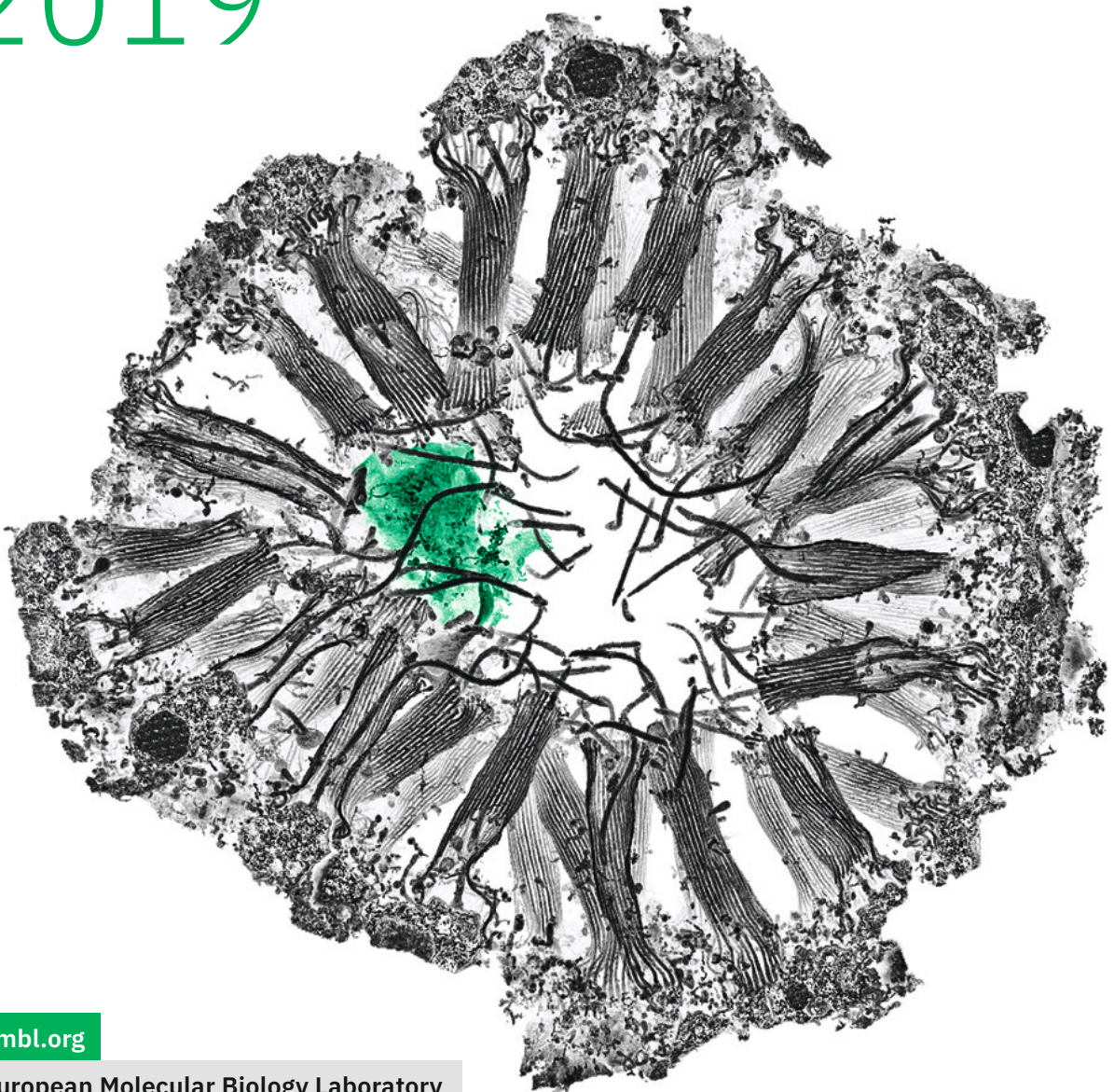


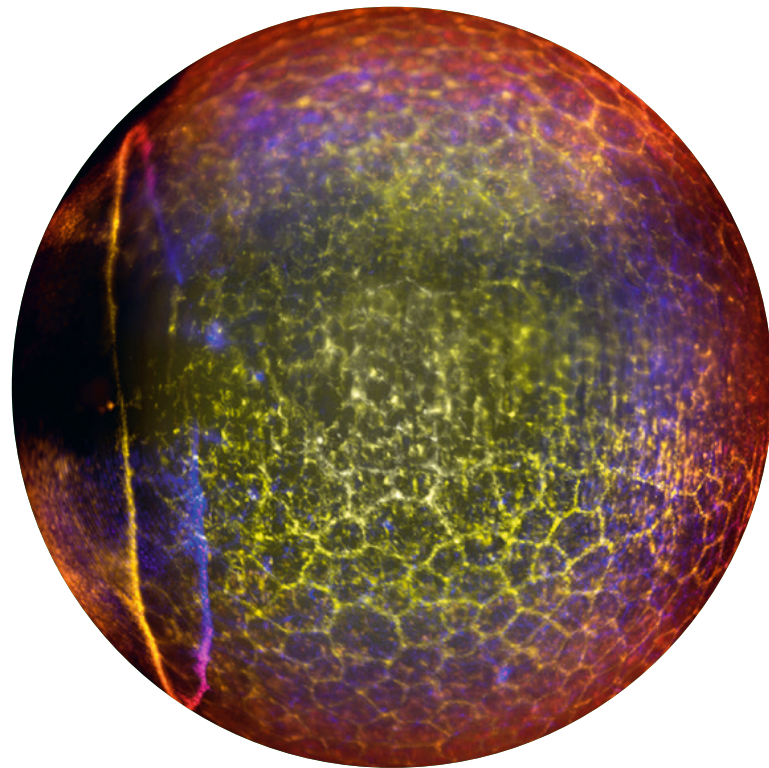
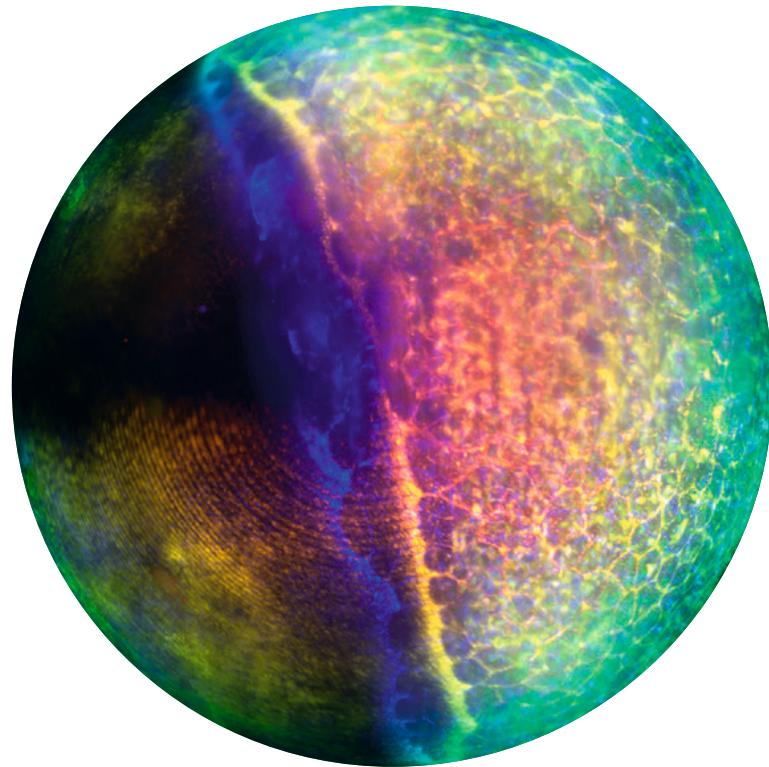
Annual Report

2019



embl.org

European Molecular Biology Laboratory



In a symphony of colours, this light-sheet microscopy image shows how zebrafish embryos start developing. This makes it possible to study the process of development and how it can be affected by environmental changes.
Krisztina Arató,
Gopi Shah/EMBL

Contents

02

Foreword

04

A vision for European science

Celebrating Edith Heard's first year as EMBL Director General

06

Research highlights

EMBL drives visionary research in molecular biology

18

Group leader profiles

Meet the newest group leaders advancing EMBL's research

21

Scientific services

EMBL offers vital services to scientists

35

Innovation and translation

Technology development and transfer, and industry relations

40

Training and public engagement

EMBL trains scientists and engages with the public, schools, and donors

48

Integrating life sciences

EMBL fosters collaboration among international scientific communities

54

Honours and awards

Celebrating individual achievements in 2019

56

Alumni

EMBL connects scientists and other professionals around the world

58

Administration

Providing services to support EMBL's missions

59

Staff Association

Supporting the EMBL community

60

Personnel statistics

62

Financial report

65

Reviews of scientific and service units

Cover image: Captured using state-of-the-art technology, this image of a marine sponge reveals a newly discovered type of neuron-like cell within a ring of digestive cells. Studies like this enable scientists to understand how the nervous system evolved and provided new ways for organisms to respond to their environment. Giulia Mizzon, Jacob Musser, Constantin Pape, Nicole Schieber/EMBL

Foreword

Welcome to the EMBL Annual Report 2019, which highlights some of EMBL's successes and important events during my first year as Director General.

This was an exciting year for EMBL on many fronts and I continue to be hugely impressed by the exceptional science and services that EMBL provides. The research highlights of 2019 range from understanding how viruses hijack their host's cells, by studying viral enzymes in atomic detail (p.8), to global analyses of more than 10 000 human gut microbiomes, which revealed almost 2 000 new bacterial species (p.7), to developing new techniques for cryo-electron tomography, allowing the creation of high-resolution 3D images of molecules inside cells (p.16).

EMBL has also built its research expertise in key areas with the recruitment of seven new research group leaders in 2019 (pp.18–19). These include two group leaders who joined EMBL Barcelona in October, enabling EMBL's newest site to expand its innovative research programme in tissue biology and disease modelling.

Over the past year I've been greatly inspired by EMBL's activities to bring together science and society on many levels. It's vital that EMBL, as the European life sciences research organisation, continues to strengthen this connection. By informing and inspiring the public about science, research organisations like EMBL can help to guide and support evidence-based discussion, policy, and practice.

This was also a year to prepare for a new era of life sciences at EMBL. Scientists from across the organisation contributed to the development of our next five-year Programme, due to start in 2022. This ambitious plan was generated through a highly collaborative process that involved multiple working groups and consultations with faculty during the year. The global vision that emerged is to understand life in the context of its environment. Today, we at last have the tools and expertise to do this at the molecular level. Understanding how organisms exist together in changing environments is of fundamental importance for our understanding of life. This coincides with urgent societal challenges, such as the breakdown of biological diversity, the acceleration in climate change, rapid environmental degradation, the spread in antibiotic resistance, and the emergence of infectious disease. All of these are contributing to a crisis in planetary health and environmentally driven human diseases. In this context, our efforts were in some respects prescient. The emergence of the SARS-CoV-2 virus in late 2019 and the resulting pandemic have graphically demonstrated the severity of the global challenges facing humanity, and which the next EMBL Programme will seek to address.

To find solutions to these challenges, we must drastically improve humanity's ability to understand



life in the context of environmental change. This requires that scientists from many areas, including molecular biology, come together to create a new era of life science research. Our Programme will build on EMBL's strengths while broadening and deepening our collaborations with new disciplines and developing a novel services portfolio that maximises value and connectivity to all our member states.

Thanks to the incredible talent, hard work, and collaborative enthusiasm that I have discovered during my first year at EMBL, I feel certain that we will be able to usher in this new era of science and knowledge, and that EMBL will continue to have a profound impact on the scientific and societal challenges that lie ahead of us and affect all of our lives.

Edith Heard, FRS
Director General

A vision for European science

Celebrating Edith Heard's first year as EMBL Director General

During this first year of Edith Heard's mandate as EMBL Director General, she tried to meet as many people as possible across the organisation. Luckily 2019 was marked by celebrations of two major anniversaries, which she joined: EMBL Rome's 20th and EMBL-EBI's 25th. At both sites, this brought together staff and alumni to celebrate the people and the science.

One of Edith's priorities in 2019 has been engagement with representatives from the EMBL member states, and with collaborators and colleagues. This has been crucial in exploring how EMBL can inspire and enable excellent science across Europe and around the world, in the context of the next Programme.

Joining forces with the Tara Ocean Foundation seemed a very natural way to engage with EMBL's host site member states in particular. As part of the Tara Ocean Foundation's Mission Microplastics, staff at each of EMBL's six sites organised and participated in public outreach activities, stakeholder receptions, alumni events, press conferences, and scientific conferences to discuss what the study of the oceans reveals about life on Earth. Edith took this opportunity to visit the EMBL sites, where she joined the events to give talks and meet EMBL staff, alumni, and visitors.

In April, the foundation stone was laid for the EMBL Imaging Centre, due to open in 2021 (p.30). This was marked by a celebration involving representatives from the Imaging Centre's public funders, industry partners, and private donors.

In September, Edith joined the first European Research and Innovation Days: a conference organised by the European Commission to shape future policy. She spoke about EMBL's successes in the Horizon 2020 framework programme and looked ahead to the next framework, Horizon Europe, emphasising the need to strengthen links between fundamental research and global challenges such as antibiotic resistance and climate change.

On 17 October, representatives from the EMBL member states, EMBL faculty, and other distinguished guests gathered for Edith's inauguration. Speakers at the inauguration symposium, 'EMBL: A Vision for European Life Sciences', discussed the need for scientists in Europe to help solve critical challenges of global importance.

- Anniversaries
- Tara stopovers
- Other events



Research highlights

EMBL drives visionary research in molecular biology

The past year has seen some remarkable discoveries and technological breakthroughs across EMBL's six sites. This is a selection of highlights.

EMBL BARCELONA

Scientists in the Sharpe group have invented a powerful new computing platform, called ya||a, for simulating the development of multicellular tissues. The platform integrates the physics and genetics of tissue formation and uses the high speed of graphics processing units – originally invented for fast computer gaming – to accelerate the simulations and enable researchers to generate testable predictions for different hypotheses. Initially created to model limb development, ya||a could also be used to model other tissues and disease processes such as tumour growth.

Germann P *et al.* (2019) ya||a: GPU-powered spheroid models for mesenchyme and epithelium. *Cell Systems* 8(3):261–266.e3. doi: 10.1016/j.cels.2019.02.007

EMBL-EBI

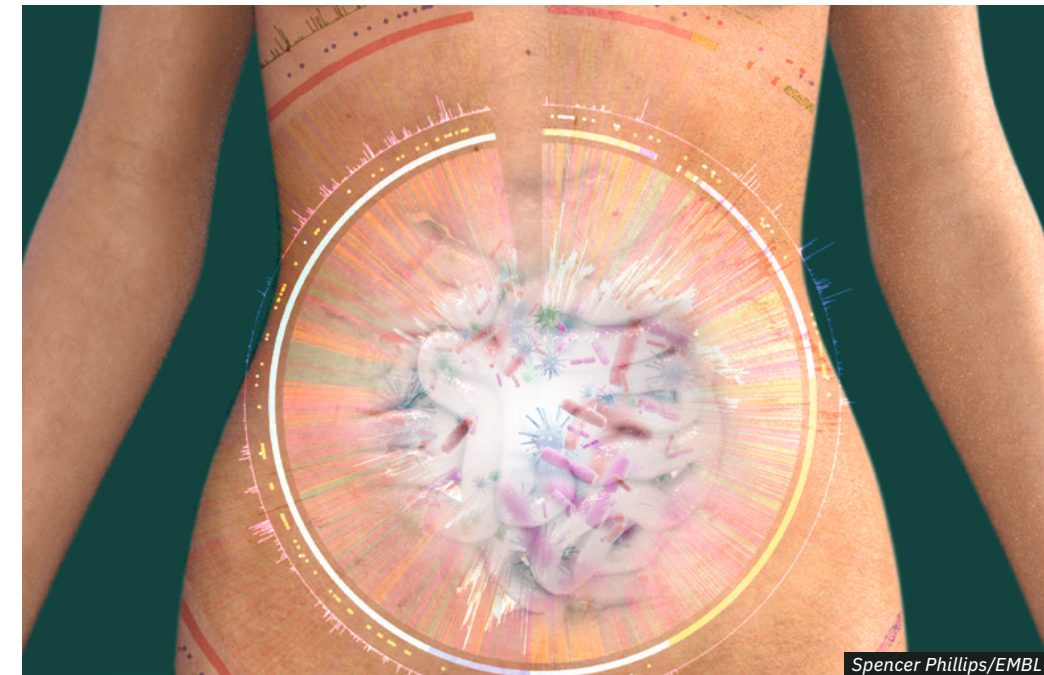
Cells regulate the activity of many of their proteins by making small chemical modifications to them. Scientists in the Beltrao group, in collaboration with the Noh group and the Savitski and Vizcaino teams, have analysed the results of thousands of experiments to study a

specific type of modification known as phosphorylation. They identified 120 000 phosphorylation sites and used machine learning to predict their importance in modifying protein function. This made it possible to produce the largest open access reference database to date of phosphorylation sites in human cells, enabling scientists to identify new sites of interest and advance research into many biological processes and diseases.

Ochoa D *et al.* (2019) The functional landscape of the human phosphoproteome. *Nature Biotechnology* 38(3):365–373. doi: 10.1038/s41587-019-0344-3

The human gut is home to a wide range of bacteria and other microbes, which together make up the gut microbiome. The Finn group has performed a large-scale genomic analysis of more than 10 000 human gut microbiomes from around the world, discovering almost 2000 new bacterial species, many of which have never been studied in the lab. This more than triples the number of known species in the human gut. Understanding more about the composition of the gut microbiome enables researchers to better study its role in human health, and could help to guide the diagnosis and treatment of gastrointestinal diseases.

Almeida A *et al.* (2019) A new genomic blueprint of the human gut microbiota. *Nature* 568(7753):499–504. doi: 10.1038/s41586-019-0965-1



Spencer Phillips/EMBL

Scientists in the Finn group have used computational methods to discover nearly 2000 previously unknown gut bacteria.

Scientists in the Marioni group and collaborators have carried out a study of gene expression in early embryos, performing single-cell analyses on over 100 000 cells to investigate a key stage of development when cells begin to take on more specialised roles. In a second study, with collaborators in the Stegle group, they expanded their analysis to include epigenetic changes, which have an effect on gene expression without changing the DNA sequence. Together, these studies provide insights into the molecular processes involved in embryo development, help researchers to understand more about the effects of gene mutations, and may lead to improved protocols for growing cells in the lab for regenerative medicine.

Pijuan-Sala B, Griffiths JA, Guibentif C *et al.* (2019) A single-cell molecular map of mouse gastrulation and early organogenesis. *Nature* 566(7745):490–495. doi: 10.1038/s41586-019-0933-9

Argelaguet R, Clark SJ, Mohammed H, Stapel LC *et al.* (2019) Multi-omics profiling of mouse gastrulation at single-cell resolution. *Nature* 576(7787):487–491. doi: 10.1038/s41586-019-1825-8

Enzymes are specialised proteins that help to speed up – or catalyse – chemical reactions. The ability to do this depends on the positioning of specific amino acids within the enzyme. Scientists in the Thornton group have performed the most extensive analysis to date of which amino acids perform which catalytic roles, by bringing together data on almost 1000 enzyme reactions from the Mechanism and Catalytic Site Atlas resource hosted at EMBL-EBI. Their results help researchers to understand the impact of mutations on enzyme function, and may assist in the design of enzymes with novel functions.

Ribeiro AJM *et al.* (2019) A global analysis of function and conservation of catalytic residues in enzymes. *Journal of Biological Chemistry* 295(2):314–324. doi: 10.1074/jbc.rev119.006289

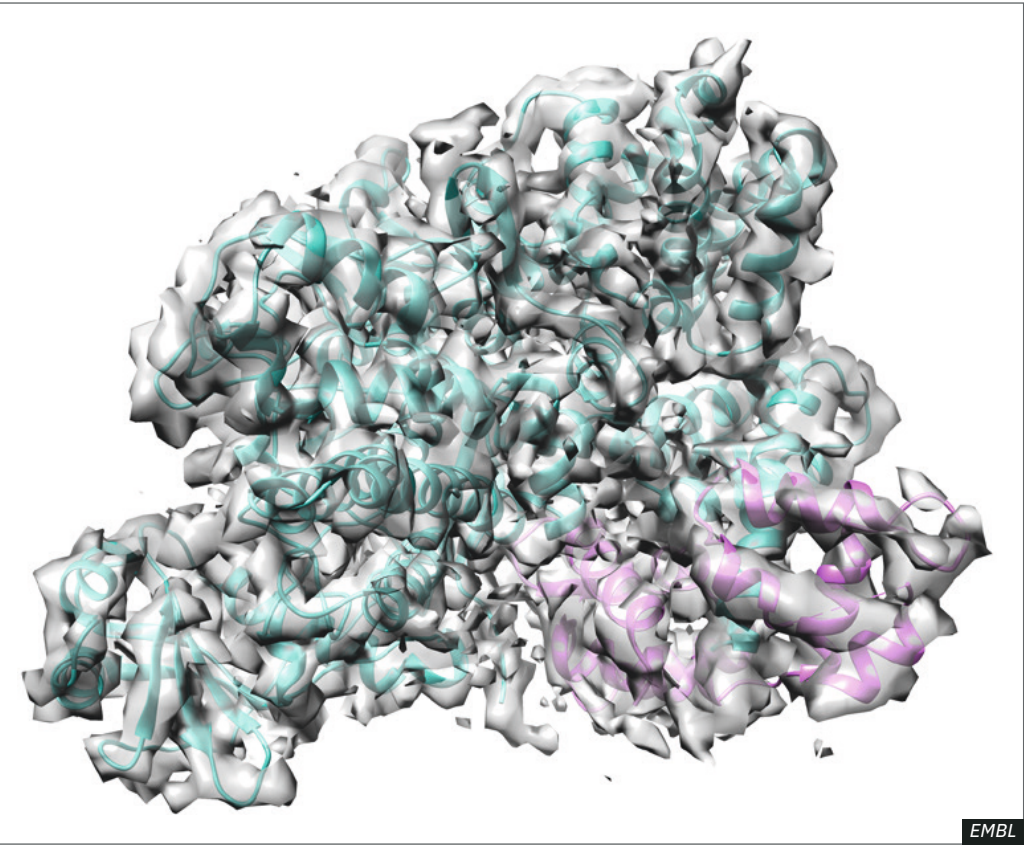
EMBL GRENOBLE

Legionella bacteria produce more than 300 toxins that they use to infect humans, making it difficult to treat infections with drugs that target a specific toxin. Scientists, including members of the Bhogaraju and Galej groups, have now revealed the function of the SidJ toxin, which is important for *Legionella* growth. They also identified part of the molecule that is a promising target for new drugs, opening up the possibility of developing treatments for *Legionella*-induced pneumonia, which has a fatality rate of over 10%.

Bhogaraju *et al.* (2019) Inhibition of bacterial ubiquitin ligases by SidJ–calmodulin catalysed glutamylation. *Nature* 572(7769):382–386. doi: 10.1038/s41586-019-1440-8

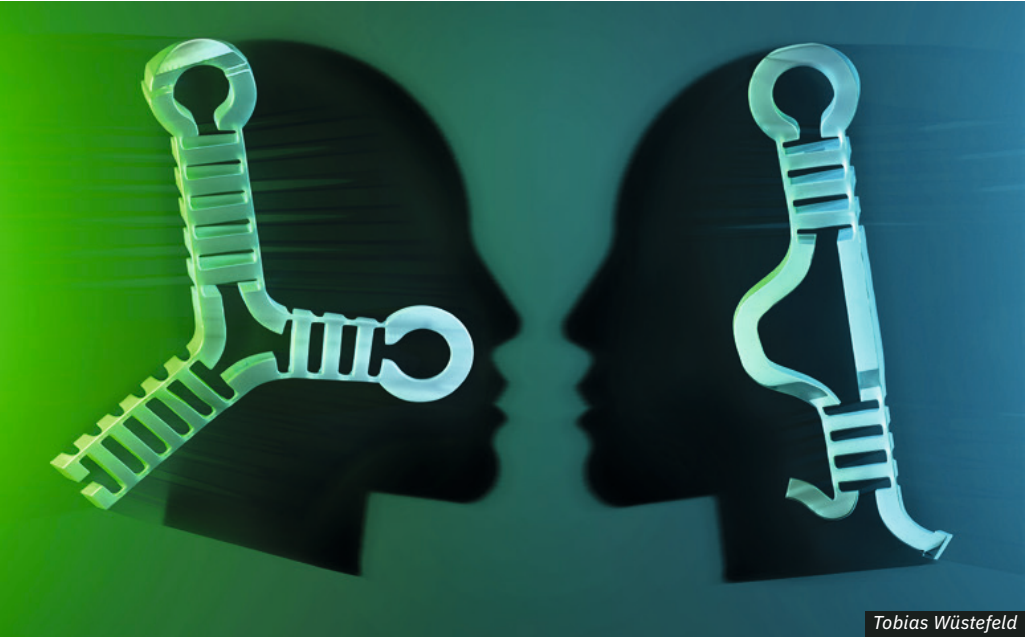
Viruses hijack their host’s cells to produce multiple copies of their genomes and assemble new viruses. Scientists in the Cusack group study influenza polymerase, the enzyme that the flu virus uses to copy its genetic material. They have observed, for the first time, how the polymerase – which acts like a molecular machine – changes structure while in action. These insights, obtained using a combination of X-ray crystallography and cryo-electron microscopy, will enable the development of new anti-influenza drugs.

Kouba T, Drncová P, Cusack S (2019) Structural snapshots of actively transcribing influenza polymerase. *Nature Structural & Molecular Biology* 26(6):460–470. doi: 10.1038/s41594-019-0232-z



Scientists in the Bhogaraju and Galej groups have revealed the cryo-EM structure of the SidJ–calmodulin complex. SidJ is shown in cyan, calmodulin in pink.

EMBL



Artist’s representation of the two important structural elements in MEG3, which biologists call ‘kissing loops’.

Tobias Wüstefeld

Many organisms express genes that regulate cell growth and division and act as tumour suppressors, preventing the development of cancer. Scientists in the Marcia group have investigated a tumour suppressor gene that expresses MEG3, a type of molecule known as a long non-coding RNA (lncRNA). Their study, which was the first to visualise the shape of a lncRNA in 3D, revealed important structural elements of MEG3 that are crucial for its function. These discoveries make it possible to identify molecules that would bind to MEG3 and modulate its activity as a tumour suppressor. Such molecules could then become the basis for new cancer treatments.

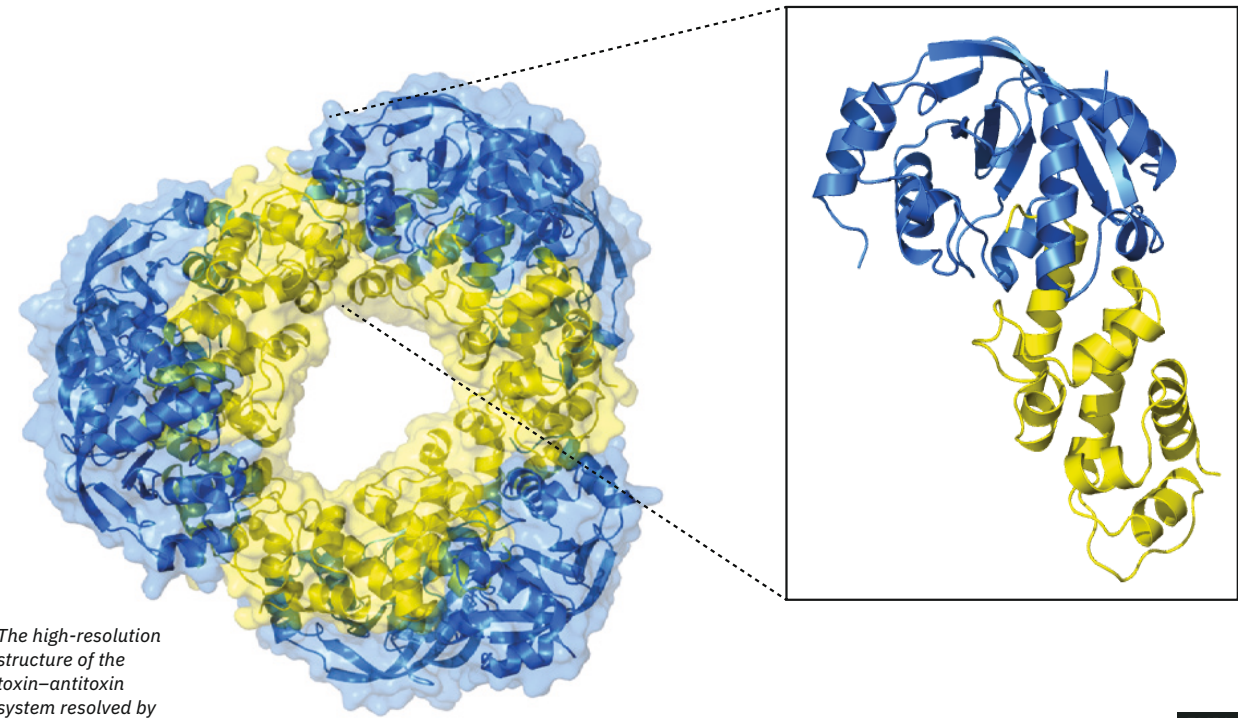
Uroda T *et al.* (2019) Conserved pseudoknots in lncRNA MEG3 are essential for stimulation of the p53 pathway. *Molecular Cell* 75(5):982–995.e9. doi: 10.1016/j.molcel.2019.07.025

EMBL HAMBURG

Because they have a penetration depth of several millimetres, high-energy X-rays can be used to image intact samples in 3D. In a proof-of-principle study, scientists in the Schneider group have used EMBL beamline P14 at DESY’s PETRA III synchrotron as an X-ray microscope to create a 3D tomogram, from which they determined the size, shape, and positions of microcrystals embedded in an optically opaque

medium. Other scientists at EMBL are already using the method, available in Hamburg, to image small organisms such as *Platynereis dumerilii* at cellular resolution, paving the way for high-throughput studies of morphological variation in response to environmental influences such as climate or pollution.

Polikarpov M *et al.* (2019) Visualization of protein crystals by high-energy phase-contrast X-ray imaging. *Acta Crystallographica Section D Structural Biology* 75(11):947–958. doi: 10.1107/S2059798319011379



EMBL

The high-resolution structure of the toxin-antitoxin system resolved by the Wilmanns group.

Scientists in the Svergun group have helped to reveal the structures of two important proteins. Together with collaborators in Belgium and France, they determined the structure of a key enzyme in cellular energy production, ATP citrate lyase. With collaborators in Italy, they solved the structure of a protein called XIAP, which is often expressed in cancers and increases their resistance to chemotherapy. These findings may help scientists to develop drugs targeting these proteins, enabling new treatments for cancer or high cholesterol.

Verschueren KHG *et al.* (2019) Structure of ATP citrate lyase and the origin of citrate synthase in the Krebs cycle. *Nature* 568(7753):571–575. doi: 10.1038/s41586-019-1095-5

Polykretis P *et al.* (2019) Conformational characterization of full-length X-chromosome-linked inhibitor of apoptosis protein (XIAP) through an integrated approach. *International Union of Crystallography Journal* 6(5):948–957. doi: 10.1107/S205225251901073X

The genome of the bacterium that causes tuberculosis contains 80 toxin-antitoxin (TA) systems: sets of closely linked genes that encode both a toxic protein and a toxin-neutralising antidote. If the antitoxin molecules are broken down, the toxins are activated and can slow cell growth, helping the bacteria to survive stressful environments. Scientists in the Wilmanns group have determined the structure and mode of action of a new TA system that has a more severe effect than most others and can kill the bacteria. Understanding this system could lead to the development of new drugs against tuberculosis, which is one of the top 10 causes of death worldwide.

Freire DM, Gutierrez C *et al.* (2019) An NAD⁺ phosphorylase toxin triggers *Mycobacterium tuberculosis* cell death. *Molecular Cell* 73(6):1282–1291.e8. doi: 10.1016/j.molcel.2019.01.028

EMBL HEIDELBERG

Directors' Research

Scientists in the Hentze group have uncovered a new dimension to RNA-protein relationships, observing an RNA molecule regulating the behaviour of a protein – a principle they term 'riboregulation'. They discovered that an RNA molecule called vtRNA1-1 regulates a protein that plays a key role in autophagy, the 'self-eating' process by which cells recycle

their components. The amount of vtRNA1-1 inside a cell varies according to the cell's nutritional status, allowing the cell to increase its supply of biological construction materials when resources are scarce.

Horos R, Büscher M *et al.* (2019) The small non-coding vault RNA1-1 acts as a riboregulator of autophagy. *Cell* 176(5):1054–1067.e12. doi: 10.1016/j.cell.2019.01.030



Tobias Wüstefeld

Scientists in the Hentze group have discovered that strands of RNA can bind to proteins to prevent the cell from carrying out autophagy, or 'self-eating'.

Cell Biology and Biophysics

When a cell divides, it has to distribute two identical copies of each of its chromosomes evenly between the two resulting cells. Errors in this process can produce cells with an incorrect number of chromosomes or broken chromosomes, which are often seen in cancer. Various molecular machines, including a protein complex called condensin, ensure that chromosomes are distributed correctly. Scientists in the Häring and Hennig groups have now revealed the molecular details of how the condensin complex organises chromosome structure, which is essential for this segregation process to happen correctly.

Hassler M *et al.* (2019) Structural basis of an asymmetric condensin ATPase cycle. *Molecular Cell* 74(6):1175–1188.e9. doi: 10.1016/j.molcel.2019.03.037

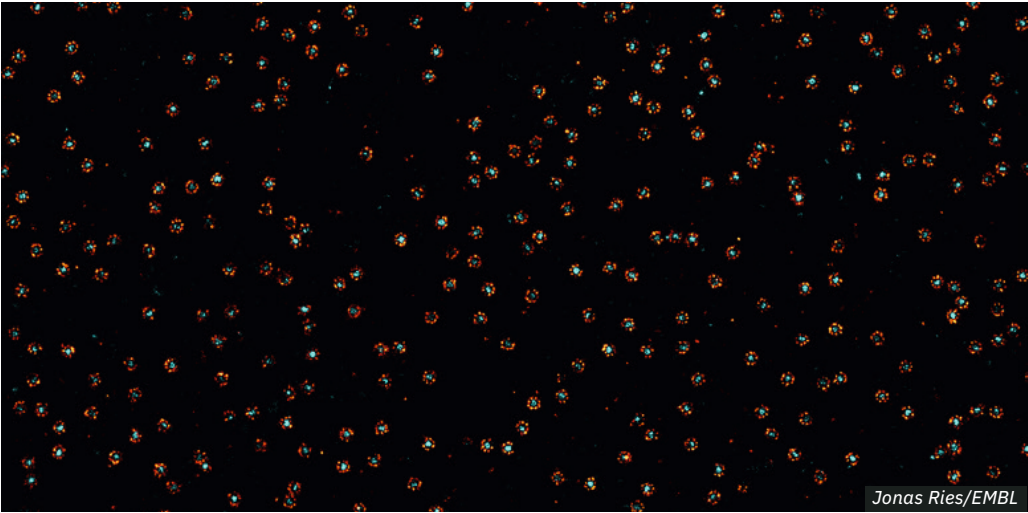
With super-resolution microscopy, it's possible to visualise single molecules on nanometre scales. However, a lack of commonly agreed standards within the field makes it difficult to compare results and draw precise conclusions. The Ries and Ellenberg groups have created four cell lines in which proteins in a structure known as the nuclear pore complex

can be fluorescently labelled. The Ries group then demonstrated their use as 3D resolution standards. The cell lines are now available to the scientific community, enabling researchers to assess the quality of their microscopes and labels, and to perform quantitative, absolute measurements.

Thevathasan JV, Kahnwald M *et al.* (2019) Nuclear pores as versatile reference standards for quantitative superresolution microscopy. *Nature Methods* 16(10):1045–1053. doi: 10.1038/s41592-019-0574-9

Scientists in the Prevedel and Hufnagel groups have developed a new light-field microscope that records up to 200 three-dimensional images per second. It also offers a resolution up to 10 times better than that of classic light-field microscopes. The new instrument allows researchers to image rapid biological processes, such as the beating heart and blood flow dynamics in medaka fish, in real time. This could become a valuable tool in developmental biology and neurobiology research.

Wagner N, Norlin N *et al.* (2019) Instantaneous isotropic volumetric imaging of fast biological processes. *Nature Methods* 16(6):497–500. doi: 10.1038/s41592-019-0393-z



Scientists in the Ries group have demonstrated the use of nuclear pore complexes as resolution standards. Here, parts of the nuclear pore complex are highlighted with red and cyan labels.

Jonas Ries/EMBL

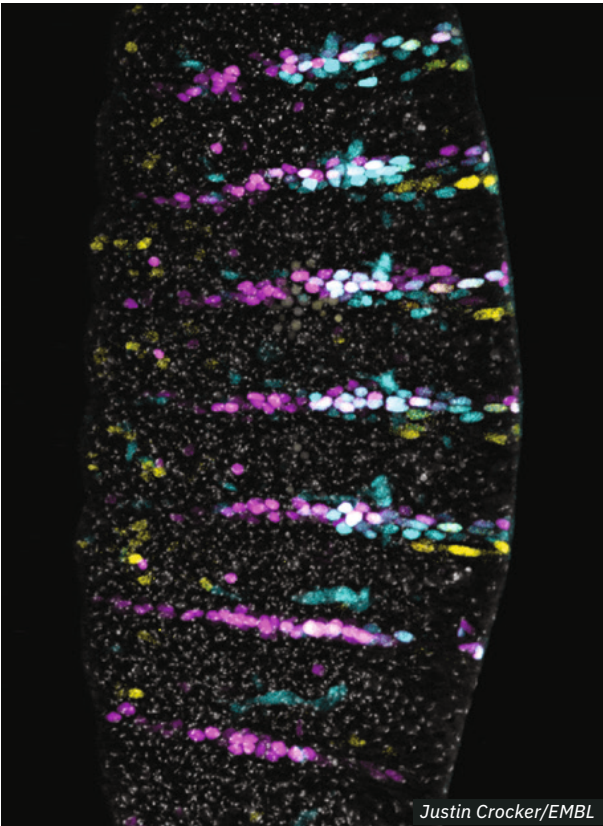
Developmental Biology

As an embryo develops, precise patterns of gene expression determine how its cells differentiate into various cell types. Regions of DNA known as enhancers – which increase the activity of certain genes when brought into proximity with them – play an important role in this process. Multiple sections of DNA that contain enhancers for the same gene can physically gather together to form a ‘transcriptional hub’. Scientists in the Crocker group have demonstrated in fruit flies that, even when one of these enhancers is deleted from its original location and inserted into a completely different chromosome, it can still find its way to the same hub. This provides new insights into how embryos are robust to environmental and genetic stresses through cooperative interactions across the genome.

Tsai A, Alves MRP, Crocker J (2019) Multi-enhancer transcriptional hubs confer phenotypic robustness. *eLife* 8:e45325. doi: 10.7554/eLife.45325

Scientists in the Hiiragi group have revealed the importance of fluid pressure in a developing blastocyst – a ball of cells enclosing a fluid-filled cavity, which is formed during mammal development. The blastocyst goes on to form the embryo and placenta. The scientists showed that the pressure inside the blastocyst plays an important role in controlling its size, and the way its cells specialise and organise themselves into tissues. Their approach to measuring fluid pressure could be used to monitor the development of human embryos in IVF clinics, and provides new opportunities to investigate the role of fluid pressure in the development of organs such as lungs or kidneys.

Chan CJ *et al.* (2019) Hydraulic control of mammalian embryo size and cell fate. *Nature* 571(7763):112–116. doi: 10.1038/s41586-019-1309-x



Justin Crocker/EMBL

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

Scientists in the De Renzis group, in collaboration with the Neveu group, have used an optogenetics approach – which allows the control of protein function with light – to study the Notch signalling pathway, which plays an important role in embryo development. By manipulating the activity of the Notch receptor, they found two modes of regulation: while Notch activation works like a simple on/off switch in individual cells, in whole tissues it is the duration of Notch activity that determines the likelihood of a cellular response.

Viswanathan R, Necakov A *et al.* (2019) Optogenetic inhibition of Delta reveals digital Notch signalling output during tissue differentiation. *EMBO Reports* 20(12):e47999. doi: 10.15252/embr.201947999

Genome Biology

Chromosomes are compartmentalised into domains, with DNA regions that control gene expression – known as enhancers – often being located in the same domain as their target gene, and coming in proximity with it through chromatin folding. It has long been thought that these domains play a crucial role in constraining enhancer activity, preventing enhancers from regulating the wrong gene. Scientists in the Furlong and Korbel groups now question that view, showing that major changes in chromatin domain organisation had surprisingly little effect on the expression of most genes. This indicates that other mechanisms must control the interactions between enhancers and their target genes.

Ghavi-Helm Y, Jankowski A, Meiers S *et al.* (2019) Highly rearranged chromosomes reveal uncoupling between genome topology and gene expression. *Nature Genetics* 51(8):1272–1282. doi: 10.1038/s41588-019-0462-3

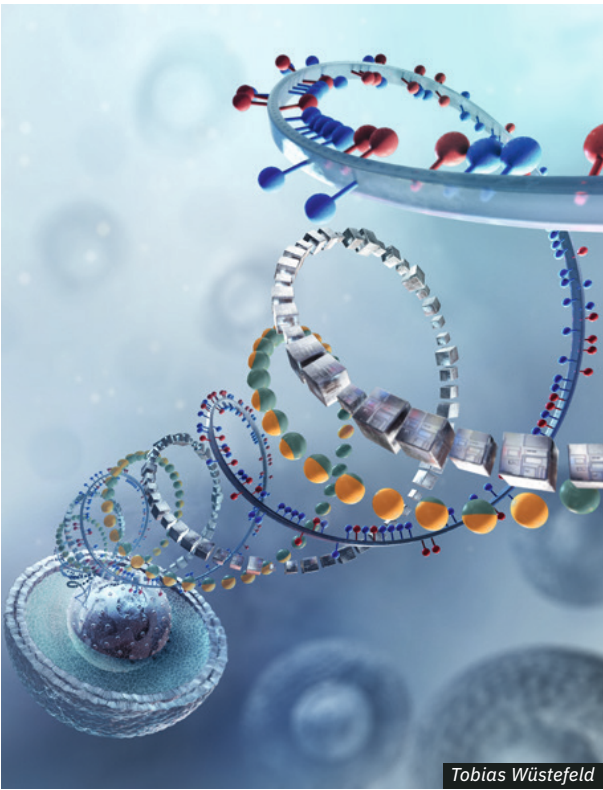
Many genes carry instructions for making proteins. Scientists in the Huber and Steinmetz groups, with collaborators at Cellzome, have investigated whether deleting a gene using the gene editing tool CRISPR is efficient in halting production of its related protein. In one-third of cases, they found that the protein was still present – sometimes at its original level – indicating a requirement for careful experimental controls when using CRISPR. The Steinmetz group was also involved in a second study, with collaborators in China, investigating the number of unintended off-target edits made by CRISPR and other gene editing tools. The scientists developed a method to experimentally test the safety and efficacy of gene editing technologies.

Smits AH, Ziebell F *et al.* (2019) Biological plasticity rescues target activity in CRISPR knock outs. *Nature Methods* 16(11):1087–1093. doi: 10.1038/s41592-019-0614-5

Zuo E, Sun Y, Wei W, Yuan T *et al.* (2019) Cytosine base editor generates substantial off-target single-nucleotide variants in mouse embryos. *Science* 364(6437):289–292. doi: 10.1126/science.aav9973

Scientists in the Korbel group and collaborators have developed a new method for detecting and measuring DNA rearrangements in single cells. Their method, called scTRIP, is cheaper, faster, and more sensitive than previous approaches. Since it enables detection of small-scale changes, scTRIP could become a new standard for the analysis of single cells, and has the potential to advance clinical diagnosis of diseases including cancer.

Sanders AD, Meiers S, Ghareghani M, Porubsky D *et al.* (2019) Single-cell analysis of structural variations and complex rearrangements with tri-channel processing. *Nature Biotechnology* 38(3):343–354. doi: 10.1038/s41587-019-0366-x



Tobias Wüstefeld

Scientists in the Korbel group and collaborators have developed a cheaper and faster method to check for genetic differences in individual cells.

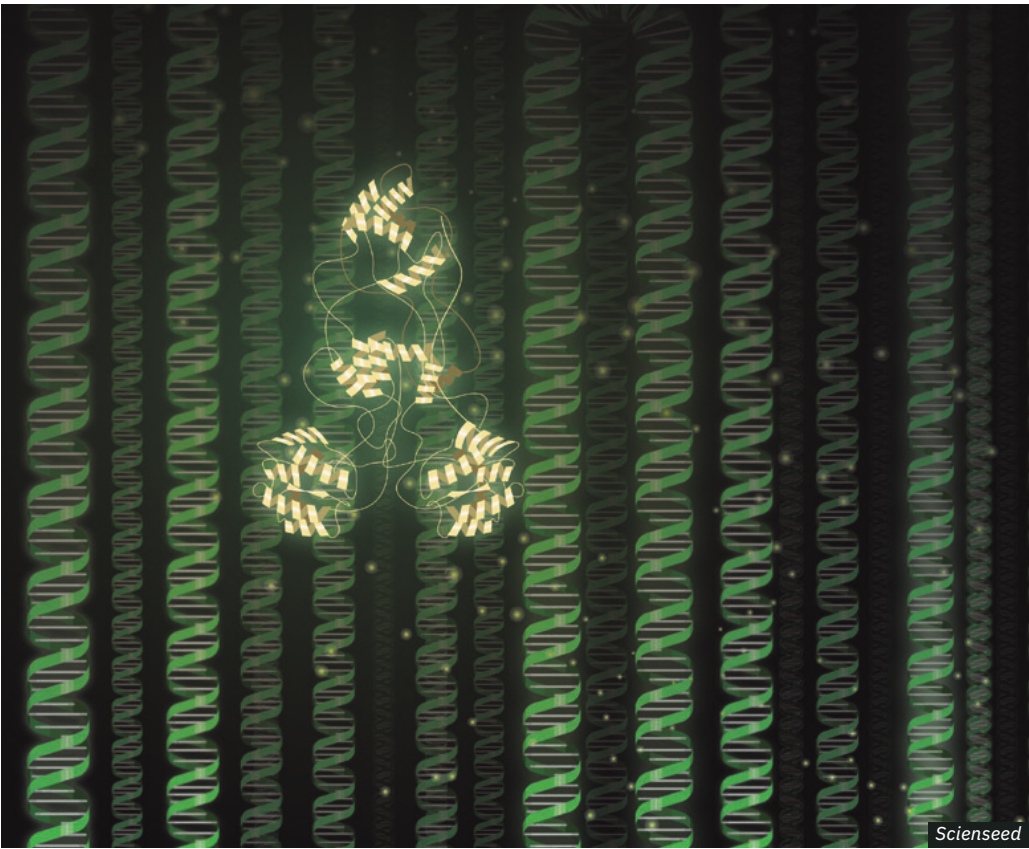
Structural and Computational Biology

Scientists in the Barabas group and collaborators have significantly improved a genome engineering tool called the Sleeping Beauty transposase – a protein that can be used to insert new DNA sequences into the genome. Their transposase is more stable and has the ability to penetrate cell membranes, making it easier to deliver into cells. This research could help to reduce the costs and improve the safety of genome engineering, and has great potential for applications in regenerative medicine and cancer immunotherapy.

Querques I, Mades A, Zuliani C *et al.* (2019) A highly soluble Sleeping Beauty transposase improves control of gene insertion. *Nature Biotechnology* 37(12):1502–1512. doi: 10.1038/s41587-019-0291-z

Every person has an individual composition of proteins in their cells – their proteotype. Scientists in the Bork and Beck groups have studied how proteotypes vary between individuals, finding that both genetic and environmental factors contribute to this individuality. For example, biological sex and diet together explain around 12% of the variation in proteotype. Understanding proteotype variation should help scientists to identify lifestyle-associated fingerprints in individuals, which may enable better personalisation of medical treatments.

Romanov N *et al.* (2019) Disentangling genetic and environmental effects on the proteotypes of individuals. *Cell* 77(5):1308–1318.e10. doi: 10.1016/j.cell.2019.03.015



Scienseed

Artist's representation of the Sleeping Beauty transposase.

The Mahamid group and collaborators have developed a new method that advances cryo-electron tomography (cryo-ET) – a technique that uses a beam of electrons to reconstruct 3D images of molecules – for applications inside cells. They used a micropatterning technique to create sample grids with areas that alternately attract or repel biological material, allowing cells to be positioned with high spatial control. This can also be used to manipulate cell shape, making it possible to study the mechanical behaviour of cells at extremely high resolution. While only a few labs currently have the expertise and technology for cellular cryo-ET, this development should help to make it a routine method by streamlining the process and facilitating automation.

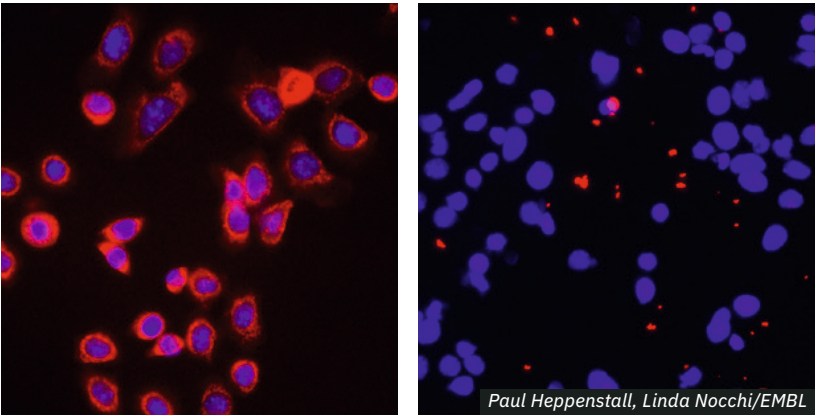
Toro-Nahuelpan M *et al.* (2019) Tailoring cryo-electron microscopy grids by photo-micropatterning for in-cell structural studies. *Nature Methods* 17(1):50–54. doi: 10.1038/s41592-019-0630-5

EMBL ROME

Scientists in the Heppenstall group have developed a dye that can be used to measure the activity of nerve cells. The dye changes its light emission in response to changes in cell activity, allowing researchers to detect even low levels of neuronal activity under the microscope. In another study, they developed a light-sensitive chemical that binds only to itch-sensing cells in the skin. By injecting an area of skin with the chemical and illuminating the area with near-infrared light, they were able to make the itch-sensing cells withdraw from the skin’s surface, stopping the itch. This may enable the development of new methods for treating inflammatory skin diseases such as eczema, which causes chronic itching.

Sundukova M *et al.* (2019) A chemogenetic approach for the optical monitoring of voltage in neurons. *Angewandte Chemie International Edition* 58(8):2341–2344. doi: 10.1002/anie.201812967

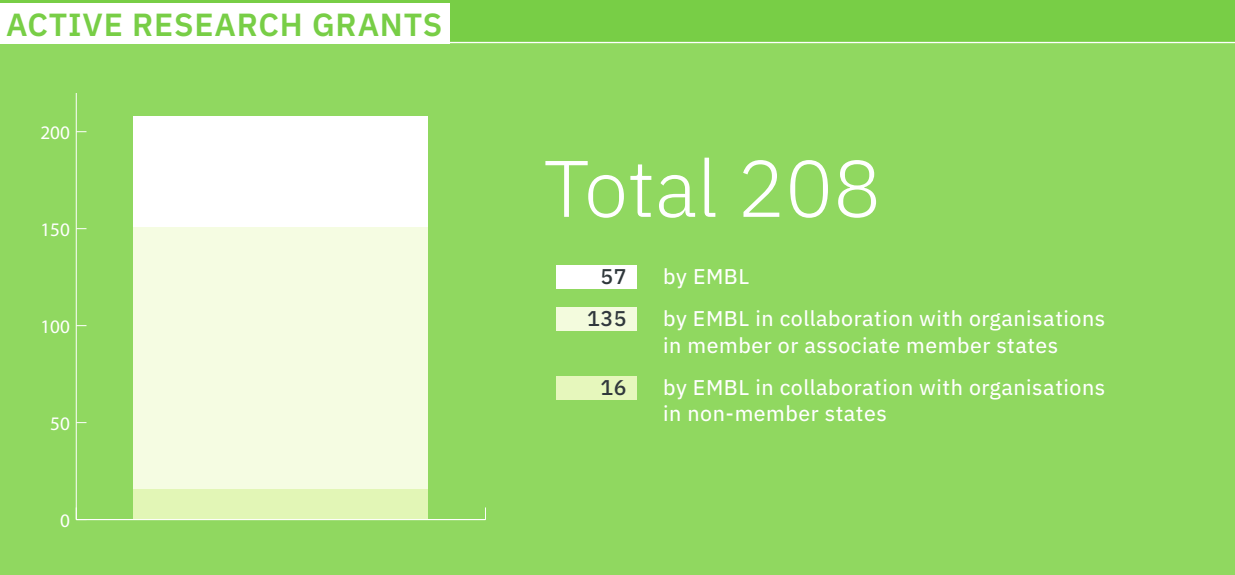
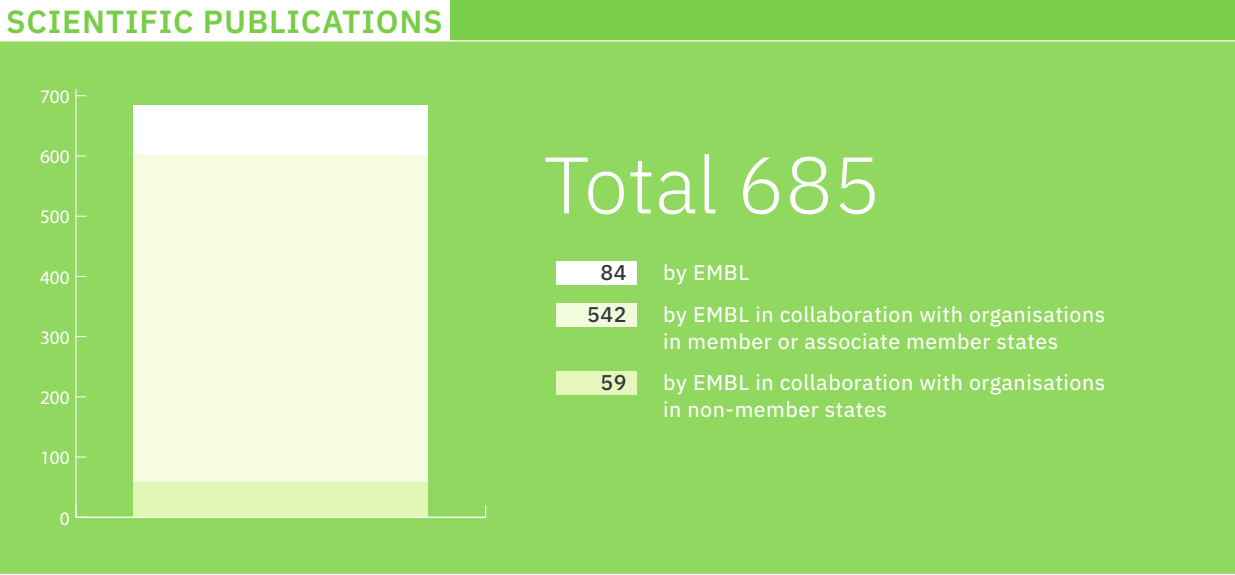
Nocchi L *et al.* (2019) Interleukin-31-mediated photoablation of pruritogenic epidermal neurons reduces itch-associated behaviours in mice. *Nature Biomedical Engineering* 3(2):114–125. doi: 10.1038/s41551-018-0328-5



Scientists in the Heppenstall group have developed a light-sensitive chemical, shown in red, that binds only to itch-sensing cells in the skin (left), but not to receptors in the control group (right).

Research in numbers

Scientific publications and active research grants in 2019



Group leader profiles

Meet the newest group leaders advancing EMBL's research



Maria Bernabeu

EMBL Barcelona

My group creates 3D blood–brain barrier models *in vitro*, and we're interested in infectious diseases, particularly malaria. I've been working on malaria for 10 years, trying to understand this complex fight for survival between human and parasite. Right now, the main goal of my lab is to model the pathogenesis of this disease, to see how human cells respond to the parasite's stimuli. Later, we'll start collaborations and use the model to study other vascular diseases of the brain.



Isidro Cortés-Ciriano

EMBL-EBI

We explore cancer genomes using diverse sequencing techniques – from whole-genome sequencing to single-cell technologies – with a particular focus on genome instability. We also integrate genomic and epigenomic data to discover genomic alterations that are predictive of response to cancer therapies. We aim to develop computational tools that could improve how we match patients to treatments.



Claire Deo

EMBL Heidelberg

In my group, we design molecules that help us to visualise highly dynamic events in biology. We're currently developing molecules that can be applied in super-resolution microscopy, which requires the ability to turn them on and off in response to light. These molecules can be applied in biological systems to visualise processes that can't be seen using conventional microscopy. I think places like EMBL, in which tool builders and tool users have a high degree of daily interaction, can really push this forward.



Sebastian Eustermann

EMBL Heidelberg

We're using cryo-electron microscopy to investigate the structure of chromatin – the complex of DNA and its associated proteins. We've used purified proteins to rebuild in the lab chromatin patterns found in the cell nucleus, which allows us to determine the fundamental requirements of chromatin organisation. Deciphering the principles of chromatin organisation will provide us with an understanding of what happens when this organisation is disturbed, for instance in cancers.



Kristina Haase

EMBL Barcelona

My group's research bridges the fields of biology and engineering. By combining human cells in millimetre-scale chips fabricated in the lab, we can effectively design tissues using their innate self-assembly process. Using different types of cells, we can engineer new tissues for regenerative medicine. While one focus of the lab will be on developing tissue patches – particularly for cardiac repair – another focus will be on developing drug screening tools and disease models.



Georgia Rapti

EMBL Heidelberg

We want to understand how the nervous system forms in the early embryo, and to identify the molecular and cellular steps driving the first events in forming neural networks and circuits. We combine advanced imaging with molecular, genetic, and genomic approaches. The nervous system is composed of neurons and glial cells, and we now know that glial cells have pivotal roles in the development and function of the nervous system. We will focus on the interactions of glia and neurons to build the structure of the brain.



Michael Zimmermann

EMBL Heidelberg

I'm interested in the metabolic interactions between our gut bacteria and ourselves. One focus is on drug metabolism: how do the bacteria in the gut contribute to this process, and do they have a role in our response to drugs? This can differ significantly: some patients have a beneficial response, others have none, and some experience toxic side-effects. Typically, we assign this variation to host metabolism, but there's so much we don't yet know about the role of microbes.

ALUMNI IMPACT

Ilaria Ferlenghi

Head of Structural Microscopy,
GSK Vaccines, Siena, Italy
PhD student at EMBL, 1994–1999



During her PhD at EMBL, Ilaria Ferlenghi studied the tick-borne encephalitis virus (TBEV), which is endemic to Europe and Asia and can be transmitted by the bite of an infected tick. While the majority of infections result in symptoms such as a mild fever, the disease can progress to causing nerve damage and even death. Ilaria's work drew on the pioneering research of Nobel laureate Jacques Dubochet at EMBL during the 1980s, which led to the development of cryo-electron microscopy (cryo-EM). Ilaria used cryo-EM to study the proteins that form the outer shell of TBEV, which allow it to attach to a host cell and infect it. By imaging this protein structure, she was able to study how it interacts with proteins on the host cell's surface and gained insights into the mechanism by which the virus enters cells.

Ilaria is now Head of Structural Microscopy at GSK in Siena, Italy, and continues to use cryo-EM to study the protein structures of potential vaccines to accelerate their clinical development. One of the successes of her team is the characterisation and development of antigens used in a vaccine recently approved by the US Food and Drug Administration to protect against meningococcus B. Infections by this bacterium can cause meningitis or septicaemia, and have a high mortality rate, but are preventable with vaccination. Ilaria recently devised and developed pioneering new software, based on the use of *in vivo* protein structure identification and machine learning, which allows fast identification of new vaccine candidates.

Scientific services

EMBL offers vital services to scientists

Bioinformatics services

EMBL's European Bioinformatics Institute (EMBL-EBI) is a global hub for open data resources and tools for the life sciences. EMBL-EBI's bioinformatics services are freely available to researchers worldwide. They improve how data is stored, shared, and analysed, and they facilitate new scientific discoveries.

In 2019, EMBL-EBI received an average of 62 million web requests per day to its websites. Web requests are defined as web traffic to a particular data resource, which includes both direct and programmatic access.

At the end of 2019, EMBL-EBI had 307 petabytes of raw storage. This is a significant increase from the 273 petabytes it had at the end of 2018, and almost double the 155 petabytes it had at the end of 2017.

Following several years of consultations with the bioimaging community, and building on the success of the Electron Microscopy Public Image Archive (EMPIAR), EMBL-EBI launched the BioImage Archive in 2019. This is a dedicated resource for archiving a wide range

of imaging data, covering scales from molecules to whole organisms. The BioImage Archive enables users to share and understand data from complex imaging studies. It includes data from several other added-value bioimaging data resources, including EMPIAR and EMBL-EBI's BioStudies database.

The Protein Data Bank in Europe (PDBe) reached 150 000 molecular structures in 2019, and also launched a sister data resource called PDBe Knowledge Base (PDBe-KB). This new community-driven resource collates annotations and predictions for structure data in the PDB archive. It also links to the UniProtKB resource, allowing researchers to easily obtain a comprehensive view of all the information available on a protein of interest.

The European Genome-phenome Archive (EGA) was awarded funding to store and share the first 50 000 genomes from UK Biobank, a unique initiative that collates genomic and health data from 500 000 UK volunteers. Enabling access to the data will contribute to many new discoveries in human health and disease.

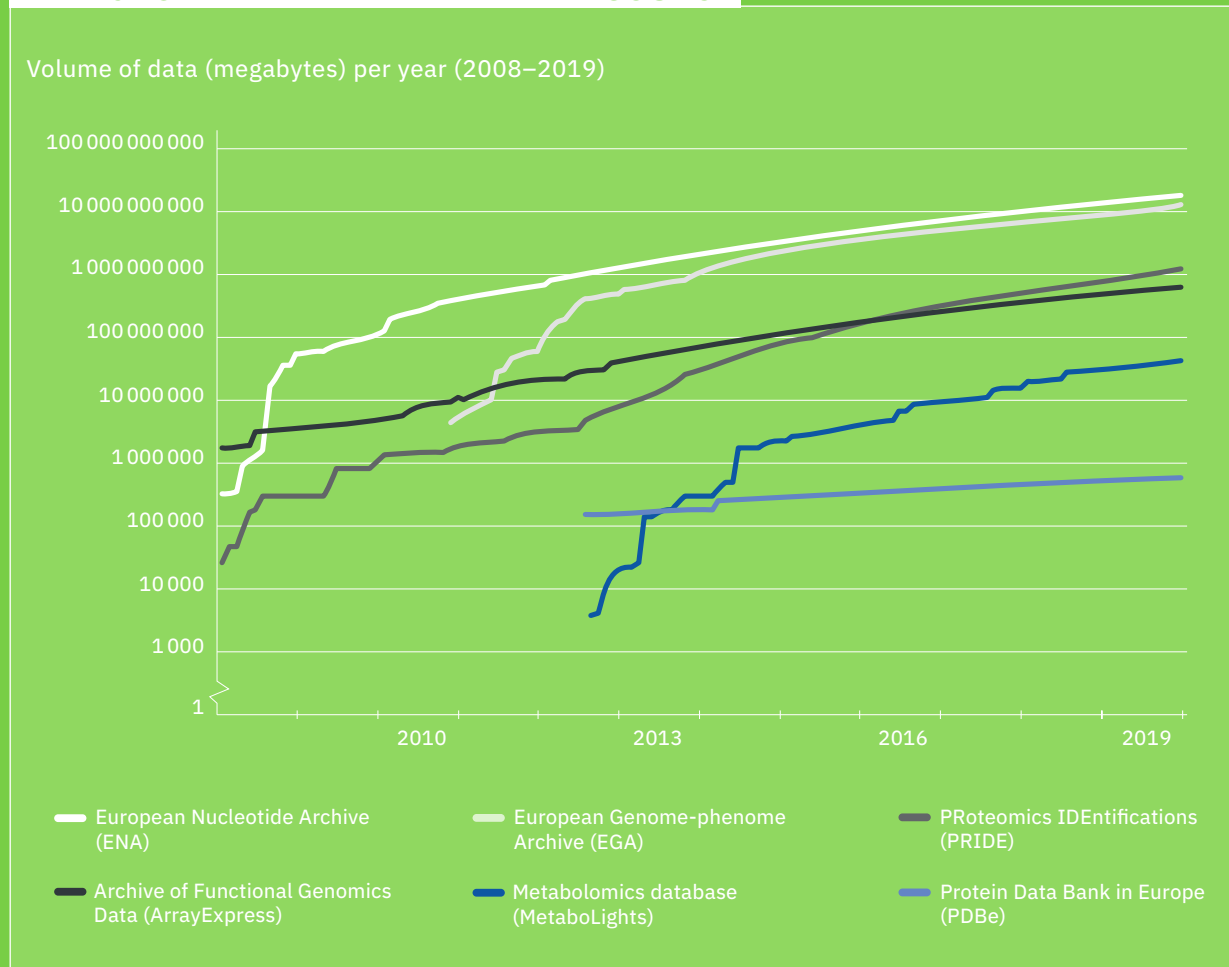
EMBL-EBI data services in numbers

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



62.6 million
web requests per day
on average in 2019

DATA GROWTH BY EMBL-EBI DATA RESOURCE



Structural biology services

EMBL GRENoble

The EMBL–ESRF Joint Structural Biology Group (JSBG), a collaboration between EMBL Grenoble and the European Synchrotron Radiation Facility, provides access to six beamlines for crystallography, one for biological small-angle X-ray scattering (Bio-SAXS), and a high-end Titan Krios electron microscope, which is installed at the ESRF and run jointly by the four institutes on Grenoble's European Photon and Neutron (EPN) science campus. In addition, EMBL Grenoble provides access to its high-throughput crystallisation and fragment screening facility, the HTX Lab, based on the CrystalDirect technology developed at EMBL for automated crystal harvesting. Access to HTX Lab pipelines is offered through the EC-funded iNEXT-Discovery project and the European Research Infrastructure Consortium for structural biology, Instruct-ERIC.

Starting in December 2018, the ESRF has undergone a major upgrade to become the ESRF Extremely Brilliant Source (ESRF-EBS), the first fourth-generation high-energy synchrotron facility in the world. During 2019, EMBL and ESRF scientists and engineers prepared the beamlines for the improved X-ray beams that will be delivered as part of ESRF-EBS. User operation is scheduled to begin in August 2020. All the JSBG beamlines have had their hardware refurbished and software upgraded for increased performance, while major improvements to beamlines BM29 and MASSIF-1 are under way. The operation of MASSIF-1 will be coordinated with HTX Lab activities to support large-scale fragment screening, and its upgrade includes the online integration of

CrystalDirect, which will open up new experimental opportunities. Other developments are in progress on beamline ID29, for the future delivery of a synchrotron serial crystallography (SSX) beamline with microsecond resolution.

In 2019, members of the HTX Lab further developed the concept of online crystallography, which comprises fully automated crystallography pipelines based on the CrystalDirect technology and the Crystallographic Information Management System (CRIMS) software, which can be operated from any desktop computer with an internet connection. The CRIMS software is able to communicate with the ESRF synchrotron in Grenoble and the PETRA III synchrotron in Hamburg to support automated and remote X-ray data acquisition, covering the whole workflow from protein to structure. Based on the same technologies, the HTX Lab has implemented an automated fragment screening pipeline by X-ray crystallography, capable of screening small-molecule libraries in excess of 1000 fragments over multiple projects, which was made available to scientists from academic institutes through iNEXT. These pipelines are also in high demand from the pharmaceutical industry, which uses them to support structure-based drug development programmes. This led to the creation in 2019 of ALPX, the first EMBL spin-off company based in France, which uses EMBL technologies to provide structure-guided drug design services to the pharmaceutical and biotechnology sectors.

EMBL HAMBURG

EMBL Hamburg operates three beamlines for applications in macromolecular X-ray crystallography and small-angle X-ray scattering at DESY’s PETRA III synchrotron, and an associated Sample Preparation and Characterisation (SPC) Facility. As an extension of the SPC Facility, EMBL also operates the High-Throughput Crystallisation and Protein Characterisation Facilities at Hamburg’s Centre for Structural Systems Biology (CSSB). CSSB is a joint initiative comprising three universities and six research institutes, among them EMBL and DESY.

EMBL began operating the High-Throughput Crystallisation and Protein Characterisation Facilities at CSSB in May 2018. As part of the services that these facilities offer to the scientific community, they hosted more than 150 users in 2019.

Users have access to quality control and characterisation techniques including calorimetry, mass spectroscopy, circular dichroism, fluorescence, microscale thermophoresis, light scattering, infrared spectroscopy, surface plasmon resonance, and biolayer interferometry. Scientists working in European academic institutions are granted access through iNEXT. Their work generates translational scientific discoveries, which have led to collaborations with hospitals and industry partners. The facilities also provide a pipeline for time-resolved studies, which offers several methods to obtain kinetic information from various read-outs in solution, such as stopped-flow experiments following absorbance, fluorescence, or Bio-SAXS. Surface-immobilised systems can also be studied using biolayer interferometry.

The first publication resulting from a collaboration at CSSB appeared in 2019. Six research groups, including two from EMBL Hamburg, developed a protocol that enables the identification of suitable conditions for making membrane proteins soluble, allowing them to be purified and studied.

Scientists from the Max Planck Institute for the Structure and Dynamics of Matter, Hamburg University, and EMBL Hamburg have developed a new method for watching biomolecules at work inside crystals. The new liquid application method for time-resolved analyses (LAMA) is tailored to the study of biologically relevant reaction timescales, which are on the order of milliseconds, up to seconds or minutes. These timescales are of particular interest to biochemists and pharmaceutical researchers, because they often reveal the structural changes relevant to a particular biochemical reaction or the turnover of a drug. LAMA makes experiments much simpler than with previous approaches. It is now available to users on the T-REXX endstation on beamline P14 at PETRA III. Applications of the technique will make it possible to answer pressing questions relating to human health or sustainable biotechnologies, such as the development of enzymes for producing industrial chemicals or recycling plastics.



The Sample Preparation and Characterisation Facility offers a pipeline from the lab bench to Hamburg’s X-ray and SAXS beamlines, helping scientists to optimise and prepare samples for structural studies.

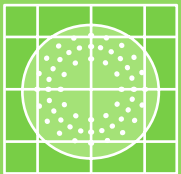
Kinga Lubowiecka/EMBL

Structural biology and imaging services in numbers

Cross-site and cross-scale services in 2019

Including beamline, cryo-electron microscopy, and light microscopy services at EMBL Barcelona, EMBL Grenoble,* EMBL Hamburg, EMBL Heidelberg, and EMBL Rome in 2019

>2500
user visits

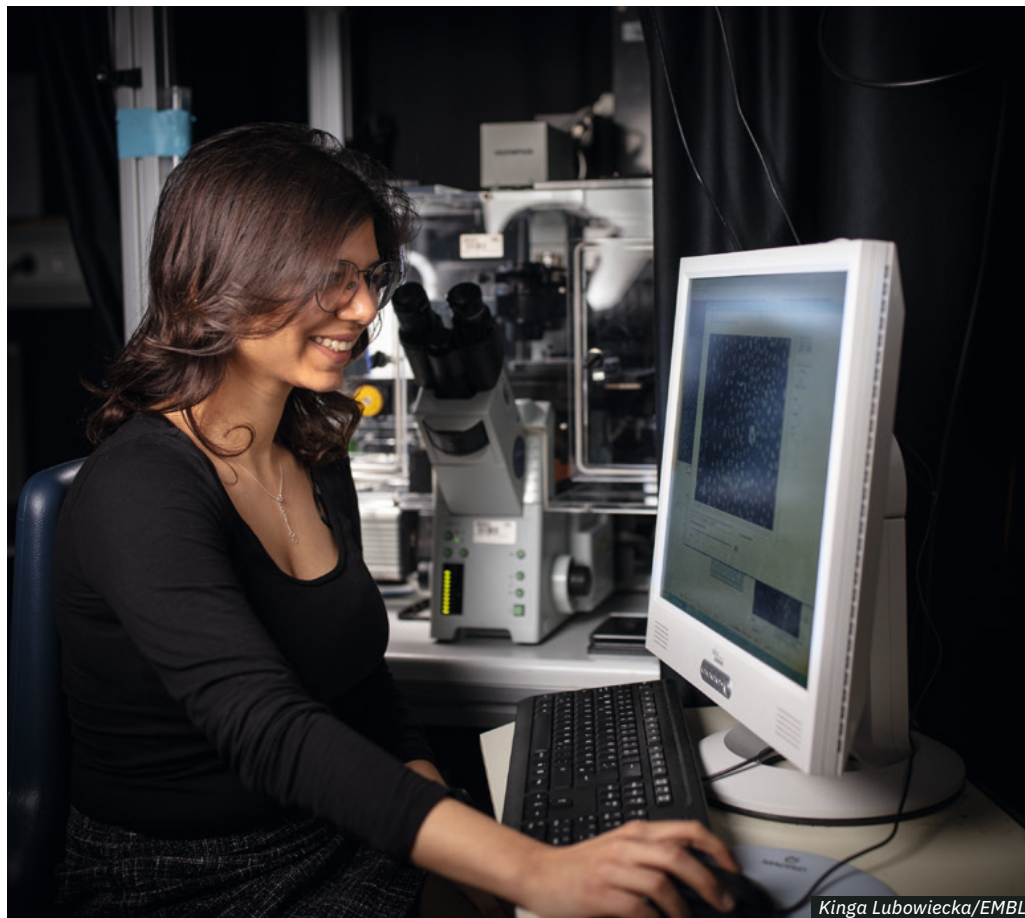


*Taking into account the ESRF shutdown in Grenoble, due to its upgrade to a fourth-generation synchrotron, the ESRF Extremely Brilliant Source

EMBL HEIDELBERG

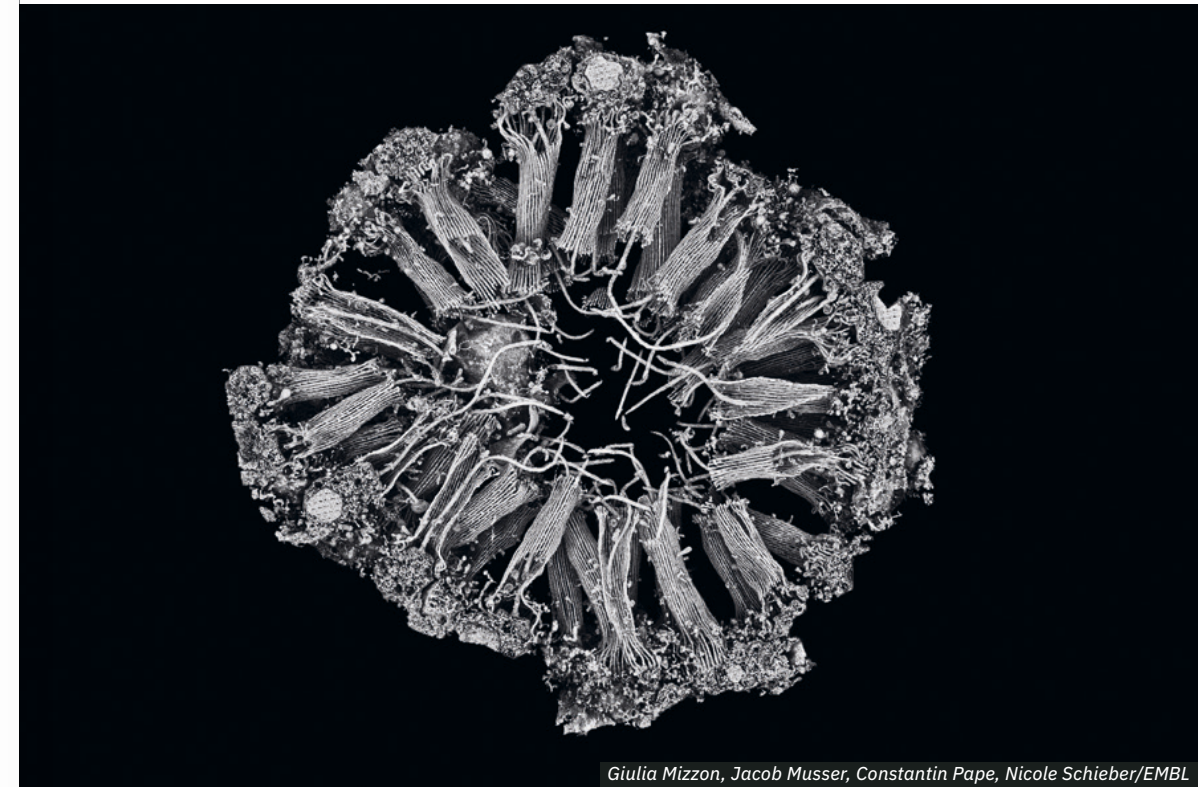
Cryo-electron microscopy service platform

Since 2017, the Cryo-Electron Microscopy (Cryo-EM) Service Platform at EMBL Heidelberg has provided services to external users for both single-particle and tomography projects. Access was initially provided through the iNEXT project, and will continue with iNEXT-Discovery in 2020. Access to the Cryo-EM Service Platform is also provided through the service access scheme, in which external academic and industrial users contribute to the running costs of the facility. In either case, an external committee reviews the projects and approves them based on scientific merit and feasibility. The Cryo-EM Service Platform will move to the EMBL Imaging Centre upon its completion in 2021. This will further extend the platform's capabilities and the number of external users it can accommodate.



The powerful advanced microscopy technologies in the ALMF enable scientists to visualise samples ranging in scale from nanometres to millimetres.

Kinga Lubowiecka/EMBL



A 3D reconstruction of a sponge feeding chamber, created using focused ion beam scanning electron microscopy (FIB-SEM) in the EMCF.

Giulia Mizzon, Jacob Musser, Constantin Pape, Nicole Schieber/EMBL

Imaging services

EMBL's imaging core facilities are the Advanced Light Microscopy Facility (ALMF) and Electron Microscopy Core Facility (EMCF) in Heidelberg, the Microscopy Facility (MF) in Rome, and the Mesoscopic Imaging Facility (MIF) in Barcelona. Together, these facilities provide a broad range of cutting-edge services in imaging and form the EMBL node of the Euro-BioImaging European Research Infrastructure Consortium, which was launched in 2019 (p. 52).

The ALMF provides state-of-the-art light microscopy equipment to visualise samples ranging in scale from nanometres to millimetres. The facility also provides image analysis services, in collaboration with EMBL's Centre for Bioimage Analysis. In response to user demand, the ALMF further increased its capacity in confocal imaging in 2019, collaborating with industrial partners to set up a new spinning-disc microscope and two additional laser scanning microscopes – one of them able to capture images with an exceptionally

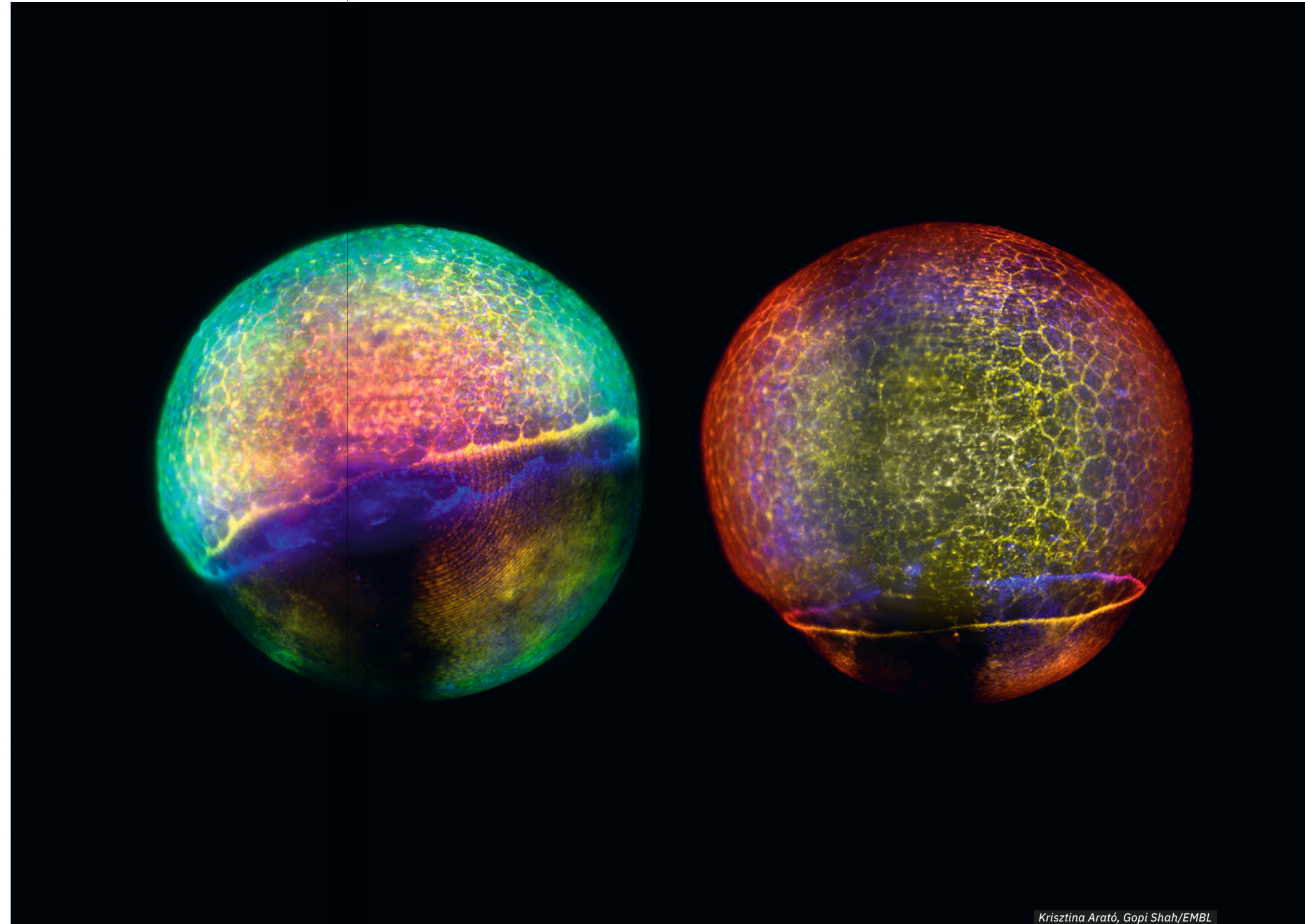
wide field of view, which is particularly suited to whole-organism imaging. The ALMF has also upgraded its capacity in STED- and STORM-based super-resolution microscopy.

The EMCF provides services and access to instruments for performing ultrastructural explorations of a diverse range of specimens, from cell lines to multicellular tissues and model organisms. Highlights in 2019 were the implementation of robust workflows for high-throughput transmission electron microscopy and electron tomography, and the installation of new microscopes: a second focused ion beam scanning electron microscope (FIB-SEM) and a serial block-face electron microscope (SBEM). The EMCF is also strengthening its portfolio in correlative light and electron microscopy (CLEM), in close collaboration with the ALMF and the Centre for Bioimage Analysis, aiming to achieve a smoother integration of multiple imaging modalities in 2D and 3D.

The MF in Rome is undergoing a full renovation of existing equipment to bring in advanced fluorescence techniques. The facility now has a new spinning-disc microscope system and a new fast wide-field microscope that deblurs and deconvolves data during acquisition. The facility also has a new structured illumination and localisation-based super-resolution microscope with an integrated fluidic device to allow multiplexed imaging techniques such as DNA-PAINT. The MF, in collaboration with research groups at EMBL Rome and the Histology Service, is developing a spatially resolved transcriptomics and connectomics analysis service. The facility has also set up collaborations with industry to facilitate multiplexing experiments and improve spinning-disc microscopy.

The MIF in Barcelona provides access to imaging platforms and support services to enable 3D imaging of biological systems in the context of an organ, body part, or whole organism. This requires specially designed technology, since most traditional microscopes are developed for looking at single cells, or small groups of cells. Scientists at the MIF use techniques such as selective plane illumination microscopy (SPIM) and optical projection tomography (OPT), which combine the ability to capture fine details with the capacity to study relatively large samples for extended periods of time. Several MIF platforms were upgraded in 2019, with additional lasers and an environmental control system for the multi-view SPIM, and the acquisition of a new light-sheet microscope designed for medium-throughput timelapse imaging of organoids and related samples.

Timelapse images taken with a MuVi SPIM light-sheet microscope show how zebrafish embryos start developing.



Krisztina Arató, Gopi Shah/EMBL

EMBL Imaging Centre

The foundation stone for the EMBL Imaging Centre was laid on 1 April 2019, in a ceremony that included representatives from the Imaging Centre's public funders, the German Federal Ministry of Education and Research (BMBF), the State of Baden-Württemberg (MWK), and EMBL; its industry partners, Thermo Fisher Scientific, Leica, and ZEISS; and private donors from the Boehringer Ingelheim Foundation and HeidelbergCement. Structural work was completed at the end of 2019, and work on the façade and internal outfitting of the building has now begun. Preparations to set up the teams that will provide Imaging Centre services and engage in technology development also began in 2019.

Construction is planned to finish in 2020, with the Imaging Centre scheduled to begin operations in 2021. It will provide access to the latest technologies in light and electron microscopy, alongside data analysis facilities and expert support. Technology developers, biological application specialists, and microscope users will work together in the creative hub to develop imaging technology prototypes. Close collaborative links with industry will facilitate the development and transfer of these technologies, providing benefits to the scientific community worldwide.



The foundation stone ceremony for the EMBL Imaging Centre. Representatives of EMBL and all involved partners attended.

ALUMNI IMPACT

Ernst H. K. Stelzer

Full Professor of Physical Biology and Advanced Light Microscopy
Buchmann Institute for Molecular Life Sciences
Goethe-Universität, Frankfurt am Main, Germany
Group Leader at EMBL, 1983–2011



Ernst Stelzer's early work at EMBL Heidelberg centred on the development of new technologies for 3D light microscopy. In confocal laser scanning, a focused laser beam excites the fluorophores in a sample point by point, while a pinhole in front of the detector discriminates against the out-of-focus fluorescence signal and creates a high-resolution 3D image. Ernst's group promoted the idea of 'optical sectioning', in which a series of 2D images are combined to reconstruct a biological sample in 3D. In their later work at EMBL, the group developed two entirely new technologies, selective plane illumination microscopy (SPIM) and digital scanned laser light-sheet fluorescence microscopy (DSLM), in which a sheet of light is used to illuminate only a thin layer inside a sample at a time. Similar to confocal imaging, moving this light sheet through the sample makes it possible to produce 3D reconstructions. Unlike confocal microscopy, SPIM and DSLM illuminate just the part of the sample that is imaged, minimising the laser light-induced damage in a biological sample by several orders of magnitude. This makes them ideally suited for the study of sensitive living systems such as developing embryos, which often need to be studied over a period of several days.

The technologies developed by Ernst and his group continue to revolutionise the life sciences, enabling discoveries in diverse fields including cell biology, developmental biology, and neuroscience. Their confocal technology inventions were commercialised by ZEISS, forming the basis of several successful series of confocal microscopes. Following Ernst's departure from EMBL, light-sheet technology has been further developed by EMBL group leaders Lars Hufnagel and Jan Ellenberg, and commercialised by Luxendo, an EMBL spin-off company that was acquired by scientific instrument manufacturer Bruker in 2017. Luxendo continues to collaborate closely with scientists at EMBL, allowing new technologies to be developed close to biological applications in EMBL's research, and to be evaluated for commercialisation. The technologies in confocal microscopy, SPIM, and DSLM that were developed at EMBL are now used in thousands of labs worldwide, and will be an important part of the instrumentation in the EMBL Imaging Centre.

Multi-omics services

EMBL HEIDELBERG

EMBL Heidelberg's facilities include services in chemical biology, flow cytometry, genomics, metabolomics, protein expression and purification, and proteomics.

In 2019, the Flow Cytometry Core Facility introduced a new service analysing cells with full-spectrum deconvolution, which provides better resolution in autofluorescent tissues. The facility also expanded its offering of several mRNA and epitope-expression single-cell sequencing approaches, in close cooperation with the Genomics Core Facility.

The Metabolomics Core Facility made an important step towards setting up highly sensitive metabolomics assays by installing a triple-quadrupole mass spectrometer for targeted metabolomics and lipidomics analyses.

The Protein Expression and Purification Core Facility established a new service offering recombinant protein expression in mammalian cells, alongside existing services for bacterial and insect cells. The facility also acquired a new SEC-MALS instrument to expand its capabilities in biophysical characterisation.

The Proteomics Core Facility improved proteome coverage and quantification accuracy by establishing and optimising new workflows on Fusion Lumos instruments acquired in previous years. The cross-linking protocol was further optimised and analysis was automated, resulting in wider use of this service.

EMBL ROME

EMBL Rome's facilities include services in flow cytometry, gene editing and embryology, genetic and viral engineering, and histology.

The Flow Cytometry Facility provides effective training, practical and theoretical assistance, and access to state-of-the-art equipment. In 2019, the facility acquired a Thermo Fisher Scientific Attune acoustic cell analyser, which is capable of high-speed analysis of samples.

The Gene Editing and Embryology Facility provides the in-house ability to rapidly generate novel transgenic mice, with strategies focusing principally on CRISPR-Cas9 genome editing. The facility also has expertise in generating transgenic mouse embryonic stem cell lines. The facility produces an average of 25 novel transgenic lines per year, with a project success rate of 94%.

The Genetic and Viral Engineering Facility designs and produces custom-made viruses. In addition to genetic engineering of viral vectors, the facility produces a wide range of genetic constructs, including reagents for CRISPR.

The Histology Service assists scientists in examining how modifications in gene expression affect cell growth, division, differentiation, transformation, and quiescence in the tissues of model organisms. Comprehensive expertise in tissue extraction, processing for histological analysis, sectioning, and staining is available. The facility is also involved in training researchers in various histology procedures and in developing and adapting new technologies.

ALUMNI IMPACT

Wilhelm Ansorge

Visiting Professor, EPFL, Lausanne, Switzerland
Head of Unit and Group Leader at EMBL, 1979–2005



Wilhelm Ansorge is one of the pioneers in the development of automated technology for genome sequencing and analysis. He developed the first automated fluorescent DNA sequencing system for large genomic DNA – subsequently commercialised by Pharmacia – and established new methods for faster and more accurate sequencing. The technologies developed in his group were used around the world and played a key role in demonstrating the feasibility of the Human Genome Project. In 2002, Wilhelm and collaborators developed the first complete human transcriptome microarray chip: a compact device that can be used to measure expression levels of all human genes in a sample. This has found wide-ranging applications in biological and biomedical research.

Another aspect of Wilhelm's work at EMBL involved the development of new methods for microinjection: a process in which an extremely fine needle is used to inject small amounts of a substance into living cells. This makes it possible to study the effects of genes, proteins, or other molecules by introducing them into a cell with precise control of quantities and timing. Wilhelm's work culminated in a fully automated microinjection system, developed in collaboration with Rainer Pepperkok, current Director of Scientific Core Facilities and Scientific Services at EMBL. This system was commercialised by ZEISS and Eppendorf, and has enabled scientists to gain insights into a wide range of biological processes, including gene expression and the cell-division cycle.

During his time at EMBL, Wilhelm's group organised more than 60 training courses, enabling thousands of scientists worldwide to use the group's technologies and methods to make new scientific discoveries.



IT services

EMBL's IT infrastructure is designed to support data-driven science at large scale. IT virtualisation and cloud technologies are vital for providing large-scale IT services that are robust, scalable, flexible, and cost effective. In 2019, EMBL IT Services made significant investments in upgrading the IT infrastructures in Heidelberg with additional GPU (graphics processing unit) compute power for the High-Performance Compute Cluster and the EMBL 3D Cloud, to support the rapidly growing demand for specialised compute capacity, and accelerating machine learning in areas such as large-scale image data analysis.

In a collaborative effort between scientists from EMBL's core facilities and groups in the Cell Biology and Biophysics Unit, IT Services in Heidelberg has continued to develop the Data Management Application (DMA), a software framework that aims to support EMBL's research groups through the whole process from data production to publication, providing improved data organisation, tracking, and data management policies. To collect feedback and to further promote the DMA, IT Services has worked with stakeholders across EMBL, including the core facilities and the Bio-IT community, to co-organise workshops and events focused on data management.

Since the beginning of 2019, EMBL's Head of IT Services, Rupert Lück, has represented EMBL, supported by EIROforum, on the Executive Board of the European Open Science Cloud (EOSC). The EOSC aims to federate existing and emerging data infrastructures in Europe, and will offer a virtual environment to store, access, share, and reuse research data across scientific disciplines and borders. The 11 members of the Executive Board serve as experts to the European Commission, assisting in the first phase of EOSC development. Rupert also leads the EOSC Sustainability Working Group of the Executive Board, which works closely with the EOSC Governance Board and representatives from 28 EU member states and 10 associated countries to ensure there is a sustainable financial foundation and solid governance for the continuing activity of the EOSC.



Innovation and translation

EMBL actively engages in technology development and transfer, and industry relations

Innovation and commercialisation activities

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 commercially available. EMBLEM has enjoyed continued success with these endeavours in 2019, and has supported EMBL in developing and expanding strategic partnerships with industry at various levels. Three spin-off companies were incorporated in 2019.

A protein engineering technology platform developed by Edward Lemke and his group at EMBL Heidelberg provides new ways to develop highly specific antibody–drug conjugates or radioisotope analogues. In August, the spin-off company ARAXA Biosciences was created to fully leverage the potential of this platform technology and offer protein engineering services for medical, biomaterial, and research applications.

In October, the spin-off company Suricube was incorporated, based on an invention from electronic engineer Alejandro Gil Ortiz and group leader Lars Hufnagel at EMBL Heidelberg. Suricube will drive the commercial development of instrument control hardware and software, allowing highly modular and versatile control of microscopes and other scientific instruments.

The CrystalDirect technology developed by José Márquez and Florent Cipriani at EMBL Grenoble enables full automation of the crystal harvesting process for X-ray crystallography. The spin-off company ALPX was created in October to establish CrystalDirect for routine services in macromolecular crystallography. Pharmaceutical companies will benefit from these services, enabling them to pursue structure-based drug development with unprecedented speed and quality.

EMBLEM in numbers

EMBLEM's technology transfer figures in 2019

€12 160 000
income



34

inventions disclosed



10

priority patent applications filed



435

licence and collaboration agreements concluded



20

patents granted

Strategic partnerships

Based on a long and successful cooperation, Leica Microsystems and EMBL have now entered into a long-term framework collaboration agreement to provide new imaging technologies to the scientific community. Leica is one of the industry partners for the EMBL Imaging Centre, which is due to open at EMBL Heidelberg in 2021 (p.30). The new framework collaboration, negotiated by EMBLEM, allows more intense collaboration between developers and users during the early stages of developing new technologies. This leads to faster iteration cycles and makes new technologies more rapidly available for research.

In 2019, the framework collaboration between EMBL and pharmaceutical company GSK, which builds on the close relationship between EMBL and its spin-off company Cellzome – now a GSK company – entered its third successful year. The collaboration aims to enhance understanding of disease and drug mechanisms through joint research. Two joint postdoctoral projects successfully concluded in 2019, and a further seven were ongoing. These collaborations produced six publications in high-ranking journals, including *Nature Biotechnology* and *Nature Methods*.

The public–private initiative Open Targets, which includes EMBL, the Wellcome Sanger Institute, GSK, Biogen, Takeda, Celgene, and Sanofi, celebrated its fifth anniversary in 2019 and began its second five-year financing phase. Open Targets uses human genetics and genomics data for systematic drug target identification and prioritisation. In 2019, it introduced target safety annotation and synthetic lethality data in cancer. It also developed eight new projects, bringing its project portfolio to more than 60 projects in total. The Open Targets public computational platform is attracting interest from outside the consortium, and the Genetics Portal – which was significantly updated

in 2019 – is gaining recognition as a robust approach to handling genetics data. Open Targets held four science integration days in 2019, which attracted over 100 scientists from its partner organisations, and worked with the EMBL-EBI Industry Programme to provide two workshops. Open Targets has also established links with similar projects in early drug discovery, notably the Structural Genomics Consortium and the Illuminating the Druggable Genome programme, run by the US National Institutes of Health.

Other highlights from 2019 include the start of a new collaboration between Unilever and the Finn group at EMBL-EBI, with the aim of studying the microbial functions present in skin microorganisms. The bioinformatics internship programme between Novo Nordisk and EMBL-EBI, which began in 2017, was extended and now includes funding for six interns. In October, US-based DNA synthesis company Twist Bioscience licensed the DNA storage technology developed by EMBL-EBI Director Ewan Birney and Joint Head of Research Nick Goldman. In November, the UN Convention on the Rights of the Child, computationally encoded by Nick Goldman and synthesised into DNA by Twist, was deposited in the Arctic World Archive in Svalbard, Norway.

Training and knowledge exchange

Corporate Partnership Programme

EMBL's Corporate Partnership Programme (CPP) facilitates cooperation with the life sciences industry sector. Two new partnership agreements were signed in 2019, bringing the total number of corporate partners to 18. The newest members are Bio-Rad Laboratories, a global leader in developing, manufacturing, and marketing a broad range of innovative products for the life science research and clinical diagnostic markets; and Stilla Technologies, a European biotechnology company that focuses on accelerating the development of next-generation genetic tests by providing biologists with tools for high-resolution genetic analysis.

The generous financial support from CPP members allows the EMBL International Centre for Advanced Training to offer course and conference registration fee waivers and travel grants to leading young scientists from around the world. In addition, the CPP provides funding for the Christian Boulin Fellowships, which help to cover travel and accommodation costs for young research scientists seeking to use EMBL's core facilities. In 2019, the CPP provided funding for 276 fellowships for course and conference participants from 54 countries. Of the 33 courses that were held in 2019 at the EMBL Advanced Training Centre in Heidelberg, 11 were co-organised with CPP partners.



A selection of the courses and conferences held in the EMBL Advanced Training Centre in 2019. The generous financial support of CPP members provided 276 fellowships for leading young scientists to participate in these courses and conferences.

Carolina Cuadras/EMBL

EMBL-EBI Industry Programme

Driven by the increased utility of genomics and biological data and the growing translational applications of bioinformatics, EMBL-EBI has set up a Strategic Partnership Office to promote broader academic and industry engagement. This includes the development of research collaborations with the private sector, and the delivery of EMBL-EBI's Industry Programme: a subscription-based scheme for major companies that make significant use of EMBL-EBI's data resources.

In 2019, the Industry Programme welcomed BioMarin as a new member and delivered 12 knowledge-exchange workshops in the UK and US, some with hands-on tutorial components. The programme also held its first agritech hackathon, bringing together plant science academics, plant breeders, agronomists, and industry partners to develop tools for data integration to help address sustainable crop protection.

ALUMNI IMPACT

Gitte Neubauer

Vice President of Omics Technologies and Head of Cellzome, GSK, Heidelberg, Germany
PhD student and postdoc at EMBL, 1994–2000



Gitte Neubauer completed her doctoral studies at EMBL in the newly established field of proteomics: the study of the full set of proteins produced by a cell or an organism. As a postdoc, she was one of the founders of EMBL spin-off company Cellzome, along with EMBL alumnus Giulio Superti-Furga. Gitte used her expertise to build Cellzome's proteomics technology platform and apply it to the development of new drugs. In 2011, she was awarded the first EU Prize for Women Innovators in recognition of her groundbreaking work in proteomics and her success in commercialising her research.

Gitte was appointed Head of Cellzome in 2012, following its acquisition by pharmaceutical company GSK. Cellzome remains on the EMBL Heidelberg campus and there is active collaboration between its scientists and those in EMBL's research groups and core facilities (see, for example, pp.14, 36). The acquisition by GSK has led to a broadening of Cellzome's research activities from its initial focus on identifying drug candidates for the treatment of inflammatory diseases and cancer. Today, Cellzome is GSK's hub for all omics technologies that are used to understand disease, drug targets, and drug mechanisms. Research at Cellzome identifies novel therapeutic targets, markers for patient stratification, and more precise drug candidates.

Training and public engagement

EMBL trains scientists and engages with the public, schools, and donors

Internal training

The Internal Training programmes at EMBL offer PhD students and postdocs outstanding training and career development opportunities, enabling them to realise their full potential.

Interdisciplinary teams are key to addressing new challenges in the biological sciences. Attracting talented people with educational backgrounds outside biology is therefore an important goal for EMBL and for the EMBL International PhD Programme. The first EMBL Lautenschläger Summer School, 'Talents teach talents', was launched in 2019, with the aim of inspiring students in STEM subjects to pursue an interdisciplinary PhD in the life sciences, while also providing an opportunity for current EMBL PhD students to teach and share their research experiences. The two-week programme was attended by 20 master's and bachelor's students from

17 countries. The event, due to be repeated in 2020, was made possible by donations pledged at the 2018 EMBL Benefit Gala and by a generous gift from the Manfred Lautenschläger-Stiftung.

EMBL's Postdoctoral Programme supports the postdoctoral community across EMBL's six sites. Postdocs join EMBL via various routes:

- A classical stream in which postdocs are supported by funding available to their group leader.
- Personal merit fellowships.
- One of EMBL's site-specific fellowship programmes.
- The EMBL Interdisciplinary Postdocs (EIPOD) programme.

The Postdoctoral Programme successfully applied to the Marie Skłodowska-Curie Actions COFUND programme to support a new version of the EIPOD programme, EIPOD4.



Marietta Schupp/EMBL

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

This programme offers three tracks for fellows to choose from. The academic track is designed for fellows interested in pursuing a traditional academic career. The industry track supports interdisciplinary research projects involving an industry partner or applied research projects. The clinical track targets medical doctors or other PhD graduates who aspire to work as physician scientists, as well as fellows with a strong interest in biomedical research.

EIPOD4 fellows work on interdisciplinary research projects involving two or more EMBL groups. Depending on the track they choose and their research interests, they may also involve an external partner from academia, industry, clinics, or museums with active researchers. The first recruitment for the programme took place at the end of 2019. The first 20 fellows were admitted to the programme and will begin their fellowships in 2020.

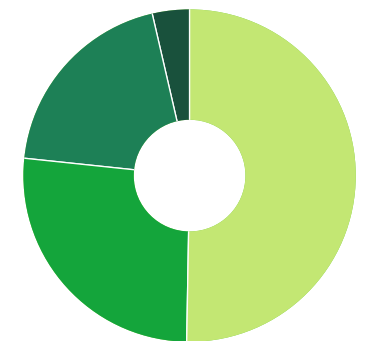
Internal Scientific Training launched two new programmes in 2019 aimed at EMBL PhD students and postdocs. The EMBL Complementary Scientific Skills Programme brings together training activities tailored for EMBL scientists, and focuses on the non-technical skills required for a scientific career. A total of 26 workshops on nine topics were held in 2019, with at least one course held at each EMBL site. Over 250 scientists participated in the workshops.

The EMBL Fellows' Career Service was launched in September 2019 to support PhD students and postdocs across all sites. The service offers individual support, and has expanded the range of career-related events and online resources available at EMBL. Within the first four months, 77 career guidance sessions were held. In addition to other events, including the annual EMBL Career Day, the service offered six 'Applying to Industry' workshops. For the first time, a Career Development Day for the new cohort of PhD students was also organised.

EMBL POSTDOCTORAL PROGRAMMES

70
new postdocs in 2019

238
postdocs in 2019 in total



- 120 Classical stream
- 63 EIPOD programme
- 47 Personal merit fellowship
- 8 Site-specific programmes

62
postdocs leaving in 2019

EMBL International PhD Programme



1771
applications



49
new PhD students



212
PhD students



50
graduations

External training

External Training at EMBL comprises the international Course and Conference Programme and the Scientific Visitor Programme. Both programmes provide excellent training opportunities to scientists from around the world.

Highlights from the Course and Conference Programme in 2019 included three new conferences: ‘Synthetic Morphogenesis: From Gene Circuits to Tissue Architecture’, ‘Reconstructing the Human Past – Using Ancient and Modern Genomics’, and ‘The Identity and Evolution of Cell Types’. The 8th Congress of the International BioIron Society was the largest conference ever held in the EMBL Advanced Training Centre, with 550 participants, three parallel conference sessions, and a connected practical course. Another large meeting was ‘Seeing is Believing – Imaging the Molecular Processes of Life’: a biennial symposium that continues to attract many scientists and engineers who are active in microscopy, imaging, visualisation, and image and data analysis. EMBL also paid tribute to the scientific legacy of its late former Director General Fotis Kafatos, in a conference held in his memory.

The first conference at EMBL Barcelona, ‘Limb Development and Regeneration: New Tools for a Classic Model System’ was held in 2019, as was the first conference in the new Centre for Structural Systems Biology (CSSB) building in Hamburg, ‘Tools for Structural Biology of Membrane Proteins’.

Outstanding practical courses trained scientists in areas such as optogenetics, single-cell omics technologies, quantitative proteomics, biology of extracellular vesicles, and microbial metagenomics.

New course topics included circular RNAs, immune profiling of single cells, and volume electron microscopy.

In 2019, the EMBL-EBI Training Programme expanded its online training offering. Among the new courses and webinars is a course on single-cell RNA sequencing, including data management, sharing, and analysis. Through its train-the-trainer courses, the team instructed 26 new bioinformatics trainers.

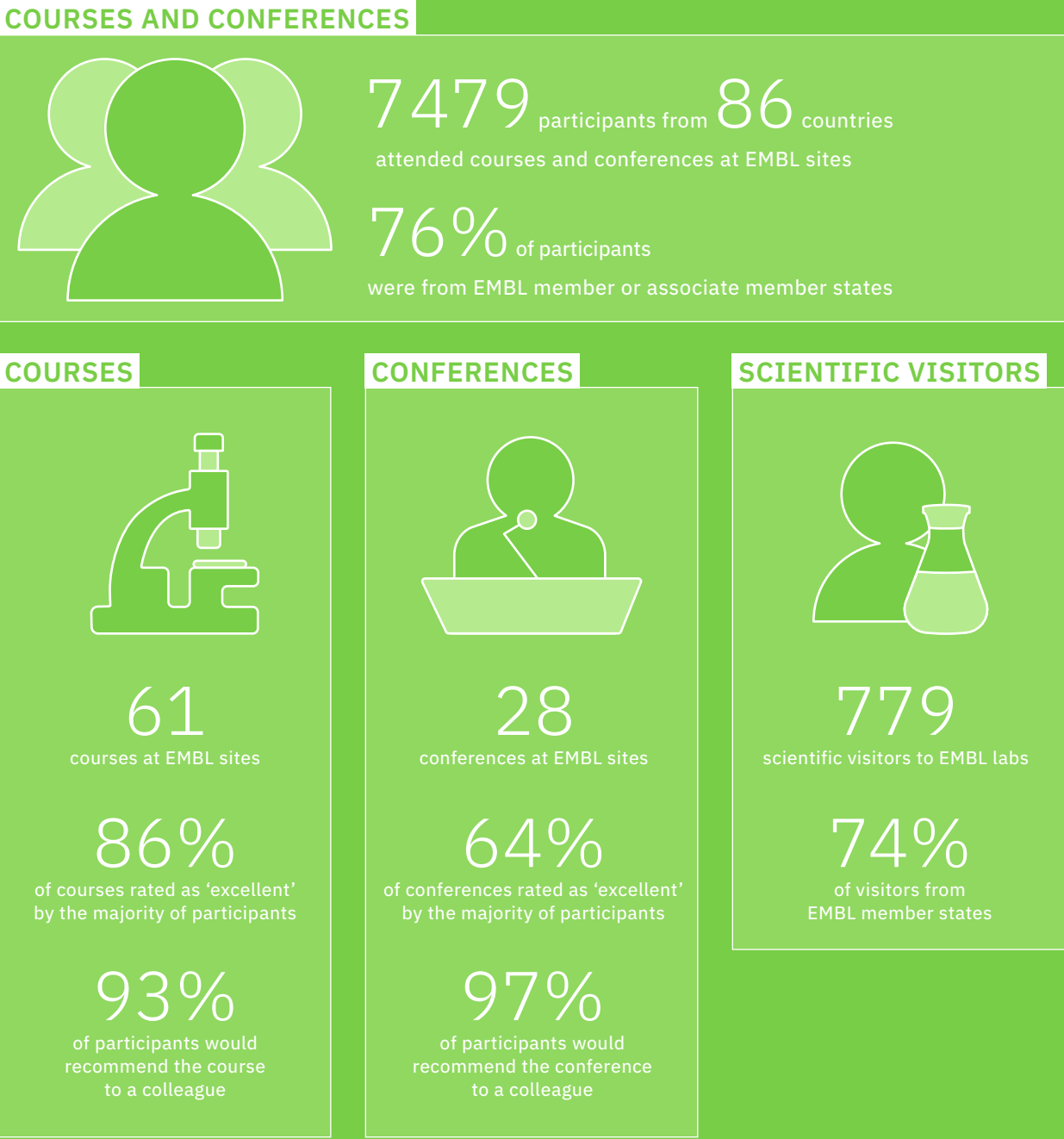
The CABANA project for building bioinformatics capacity in South America, which began in 2018, continued to build momentum. CABANA has now hosted more than 20 scientists on secondments, and in 2019 alone delivered 11 workshops throughout South America, as well as train-the-trainer activities in Brazil and Peru.

Together with collaborators in Africa, Canada, and mainland Europe, EMBL-EBI Training developed a training and outreach strategy for the new Common Infrastructure for National Cohorts in Europe, Canada, and Africa (CINECA) project, which aims to accelerate disease research and improve health by facilitating transcontinental human data exchange.

EMBL also promotes scientific excellence through its Scientific Visitor Programme. The programme enables visiting scientists and students – 74% of whom are from EMBL member states – to access EMBL’s technologies and equipment, and to build collaborations with groups across all EMBL sites.

External training in numbers

EMBL’s courses, conferences, and scientific visitors in 2019

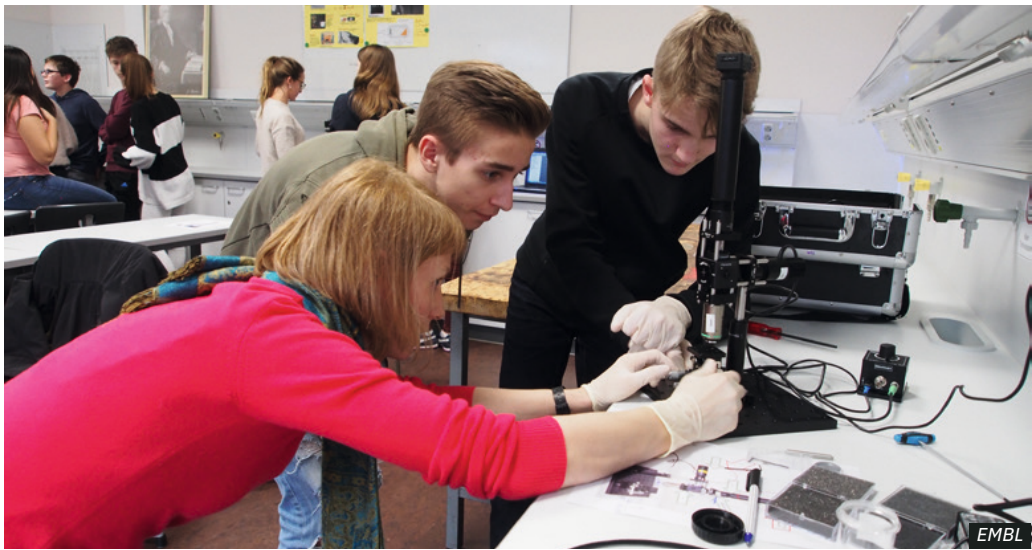


Public engagement, communications, and outreach

Together, EMBL’s Communications team, the European Learning Laboratory for the Life Sciences (ELLS), EMBL’s Science and Society Programme, and the EMBL Archive seek to inspire and educate people in engaging ways.

In 2019, ELLS – EMBL’s educational programme – carried out engagement activities that reached 217 high-school teachers and more than 1850 students, and engaged directly with around 1100 members of the public. ELLS welcomed 250 students to EMBL Heidelberg and organised two practical courses in molecular biology for science teachers. Visits carried out as part of their School Ambassador Programme involved 247 students in France, Greece, Italy, Portugal, and Colombia. The 2019 EMBL Insight Lecture, organised by ELLS, was attended by 70 students and nine teachers on site, and was broadcast live to 35 schools in nine countries. The lecture was given by Professor Dame Janet Thornton, group leader and senior scientist at EMBL-EBI, who spoke on the subject of ageing and disease.

ELLS also continued the development of its educational resource ‘From Nature to Technology: Microscope in Action’, which aims to engage teenagers with biology by enabling them to build and use their own fluorescence microscope. Carried out in collaboration with the Prevedel group at EMBL Heidelberg, the project reached the end of its second developmental phase, involving further development of the microscope and the preparation of teacher resources. The Microscope in Action project was tested in several schools, with plans to make it more widely available in 2020.



Pupils assemble EMBL’s ‘Microscope in Action’.

EMBL’s Communications team supports an extensive programme of visits to EMBL throughout the year. In 2019, 28 visitor groups came to EMBL Heidelberg, including a total of 755 people. Each group spends half a day at EMBL, getting to know the organisation by attending scientific talks tailored to their interests, discussing careers with EMBL staff and career advisors, and looking behind the scenes during tours of laboratories and service facilities. Groups come from around the world, with most consisting of students in the life sciences, IT, or engineering. Groups also include members of the local community, journalists, and distinguished scientists.

Colleagues at EMBL-EBI were involved in 46 visits to campus, engaging with more than 2400 people. Visitors include groups from primary and secondary schools, university students, teachers engaged in continuing professional development, community groups, and other members of the public.

On 20 February 2019, more than 250 local supporters, collaborators, and friends gathered at EMBL Heidelberg for the Annual Reception. This was an opportunity to meet Edith Heard, then newly arrived as EMBL Director General, to celebrate the successes of the past year, and to discuss future projects.

The Friends of EMBL Science Movie Nights provide an opportunity for an audience of EMBL Teens, Friends of EMBL, and members of the public to understand more about their favourite films. For the Science Movie Night in May 2019, the film *Pacific Rim* was chosen, with EMBL scientists taking a closer look at the science behind the movie and answering the audience’s questions.

During three days in May, scientists from EMBL’s Barcelona, Grenoble, Hamburg, and Heidelberg sites took part in the global festival Pint of Science, in which scientists join events at local pubs or bars to explain their research to the public. In Hamburg, this was followed in June by Summer of Science: a three-day science festival in the heart of the city, visited by 50000 people. Members of the EMBL community were present to offer activities for children and adults.

European Researchers’ Night took place on 27 September, and included events in Heidelberg and its neighbouring city Mannheim, as well as three cities in Cambridgeshire, where EMBL-EBI is located. ELLS led the organisation of the Nacht der Forschung Heidelberg | Mannheim, during which around 1000 guests visited EMBL Heidelberg. The External Relations team at EMBL-EBI supported events in Cambridgeshire, which attracted 3500 guests. On 12 October, EMBL Grenoble participated in the Parvis des Sciences at the Grenoble Innovation for Advanced New Technologies (GIANT) campus. More than 1800 visitors attended the talks and hands-on activities at this event.

A highlight of EMBL’s programme of public engagement is the annual Science and Society Conference. The 2019 conference, ‘Science as Storytelling: From Facts to Fictions’, explored the interplay between persuasive narrative formats and seemingly objective scientific results. This sparked much interest and debate, with the conference attracting 400 participants.

The Communications team continued to build EMBL’s social media following in 2019. EMBL’s LinkedIn account showed an increase in followers of 55%, accompanied by very high engagement with EMBL content.

EMBL AND TARA

EMBL and the Tara Ocean Foundation raise awareness of the risks of microplastic pollution

From June to November 2019, the Tara Ocean Foundation carried out Mission Microplastics: a voyage around Europe to study the nature of plastic pollution entering the ocean from the European mainland. This involved taking samples of microplastics flowing from the estuaries of 10 of Europe’s major rivers.

Members of the EMBL community joined the Tara Ocean Foundation during the stopovers of its research vessel *Tara* in London, Hamburg, Rome, Marseille, and Barcelona. EMBL’s Alumni Relations team organised the ‘EMBL in France’ and ‘EMBL in Spain’ events to coincide with the stopovers in Marseille and Barcelona, respectively. The stopover in Barcelona also coincided with the open day of the Barcelona

Biomedical Research Park (PRBB), where EMBL Barcelona is situated. EMBL Barcelona opened its doors to the public for a day of talks, tours, and activities, including imaging samples of aquatic organisms at EMBL’s Mesoscopic Imaging Facility.

Various receptions were organised on board *Tara* to strengthen relationships with local institutes, partners, and stakeholders, and press conferences were co-organised by EMBL and the Tara Ocean Foundation to raise awareness and reach out to local media. EMBL’s press campaign around Mission Microplastics resulted in 39 press clippings mentioning EMBL alongside the Tara Ocean Foundation, reaching a potential readership of 58.7 million.



As part of Mission Microplastics, the schooner *Tara* docked within view of the Barcelona Biomedical Research Park (PRBB), where EMBL Barcelona is situated.

Jordi Casañas/EMBL



EMBL Director General Edith Heard joined women from academia, business, and politics on 14 November for an inspiring evening of talks and networking at EMBL Women’s Night.

Kinga Lubowiecka/EMBL

Private support

EMBL partners with an ever-growing community of individuals, foundations, and companies that enable key projects to advance science and benefit society.

Among these key projects is the EMBL | Stanford Life Science Alliance, which receives vital support from the Dieter Schwarz Foundation. This enables the Alliance to create interdisciplinary, cross-border scientific collaborations that aim to address scientific challenges in the fields of genomics, computational biology, biological imaging, and structural biology.

The Friends of EMBL is a community of individuals and businesses who support EMBL’s work with annual donations. In 2019, support from the Friends of EMBL benefitted EMBL’s initiative for the Advancement of Women in Science. This initiative aims to foster the talent of women as they advance in their scientific careers towards leadership positions. The initiative

was launched at EMBL Women’s Night, now in its third year, which brought together women from science, business, and politics to be inspired by talks and discussion around this year’s motto, ‘Courage to Succeed’.

The Fuchs Fund continues to enable PhD students at EMBL to take up professional development opportunities, and provides help to fellows who are confronted with challenging personal circumstances.

The end of 2019 saw the launch of the Environmental Research Initiative, made possible by private support. This initiative aims to support and enable new research with the potential to find solutions to society’s biggest environmental challenges. EMBL would like to thank everyone who has contributed to this important endeavour.

Integrating life sciences

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

Member state relations

Director General Edith Heard joined EMBL in January 2019 with a vision for the future of life science research in Europe, and a determination to use science to build collaborations between countries in Europe and around the world. To maintain and strengthen EMBL's close relationships with its member states, Edith has undertaken many activities throughout 2019 to engage with member state representatives.

Many new interactions between EMBL and the research community in France took place in 2019. In July, a group of representatives from France's Institute of Biological Sciences (INSB) came to EMBL Heidelberg to introduce their work, find out more about EMBL, and explore possibilities for future interaction. In September, Edith met with Marie-Hélène Tusseau-Vuillemin, Director of the Unit for Environment, Geoscience and Astronomy in the Ministry for Higher Education, Research and Innovation (MESRI), and also with Brune Poirson, State Secretary for Environment and Sustainable

Transition. These meetings laid the groundwork for future research collaborations in line with plans for the new EMBL Programme.

In April and July 2019, Edith travelled to Italy to meet with high-level representatives from the Ministry of Education, University and Research (MIUR), the National Research Council (CNR), the Italian Institute of Technology (IIT), and Sapienza University of Rome. These visits strengthened collaborations and provided an opportunity to discuss the EMBL Rome site and plans for its renovation.

The new Swiss delegates to EMBL Council, from the State Secretariat for Education, Research and Innovation, visited EMBL's headquarters in Heidelberg in August, to learn about EMBL's missions and future ambitions for research and technology development. In November, Edith met with Matthias Egger, the President of the Swiss National Research Council, and Martina Hirayama, the State Secretary for Education, Research and Innovation, to present EMBL's next Programme.



Edith Heard (centre) and representatives from the EMBL member states, EMBL faculty, and other distinguished guests on the day of her inauguration.

Kinga Lubowiecka/EMBL

In June, Edith travelled to Austria and met Iris Rauskala, Federal Minister of Education, Science and Research. She also visited two Austrian research institutes, meeting senior leadership at the Vienna BioCenter and the Institute of Science and Technology Austria.

Based on a framework agreement signed with the Luxembourg National Research Fund (FNR), EMBL-EBI team leaders Rob Finn and Juan Antonio Vizcaino have been awarded funding for their project MetaPUF (Metagenomics: Proteins of Unknown Function), in collaboration with Paul Wilmes and Patrick May from the Luxembourg Centre for Systems Biomedicine at the University of Luxembourg.

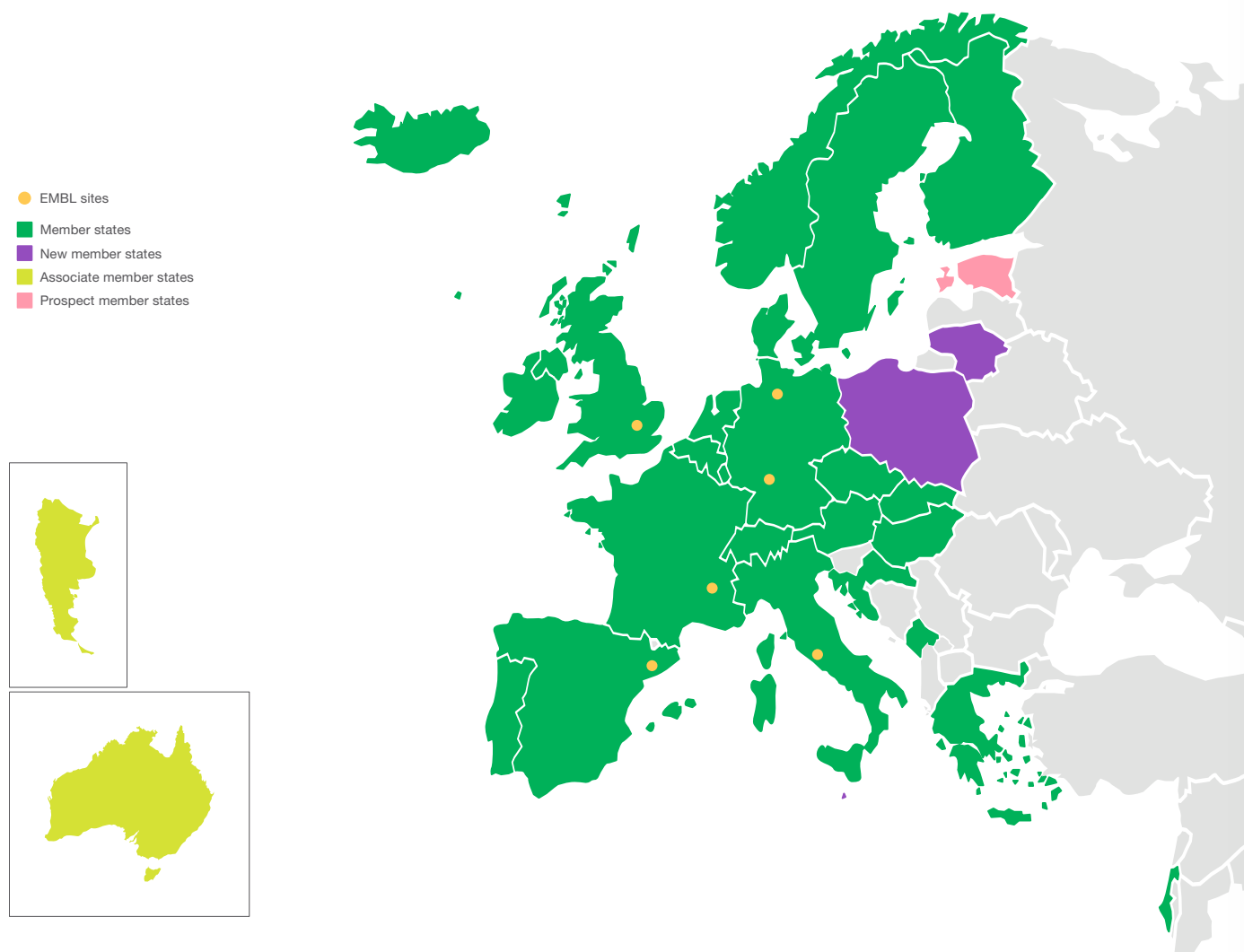
In September, a Portuguese technical graduate joined EMBL's Cell Biology and Biophysics Unit in Heidelberg to receive on-the-job training in technologies available at EMBL. The graduate was selected by the Portuguese Foundation for Science and Technology (FCT) via a call for applications as part of an agreement between FCT and EMBL that aims to advance scientific and technical knowledge within the Portuguese research community. A second call was launched at the end of 2019.

In October, EMBL organised a symposium, 'EMBL: A Vision for European Life Sciences' to celebrate Edith's inauguration. The event was attended by representatives from the member states, and by EMBL faculty and other distinguished guests. It was an opportunity to reflect on previous successful collaborations and to exchange ideas for future projects. The symposium was organised by Patrick Cramer, Chair of EMBL Council, and included

addresses from Sir Paul Nurse, Chair of EMBL's Scientific Advisory Committee; from Edith, on her vision for the future of EMBL research; and from ministerial representatives of all of EMBL's host site countries and its newest member state, Lithuania.

At the end of 2019, EMBL's member states comprised 27 full members, 2 associate members, and 1 prospect member. EMBL continues to grow and use its connections to foster international research

collaboration. In February 2019, EMBL welcomed Poland as a full member state, with Lithuania following in June. The same month, another Baltic state – Estonia – joined EMBL as a prospect member. A delegation from EMBL travelled to Tallinn and Tartu in September 2019 to meet members of the research community in Estonia and inform them about the benefits of EMBL membership, including access to EMBL training schemes and the use of EMBL's facilities and services.



EMBL partnerships

In addition to regular exchange with its member states and associate member states, EMBL actively engages in building and maintaining formal partnerships with other centres of scientific excellence in its member states.

In September 2019, EMBL held its third Partnership Conference, 'Perspectives in Translational Medicine', which took place at EMBL Barcelona. The event brought together more than 200 people from EMBL and its partner institutes to exchange expertise and build new collaborations and research networks. This provided an opportunity for group leaders and senior representatives from the partner institutes to meet one another, and to identify future directions for collaborative research. Following the conference, a

Young Investigators Meeting was held for early-career researchers. This included panel discussions with young group leaders, and workshops exploring job opportunities in industry, academia, and beyond.

A new partnership was successfully established in March 2019 with Poland's Nencki Institute of Experimental Biology. The Nencki-EMBL Partnership BRAINCITY specialises in neural plasticity and brain disorders. The establishment of this partnership shows the strong international connections that had already been made between researchers during Poland's prospect membership, as Poland had only become a full member state one month before the new partnership was established.

EU relations

Supported by a memorandum of understanding, EMBL maintains close relationships with the European Commission (EC), and with key members of the European Parliament. Throughout 2019, EMBL's Government and EU Relations team responded to multiple public consultations from the EC.

In April, EMBL welcomed Jean-Eric Paquet, Director General of Research and Innovation at the EC, to EMBL Heidelberg, where he met EMBL Director General Edith Heard and other senior EMBL faculty. Discussions during the day covered topics such as interdisciplinarity, research infrastructures, and collaboration with industry. In September, Edith Heard and Joint Head of Government and EU Relations Jana Pavlic represented EMBL at the EC's first European Research and Innovation Days. In March, EMBL celebrated the award of its 100th Horizon 2020 grant.



EIROforum

The European Intergovernmental Research Organisation forum, or EIROforum, is an association of eight of Europe's largest intergovernmental research organisations, together aiming to strengthen the impact of European research. Following the ratification of a new statement of intent with the EC during EMBL's chairmanship, the dialogue between EIROforum and EU institutions continues on various topics, including the future of research infrastructures, the European Open Science Cloud (p. 34), the mobility of researchers, and diversity.

In 2019, EIROforum published a position paper on the value of European Research Infrastructures and the need to fund them adequately. Through EIROforum, EMBL representatives also attended several conferences on the future of the European Research Area, to ensure that funding and future policy take into account the important roles of Research Infrastructures and of fundamental research.

European Research Infrastructures

With the benefit of its experience in operating and administering its own distributed life science research infrastructures, EMBL has actively participated in the development and coordination of projects relating to biological and medical sciences, outlined on the European Strategy Forum on Research Infrastructures (ESFRI) roadmap. EMBL is involved particularly in the governance of two projects: Euro-BioImaging and ELIXIR.

ELIXIR is a research infrastructure for biological data, which coordinates bioinformatics services across its member states. Three new ELIXIR Communities were established in 2019, in the fields of structural

bioinformatics, intrinsically disordered proteins, and microbial biotechnology. In August, the four-year Horizon 2020 project ELIXIR-EXCELERATE was successfully concluded. It reached its goal to pool bioinformatics resources across Europe and integrate them into a federated infrastructure for life science data. ELIXIR strengthened and diversified its services with the launch of 28 new projects in 2019, and involvement in more Horizon 2020 initiatives is expected.

Euro-BioImaging, which had already been recognised as a landmark European Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences by ESFRI, was officially established as a European Research Infrastructure Consortium (ERIC) by the EC in November 2019. The project was initiated many years earlier at EMBL as part of its mission to integrate the life sciences in Europe, and the achievement of ERIC status is an enormous success. Euro-BioImaging also continued its collaboration with other international partners via the EU-funded Global BioImaging project in 2019. The access that Euro-BioImaging provides to high-end imaging technologies enables the research community to make breakthrough biological discoveries and translate them into innovations in the fields of medicine, diagnostics, drug development, biotechnology, and molecular ecology.

In December, EMBL became the first intergovernmental organisation to join Instruct-ERIC: an ERIC in the field of structural biology that is distributed across 13 member states and offers high-end technologies to the life science research community. Instruct-ERIC and EMBL share a history of collaboration in molecular and structural biology, which will now be deepened and expanded. EMBL will offer structural biology expertise and services via Instruct-ERIC at its sites in Grenoble, Hamburg, and Heidelberg.

Further broadening horizons

Although EMBL's sites are based in Europe, its science extends worldwide. EMBL therefore looks not only within Europe but also to the rest of the world to forge meaningful connections that bring the benefits of its research to society.

Relations with Japan were fostered by a visit to EMBL Heidelberg from the Vice President of Japan's National Institutes of Natural Sciences and the Deputy Director General of the National Institute for Basic Biology in July. On that occasion, an extension of EMBL's memorandum of understanding with these institutes was signed, paving the way for future cooperation with a particular emphasis on imaging.

In May, representatives from Brazil visited EMBL Heidelberg. A special focus of this visit was on communications at EMBL, and on the synchrotron facilities provided by the EMBL network.

In 2019, the EMBL | Stanford Life Science Alliance extended its memorandum of understanding for a further five years, and expanded its scientific cooperation to include the area of computational biology. The Alliance offers a joint postdoctoral fellowship programme and a researcher exchange programme, thereby supporting transatlantic collaboration.

EMBL's Director of International Relations, Silke Schumacher, travelled to Latvia in September 2019 to discuss prospect membership of EMBL. She visited several research institutes and universities, and gave a presentation at the University of Latvia on the benefits that EMBL membership can provide to the Latvian life science community. She also met with the Minister of Education and Science, and members of the Ministry's Higher Education, Science and Innovation Department, to answer their questions and discuss possible opportunities for collaboration.



An extension of EMBL's memorandum of understanding with Japan's National Institutes of Natural Sciences and National Institute for Basic Biology was signed in July.

Massimo Del Prete/EMBL

Honours and awards

Celebrating individual achievements in 2019



SISSY KALAYIL

Postdoctoral Fellow, Cusack group
Young Talent France 2019
L'Oréal–UNESCO Prize for Women in Science
L'Oréal Foundation and UNESCO



TOBY HODGES

Bioinformatics Community
 Project Manager, Zeller team
AAAS Community Engagement Fellow for 2019
American Association for the Advancement of Science



ANNE-FLORE LALOË

EMBL Archivist
Selected for New Professionals Programme
International Council on Archives



MARIA LUKARSKA

PhD student, Cusack group
Prix de thèse
Université Grenoble Alpes



ANDREA IMLE

Postdoctoral Fellow (EIPD),
 Díz-Muñoz and Korbelt groups
2019 L'Oréal–UNESCO for Women in Science fellowship
L'Oréal Foundation and UNESCO



MARIA LEPTIN

EMBO Director
Doctor Honoris Causa
EPFL



ISIDRO CORTÉS-CIRIANO

Group Leader
MGMS Frank Blaney Award
Molecular Graphics and Modelling Society



PEER BORK

Head of Unit, Senior Scientist, and
 EMBL Heidelberg Strategic Head of Bioinformatics
Honorary professorship
Heidelberg University



SARA CUYLEN-HÄRING

Group Leader
Career Development Award
Human Frontier Science Program



EDITH HEARD

EMBL Director General
Hansen Family Award
Bayer Science & Education Foundation
Karl Friedrich Bonhoeffer Medal
Max Planck Institute for Biophysical Chemistry



MIKI EBISUYA

Group Leader
Jun Ashida Award for Brilliant Female Researchers
Japan Science and Technology Agency

Alumni

EMBL connects scientists and other professionals around the world

In 2019, the EMBL Alumni Association marked its 20th anniversary. From its beginnings as a network that grew organically and was largely run by members on a voluntary basis, it has expanded into a rich and vital resource for EMBL, providing expertise, support, and access to networks. The Alumni Relations team works strategically to harness this resource and the goodwill of the alumni community through a targeted programme of events, communications, and other engagement activities. This ensures that alumni remain involved in EMBL and connected with each other wherever they are, while EMBL benefits from the tremendous strengths of its almost 9000 former staff.

The community is diverse. Former scientific, technical, and administrative staff, visitors, and fellows of EMBL, EMBO, EMBLEM, and EMBL Ventures are considered alumni – as are former Council delegates and members of the Scientific Advisory Committee. Of those eligible, more than half are registered members of the Alumni Association. The appointment of a dedicated Alumni Volunteer Officer in 2017 has enabled the team to capitalise on this resource, with volunteering actions increasing from 156 in 2018 to 340 in 2019.

There was also growth in the number of events and the reach of the ‘EMBL in...’ event series in 2019. More than 60 alumni volunteered as event hosts, co-organisers, or speakers in 2019 at seven ‘EMBL in...’ events in Europe and the US, which

together attracted nearly 500 guests. There remains significant potential to enhance the value of these events for participants by further engaging with industry partners and granting access to members of the EMBL community. These events are a prime example of the crucial role that the alumni community plays in representing EMBL internationally, in member states and beyond.

In 2019, the Alumni Relations team launched the first EMBL World Alumni Day. This is an online global event to connect the community of EMBL staff and alumni across sites and countries at one time. The event was coordinated by 60 alumni, with 70 sharing inspiring stories on social media, highlighting how their time at EMBL has shaped their lives and careers. World Alumni Day was attended by 150 alumni online, and by 300 staff and alumni in person.

In 2019, a new EMBL Alumni Association Board of 15 members representing the community was elected for a term of four years. EMBL would like to thank the previous board for their contributions, and all other volunteers who have served in various capacities.

Alumni continue to draw upon their experience gained at EMBL to drive scientific investigation and discovery. The annual John Kendrew and Lennart Philipson awards, sponsored by philanthropist Roland Specker and EMBLEM, respectively, are just one way that the EMBL Alumni Association celebrates the



EMBL in Italy at Nouscom/ReiThera, Rome, March 2019; the first meeting of the new EMBL Alumni Association Board in Barcelona, January 2020; Angus Lamond and Mehrnoosh Rayner at EMBL World Alumni Day in Heidelberg, July 2019.



Erin Tranfield

achievements of alumni. The 2019 Lennart Philipson Award, which recognises outstanding contributions to translational research and technology development, was presented to Patrick Baeuerle, Executive Partner at MPM Capital, for his pivotal role in the development of immunotherapy drugs to treat cancer. The 2019 John Kendrew Young Scientist Award was presented to Tanmay Bharat, a group leader in the Sir William Dunn School of Pathology at the University of Oxford, UK, for novel applications of cryo-electron tomography in visualising the molecular structures of bacterial communities.

“My time at EMBL was instrumental in shaping my career...We were a group of scientists all pulling together in the same direction. Really collaborative and really exciting. I miss those times!”

Tanmay Bharat
Group leader, University of Oxford
Former PhD student, EMBL Heidelberg, 2008–2013

Administration

Providing services to support EMBL's missions

Throughout 2019, EMBL Administration was actively involved in preparations for EMBL's new Programme and Indicative Scheme, which are currently in development. Administration conducted workshops to define the services it will provide during EMBL's future research programme, and how it will continue to support scientists and other staff members and respond rapidly to their needs.

EMBL's environmental impact has been an important focus in the past year, with the establishment of a Green EMBL Working Group, which carried out an EMBL-wide staff survey and began several initiatives to raise awareness and promote more sustainable practices. EMBL Facility Management supported these initiatives with investments in new solar panels and electronic mobility in Heidelberg, funded by the German government, and with the installation of the first green façade in Heidelberg. Many other improvements were carried out at all sites, including reductions in plastic usage and other measures to reduce waste.

EMBL Council's Working Group on Pensions, led by the Pension Advisory Board, carried out a five-yearly review of the EMBL pension scheme in 2019. The review identified potential issues with the future funding of the pension scheme, similar to those faced

by many other such schemes worldwide. The Working Group and EMBL management developed a range of options to ensure the pension scheme would be sustainable into the future. Council debated these options at its November meeting and agreed that it was fair for EMBL, its member states, and its staff to share the necessary burden between them. Staff were informed of the developments by the Staff Association, and by communications from the Director General.

Following a 2018 report from the Council Working Group on Terms and Conditions of Employment at EMBL, and decisions made by EMBL Council in November 2018, the required adjustments to employment conditions were successfully implemented by Human Resources, Finance, and Legal Services in 2019. These included changes to maternity, paternity, parental and special leave; childcare and flexible working arrangements; and the administration of the EMBL Health Insurance Scheme.

EMBL-EBI Administration made preparations for the UK's exit from the EU and provided support to staff, including practical help and information about the EU Settlement Scheme, whereby staff from the EU, EEA, or Switzerland can apply for settled or pre-settled status in the UK.

Staff Association

Supporting the EMBL community

The Staff Association continues to support EMBL staff by offering advice and information, and by engaging with management on matters of importance for staff. In 2019, the Association was involved in extensive discussions on the review of the EMBL pension scheme and changes to the administration of the health insurance scheme, ensuring that staff were kept informed by updates on its website, online forums, conversations with staff representatives, and information sessions held in collaboration with Human Resources.

The Staff Association provided extensive input into EMBL's Whistleblowing Policy, which was introduced in July. The Association has also been actively supporting initiatives on work-life balance and mental health, and is establishing lists of mental health resources for all EMBL sites, including emergency numbers, a database of physicians and therapists, and training and talk sessions. A seminar, 'Cultivating Mental Health in Academia', was held on 23 September and streamed to all sites.

The Staff Association continued its involvement in various EMBL committees, such as the EMBL Equality and Diversity Committee, the Health and Safety Committee, and the Green EMBL Working Group. With these collaborations, the Staff Association supported

EMBL-wide initiatives such as Fit for Spring and Green Mobility Day. The Staff Association also reviewed and updated its statutes, which included revising various roles and updating its code of conduct and internal financial regulations.

EMBL Aid

EMBL Aid is a platform for staff to raise awareness and organise fundraising activities. Since it was set up in 2014, it has raised more than €30 000 for various charities.

In 2019, almost €14 000 was raised as part of the Mont Blanc Challenge, in which staff climbed the helix of the EMBL Advanced Training Centre 58 times to simulate a climb of Mont Blanc. The funds were donated to Das Frühchen, a Heidelberg charity that supports premature babies and their families. The 2019 EMBL Calendar, organised by EMBL's Photography Club, raised over €2 000 for the Child Care Project, to help build a school in Uganda. Other activities raised €1 250 for Aid for Labs, €870 for Make Change Possible e.V., €590 for Johann-Peter-Hebel-Heim, and €350 for Caritasverband Heidelberg e.V. The Staff Association would like to thank all staff who supported these activities.

Personnel statistics

EMBL hires talented people from around the world

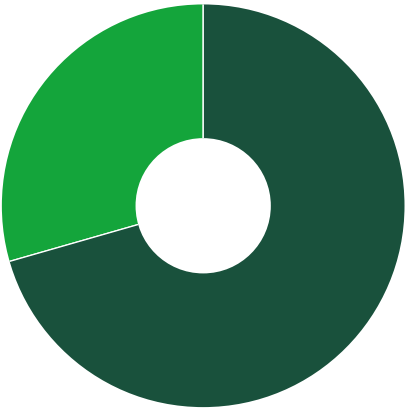
PERSONNEL CATEGORIES IN 2019



Total 1791
in full-time equivalent (FTE)

- 1098 Staff members
- 246 Postdocs
- 212 PhD students
- 133 Supernumeraries and ancillaries
- 102 Diploma students and trainees

STAFF NATIONALITIES IN 2019



Total 1791
in full-time equivalent (FTE)

- 1268 EMBL member or associate member states
- 523 Non-member states

STAFF CLASSIFICATION IN 2019

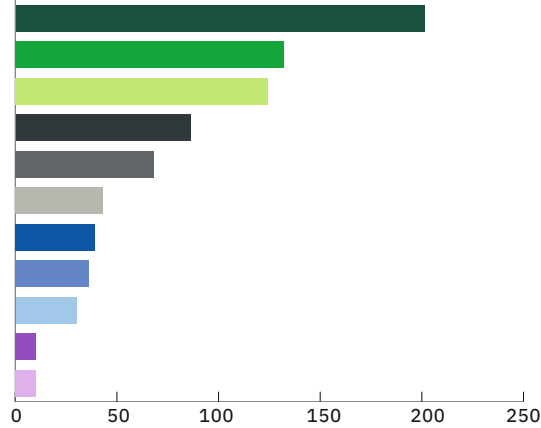


Total 1791
in full-time equivalent (FTE)

- 783 Research
- 482 Scientific services
- 189 Scientific or technical support
- 91 Training and outreach
- 120 Administrative support
- 126 General support

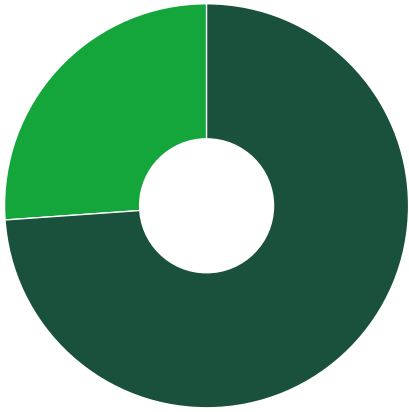
SCIENTIFIC VISITORS IN 2019

EMBL UNITS



- 201 EMBL-EBI
- 132 Structural and Computational Biology
- 124 Core Facilities and Scientific Services
- 86 Cell Biology and Biophysics
- 68 Genome Biology
- 43 EMBL Rome
- 39 Developmental Biology
- 36 EMBL Hamburg
- 30 Directors' Research
- 10 EMBL Grenoble
- 10 EMBL Barcelona

VISITORS' NATIONALITIES



- 576 EMBL member or associate member states
- 203 Non-member states

Total 779

Financial report

EMBL’s financial figures for 2019

EMBL TOTAL INCOME IN 2019

€ 266 million

INCOME

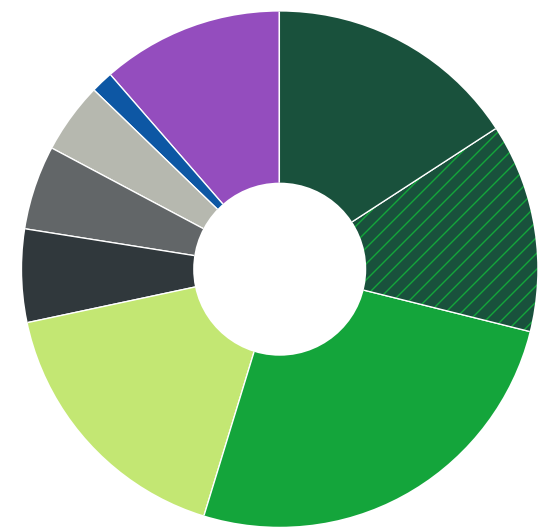


- 41.5% Member state contributions
- 6.0% Member state special contributions*
- 16.6% Internal tax
- 21.8% External grant funding
- 5.0% Other external grant funding†
- 9.1% Other receipts‡

EMBL EXTERNAL GRANT FUNDING IN 2019

€ 57.8 million

EXTERNAL GRANT FUNDING

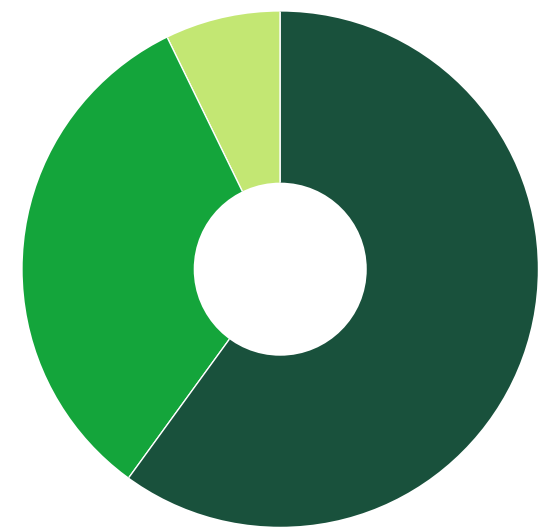


- 15.9% EC
- 13.2% ERC
- 25.7% NIH
- 16.9% Wellcome Trust
- 5.9% BBSRC
- 5.3% BMBF
- 4.4% DFG
- 1.4% MRC
- 11.3% Others

EMBL TOTAL EXPENDITURE IN 2019

€ 267 million

EXPENDITURE



- 60% Staff costs
- 33% Operating costs
- 7% Equipment expenditure, including depreciation

EXPENDITURE BY AREA OF ACTIVITY



- 32% Research
- 28% Scientific services
- 12% Scientific or technical support
- 8% Training and outreach
- 9% Administrative support
- 11% General support

*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 Imaging Centre at EMBL Heidelberg

†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

	× €1000	%		
Ordinary contributions				
Austria	2 372	2.2		
Belgium	2 908	2.7		
Croatia	294	0.3		
Czech Republic	997	0.9		
Denmark	1 911	1.8		
Finland	1 417	1.3		
France	16 008	15.0		
Germany	21 761	20.4		
Greece	1 312	1.2		
Hungary	325	0.3		
Iceland	73	0.1		
Ireland	1 134	1.1		
Israel	1 659	1.6		
Italy	11 883	11.2		
Lithuania	137	0.1		
Luxembourg	210	0.2		
Malta	53	< 0.1		
Montenegro	7	< 0.1		
Netherlands	5 081	4.8		
Norway	3 023	2.8		
Poland	908	0.9		
Portugal	1 207	1.1		
Slovakia	210	0.2		
Spain	7 841	7.4		
Sweden	3 317	3.1		
Switzerland	4 146	3.9		
United Kingdom	16 366	15.4		
	106 560	100		
Currency adjustment				
for sterling adjustments			× €1 000	(1 044)
Entry fees				
Hungary				124
Lithuania				66
Montenegro				4
Poland				732
Slovakia				100
				1 026
Associate member state contributions				
Australia				3 114
Argentina				675
				3 789
Additional contributions				
United Kingdom				9 627
Germany				6 292
				15 919

Reviews of scientific and service units

EMBL Hamburg Unit review

The EMBL Hamburg Unit was reviewed on 25–27 February 2019 by a panel of 15 international experts, including five members of the Scientific Advisory Committee (SAC). The review was chaired by Poul Nissen, Interdisciplinary Nanoscience Center, Aarhus, Denmark.

Evaluation summary

The overall performance of EMBL Hamburg was rated as outstanding by the panel, based on the quality of the unit’s research and services, as well as the training and development of young scientists. The panel applauded the unit’s capacity to facilitate outstanding research programmes and projects, both locally and across the world. This is being achieved through the excellent running of the synchrotron beamlines, Sample Preparation and Characterisation Facility, software programmes, and governance. Since the previous review, the unit has consolidated and further developed its position at the forefront of X-ray sciences, structural biology, and life sciences. Research programmes and projects of the unit address a broad range of important questions in structural biology and infection biology. These include elucidating the structures of a wide range of membrane proteins, understanding complex biological networks and pathways such as the influenza virus infection cycle, and advanced modelling based on core principles of protein structure and dynamics. The results are disseminated with high recognition from the community. The current beamlines P12, P13, and P14, for which EMBL Hamburg is fully responsible, provide a robust, high-end service to a large and growing user community.

Alongside the latest software and database developments, these services are of immense importance to the structural biology community, and mail-in and remote access user support must also be encouraged. These achievements are made possible by the strong leadership and vision of the Head of Unit Matthias Wilmanns and the Joint Heads of Research Infrastructures Dmitri Svergun and Thomas Schneider.

The panel discussed many of the unit’s excellent research highlights, including the development of a time-resolved pump-probe protein crystallography station at P14 with Arwen Pearson’s group from the University of Hamburg. This development highlights a very important transition to ‘4D structural biology’ and has the potential to attract a growing user community focusing on cutting-edge research problems of structural biology and biocatalysis. A novel analysis method which allows the ‘soft’ refinement of high-resolution protein structures guided by agreement with small angle X-ray scattering data was also highlighted by the panel. There was a recommendation that excellent work such as this must adhere to EMBL’s open source policy of software.

The panel noted that EMBL Hamburg is tightly integrated into a complex, local research structure, not least with the newly opened Centre for Structural Systems Biology (CSSB), on the German Synchrotron (DESY) campus, with contributions of ten research partners including EMBL. The panel recommended that EMBL Hamburg and CSSB should improve coherence and establish a joint scientific culture and community. Additionally, it was recommended that a partnership between EMBL Hamburg and the European X-Ray Free-Electron Laser Facility Biology Infrastructure (European XFEL XBI) should be further explored, and an XFEL-oriented group leader recruitment could be a wise strategy. Further afield, EMBL Hamburg has fruitful collaborations to ensure complementing expertise with EMBL Grenoble and integrates exceptionally well into the European life science research community.

Looking into the future, the Hamburg Advanced Research Centre for Bioorganic Chemistry (HARBOR) initiative, specialising in time-resolved studies using X-ray and imaging infrastructures, is under construction, and plans for a PETRA IV upgrade have been launched. The panel recommended that, prior to transition to PETRA IV, EMBL carefully evaluates the potential for biological X-ray imaging as well as considering that administrative burdens of general user support and beamtime allocation are released from the responsibility of the beamline managers and better transferred to the administrative support team of the Hamburg Unit. The panel welcomes further steps (including a symposium) to explore the possibilities for research in X-ray imaging of biological

samples at PETRA IV. The panel noted that the recruitment of a small-angle X-ray scattering (SAXS) group or team leader must be carefully considered in light of highly dynamic developments in structural biology. In addition to the PETRA IV upgrade, it was recommended that the unit should join other EMBL units in applying cryo-electron microscopy (cryo-EM) as a core method in structural biology, and a potential target for method development.

The review panel engaged in wide-ranging discussions with predoctoral and postdoctoral fellows over many aspects of research, training, mentoring, and work-life balance at EMBL Hamburg. On the whole, training and development of young scientists is maintained to an outstanding level at the unit. In the context of training, some students expressed concern that they are not given sufficient time to write their thesis, and the review panel felt that a mentor outside of the thesis committee would be beneficial. Mentoring was also recommended for young group leaders to ensure future career progression. Combined with general EMBL procedures and structures, the young scientists overall have great opportunities to leave the unit well prepared for a future career.

Response to the panel's recommendations

I would like to begin by thanking the review panel for their detailed evaluation of the activities of EMBL Hamburg. I am delighted with their overwhelmingly positive report of the unit's performance. The review panel were very positive about the leadership and research performance

of the unit management team and this opinion reflects my own. I would like to congratulate them for leading by example and creating a stimulating research and service environment.

Several recommendations were made by the panel. Concerning the future transition to PETRA IV on the DESY campus, EMBL will carefully evaluate the potential implications and opportunities that PETRA IV will bring for biological research and in particular X-ray imaging. Part of the brainstorming around this will involve the organisation of a workshop to explore these possibilities.

Another point raised concerned the European XFEL XBI partnership, which is currently being explored, and an XFEL-oriented group leader recruitment was suggested to be a wise strategy. This consideration will be balanced alongside skills needed for the upcoming PETRA IV upgrade, to prioritise resources in the best interest of EMBL and the external research community.

Several points were raised by the panel concerning the future of SAXS at EMBL Hamburg, particularly in the context of the upcoming retirement of Dmitri Svergun. After discussion with the unit leadership, and given the success of SAXS, it is considered important that this activity is maintained and a call will be launched in the near future.

Another point raised in the context of SAXS concerned possible transfer of the Small Angle Scattering Biological Data Bank (SASBDB) standardisation and

development to EMBL-EBI. SASBDB is still being refined by the Svergun group and its curation requires active expert interactions with the depositors, which would be more difficult if the curation was moved elsewhere. As of July 2019, a postdoctoral fellow, funded by the German Federal Ministry of Education and Research (BMBF), will curate and further develop SASBDB, and this will help to free internal resources. These funds will also go towards identifying and implementing a forward-looking solution to ensure long-term sustainability of SASBDB, in cooperation with Protein Data Bank in Europe (PDBe), hosted at EMBL-EBI.

The panel also raised the general issue of EMBL open source policy of software and models for the commercialisation of open source software. In line with EMBL's founding principles, the Laboratory endeavours to publish or otherwise make generally available its results and developed software. This is in line with established general open access principles. I agree that it is critical to ensure that software developments remain accessible, ideally with options for further developments, for example when an individual leaves EMBL. To ensure this, I will create a small working group to formulate a forward-looking EMBL-wide solution.

The panel strongly recommends the construction of a new building, possibly as a new wing of the CSSB, which would host EMBL. I am keen to take this project on board with high priority for timely realisation, to unify the activities of the unit.



The recommendation that the unit should consider cryo-EM as a core method and a potential target for method development at the same level as other techniques has been taken on board. This will be weighed up against other methods that are available and will be part of more general discussions concerning the development of the DESY campus.

Finally, the review panel recommended that the general user support and beamtime allocation should be released from the responsibility of the beamline managers and transferred to administrative support. This has been discussed with the unit leadership and

efforts will be made to find the appropriate balance between beamline and administrative support. Furthermore, mail-in and remote access user support will be encouraged for outside users.

In summary, I would like to congratulate the unit leaders and members for their performance over the last review period, and give credit to Matthias Wilmanns for providing visionary leadership.

*Professor Edith Heard, FRS
Director General
12 June 2019*

EMBL-EBI services review

EMBL-EBI services were reviewed on 26–28 March 2019 by a panel of 18 international experts, including four members of the Scientific Advisory Committee (SAC). The review was chaired by Edward Marcotte from the Center for Systems and Synthetic Biology, Institute for Cellular and Molecular Biology, Austin, US. The Chair of SAC, Paul Nurse, attended the review as an observer.

Evaluation summary

By all metrics, EMBL-EBI services are a success, vital in delivering biological data worldwide. The services at EMBL-EBI appear more cohesive and coherent than ever before, particularly in the context of the explosion of data that has occurred since the last review in 2015. This is in part due to the structuring of the service teams into thematic clusters under Rolf Apweiler and Ewan Birney’s leadership. This has

improved the coordination and integration between related EMBL-EBI service areas and facilitated user access to resources. Thanks to this exceptional leadership, EMBL-EBI is placed at the forefront of many of the most important data initiatives worldwide, such as the Global Alliance for Genomics and Health (GA4GH), the Human Cell Atlas (HCA), and ELIXIR, within which 13 EMBL-EBI resources are selected as Core Data Resources in Europe. EMBL-EBI



websites serve tens of millions of web requests every day and they provide biological and biomolecular data, services, and infrastructure to the academic, clinical, and industrial life science communities. This includes archiving, curating, and integrating data that span the chemical, molecular, cellular, phenotypic, and literature realms.

Several notable achievements were highlighted by the panel, including the successful deployment of the Open Targets Platform in 2015. The panel felt that Open Targets was an important driver of integration across multiple cluster resources and encouraged the unit to consider how to take advantage of this in other domains that are of interest to the user community. The review panel was enthusiastic about EMBL-EBI’s growing efforts in the Global Biodata Coalition, whose aim is to coordinate long-term funding for core resources, and strongly supports further efforts in this area.

The panel also highlighted the development of the Electron Microscopy Data Bank (EMDB) and the associated Electron Microscopy Public Image Archive (EMPIAR), both of which are having an enormous impact in the cryo-electron microscopy field. Additionally, the panel commended the remarkable growth of the European Nucleotide Archive (ENA), EMBL-EBI’s main archive for primary nucleotide sequence data and derived analyses, which support many critical downstream services. Alongside this, the PRoteomics IDentifications (PRIDE) database has become the leading proteomics data repository in the world, and has transformed the field of proteomics by being the dominant driver of open data culture.

EMBL-EBI is commended for expanding into biodiversity and ecology genomics, with a large network of partners in place around the world in various tree of life sequencing projects. In this context, the panel commends EMBL-EBI for embracing the Nagoya Protocol, actively participating in talks about ethical hosting of data, and developing pilot projects around data provenance tracking. The panel recommends that EMBL-EBI take a leadership role in promoting good practices for considering ethical and moral aspects of sequencing datasets and analyses.

The panel felt that the plan to develop a bioimage database was exciting and timely. It will need to start with a clear remit, and it was recommended that a new staff member move this forward, together with Ardan Patwardhan and Alvis Brazma, as proposed. There was enthusiastic support for the mechanism by which ArrayExpress, within the Molecular Atlas Cluster, was phased out as a major resource. The panel recommended that this effort should be taken as a basis for a procedure for future decommissioning decisions. The panel also noted that consideration be given as to how to strengthen this cluster and sustain key resources, given the small size of the cluster and potential for destabilisation. This could be applicable to the context of rapid developments in data science at large, and of which EMBL-EBI needs to take note. The panel recommended that EMBL-EBI set up a small service unit that will provide data science expertise across the institution.

With the continuous growth of data and of data types in life sciences, it is difficult to attract all necessary

expertise in bioinformatics at the current EMBL-EBI site. The panel recommended that this calls for some distribution of data resources across other European sites. ELIXIR appears to be the natural ecosystem for these to emerge and consolidate, but some new service areas could be directly deployed by EMBL-EBI away from the main site. This will engage the member states more strongly and facilitate investments into infrastructure by other European governments, similar to those by the UK government.

Moving forward, EMBL-EBI's plans for the next four-year period appear to be appropriate, with a strong emphasis on human health and increasing efforts on agriculture, biotechnology, and the environment. The panel is pleased to note this is planned to be done in the context of building stronger connections to other EMBL units, industry, and international research consortia.

Response to the panel's recommendations

I would like to extend my thanks to the panel for their time and effort in reviewing EMBL-EBI's service activities. It is wonderful to hear the exceptionally positive report of the services provided by EMBL-EBI and I echo the panel's commendation of EMBL-EBI's leadership. I would like to congratulate Ewan Birney and Rolf Apweiler for creating a cohesive and well-structured working environment that provides world-leading data services to users in academic, clinical, and industry areas alike. The excellent integration and interconnectivity of services within EMBL-EBI further builds on EMBL's pre-existing collaborative strengths. In this context, I am pleased to recognise

the success of Open Targets as a driver in integrating multiple cluster resources. The panel recommended applying this successful model to other domains. The very substantial groundwork and manpower that would need to be deployed in launching another such operation would need to be considered carefully.

As recommended by the panel, I would like to note that the Global Biodata Coalition is a good opportunity to coordinate long-term funding for core resources. However, I am aware that shifting external funding landscapes means we cannot depend on this, and EMBL is highly appreciative of vital funding given by its member states. In line with EMBL's service mission, this core funding drives these data services, without which researchers and clinicians in the member states and beyond would be at a complete loss.

I would also like to highlight that in his capacity as the leader of the GA4GH consortium, Ewan Birney is uniformly trusted around the world as an expert in health data and he has my full support in this endeavour.

The recognition of EMBL-EBI's expansion into biodiversity and ecology genetics is greatly appreciated. I would like to take this opportunity to highlight the research and service links this forms with other areas of EMBL that explore the molecular mechanisms behind biodiverse organisms, in particular EMBL's collaboration with Tara Oceans. As part of this hugely successful global project, EMBL-EBI services have been integral to making unique and novel oceanic genomic data globally accessible. Across units, EMBL is also actively discussing how to

further integrate these topics into EMBL's activities across all of the missions. I would like to praise EMBL-EBI for its proactive and responsible approach to the ethical hosting of data and I fully support the recommendation that EMBL-EBI take a leadership role in promoting good practices for considering ethical and moral aspects of sequencing datasets and analyses. EMBL-EBI should also be congratulated for setting global standards as an open access provider for exceptionally high-quality data.

I agree with the recommendation that it is vital to maintain a broad and full understanding of the data services required by the community and to respond accordingly. This is exemplified by the elegant decommissioning of ArrayExpress and the ongoing discussions regarding the setting up of the BioImage Archive. The BioImage Archive is an ambitious initiative that would further integrate current and future imaging services and infrastructures across many of EMBL's sites. However, the funding and personnel required to make this a success must be carefully considered within the context of current funding for the EMBL Programme.

The panel's recommendation to consider the rapid developments in data science and setting up of data science institutes was also noted. EMBL-EBI and other EMBL sites are already actively involved in using AI and other approaches. Indeed, all of EMBL would like to move towards powerful data science approaches in the future, and this topic will be considered more generally in the context of the preparation of the next EMBL Programme and Indicative Scheme.

EMBL-EBI has grown both because of, and in response to, its continued success. As biology becomes more data driven and dependent on informatics, the service component of EMBL-EBI will need to be further developed. The recent £44.5 m funding awarded by the UKRI's Strategic Priority Fund will enable the substantial increase in EMBL-EBI infrastructure that is necessary to meet the rapidly increasing demands made on its services. There are also plans for a potential new building on the Wellcome Genome Campus. I am supportive of this on-site growth for EMBL-EBI, as part of EMBL's service mission. I will maintain an awareness of EMBL-EBI's continued expansion in the context of funding for the next EMBL Programme. The panel suggested that some new service areas might be directly deployed by EMBL-EBI off their main site and within other member states. It is my opinion that the distribution of data resources should be limited to the infrastructure provided by ELIXIR; nevertheless, EMBL-EBI will continue to collaborate and advise actively across Europe.

To summarise, I would like to congratulate EMBL-EBI services for their performance over the last four years and credit Ewan Birney and Rolf Apweiler for their cohesive and exceptional leadership.

*Professor Edith Heard, FRS
Director General
5 June 2019*

EMBL Developmental Biology Unit review

The EMBL Developmental Biology Unit was reviewed on 14–16 May 2019 by a panel of 14 international experts, including six members of the Scientific Advisory Committee (SAC). The review was chaired by Stefano Piccolo, University of Padua, Italy. The Chair of SAC, Paul Nurse, attended the review as an observer.

Evaluation summary

The EMBL Developmental Biology Unit is one of the world's leading departments for the study of developmental processes. The unit is characterised by consistent and outstanding scientific productivity. This ensures visibility and impact on the international stage and attracts brilliant students and postdocs. As Head of Unit for the past 12 years, Anne Ephrussi's contribution can be defined as remarkable. In addition to pursuing her own innovative work on RNA transport in germ cells, Anne Ephrussi deserves considerable credit for generating a productive, highly collegial, and positive atmosphere that permeates the whole unit. She has successfully managed the high turnover in the unit by hiring new group leaders and mentoring them. Her key work directing the EMBL International Centre for Advanced Training (EICAT) is recognised by the panel and Anne is commended for her effective mentoring of young faculty staff and trainees.

The Developmental Biology Unit brings to EMBL an essential organismal, 'system-level', and quantitative perspective to biological processes. As such, the unit is complementary and synergistic with other cell biology and technology-driven efforts of EMBL. The unit studies the basic principles underlying the development of complex organisms, adopting a rich variety of model systems and methodological approaches, while managing to remain coherent in its scope. Researchers of the unit aim to understand

the emergent properties of living systems, the mechanisms of tissue patterning and differentiation, and their evolution. This includes investigations on how cell fate is determined through cell–cell and cell–environment relationships in time and space, such as symmetry-breaking events, cell shape changes, collective cell behaviours, and tissue self-organisation. The Developmental Biology unit adopts a variety of data-driven and hypothesis-driven approaches toward these objectives. This is partly done through an extensive network of collaborations with other groups throughout the EMBL community, epitomising the highly collaborative atmosphere of EMBL.

There were many excellent research highlights discussed by the panel, including work by Detlev Arendt's group that builds a framework with which to infer evolutionary connections between different cell types. This offers entirely new perspectives to animal evolution with the 'cell tree of life': an initiative involving 20 labs, which Arendt leads. Alexander Aulehla's work on collective cell behaviour during segmentation was also praised. He has developed highly innovative approaches, involving *in vitro* cell systems and microfluidic devices to control oscillatory dynamics experimentally. With these tools, he was able to reveal that the relative timing of signalling oscillations carries key information for mesoderm patterning. The panel recognised that embracing new applications of physical principles is advancing our

understanding of development in new and unexpected directions. Also along these lines, Takashi Hiragi's group has applied EMBL-customised light sheet microscopy and high-resolution mechanical measurements to monitor mouse peri-implantation development. Using fly embryos, Stefano De Renzis's group has implemented optogenetic methods that allow protein activity to be controlled with high spatio-temporal precision in order to analyse and provoke cellular relocalisation during gastrulation processes. Finally, Francois Spitz's group provided novel insights into the role of cohesins for chromatin structure by showing that depletion of cohesin, a ring-shaped protein complex, dramatically alters three-dimensional genome structure.

The panel noted that PhD students often graduate before publishing a first author paper and recommended that group leaders try to combine more ambitious projects with smaller-scale, more concrete and feasible research goals. The turnover and hiring of group leaders was discussed by the panel. It was recognised that the high turnover of group leaders means that productive areas of research can be lost, but that this also ensures the hiring of new talents as well as fresh scientific perspectives, biological models, and experimental approaches. The review panel also insisted on the importance of actively striving to establish and maintain a good gender balance at all levels, but particularly when hiring group leaders. Additionally, it was recommended that policies aimed to accompany and prepare group leaders for transition out of EMBL before their nine-year term be implemented, for example by

encouraging young recruits to apply for prestigious grants even before their first renewal.

The review panel endorsed the proposal by the Head of Unit to support the unit's needs for in-house computational and theoretical experts to enable predictive modelling. Overall, the review panel was positively impressed with the unit's interdisciplinarity, as well as its intellectually diverse, positive, and collegial climate.

Response to the panel's recommendations

I would like to thank the panel for their extremely positive evaluation of the Developmental Biology Unit. I join the panel in congratulating Anne Ephrussi as an excellent Head of Unit who has enabled a collaborative and positive research atmosphere. As highlighted by the panel and reflected in the research highlights, the unit is intellectually diverse, stands out due to the variety of model systems studied, and offers many fresh scientific perspectives. For this and the consistently high standard of research performed within the unit, Anne Ephrussi and the entire Developmental Biology Unit should be commended.

In response to the panel's recommendations, I agree that this unit has a need for computational and theoretical experts to enable predictive modelling approaches. Theoretical biology would be highly complementary to much of the ongoing research within the unit, but also in other units. Indeed this is an area that I would like to consider across EMBL in the context of the upcoming EMBL Programme.

The panel noted that some PhD students graduate without a first author paper. Nevertheless many of them go on to publish their paper shortly after their PhD. I would also like to note that the scientific complexity of developmental biology research is likely to be a contributing factor. However, the panel's recommendation to combine both ambitious and smaller-scale research goals is noted.

I firmly agree with the panel's recommendation to improve the gender balance of the unit, particularly at the group leader level. The gender balance will be somewhat helped by the latest group leader recruitment who will arrive later in 2019. However, I will continue to ask recruitment panels to keep this issue at the forefront of their minds. Future recruitment will involve gender-balanced panels.

The upcoming recruitments will also be an opportunity to further diversify the unit in terms of biological models and experimental approaches. This refresh of scientific perspectives is one of the benefits of EMBL's nine-year turnover rule.

To ensure that both the incoming and outgoing processes for group leaders remain as smooth as possible, I agree with the recommendation by the panel that young group leaders should be encouraged to apply for prestigious grants. I am discussing additional mechanisms that could be put in place to help better prepare young group leaders for their departure from EMBL by providing targeted career advice at strategic time points during their nine-year term. It should be noted that these issues do not

exclusively affect the Developmental Biology Unit and should be addressed more broadly across EMBL to improve career development.

Once again, I would like to congratulate Anne Ephrussi and the entire Developmental Biology Unit for a highly successful review. One in which the unit's collaborative and innovative philosophy shone through and provides an example for many of EMBL's values.

Professor Edith Heard, FRS

Director General

11 June 2019

Imprint

Publisher

EMBL

'A vision for European science' image credits

Tara in London by Phil Mynott

Tara in Barcelona by Jordi Casañas

European Research and Innovation Days by European Union

EMBL-EBI's 25th anniversary by Phil Mynott

All events not listed here were photographed by Kinga Lubowiecka or Massimo Del Prete on behalf of EMBL

Profile image credits

Sebastian Eustermann by Kilian Knoll

Ilaria Ferlenghi by Fabiola Giusti

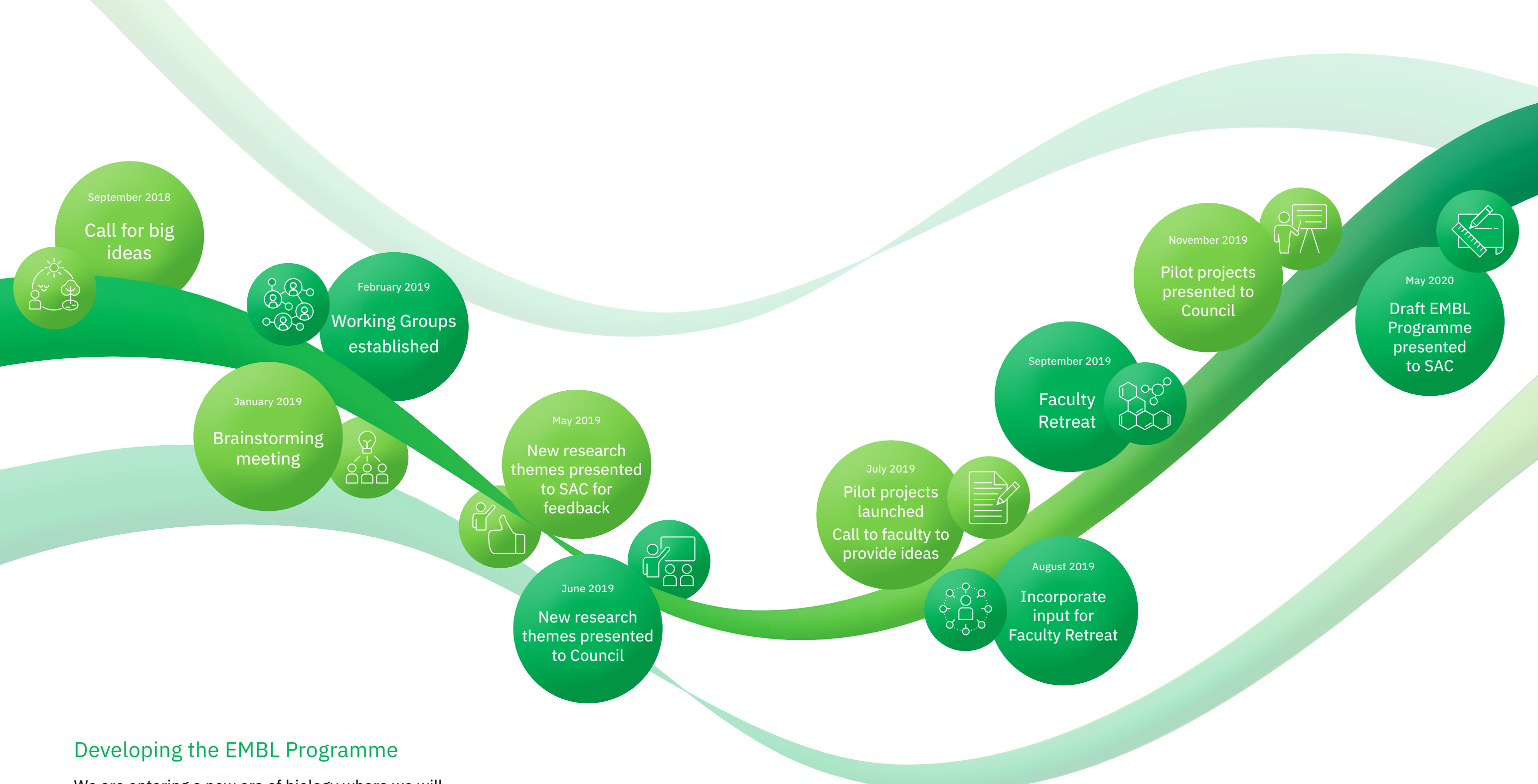
Georgia Rapti by Joseph Franciosa/FranciosaFotograf

Ernst Stelzer by Goethe University Frankfurt

All portraits not listed here were from personal collections or taken on behalf of EMBL by Montserrat Coll Lladó, Massimo Del Prete, Kinga Lubowiecka, Udo Ringeisen, Marietta Schupp, or Oana Stroe

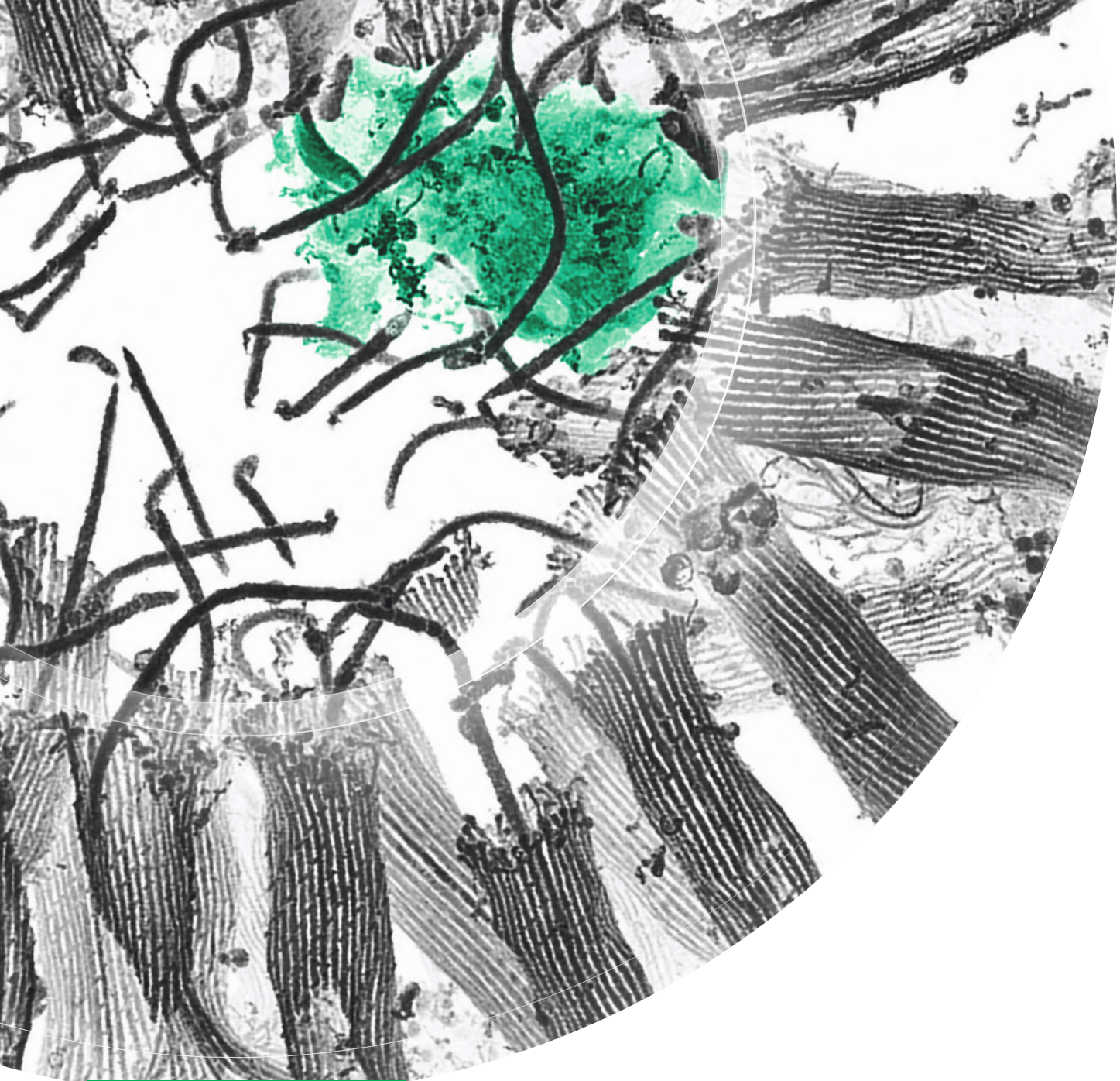
EU relations

Edith Heard, EMBL Director General, and Jean-Eric Paquet, Director General of Research and Innovation at the European Commission, by Marietta Schupp/EMBL



Developing the EMBL Programme

We are entering a new era of biology where we will understand how organisms function together and respond to changing environments. Together we are developing a new EMBL Programme that will build on EMBL’s strengths in molecular biology to tackle the grand challenge of understanding life in context.



EMBL prospect member states

Estonia

EMBL member states and associate member states

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