. The development and implementation of on-section correlative lightelectron microscopy and correlative focused ion beam scanning electron microscopy services by the EMCF and of a complete multiplexed proteomics service workflow by the Proteomics Core Facility were highlighted as particular examples. The panel was impressed by the multidisciplinary approach of the Core Facilities' activities - based on the combination of complementary enabling technologies used in different facilities - for example, in the areas of correlative light-electron microscopy and single-cell technologies. The Core Facilities' training efforts both in supporting individual users and in organising courses and workshops for the wider community - as well as their integration into the European landscape through participation in international initiatives and networks were valued as exceptional.

In total, the panel was very impressed with the overall competence, commitment and transparency of the Core Facilities staff, and greatly appreciated their

efforts and unique enthusiasm in serving their user communities. In its thorough analysis of the unit's activities, the panel highlighted a need for additional expertise and user training in image processing and analysis, particularly for users of the ALMF and the EMCF, and thus recommended strengthening support in this area. The panel made several other recommendations - relevant either to the entire unit or to specific facilities - aimed at further improving and/or expanding the excellent service provided.

A dedicated sub-panel focused on the review of EMBL's IT Services, which was found to function extremely well and was rated as outstanding. The panel noted significant improvement and highly effective investments over the review period that had dramatically increased the IT service level and overall capacity. Moreover, the panel commended IT Services' contribution to integrated activities in European life sciences research, such as the European Open Science Cloud and work carried out in the context of EIROforum.

The panel expressed some concerns regarding the sustainability and scalability of the IT infrastructure, particularly the 3D Cloud, in view of the planned expansion of EMBL's imaging facilities, and recommended that the IT team be involved early in the planning phase, to define and respond to the new requirements. Other concerns related to securing the funding required for adequate bandwidth for all EMBL sites, and to the involvement of IT Services in setting up and operating the IT infrastructure, particularly at the sites in Grenoble and Hamburg. To ensure

that IT Services maintains its high quality of service, the panel recommended looking into recovering additional funding from user fees, intensifying user training in the areas of IT security and data management, and potentially strengthening activities in the area of desktop support.

Finally, the panel provided some suggestions to EMBL for the organisation of the next Core Facilities and IT Services review, aimed mainly at providing the reviewers with additional information ahead of the review and maximising their opportunities to collect feedback from various stakeholder groups.

#### Response to the review panel's recommendations

I would like to start by thanking the panels for their detailed analysis of EMBL's Core Facilities and IT Services and for the constructive recommendations and advice they provided. I am delighted with their extremely positive evaluation of the services under review and grateful for their suggestions as to how the materials presented for future reviews might be improved.

The reviewers attribute much of the success of these services to the efforts of Rainer Pepperkok and Rupert Lück, and I share the opinion that both have performed in an outstanding way. Rainer Pepperkok has proven to be an exceptional Head of Core Facilities, with his commitment as Head of the ALMF not affecting – and possibly even reinforcing – this important role. Rupert Lück has done an impressive job of scaling up the capacity and performance of

IT Services, particularly against the background of the recent data explosion arising from the use of new research technologies. Furthermore, the panel also highlights the high level of commitment and enthusiasm of the Core Facility staff at all levels. Indeed, the panel members identify this as one of the key features of the unit's overall success.

In reviewing the activities of the Core Facilities, the panel noted the need for additional user support in advanced image analysis. This issue was also highlighted recently during the review of specific EMBL research units; it is one that we are aware of and have been addressing, although previous attempts to recruit in this specific area have not been successful. One of the expert ALMF staff members has recently left the facility to head the new EMBL Centre for Bioimage Analysis, which provides support and training to scientists across EMBL and collaborates closely with both the ALMF and EMCF. I will say more below about the various staffing and upgrading recommendations made by the panel.

The panel felt that the activities of the Chemical Biology Core Facility (CBCF) are greatly affected by the uncertainty concerning its relationship with one of EMBL's external partners. The CBCF is indeed different from other EMBL Core Facilities in that it is a shared service, funded equally by EMBL, the German Cancer Research Centre (DKFZ) and the University of Heidelberg. The panel noted that its successful operation requires a sustainable funding model, which it believes should be based on a fiveyear commitment from EMBL and its partners. This

would allow for long-term planning and recruitment and retention of high-quality staff. The complexity of decision-making in the University has led to delays and shortfalls each time our agreement has had to be renewed. I fully agree with the panel's comments. Lack of continuity is bad for any service or support activity, and the CBCF is no exception. We have already engaged in discussions with our partner institutions around this topic and will continue to work with them until a suitable solution can be reached. We are also considering the possibility of adding an additional partner to help provide stability. I am happy to report that the acute funding problem at the time of the panel review has now been resolved.

Another concern highlighted by the reviewers regards the Metabolomics Core Facility. Although they regard it as having started very well, they believe it now needs further development and additional staff to achieve its promised goals. Again, I will comment on the recommendations for expansion of activities below.

In relation to EMBL's IT Services, perhaps the major recommendation made by the reviewers regards the development and implementation of a clear policy on data management, ideally to be complemented by offering training in this area to EMBL staff. In discussion with EMBL groups and teams, IT Services has been developing an application that helps to track the location of all stored data files on the storage servers. This protects against data loss when people leave EMBL and protects ownership,

among other things. The next step in this process is to connect this application in an appropriate way to enable easy data sharing and open access, as increasingly demanded by external funders. This is in progress, and IT Services is participating actively in these developments.

The panel also recommended that IT Services be closely involved in the implementation of the EMBL General Data Protection Regulation (GDPR) policy, currently under development, to raise awareness of the IT-related issues relevant to personal data privacy and management. As I mentioned to the review panel, IT Services has indeed been deeply involved in EMBL's discussions and development of our internal policy on data protection.

As a general suggestion, the panel encouraged the adoption of additional and more standardised performance metrics - to facilitate comparison among EMBL's facilities and services and with other service providers - that could be used for internal policy and decision-making as well as for future reviews. I will explore this topic with the senior staff involved and discuss how useful metrics could best be generated. Similarly, I will address and follow up with the units' leadership or in the appropriate EMBL-wide context on other recommendations provided by the panel that I do not discuss here.

The panel made a significant number of recommendations concerning equipment upgrades and increased staffing. In total, the panel recommended the addition of 10-12 staff

members to the combined Core Facilities and several more (depending to some extent on which other recommendations EMBL follows) in IT Services. In addition, the panel recommended very significant spending on the replacement, upgrade and addition of new equipment. These recommendations were justified by two requirements: to maintain the Core Facilities at state-of-the-art levels, and to ensure that EMBL is able to store and manage ever-increasing quantities of data. Neither type of expenditure is in a category where external funding can be raised, meaning that any increases must come from internal budgets. Although I am very sympathetic to these recommendations and agree that these investments into critical support functions should be a high priority, I told the panel that there is no possibility that I will be able to provide them during a period in which member state funding, across the Indicative Scheme, will decrease in real terms. Inevitably, this will have an ongoing effect on the quality of the Core Facilities and IT Services, as well as on any capacity they have to serve external users.

I would like to conclude by congratulating my colleagues in the Core Facilities and IT Services for the very successful outcome of this review and by thanking them for the crucial support they provide to EMBL's research and overall activities.

Iain W. Mattaj, FRS, FMedSci **Director General** 

26 April 2018

### EMBL Structural and Computational Biology Unit review

The EMBL Structural and Computational Biology Unit was reviewed on 15–17 May 2018 by a panel of 16 international experts, including seven members of the SAC. The review was chaired by Jan Löwe, MRC Laboratory of Molecular Biology, Cambridge. SAC Chair Paul Nurse and EMBL Director General Elect Edith Heard attended the review as observers.

#### **Evaluation summary**

EMBL's Structural and Computational Biology Unit currently comprises 11 group leaders, three team leaders, and Heads of Unit Peer Bork and Christoph Müller. The unit employs an array of integrated structural, biochemical, genomics and computational approaches to investigate the structural and functional organisation of molecular networks. The panel was impressed by the level of integration of the diverse approaches and the unique ability to combine detailed biochemical and structural approaches with large-scale genomics and computational approaches.

The overall performance of the unit, including the quality of research and the training and development of young scientists, greatly impressed the review panel, as did the leadership shown by the Heads of Unit. The Heads of Unit were particularly commended for their open-door policies, for their nurturing of young scientists, and for generating an environment that encourages excellence. The panel noted that a transition phase was about to begin, with five group leader departures expected within the next two years. The panel recommended that the balance between computational approaches and mechanistic/ biochemical studies should be maintained and, in

Several research highlights were identified by the panel as pushing the scientific boundaries of structural and computational biology. These included the work on the potential risk of non-antibiotics promoting antibiotic resistance, a study on the molecular organisation of the inner ring core of the human nuclear pore complex, and research on the structures of RNA polymerase III complexes.

particular, that critical mass in cryo-EM research and training should be maintained or increased.

The panel congratulated the unit members for being highly collaborative, but noted that a few group leaders could benefit from focusing on the most interesting and far-reaching questions raised by their research. The leadership was particularly commended for strategic recruitments and rapid changes that have enabled scientists in the unit. and within EMBL. to access high-resolution and cellular electron microscopy techniques. The Bio-IT programme, coordinated by the unit, was recognised as an original and creative approach in both data science training and fostering collaborations across EMBL and partner institutions in the area of IT. Panel members noted, however, that Bio-IT appeared to be understaffed.

In terms of infrastructure, the panel noted the need for continued investment in the areas of cryo-EM and mass spectrometry. For cryo-EM in particular, more investment is anticipated with the establishment of the new EMBL Imaging Centre; thus, the panel recommended a thorough search for experts to run the equipment, given the limited number of scientists in the field. In relation to the strong cryo-EM activity, the panel members further advised an increase in the number of people working on software related to the processing and visualisation of datasets. Spatially resolved mass spectrometry is a promising new area recently recruited to the unit and EMBL, but it will require further investment in equipment and staff to achieve its potential.

## Response to the review panel's recommendations

I would like to thank the panel members for their time and effort in reviewing the Structural and Computational Biology Unit. I am pleased with the very positive evaluation of the unit's performance since the last review and grateful for the constructive feedback. All the group leaders received a detailed evaluation and constructive suggestions from the panel.

The review panel was very positive about the leadership and research performance of the Heads of Unit, Peer Bork and Christoph Müller. I take this opportunity to congratulate them for leading by example and creating a highly unusual, creative environment that facilitates original research approaches and collaboration between disciplines. Some concern was expressed regarding the anticipated departures of five group leaders within the next two years and the potential loss of expertise, especially in mechanistic and biochemical studies, as well as in single-molecule microscopy. While I share the panel's concerns, I agree with their comment that this new phase presents interesting opportunities for shaping the future direction of the unit. The EMBL model is based on regular turnover, and we use such opportunities to explore promising new directions and remain at the cutting edge of quickly evolving fields. As an example, the last major phase of turnover in the unit led to the recruitment of three group leaders who have become leaders in the cryo-EM field.

The panel recommended maintaining this strength in the rapidly growing area of cryo-EM. I agree that cryo-EM is a key technique for structural biology and that it is essential to maintain a critical mass of expertise in this strategic area, in particular with a view to the future EMBL Imaging Centre, which will provide user access to services in cryo-EM. The recent recruitment of Julia Mahamid shows EMBL's commitment to and ability to attract promising young talent in this field. Cryo-EM remains a high priority for future recruitment on both the research and technical sides.

The reviewers also suggested that the unit would benefit from providing enhanced cryo-EM training. We have started taking steps in this direction by establishing the cryo-EM service platform and by organising specialised practical courses in cryo-EM and 3D image processing. Finally, the panel recommended increasing the number of people working on software related to the processing and visualisation of imaging datasets. This expertise is crucial for several of EMBL's research units, and we have recently recruited two group leaders, in Heidelberg and at EMBL-EBI, who focus on developing algorithms and machine learning-based methods at the intersection of biology, computer science and mathematics. Recruiting support staff in this area, to train non-experts, remains a priority.

The panel noted the successful Bio-IT programme and recommended supporting the programme with additional personnel. The Bio-IT programme in its current form is a relatively recent addition to the unit's activities and has proven tremendously valuable for computational scientists across EMBL Heidelberg and at other EMBL sites. The Heads of Unit will consider the panel's recommendation in their continuous effort to evolve and improve the support provided to the Bio-IT community, but finding internal funding for this activity, given the current constraints on member state contributions to the Indicative Scheme, will be very difficult.

The panel also made recommendations regarding scientific equipment available to the unit. With regards to the MALDI imaging platform, the panel considered the current platform adequate for the work performed to date, but recommended upgrading the instrumentation available to the group as well as increasing staff numbers. These recommendations have been noted. Iain V

19 June 2018

In summary, I would like to congratulate all unit members for their performance over the last review period and give credit to Peer Bork and Christoph Müller for providing visionary leadership.

Iain W. Mattaj, FRS, FMedSci Director General

#### Publisher EMBL

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**Printed by** ColorDruck Solutions, Leimer A confocal microscopy image of a six-day-old larva of the marine worm Platynereis. Genes in muscle cells are shown in green, and genes in different neurons in the brain and ventral nerve cord are shown in red, pink and yellow.

Paola Bertucci and Hernando Martinez Vergara/EMBL

#### EMBL member states and associate member states

Argentina | Australia | Austria | Belgium | Croatia Czech Republic | Denmark | Finland | France Germany | Greece | Hungary | Iceland | Ireland Israel | Italy | Luxembourg | Malta | Montenegro Netherlands | Norway | Portugal | Slovakia | Spain Sweden | Switzerland | United Kingdom

**Prospect member states** 

Lithuania | Poland