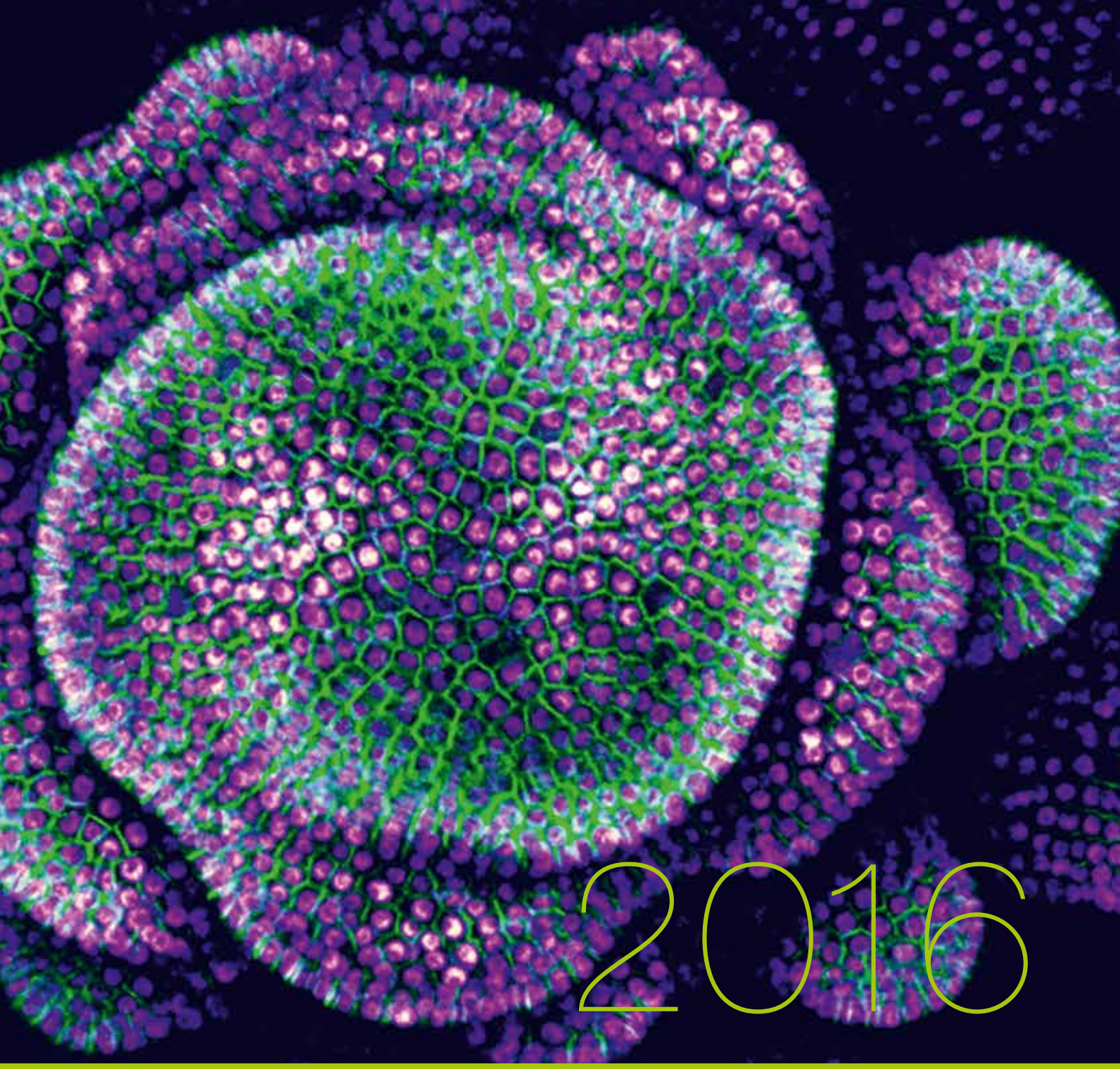

2016

Annual Report

EMBL

Cover image

This flower-like image shows a plant whose leaf-placing feedback loop is not quite right, causing its leaves to grow in a spiral (image EMBL/Neha Bhatia).

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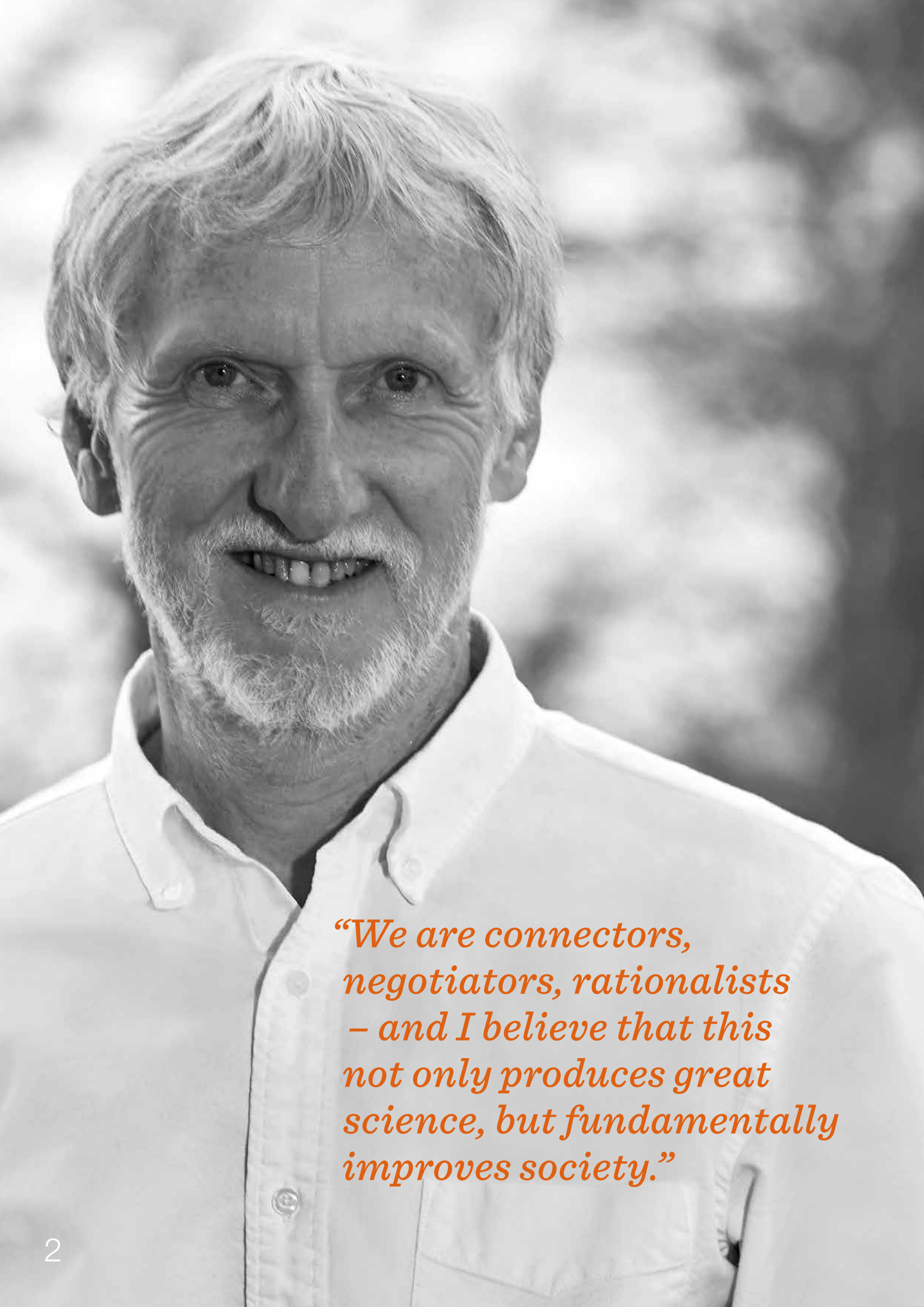


"We are connectors, negotiators, rationalists – and I believe that this not only produces great science, but fundamentally improves society."

Foreword

Like every year, 2016 was a year of dialogue at EMBL. It was a time to consolidate our plans to lead basic life science research into the era of digital biology. Securing the support of EMBL's scientists and member states for our ambitious five-year programme was a collaborative process that made the programme stronger. It involved embracing, not shying away from, a diversity of viewpoints, interests and needs. This, at its heart, is what we do best at EMBL. We are connectors, negotiators, rationalists – and I believe that this not only produces great science, but fundamentally improves society.

Intergovernmental research organisations like EMBL, CERN and the European Space Agency were explicitly set up to promote peaceful interactions between countries after World War II. By bringing together international teams diverse in discipline, gender, language and culture, we are able to tackle problems that do not respect national boundaries and whose solutions are important to every one of us. The way in which we reach these solutions, through dialogue and collaboration, is itself as important as the science.

Dialogue leads to progress. Scientists exchange despite differences between nations and despite political tensions; they can inspire us to think differently about how we live and work together.

I look ahead to EMBL's new programme of digital biology with excitement and pride. This pride comes from the sense not only that we are doing important work – as I sincerely believe we are – but that the way we do it is a model that offers hope to our larger communities and societies.

Iain Mattaj

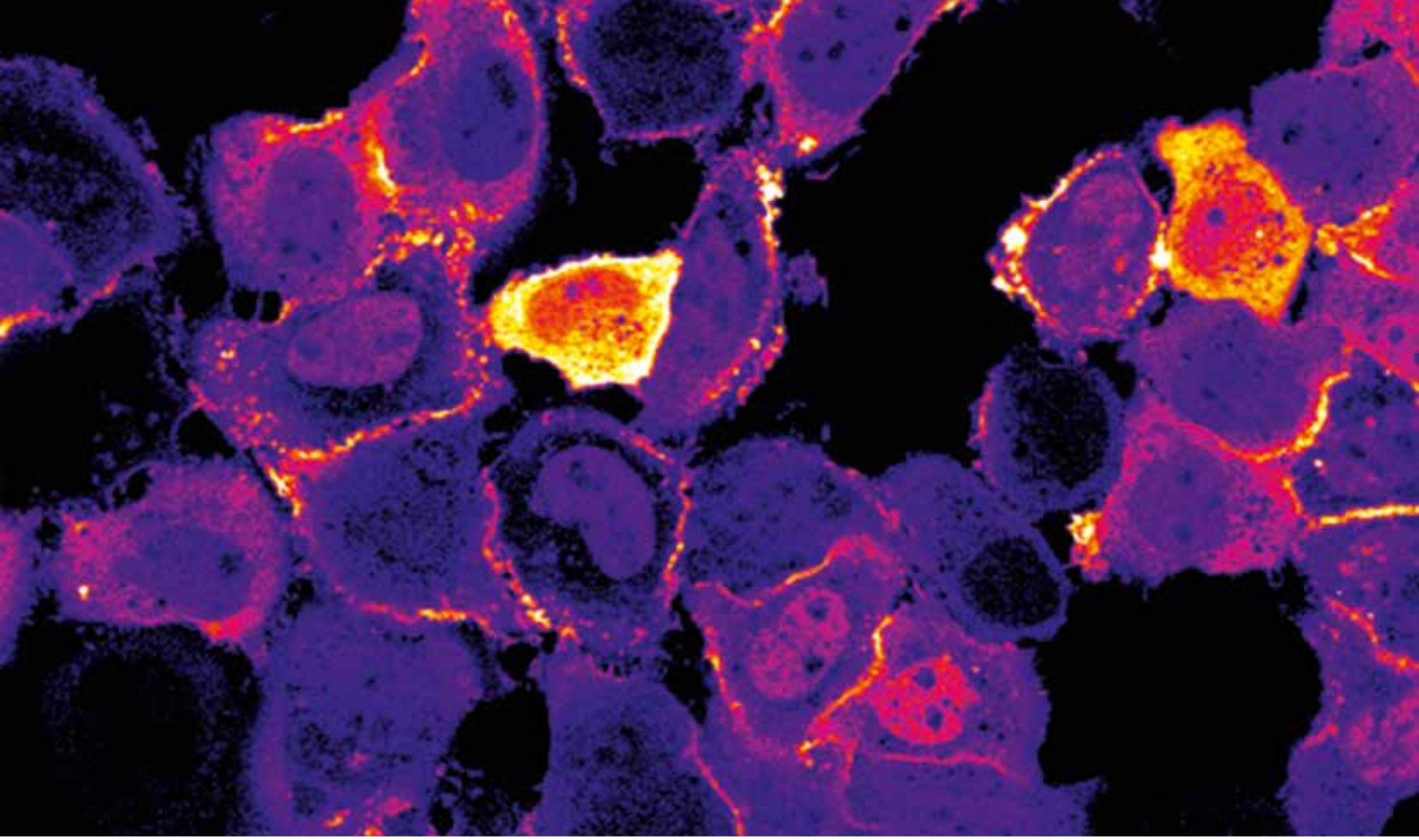
Research Highlights

25%
of research group leaders have ERC grants

From local partnerships to large international consortia, research at EMBL thrives on – and nurtures – collaboration across borders. By combining resources, expertise and approaches with colleagues near and far in 2016, EMBL scientists advanced our understanding of the intricacies of life on Earth.

Cell Biology and Biophysics

Cells in our body often have to react to cues from their surroundings: your heart beats faster in response to adrenalin; in response to light or sound, neurons pass a signal through the brain. Each of these responses entails detecting the external stimulus and triggering reactions inside the cell.



The Schultz group and collaborators have modified a signaling molecule to switch it on with a flash of ultraviolet light, and then switch it off using blue light

To detect external cues, cells have receptors on their surface. For a cell to respond appropriately – neither over-reacting to a signal nor letting it go undetected – the number of receptors on its surface must be correctly calibrated. The Pepperkok group found a link between the process that removes a certain type of receptor from the cell surface and the one that transports new receptors to the surface to take its place. Problems in the way these processes are regulated are thought to give rise to certain types of cancer.

Scharaw S *et al.* (2016) The endosomal transcriptional regulator RNF11 integrates degradation and transport of EGFR. J *Cell Biol* 215:543-58. doi: 10.1083/jcb.201601090

In many cells, when receptors detect a signal, they activate chemical intermediaries called diacylglycerides (DAGs), which in turn trigger further reactions inside the cell. The Schultz group, in collaboration with researchers at Ludwig Maximilians University Munich, modified a certain type of DAG so that it was inactive until switched on with a flash of ultraviolet light, and could then be switched off using blue light. This gave the team the precise control needed to study the way this DAG works in cells. The tool will enable scientists to investigate how this DAG causes cells in the pancreas to produce the insulin that controls blood sugar levels, as well as its role in the transmission of nerve signals. The new approach could also be applied to other DAGs, boosting our understanding of how cells react to external cues.

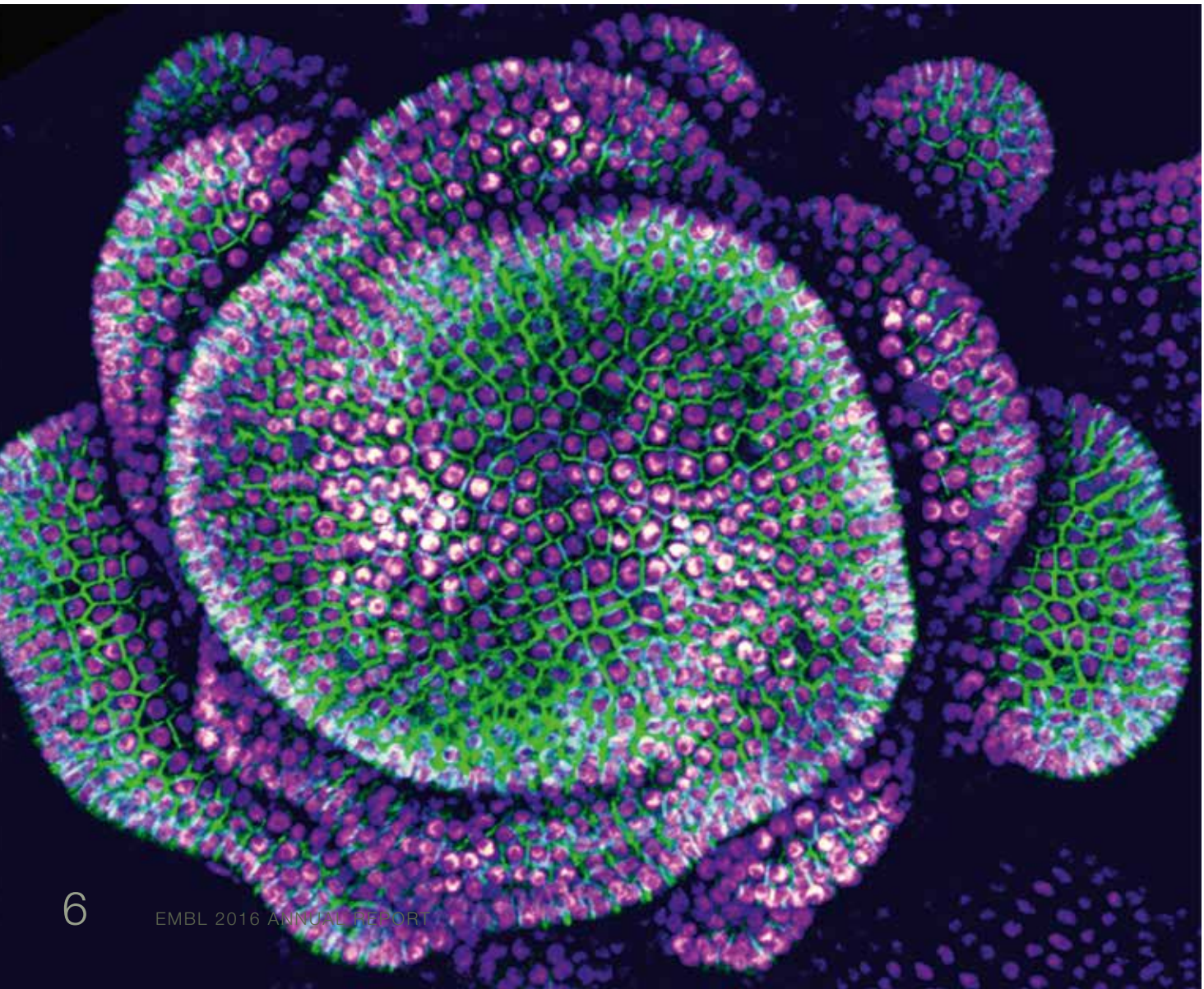
Frank JA *et al.* (2016) Photoswitchable diacylglycerols enable optical control of protein kinase C. *Nat Chem Biol* 12:755-62. doi: 10.1038/nchembio.2141

Developmental Biology

As part of in vitro fertilisation procedures, embryos are screened for genetic disorders before being implanted into the mother. This entails taking a cell from the embryo to analyse its DNA. However, not all the cells in this early embryo will become part of the baby. The Hiiragi group, working with the Nédélec group in the Cell Biology and Biophysics Unit, gained insights into how that distinction comes about. As a mammalian embryo develops, some of its cells move inwards to become the new organism, while others remain near the surface to form the placenta, which supports the developing embryo in the womb. The Hiiragi and Nédélec groups found that the positioning of a cell in the embryo depends on how strongly it can contract. They determined that cells that contract at least one and a half times more than their neighbours move inwards. Hence, sensing the forces around them is likely to be important in telling cells where they are and what type of cell to become. Discoveries like these could one day help clinicians to pick either placental or embryonic cells for genetic testing.

Maître JL *et al*. (2016) Asymmetric division of contractile domains couples cell positioning and fate specification. *Nature* 536:344-8. doi: 10.1038/nature18958

This flower-like image shows a plant whose leaf-placing feedback loop is not quite right, causing its leaves to grow in a spiral



For centuries, artists, biologists and mathematicians have been inspired by the recurring patterns of the plant world: the exquisite symmetry of flowers, and the sweeping spirals of seeds, spines and leaves. These patterns naturally emerge if a plant is able to grow organs at regular intervals, which it does by creating local hotspots of the plant hormone auxin. The Heisler group, in collaboration with scientists at the University of Sydney, investigated this process. They found that when a cell detects a sufficiently high level of auxin, it causes neighbouring cells to transport the hormone towards it, creating a hotspot. At the same time, this depletes auxin levels in the surrounding area, so another hotspot can only form some distance away. This creates the regular spacing between auxin hotspots, and therefore between leaves.

Bhatia N *et al*. (2016) Auxin acts through MONOPTEROS to regulate plant cell polarity and pattern phyllotaxis. *Curr Biol* 26:3202-8. doi: 10.1016/j.cub.2016.09.044

Directors' Research

The DNA inside each of our cells is in constant use. It is transcribed into a multitude of RNA molecules. Some of those RNAs serve as templates for making proteins, which are crucial components of most cellular machines. Other RNAs play pivotal roles in controlling processes such as protein production and gene expression. But before an RNA molecule can perform its job, it often has to be edited and transported to the right place in the cell. This editing and transport is carried out by proteins that bind to the RNA. Many of the proteins in our cells can bind to RNA, and scientists have identified common features that allow them to do this. But there are also many proteins that lack any of these features and are still able to bind to RNA. A comprehensive survey by the Hentze group uncovered more than 1000 new RNA binding sites in over 500 proteins. The researchers now intend to investigate how these RNA binding sites work, probing how RNA binding influences the way cells respond to stresses like starvation and disease.

Castello A, Fischer B *et al*. (2016) Comprehensive identification of RNA-binding domains in human cells. *Mol Cell* 63:696-710. doi: 10.1016/j.molcel.2016.06.029

Genome Biology

Small differences in genetic sequence can have a big impact, for example by influencing whether one person is more susceptible to a disease than another. Cells have evolved ways to counteract the detrimental effects of genetic variation. In a collaboration with the Birney group at EMBL-EBI, the Furlong group showed that some variants have a severe effect on the regulation of gene expression in fruit flies, but thanks to the presence of 'buffering' variants that cancel out these effects during embryonic development, they are tolerated within healthy individuals.

Cannavò E *et al.* (2016) Genetic variants regulating expression levels and isoform diversity during embryogenesis. *Nature* 541:402-6. doi: 10.1038/nature20802

The Savitski team, in collaboration with EMBL spin-off company Cellzome, revealed the molecular causes behind the side effects of panobinostat, a drug widely used to treat leukaemia, by tracking the drug's impact on proteins inside living cells. The study also had an unexpected positive outcome, as the scientists showed that the drug has the potential to be repurposed to treat tyrosinemia, a rare genetic disorder that can lead to liver, kidney and neurological problems.

Becher I *et al.* (2016) Thermal profiling reveals phenylalanine hydroxylase as an off-target of panobinostat. *Nat Chem Biol* 12:908-10. doi: 10.1038/nchembio.2185

EMBL-EBI

T cells – white blood cells that recognise invaders and trigger our defences – are equipped with receptors that can latch onto an invader. Our bodies come into contact with thousands of different invaders – from viruses and bacteria to cancer cells – so we have thousands of T-cell receptors, each attuned to one particular threat. The Teichmann group at EMBL-EBI and the Wellcome Trust Sanger Institute developed a new single-cell tool called TraCeR, which enabled them to look simultaneously at the DNA and RNA sequences of these highly variable T-cell receptors. They found that the DNA and RNA sequences of the receptors on each T cell are unique. The only cells with the same sequences were 'sister' cells, whose parent had come into contact with an invader and multiplied to fight it. By continuing to use this tool on T cells and developing similar tools for analysing B cells, the scientists aim to better understand the adaptive immune system as a whole.

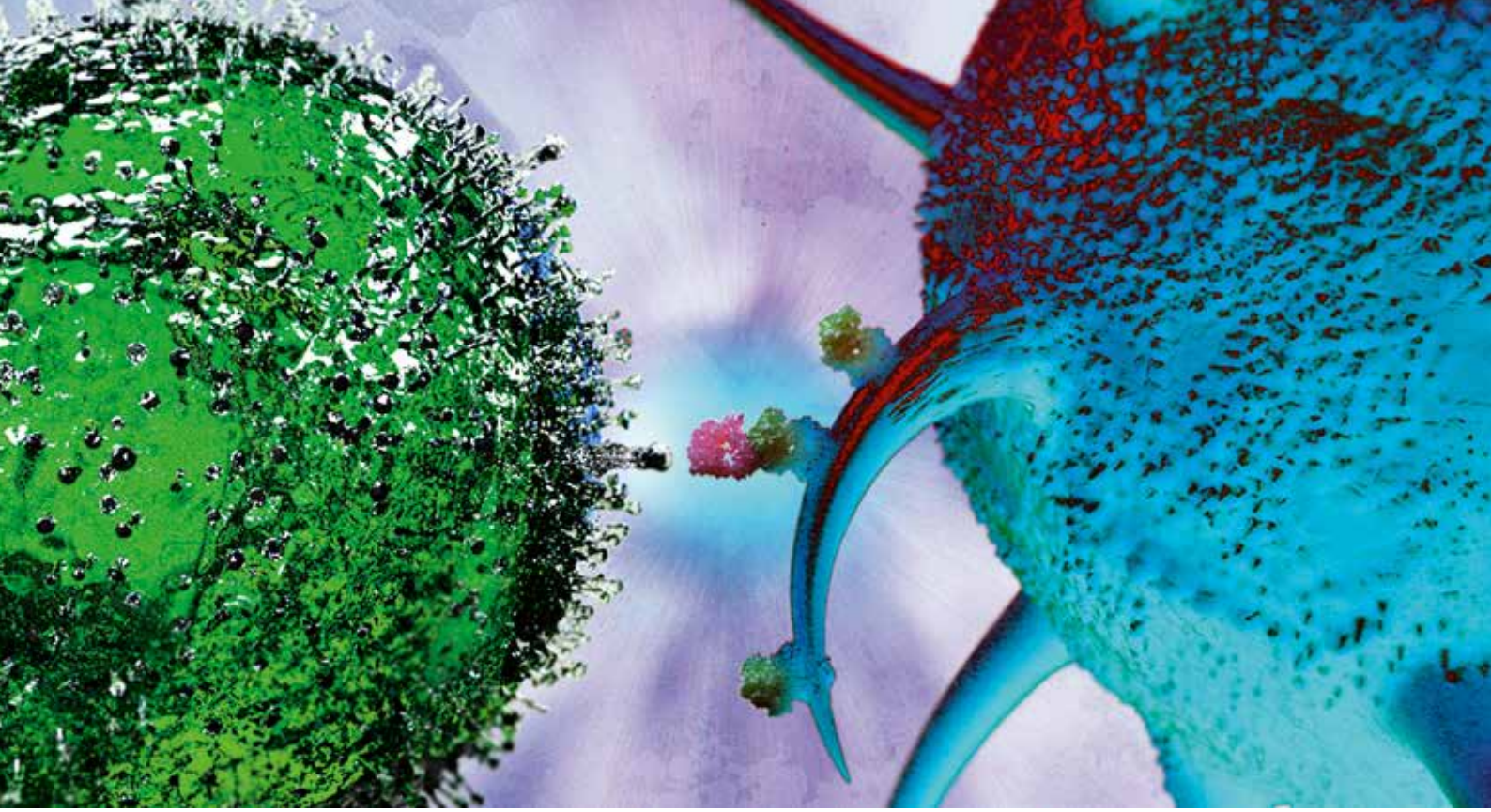
Stubbington MJ, Lönnberg T, *et al*. (2016) T cell fate and clonality inference from single-cell transcriptomes. *Nature Methods* 13:329-332. doi: 10.1038/nmeth.3800

An international team led by the Saez-Rodriguez group and colleagues at the Wellcome Trust Sanger Institute and the Netherlands Cancer Institute discovered a strong link between many mutations in DNA from cancer biopsies and the patients' sensitivity to particular drugs. This was the first systematic large-scale study to combine molecular data from patients, laboratory cancer cell lines and drug sensitivity. The findings will help increase the success rate for developing new, more personalised cancer treatments by assisting doctors to predict the best available drugs or the most suitable clinical trials for each individual patient.

Iorio F *et al.* (2016) A landscape of pharmacogenomic interactions in cancer. *Cell* 166:740-54. doi: 10.1016/j.cell.2016.06.017

Research led by the Beltrão group and colleagues at the University of Washington showed that the biological diversity needed for evolution can be generated by changes in protein modifications. They discovered that the rapid, versatile mechanism known as phosphorylation is crucial for the evolutionary process. Their work provides valuable insights into how different species adapt to different environments and could shed light on how pathogens evolve and become resistant to drugs.

Studer RA *et al.* (2016) Evolution of protein phosphorylation across 18 fungal species. *Science* 354:229-32. doi: 10.1126/science.aaf2144



A new single-cell tool called TRaCeR helps us better understand differences between T cell populations

In 2016, blood disease research was taken to a new level, with 47 scientific papers published in high-profile journals by the International Human Epigenome Consortium. Collectively, these papers illuminate how changes to chromatin – DNA and the proteins that it wraps around – contribute to cell type-specific biology, development, variation between individuals, and disease. The Cochrane, Flicek and Stegle teams provided data coordination, analysis and infrastructure to the project as well as contributing directly to research findings. Over 1000 datasets from this work were made freely available by the consortium and the European Union (EU)-funded BLUEPRINT project. They will be a valuable resource for biomedical research for years to come.

The full collection of papers can be accessed at: www.cell.com/consortium/IHEC

EMBL Grenoble

When the flu virus gets inside our cells, it needs to use an enzyme – influenza polymerase – to convert its genetic material into a form called messenger RNA, which is used to make viral proteins. To produce this messenger RNA, the polymerase needs a special starting RNA sequence called a primer, which it cannot make itself. The Cusack group discovered that influenza polymerase solves this problem by binding to the human RNA polymerase enzyme and stealing its primers. Developing new drugs to target the interaction between the polymerases could therefore be an important step in the fight against influenza.

Lukarska M *et al*. (2016) Structural basis of an essential interaction between influenza polymerase and Pol II CTD. *Nature* 541:117-21. doi: 10.1038/nature20594

The Cusack group have also made steps toward tackling four other widespread and debilitating diseases, including tuberculosis and malaria. They investigated benzoxaboroles – a family of molecules developed by Anacor Pharmaceuticals – which work by inactivating the enzyme leucyl-tRNA synthetase, or LeuRS. Blocking LeuRS kills pathogens by preventing them from making proteins. Because the four pathogens they studied all have similar versions of LeuRS, a single type of benzoxaborole was effective against all of them. Research on benzoxaboroles offers a promising avenue for the development of new drugs.

Palencia A *et al*. (2016) Discovery of novel oral protein synthesis inhibitors of Mycobacterium tuberculosis that target leucyl-tRNA synthetase. *Antimicrob Agents Chemother* 60:6271-80. doi: 10.1128/AAC.01339-16

Palencia A *et al.* (2016) Cryptosporidium and Toxoplasma parasites are inhibited by a benzoxaborole targeting leucyl-tRNA synthetase. *Antimicrob Agents Chemother* 60:5817-27. doi: 10.1128/AAC.00873-16

Sonoiki E, Palencia A *et al.* (2016) Anti-malarial benzoxaboroles target P. falciparum leucyl-tRNA synthetase. *Antimicrob Agents Chemother* 60:4886-95. doi: 10.1128/AAC.00820-16

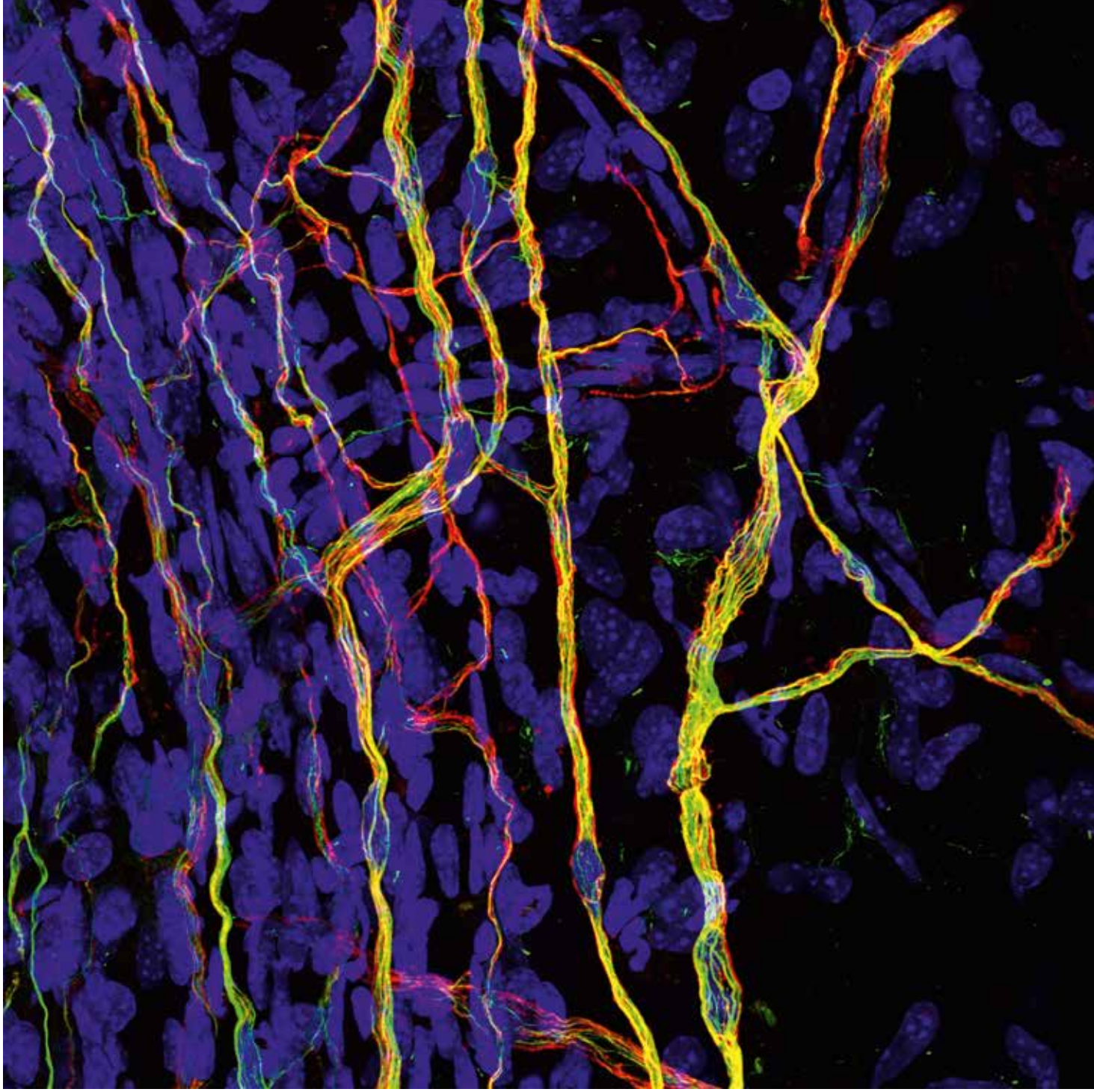
EMBL Hamburg

The Schneider group determined the structure of the cell's waste-disposal unit, the proteasome. The researchers were also able to resolve the structure of the molecule bound to four different inhibitor drugs. Their surprising results show that cancer drugs interact with the proteasome somewhat differently than previously thought, paving the way for the development of more effective cancer therapies.

Schrader J, Henneberg F *et al*. (2016) The inhibition mechanism of human 20S proteasomes enables next-generation inhibitor design. *Science* 353:594-598. doi: 10.1126/science.aaf8993

The Wilmanns group revealed a plot twist in a group of enzymes called death associated protein kinases (DAPK). These enzymes can trigger the death of cells, ensuring cells die off if they start to grow uncontrollably. The study revealed an unexpected dual-purpose loop in the folded string of amino acids that makes up the enzymes: the loop is crucial not only for inactivating the kinase but also for the enzyme's active form to trigger the chain reaction that can lead to cell death.

Simon B *et al.* (2016) Death-associated protein kinase activity is regulated by coupled calcium/calmodulin binding to two distinct sites. *Structure* 24:851-61. doi: 10.1016/j.str.2016.03.020



The Heppenstall group have found that a nerve cell's sensitivity to touch depends on how the microtubules are modified by Atat1 (yellow), a molecule that affects the stiffness of nerves

EMBL Monterotondo

To understand the workings of the brain, it is not enough to know what each region of the brain does – we also have to know how they are connected. In 2016, the Gross group traced the role of two such connections. For the first time, they linked a specific neural pathway to forgetting. Their study suggests that while learning, the brain also has to actively forget.

Madroñal N *et al.* (2016) Rapid erasure of hippocampal memory following inhibition of dentate gyrus granule cells. *Nat Commun* 7: 10923. doi:10.1038/ncomms10923

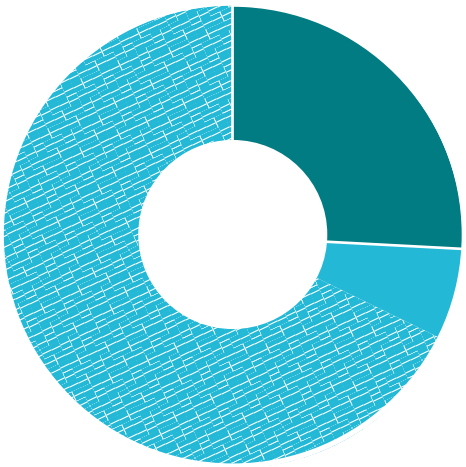
The Heppenstall group focused on neurons that help us sense our environment. They discovered how the stiffness of our nerve cells influences sensitivity to touch and pain. Their findings point to a potential new avenue for producing painkillers that specifically treat chronic pain. Such medications would help patients for whom any light touch – even just their clothes brushing their skin – can be agony.
Morley SJ Qi Y *et al.* (2016) Acetylated tubulin is essential for touch sensation in mice. *eLife* 5:e20813. doi: 10.7554/eLife.20813

Structural and Computational Biology

An international team led by the Bork group found that in faecal transplants, compatibility between donor and patient likely plays a bigger role than previously thought. For the first time, the team was able to track which strains of bacteria from a donor take hold in a patient's gut after a transplant. The study could help make stool transplants a valid treatment option for even more conditions.
Li SS *et al.* (2016) Durable coexistence of donor and recipient strains after fecal microbiota transplantation. *Science* 352:586-9. doi: 10.1126/science.aad8852

A virus's genome is protected by a protein shell called a capsid. The Briggs group, working in the Molecular Medicine Partnership Unit (MMPU), visualised the intricate structure of human immunodeficiency virus (HIV) capsid proteins in the virus itself for the first time. The group also discovered how a new type of HIV drug works, and why some mutations make the virus resistant to it. The drug, which is currently in clinical trials, stops the HIV virus from maturing. The scientists discovered that the drug locks the virus's immature structure in place, preventing it from rearranging into the mature form. They also found that the mutations

Scientific Publications in 2016

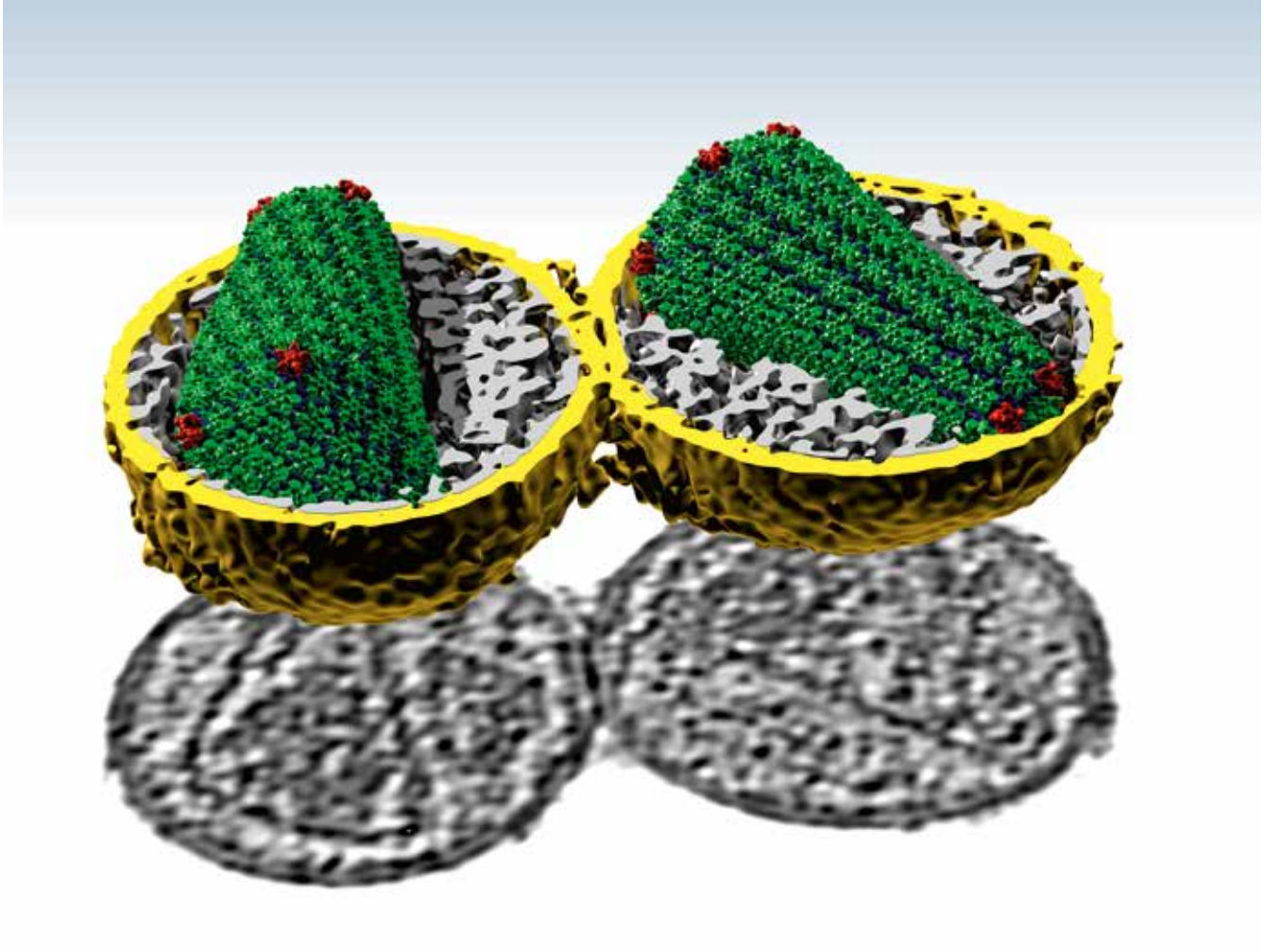


175 By EMBL

506 By EMBL in collaboration with over 600 organisations worldwide

462 By EMBL in collaboration with organisations in member and associate member states

681 Total



For the first time, the intricate structure of HIV capsid proteins has been visualised in the virus itself.

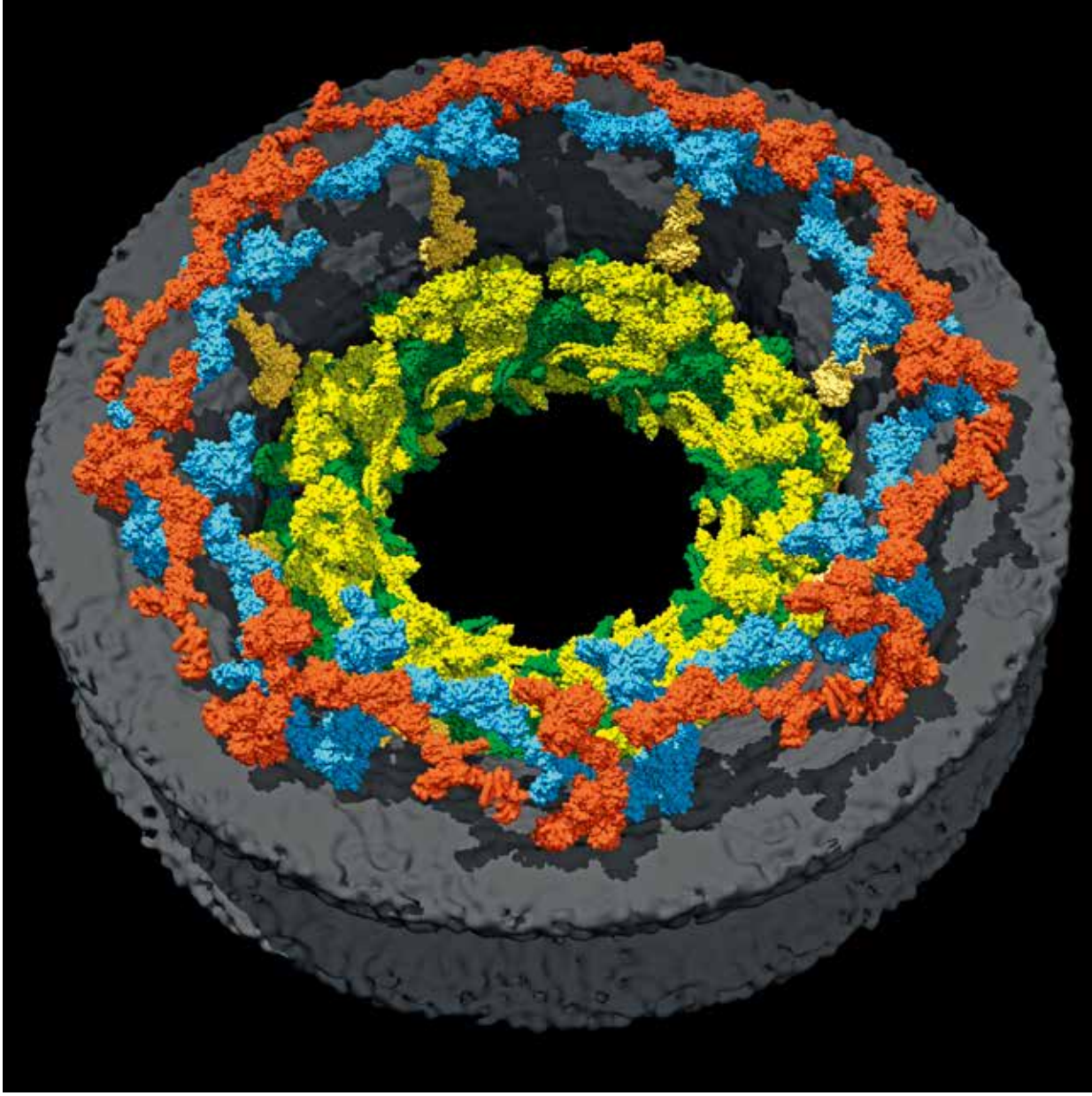
that confer the virus's resistance circumvent that lockdown by making the immature structure unstable, so that the virus can still rearrange its building blocks. Once we understand exactly how the drugs attach themselves to the viral proteins, scientists may be able to search for – or design – better drugs.

Mattei S *et al.* (2016) The structure and flexibility of conical HIV-1 capsids determined within intact virions. *Science* 354:1434-7 doi: 10.1126/science.aah4972

Schur FKM *et al.* (2016) An atomic model of HIV-1 capsid-SP1 reveals structures regulating assembly and maturation. *Science* 353:506-8. doi: 10.1126/science.aaf9620

The Barabas group increased the efficiency of a genome-engineering tool called Sleeping Beauty, which is showing promise in clinical trials as a treatment for leukaemia and lymphoma. In these trials, Sleeping Beauty is used to modify a patient's T cells, part of the immune system, so that they can seek out and destroy the cancer cells. Based on the structural information they obtained, the Barabas group worked with colleagues from the Paul Ehrlich Institute in Germany to design new variants of this tool that are 30% more efficient than currently available variants. The group is pursuing several avenues to increase that efficiency even further.

Voigt F *et al.* (2016) Sleeping Beauty transposase structure allows rational design of hyperactive variants for genetic engineering. *Nat Commun* 7:11126. doi: 10.1038/ncomms11126



The architecture of the nuclear pore. The outer ring is coloured in orange and blue, whereas the newly characterised inner ring is seen in green and yellow

The nuclear pore plays a key role in controlling molecular traffic into the cell's nucleus. It is also the biggest, most complicated stable protein complex in a human cell, making it a huge challenge for structural biologists. In 2016, the Beck group in Structural and Computational Biology and the Ellenberg and Schwab groups in the Cell Biology and Biophysics Unit solved major parts of this puzzle, discovering how the pore is formed at different times in the cell cycle, and revealing how embryos use stockpiled pre-formed pores to enable rapid growth.

Kosinski J Mosalaganti S, von Appen A *et al*. (2016) Molecular architecture of the inner ring scaffold of the human nuclear pore complex. *Science* 352:363-5. doi: 10.1126/science.aaf0643

Hampoelz B *et al*. (2016) Pre-assembled nuclear pores insert into the nuclear envelope during early development. *Cell* 166:534-5. doi: 10.1016/j.cell.2016.06.015

Otsuka S *et al.* (2016) Nuclear pore assembly proceeds by an inside-out extrusion of the nuclear envelope. *eLife* 5:e19071. doi: 10.7554/eLife.19071

Services

>100

petabytes of scientific data managed by EMBL

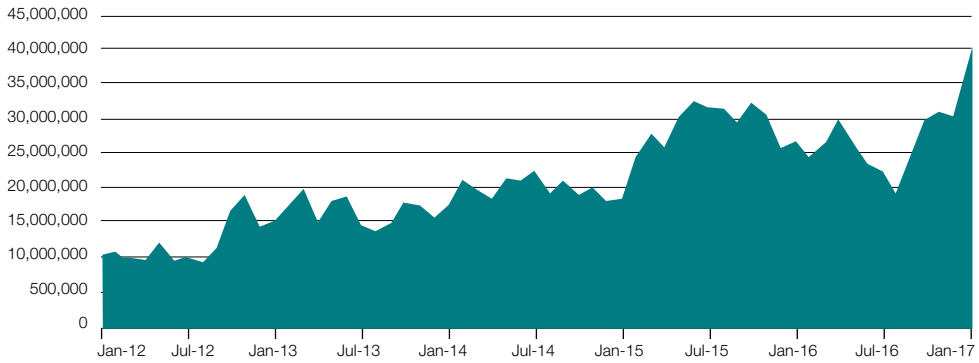
Bioinformatics Services

EMBL delivers high-impact data services to academic and commercial researchers worldwide. On an average day at the end of 2016, there were approximately 27 million requests to the websites of EMBL's European Bioinformatics Institute, which provide the entrance portal to the breadth of biomolecular databases hosted at EMBL-EBI. Along with its user community, EMBL-EBI's core data resources maintained their steady growth in 2016. To prepare for even further growth in the future, EMBL-EBI continued to develop and implement innovative methods for data storage. Several new tools for rapid access to and analysis of biomolecular data were launched, for example HMMER3 for the rapid detection of distantly related proteins and Gene2Phenotype for exploring high-quality data linking genotypes with disease.

In addition to providing data coordination services for the International Human Epigenome Consortium and the EU-funded BLUEPRINT project (p.9), EMBL-EBI managed the International Mouse Phenotyping

Usage of EMBL-EBI Websites

Requests per day, 2012 through 2016



Consortium's data, which in 2016 supported the identification of over 400 genes essential to life in the mouse, and promising candidates for studying human disease. The service integrated new data from PhenoImageShare, a project funded by the UK's Biotechnology and Biological Sciences Research Council that enables discovery and annotation across a variety of phenotype imaging repositories.

In 2016, the Protein Data Bank in Europe (PDBe) resource for structural data of large biological macromolecules celebrated its 20th year in operation and the annotation of its 25,000th structure. The UniProt service for protein sequence and functional data also marked a milestone as its founding database, SwissProt, turned 30. The continuous and successful collaboration between EMBL-EBI and its UniProt Consortium partners, the Swiss Institute of Bioinformatics and the Protein Information Resource, and the fundamental value of this resource for biomedical research were showcased at the Biocuration 2016 Conference in Geneva in April.

EMBL-EBI launched the new BioStudies database, which provides links to all of the data supporting an article, study or project. The repository particularly enables the archiving of unstructured data, for which there is no public repository, thus helping establish standards for new data types. Fully integrated with the European PubMed Central literature database, BioStudies allows for easy data submission by dataset authors.

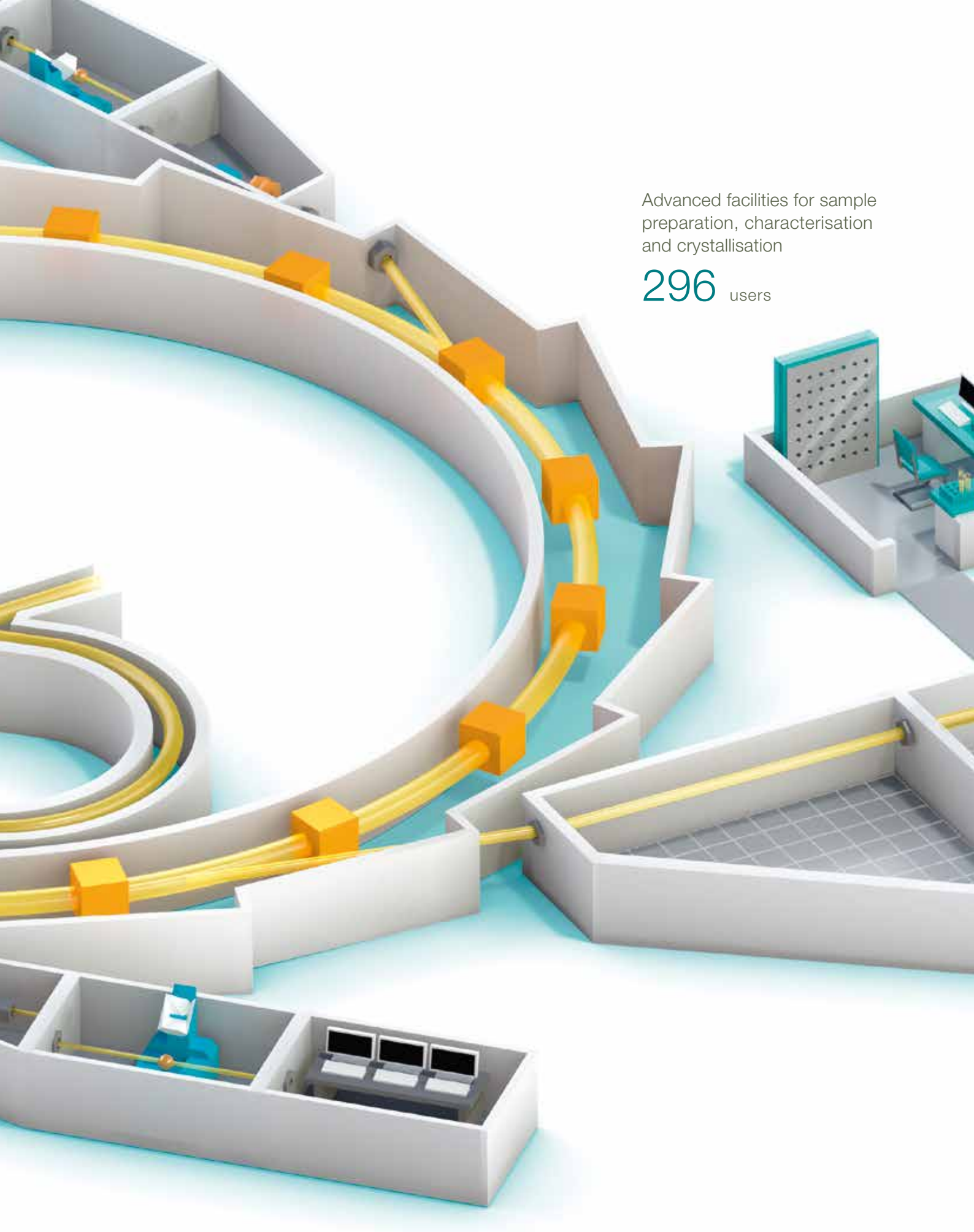
The European Nucleotide Archive team at EMBL-EBI also launched a new service, a cloud platform specifically aimed at facilitating pathogen genomic data analysis and sharing. The EMBL-EBI Metagenomics resource for metagenomic and metatranscriptomic data grew 11-fold in 2016. In collaboration with its US counterpart MG-RAST, the service launched Metagenomics Exchange, a computational framework that enables different metagenomics datasets and the results of their analyses to be linked.

EMPIAR, the Electron Microscopy Public Image Archive, is EMBL-EBI's global public data resource for raw 2D electron microscopy images. By providing easy access to state-of-the-art raw data, EMPIAR facilitates the development of new approaches to data processing, interpretation and validation, which lead to better 3D structures. In response to the growing demand for public infrastructure to store, share and link the massive datasets produced using new imaging techniques, the EMPIAR data service was expanded to accommodate new high-resolution imaging modalities such as scanning electron microscopy.

Structural Biology Services

At the German Electron Synchrotron (DESY) in Hamburg and the European Synchrotron Radiation Facility (ESRF) in Grenoble, EMBL provides access to crucial infrastructure for structural biology users from all over Europe. At both EMBL Grenoble and EMBL Hamburg, the operation of synchrotron beamlines for macromolecular crystallography (MX) and small-angle X-ray scattering (SAXS) is complemented by advanced facilities for the preparation, characterisation and crystallisation of biological samples and by computational resources and EMBL-developed software packages for the analysis of structural data. Through these integrated resources and facilities, EMBL offers access to service, expertise and user training across the entire structural biology workflow (pp.18-19).

Scientists from EMBL Grenoble and EMBL Hamburg gathered in Grenoble for the 12th annual bilateral meeting

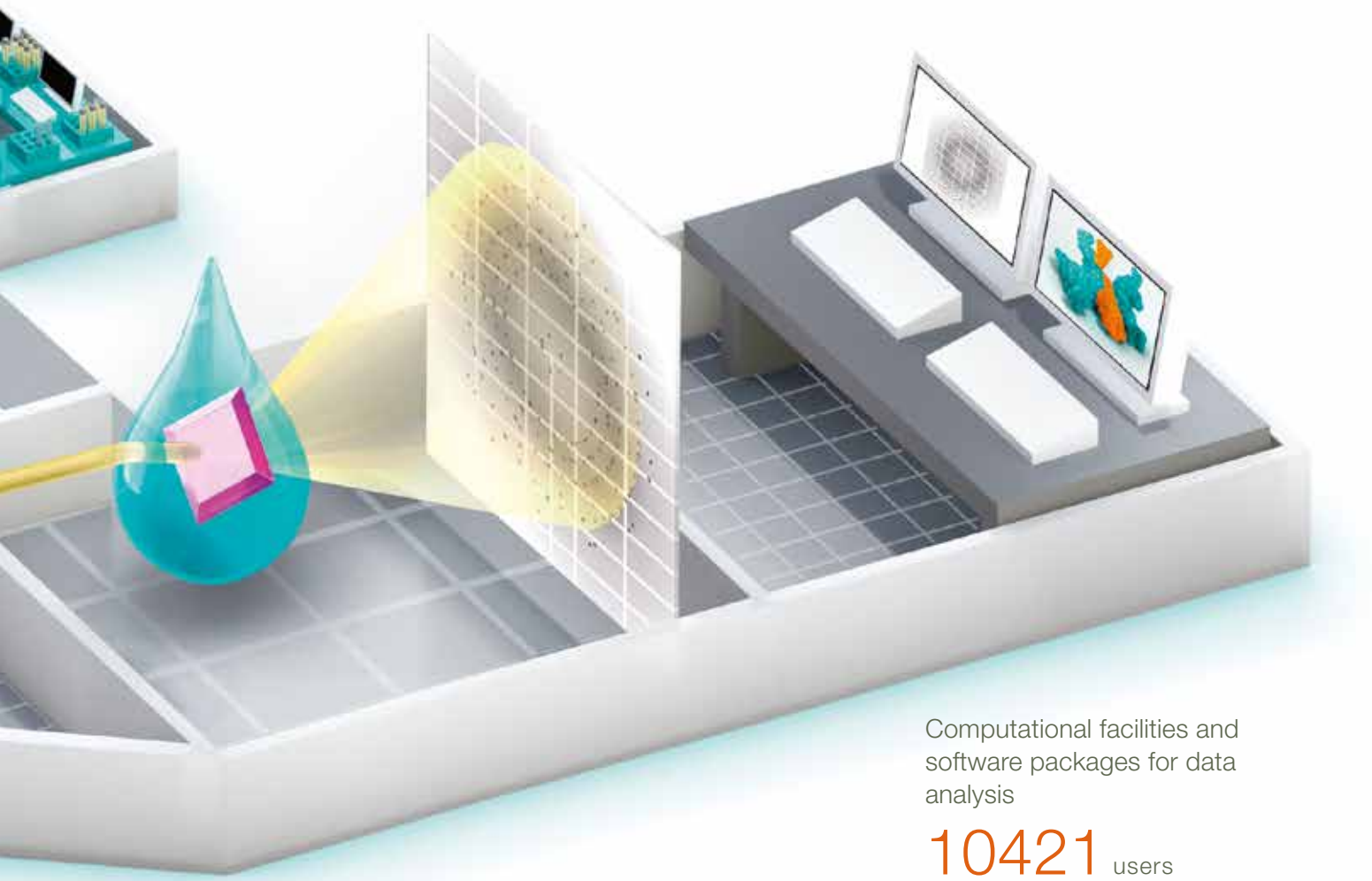


Advanced facilities for sample preparation, characterisation and crystallisation

296 users

Structural biology services in 2016

EMBL's facilities in Hamburg and Grenoble (where beamlines are operated together with ESRF) support users throughout the whole process of biological structure determination.



Computational facilities and software packages for data analysis

10421 users

Beamline services

3421 users

Scientists at EMBL Hamburg and EMBL Grenoble collaborate closely to provide structural biology users with the best possible service. Technology advances are rapidly shared between the two sites and directly implemented into the service platforms to benefit the large external user community. Regular meetings of the synchrotron instrumentation groups in Grenoble and Hamburg ensure exchange of information and often result in joint technology development projects. At the 12th bilateral beamline technology meeting, held in October 2016 in Grenoble, beamline scientists, engineers and technicians from the two EMBL sites and from partner institutes gathered to prepare for the future of the MX and SAXS beamlines and explore common challenges.

EMBL Grenoble

Following the successful completion of the first phase of the ESRF upgrade programme in 2015, EMBL scientists in Grenoble worked alongside ESRF colleagues in 2016 on further updates to the design and operation of the EMBL-ESRF synchrotron beamlines. The extensive modernisation programme aims to improve the speed and accuracy of structural biology experiments and will enable international users to choose from a wider range of techniques, such as serial and time-resolved crystallography.

At the end of 2016, EMBL Grenoble launched a refurbished and upgraded High-Throughput Crystallisation (HTX) platform offering robotics for protein crystallisation and crystal harvesting for MX. Led by EMBL scientists, the new HTX platform is a joint effort between EMBL Grenoble and the Institut de Biologie Structurale (IBS). It brings together service facilities and expertise from the two institutions: the EMBL HTX platform, which offers services in the crystallisation of water-soluble proteins and automated crystal harvesting, and the IBS platform, which specialises in the crystallisation of membrane proteins.

Stephen Cusack, Head of EMBL Grenoble, and Winfried Weissenhorn, IBS Director and EMBL alumnus, officially opened the new EMBL-IBS High-Throughput Crystallisation platform

Thanks to the seamless interface between the EMBL-developed CrystalDirect system for automated crystal manipulation (p.26) and the automated data collection beamlines at the ESRF, the new HTX platform also offers access to high-throughput ligand screening pipelines. These enable scientists, from both academia and pharmaceutical companies, to screen increasing numbers of small molecules for their ability to bind proteins, thus making the search for drug candidates and chemical probes easier and more efficient.

As the demand for storage and computational power is growing due to the increasing volumes of data generated and analysed at EMBL Grenoble, the site also engaged in an upgrade and restructuring of its computer servers. These improvements were undertaken in view of plans with the ESRF for a user facility for high-resolution electron microscopy, an extremely data-intensive technology, due to become operational in 2017.

EMBL Hamburg

EMBL Hamburg operates three beamlines for structural biology applications for the international user community at DESY's PETRA III storage ring – two for MX and one for SAXS experiments. Beamlines at EMBL Hamburg continued to be upgraded and optimised for the benefit of users over the course of 2016. This included the integration of new tools to enable the investigation of heterogeneous samples, the characterisation of changes in protein structure over time, and the collection of serial data.

To bridge the gap between high-throughput crystallisation and data collection on the MX beamlines, a CrystalDirect harvester system (p.26) was installed in 2016. By using highly accurate robotics to harvest and manipulate crystals, the system has the advantages of enabling harvesting of the most fragile crystals and of being remotely controllable, which means users no longer have to be physically present at the beamline.

Groundwork was also undertaken towards establishing a programme of research, development and user services dedicated to time-resolved crystallography. This method, which involves taking several snapshots of a protein in quick succession to observe how its shape changes following a reaction, holds great potential for studying proteins that may lead to new biotechnological applications in the fields of agricultural, food and environmental science. In 2016, a project was started – in collaboration with the University of Hamburg and funded by the German Federal Ministry of Education and Research – that will involve extending the MX P14 beamline to include a dedicated time-resolved crystallography endstation, making the experimental set-up more efficient and versatile.

Upstream of EMBL Hamburg's beamline services, the Sample Preparation and Characterisation (SPC) facility offers users an integrated pipeline and expert support for preparing, optimising and characterising their protein samples for structural biology experiments. The facility reached a milestone in 2016, receiving visits by over 100 external scientists. The

Arwen Pearson, Professor at the Centre for Ultrafast Imaging of University of Hamburg (left), and Thomas Schneider, EMBL group leader, are collaborating to establish time-resolved crystallography at EMBL Hamburg

SPC developed new screens to optimise sample purification and storage that were commercialised by the company Molecular Dimensions in 2016. In 2017, the SPC is set to extend its services in the characterisation of protein-protein and protein-ligand interactions to the Centre for Structural Systems Biology – a joint initiative of EMBL Hamburg and nine research partners from northern Germany to investigate the mechanisms underlying infection. In preparation for these future developments, a wide array of biophysical equipment was commissioned and made available to beamline users.

Core Facilities and IT services

EMBL's Core Facilities supported more than 1000 scientists at EMBL and in its member states in 2016 by offering access to state-of-the-art equipment and expert support in a diverse range of technologies. The services offered by the Core Facilities develop flexibly in response to changing demands and requirements in the scientific community, and benefit from the close interaction with advanced users and technology developers at EMBL. As a result, cutting-edge methods previously developed and applied in specialist groups are made available to facility users. Examples of new services introduced in 2016, by the Electron Microscopy Core Facility and the Proteomics Core Facility, respectively, include advanced techniques for high-accuracy correlative light and electron microscopy and a new pipeline for multiplexed large-scale proteomics experiments.

The Core Facilities contribute to EMBL's training activities by organising courses, workshops and meetings – over 50 in 2016 – often in cooperation with academic or industrial partners. EMBL Core Facilities also co-organised and hosted the CTLS (Core Technologies for Life Sciences) meeting in June 2016. The meeting attracted scientists, technicians and managers involved in operating core technology facilities and infrastructures across Europe, and offered a forum to discuss all aspects – scientific, technical, managerial, funding and educational – related to their operation . The meeting led to the foundation of a pan-European CTLS association that offers professionals working in core facilities a

platform for collaboration and training in relevant technologies. In addition to organising regular conferences, workshops and networking events, the association will support individual national institutions in setting up their own core facilities.

Life science research has become extremely data-intensive, with IT infrastructure and services underpinning virtually all of EMBL's research and service activities. Helix Nebula is a consortium of over 50 academic and industry partners aimed at establishing a pan-European cloud infrastructure for science. As a co-founder and the life science flagship of Helix Nebula, EMBL hosted the initiative's 7th General Assembly at EMBL Heidelberg in January 2016. A highlight of the meeting was the Open Day Event 'Towards the European Open Science Cloud,' which brought together representatives from the most renowned international research organisations, e-infrastructures, cloud projects, cloud service providers, IT advisory bodies and funding agencies. The HNSciCloud project, a European Commission (EC) co-funded pre-commercial procurement action to build a hybrid public-private cloud platform for Europe's research communities, was also officially launched.

Technology

Development and Transfer

18

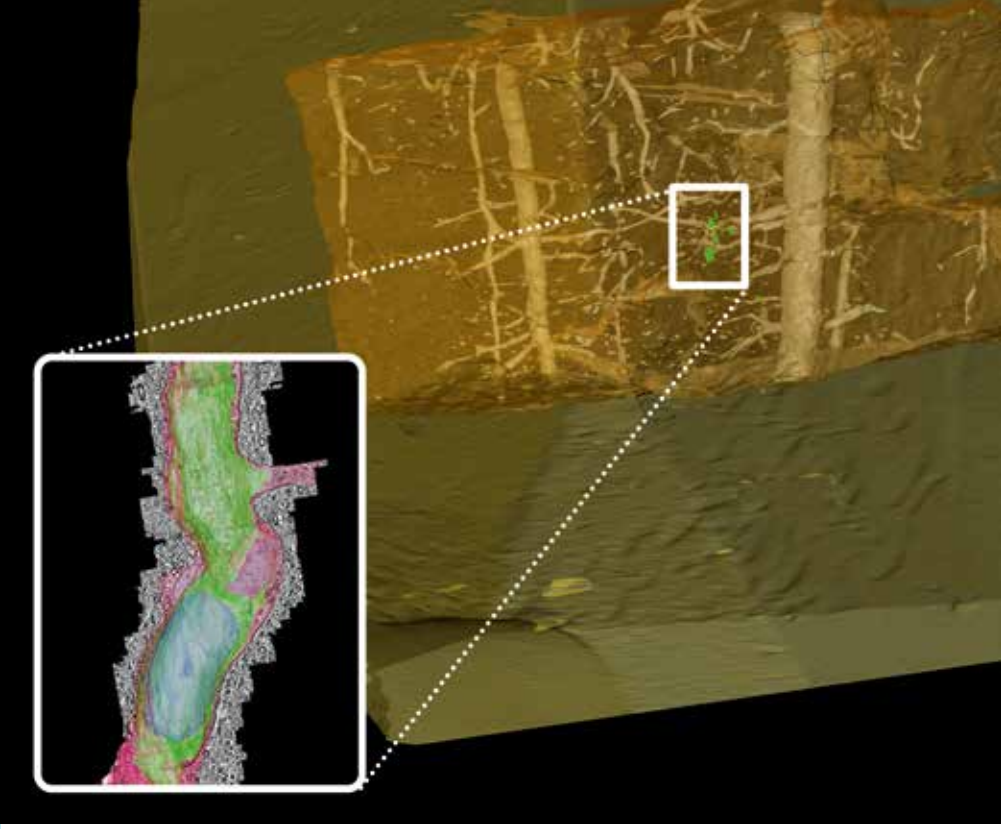
spin-off companies since 1999

Technology Development

Technology development is complementary to and closely intertwined with EMBL's research mission. In solving challenging problems through the course of their research, EMBL scientists develop new tools, methods and resources for life science research that greatly benefit the broader scientific community. EMBL's traditional strengths in technology development lie in the areas of imaging, structural biology and computational methods.

In 2016, EMBL scientists developed a new imaging method called multimodal correlative microscopy. This X-ray-based technique combines information obtained at different scales by electron and fluorescence microscopy and allows the tracking of specific biological structures within large samples. Another example of imaging technology development at EMBL was an innovative method to induce and control the movement of cells, for example cancer cells, towards a specific location using light.

In the area of structural biology, EMBL scientists in Hamburg developed an optimised method for the production of large amounts of Mycobacterium



The new multimodal correlative microscopy technique developed at EMBL allows scientists to find tiny structures in large samples

tuberculosis (Mtb) proteins to be used in structural studies. In 2016, a broad collaboration between EMBL scientists in Grenoble and Heidelberg also yielded the MultiBacTAG protein production platform, a protein engineering method that enables researchers to efficiently produce recombinant proteins carrying specific amino-acid modifications in insect cells. This new platform has a wide range of applications, particularly in protein binding and human tissue studies.

Major achievements were also seen in the development of bioinformatics tools and resources. Scientists at EMBL-EBI created OmniPath, which gives a much clearer view of complex biological interactions by combining the power of multiple signalling pathways data resources. Using expertise in computational biology and metabolomics, scientists at EMBL Heidelberg developed the first bioinformatics framework and open-source software for identifying metabolites in large datasets from imaging mass spectrometry.

Technology Transfer and Industry Relations

Through its knowledge-transfer arm EMBLEM, EMBL facilitates the translation of basic research discoveries into practical applications and makes technologies and instruments developed at EMBL commercially available. The success of EMBL's technology transfer activities is reflected both in the broad engagement of scientific staff – more than 700 EMBL scientists are on record as inventors with nearly 1000 invention disclosures since 1999 – and in the number of commercial licensees of EMBL technologies (now more than 400).

Spin-off companies are created to make EMBL's unique products and services available to the wider scientific community as rapidly as possible. A recent example is Luxendo, founded in 2015, which develops and internationally markets microscopes based on its proprietary single-plane illumination microscopy (SPIM) technology. In 2016, Luxendo launched two different microscopes: the MuVi-SPIM, which allows fast 3D imaging of living objects, including whole embryos of model organisms, for extended periods of time; and the InVi-SPIM, which allows extremely gentle sample handling and is designed for fast 3D imaging of living objects, such as cell cultures and samples of developing mouse embryos. Following a funding extension by Life Science Partners from Amsterdam, EMBL Ventures and EMBLEM, Luxendo raised a total of €8 million in capital by the end of 2016 – in just over one year of activity.

BioSAXS, the other most recent example of an EMBL spin-off company, emerged from EMBL Hamburg at the end of 2015. In its first year, over 15 pharmaceutical companies became customers of its professional small-angle scattering services. Active in the development and commercialisation of hardware and software for structural biology applications, BioSAXS concluded several commercial license agreements for the ATSAS software, a powerful EMBL-developed programme suite for structural data analysis of biological macromolecules in solution.

The innovative CrystalDirect technology, developed at EMBL and available through the HTX laboratory in Grenoble (pp.20-21), provides automated crystal harvesting and processing services and forms the basis for establishing fully automated protein-to-structure pipelines. CrystalDirect services continued to be in high demand in 2016, with a number of evaluation service projects for pharmaceutical companies successfully completed. New Crystallographic Ligand Screening Services were officially launched at the Protein Structure Determination in Industry Conference in Malmö, Sweden, in November 2016. Following the commercialisation of the CrystalDirect platform in collaboration with the company Arinax, the first automated crystal harvester was also installed at EMBL Hamburg (p.21).

EMBL collaborates closely with industry in multiple ways to provide corporate partners with access to its scientific expertise, infrastructure and training events, and to ensure that the knowledge and technologies resulting from EMBL's fundamental research are translated for the benefit of society. The Advanced Training Centre Corporate Partnership Programme (CPP) acts as a facilitating platform for collaboration between EMBL and industry in the co-development of training, products and services. At the CPP annual meeting in February 2016, EMBL's corporate partners had the opportunity to learn about the latest scientific developments at EMBL, particularly in the area of advanced imaging technologies, and to engage in strategic discussions with EMBL scientists and leadership. At the end of 2016, the CPP welcomed Sartorius, a leading international pharmaceutical and laboratory equipment provider, to its circle of corporate partners.

The EMBL-EBI Industry Programme provides a forum for interaction and knowledge exchange for corporate partners working at the forefront

of commercial bioinformatics. In 2016, it continued to help industry make the most of advances in bioinformatics by developing resources and services for the benefit of its members and by organising strategy meetings and tailored expert-level workshops on a variety of topics. It further extended the international reach of its membership with the addition of three life science companies with global R&D programmes: AbbVie (USA), Takeda (Japan) and MSD (USA).

A new partner company also joined the Centre for Therapeutic Target Validation, the public-private partnership between GlaxoSmithKline, the Wellcome Trust Sanger Institute and EMBL-EBI that was established in 2014 to leverage genome-scale experiments and analyses to improve the success rate of drug discovery. In an interaction facilitated by EMBLEM, the multinational biotechnology company Biogen joined the partnership – then renamed Open Targets – in February 2016. Following the successful launch of its Target Validation platform at the end of 2015, Open Targets released its first experimental datasets in 2016, demonstrating its commitment to share data openly with the scientific community to accelerate the development of novel therapies for a wide range of human diseases.

Also in the area of drug discovery, EMBL joined forces with Merck in a research collaboration focused on cancer metabolism. The three-year project, negotiated by EMBLEM, makes use of EMBL's capabilities in the area of metabolomics and its expertise in combining modelling and bioinformatics with experimental approaches. By uncovering cancer metabolic pathways and their control mechanisms, the project's ultimate goal is to deliver novel therapeutic targets and biomarkers.

EMBLEM Technology Transfer in Numbers 2016

€ 8 400 000
Income

45
Invention disclosures

22
Priority patent applications filed

353
Licence & collaboration contracts

20
Patents granted

Training and Outreach

7290

attendees at courses and conferences at EMBL sites

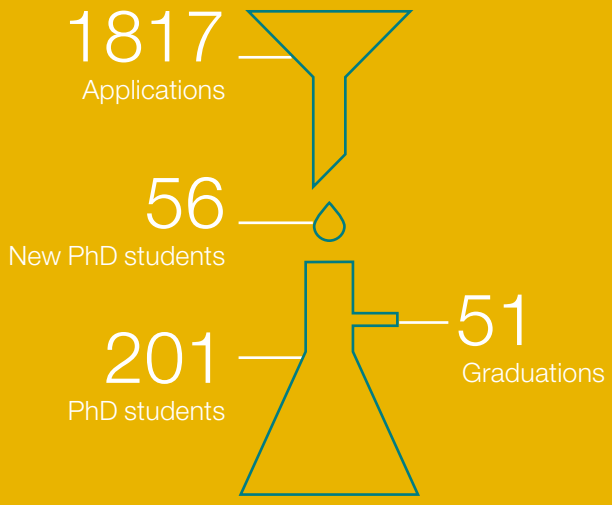
Internal Training

Advanced training is core to EMBL's activities and its service to the member states. Through its prestigious PhD and postdoctoral programmes, EMBL trains and helps shape the careers of Europe's most promising researchers. EMBL's internal training programmes leverage the interdisciplinary and dynamic scientific environment at EMBL and host a total of more than 500 PhD students and postdocs at any time.

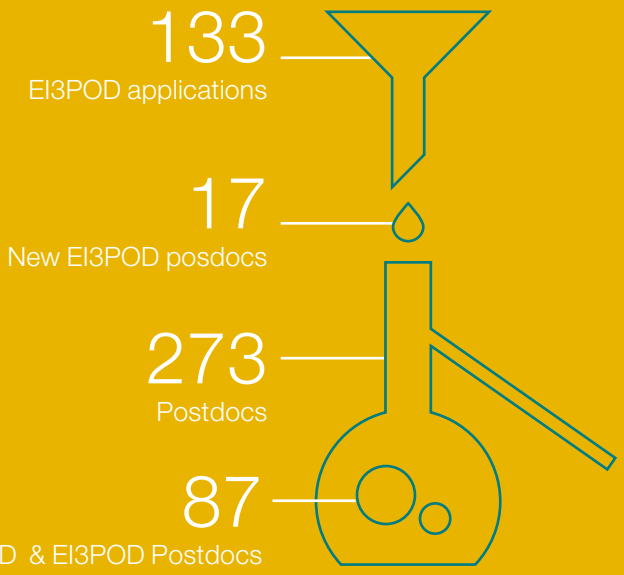
This year marked a major changing of the guard in the leadership of the internal training programmes, as EMBL's Academic Coordinator and Dean of Graduate Studies Helke Hillebrand's term came to an end in December 2016. During the previous nine years, she developed and shaped EMBL's internal training, raising EMBL's profile and acting as a driving force for the implementation of important changes to the benefit of predoctoral and

Internal Training in Numbers 2016

EMBL International PhD Programme



EMBL Postdoctoral Programmes



postdoctoral fellows. Monika Lachner from the Max Planck Institute for Immunobiology and Epigenetics was recruited to the positions of Academic Coordinator and Dean of Graduate Studies from the beginning of 2017.

The EMBL International PhD Programme (EIPP) is a flagship of EMBL's commitment to training and is characterised by a combination of dedicated mentoring and creative freedom to support early independence. In its history of more than 30 years, the EIPP has served as a role model for institutions in Europe and beyond. It remains a very attractive and competitive programme, each year receiving around 1800 applications from across the globe and admitting only 50–60 students. EIPP had its largest class to date in 2016, with 56 students attending the initial intensive predoc course, which aims to provide interdisciplinary training in molecular biology and to familiarise students with EMBL's research and culture. The programme's long-serving organiser, Lars Steinmetz, stepped down at the end of the year, handing over the course organisation to Judith Zaugg from 2017.

The EMBL Interdisciplinary Postdoc Programme (EIPOD), co-funded by the EC Marie Skłodowska-Curie actions, enables young researchers to work on highly collaborative and interdisciplinary projects across different groups and units at EMBL. From 2015, the third-generation EI3POD Programme also enables collaborations with other academic institutions and industry, thus allowing postdocs to establish and maintain connections that prove useful in building their careers beyond EMBL. Several research institutes, including the Italian Institute of Technology, the University of Geneva and Yale University, joined the EI3POD Programme as external

Helke Hillebrand at EMBL's 2016 graduation ceremony – her last as EMBL's Academic Coordinator and Dean of Graduate Studies

partners in 2016. A cornerstone of the new programme is offering dedicated career support for postdocs, with a career advisor recruited in 2016 to set up structured EIPOD career development services. In this context and alongside other initiatives, individual career counselling sessions for EIPOD postdocs were introduced and have been in high demand throughout the year.

External Training

External training activities at EMBL focus largely around the events in the Course and Conference Programme, which in 2016 was the largest to date. With 29 conferences and 42 courses held in the Advanced Training Centre (ATC), the training facilities in Heidelberg were close to capacity.

External Training in Numbers 2016

31
Conferences at EMBL sites

65
Courses at EMBL sites

7290
Participants across EMBL sites

EMBL continuously adapts its training to emerging trends in molecular life science research, and several new conferences on innovative scientific topics were launched in 2016. As a prominent example, the EMBL Conference 'The Epitranscriptome' focussed on epigenetic mechanisms of transcriptional regulation and their impact on genomic output and RNA function.

An important development for EMBL conference attendees was the introduction – following a successful pilot in 2015 – of the EMBL PlayLab, on-site childcare during conferences at EMBL Heidelberg. The new service, provided by EMBL Kindergarten teachers, makes it easier for parents to attend scientific conferences.

EMBL's cutting-edge courses covered exciting topics in 2016, ranging from single-cell gene expression analysis to optogenetics and super-resolution microscopy. In addition to those held in the ATC in Heidelberg, events were organised at other EMBL sites, such as the very successful Protein Expression, Purification and Characterisation course at EMBL Hamburg, which reached its tenth anniversary in 2016 and was complemented by a celebratory mini-symposium involving tutors and students from its early days. As in previous years, bioinformatics training, delivered mainly by EMBL-EBI, represented a large component of the EMBL courses, confirming the high demand for training in this area. Altogether nearly 7300 attendees were welcomed at EMBL events across all sites – almost 1000 more than in 2015.

EMBL's on-site training programme is increasingly complemented by e-learning opportunities. TrainOnline, EMBL-EBI's web-based resource for training in bioinformatics, offered 17 new webinars and 10 new courses, and grew its user community by 70% in 2016. Building on the strong TrainOnline portfolio, EMBL plans to expand its online training services to the complete range of EMBL's research, so as to establish an EMBL-wide e-learning portal for advanced training. A dedicated scientific project manager for e-learning was recruited to drive this effort.

Participants from

83

countries

77%

from EMBL member and associate member states

The wider research community also benefits from scientific training offered by EMBL group and team leaders outside of EMBL, for example when they participate in external courses as instructors or co-organise training events worldwide. In 2016, nearly 60 conferences, courses and workshops were organised by EMBL faculty in 17 countries. In addition, EMBL group and team leaders delivered over 500 lectures and seminars at universities and research institutes in 39 countries. Finally, under the auspices of EMBL's Scientific Visitor Programme, more than 600 scientists from our member states and beyond visited EMBL through internships or to collaborate on specific research projects with EMBL laboratories and core facilities.

Outreach

EMBL's communications saw important developments in 2016, as Dan Noyes, who joined EMBL from CERN, and Anna-Lynn Wegener, former Head of EMBL's Strategy Development and Analysis team, were appointed as Joint Heads of a new, restructured Strategy and Communications team. With the aim to streamline communication activities across the organisation and increase public awareness of EMBL, the new team brings together the former Office of Information and Public Affairs, Strategy Development & Analysis and EMBL-EBI External Relations. The new team started several major long-term projects in 2016, including a digital redesign of EMBL's public web presence and intranet, a revamp of the organisation's visual identity, and systematic internal communications across EMBL's sites. Their efforts have already produced positive results: in the area of social media, for example, the number of EMBL's followers on Twitter increased by a third in the course of 2016.

The European Science Open Forum – held every two years and attended by representatives of research, technology, industry, journalism and policy – took place in Manchester in July 2016 and offered a great opportunity to showcase EMBL's scientific achievements and unique spirit. In addition to organising sessions on microbiome research and

Iain Mattaj, Director General of EMBL, took part in a plenary session with the Director General of CERN and the Director for Science of ESO at the European Science Open Forum

Matthias Hentze, EMBL Director, talking to guests during the EMBL Fall Gala reception

scientific community engagement, EMBL presented its technology transfer activities and demonstrated fundamental research benefits for society in a joint exhibition stand with EIROforum partners (p.40). In a plenary session, EMBL Director General Iain Mattaj discussed the importance of collaboration in European science with CERN Director General Fabiola Gianotti and European Southern Observatory Director for Science Rob Ivison.

Smaller-scale outreach activities kept different parts of EMBL busy in 2016. Together with their neighbours on the European Photon and Neutron (EPN) campus, staff from EMBL Grenoble explained molecular biology and protein crystallography to nearly 3000 enthusiastic visitors as part of the Fête de la Science in October. A Science Movie Night in Heidelberg paired the screening of Hollywood blockbuster 'X-Men' with commentary and discussion from young EMBL scientists. EMBL Hamburg took part in the city's first Day of Science in September, and EMBL-EBI launched the 'Science is Global' event series, in which staff shared their fascinating global career stories to celebrate the diversity and internationality of science.

An artistic perspective on EMBL's science was offered by the 'Life in Perspectives' exhibition, based on the visualisation of stunning 3D microscopy images as lenticular images and displayed at the Heidelberg City Library in October and November 2016.

In 2016, the European Learning Lab for the Life Sciences (ELLS), EMBL's educational programme, reached nearly 170 high-school teachers and 1800 students. In addition to welcoming numerous school visits to EMBL, ELLS

organised two practical courses for teachers to gain hands-on experience in molecular biology experiments, including a two-day training workshop on protein crystallography organised in collaboration with EMBL Hamburg on the DESY campus. For 2016's Insight Lecture, EMBL-EBI Director Ewan Birney explored opportunities and challenges of big data with more than 900 students and over 50 teachers from 14 countries. EMBL researchers also shared their excitement for science with hundreds of students in Mexico, Italy, Spain, Colombia, Czech Republic and Germany through the EMBL School Ambassador Programme.

EMBL's Science and Society Programme organised the 17th joint EMBL/EMBO Science and Society Conference, 'The Past in the Present: The Making of memories', and the 8th EMBL-EBI Science and Society symposium – focused on the science and ethics behind genome editing – in addition to a series of smaller seminars and discussion meetings across EMBL sites. Selected seminars were made freely available to the general public on EMBL's website.

Members of the public interested in the future of the life sciences and how these may impact on society were also among the attendees of the first European Conference of Life Science Funders and Foundations in April 2016. The meeting, organised in collaboration with the Volkswagen Foundation and held at EMBL Heidelberg, explored opportunities to accelerate discoveries and their translation into practical applications.

Private Support

EMBL's resource development efforts are geared towards building an active network of influential and philanthropic individuals to advise and support the institute. The Friends of EMBL Programme contributes to these efforts by bringing potential individual donors and businesses into closer contact with EMBL science and scientists. Under its auspices, local supporters and Friends of EMBL were invited to EMBL Heidelberg for a PhD lunch where they learned about young scientists' projects. At a new event at a local monastery brewery close to Heidelberg, guests learned about brewer's yeast while enjoying a glass of beer. Events more specifically tailored to companies included the organisation of EMBL lectures at selected companies' sites as well as events at EMBL sites, all aimed at raising interest in and fascination with EMBL research and identifying new research funding opportunities.

The largest single event aimed at raising support for EMBL science in 2016 was the EMBL Fall Gala in September. EMBL put on its finest dress as 140 guests from the worlds of science, business, politics and journalism convened at the ATC in Heidelberg for an evening of discussions and performances around the topic of EMBL's ocean biodiversity research.

Integrating Life Sciences

in Europe and Across the World

9

partnerships with research institutes in member and associate member states

EMBL plays a leading role in promoting cooperation and integration by fostering international relations at a political, institutional and scientific level in Europe and worldwide. As Europe's only intergovernmental research organisation in the life sciences, EMBL also helps shape science policy and strategy by engaging with European policy-making bodies.

Member State Relations

Following completion of its national ratification process, Malta officially became the 22nd EMBL member state in August 2016, paving the way to further strengthen its ties to the European life science research community. Collaboration with the Czech Republic, the last country to join EMBL before Malta in 2014, was very intense throughout the year, particularly in the context of the EC-funded MEDGENET Twinning project – between

EMBL and the Central European Institute of Technology – for training and exchange of scientific expertise in the areas of medical genomics and epigenomics.

In addition to hosting young scientists who came to refine their knowledge in various techniques, EMBL welcomed visits from important political representatives of its host countries in 2016. The German Federal Minister of Health gained insights into EMBL research and facilities during a visit to EMBL Heidelberg in August, which was followed by a visit by the Minister-President of Baden-Württemberg in November. Also in November, UK Prime Minister Theresa May visited EMBL-EBI's campus in Hinxton, where she toured the site and met with the EMBL-EBI Directors. Over the course of the year, high-level meetings also took place between EMBL leadership and representatives of the governments and national research councils of Austria, Belgium, France, Israel, the Netherlands, Norway, Portugal, Sweden and the UK.

In an effort to tighten EMBL's links and foster integration with the Italian research community, scientific meetings were organised jointly with the Italian Institute of Technology to explore areas and opportunities for future collaboration. Close interactions, including the organisation of joint meetings and seminar series, were also developed with Sapienza University.

Malta became EMBL's 22nd member state

After Australia renewed its associate membership in 2015, EMBL participated in the National Collaborative Research Infrastructure Strategy mapping action in 2016, which aims to inform the Australian Government on future priorities for strategic investment in collaborative research infrastructures. Visits to EMBL Heidelberg by the new Scientific Head and the new Chief Operating Officer of the EMBL Australia Partnership Network offered the opportunity to further discuss the road map for collaboration.

Joint activities were carried out throughout the year with Argentina, EMBL's second associate member state. In February 2016, EMBL supported the launch of a joint Tara/FFEM (French Facility for Global Environment) project that will allow postdoctoral fellows from South America to visit Europe to conduct research on the findings from the Tara Oceans project on oceanic plankton. High-level discussions on research and development took place at the newly inaugurated Scientific and Technological Center of the Ministry of Science, Technology and Productive Innovation (MINCYT) in Buenos Aires. Together with MINCYT, EMBL faculty organised an advanced course in correlative light and electron microscopy in Mendoza and an EMBL-EBI industry workshop in Buenos Aires that focussed on industrial applications of biotechnology and genomics. A delegation led by the Minister Lino Barañao visited EMBL-EBI in November 2016. Alongside the visit, EMBL signed a Memorandum of Understanding with MINCYT to work together towards establishing an EMBL partner institute in Argentina.

EMBL worked intensely throughout 2016 to further integrate its prospect member states – Hungary, Lithuania, Poland and Slovakia – into EMBL

Anna Steyer (Phd student in the Schwab team) explains the concept of correlative light and electron microscopy to Hermann Gröhe, German Federal Minister of Health, during his visit to EMBL Heidelberg

and the wider European life science landscape. Cooperation with Hungary was greatly accelerated by the advancement of the HU-MOLMEDEX Teaming proposal, which received €15 million of phase-two funding from the EC to establish the Hungarian Centre of Excellence for Molecular Medicine. Under the coordination of the Hungarian National Research, Development and Innovation Office, the new institute will be a joint venture between EMBL's Teaming partners, including the University of Szeged, Semmelweis University, the Biological Research Centre of the National Academy of Sciences, and the University of Debrecen. In the context of driving further cooperation with Slovakia, EMBL jointly organised a workshop with the Institute of Molecular Biology in Bratislava to raise awareness of the opportunities offered by EMBL to Slovakian scientists. Collaborations with Hungary and Slovakia culminated in applications by both countries to join EMBL as full member states, which were endorsed by EMBL Council in November 2016. Hungary and Slovakia's memberships will become effective following ratification by their national governments. EMBL continued to engage in scientific cooperation with Lithuania in 2016, with the participation of EMBL scientists and EMBLEM in major national life science initiatives and conferences. The visit of a delegation from the University of Vilnius to learn about EMBL's core facilities and subsequent discussions with EMBL leadership resulted in the signing of a Memorandum of Understanding with the university's Life Sciences Center.

EMBL Partnerships

EMBL's institutional partnerships are close cooperative affiliations based on scientific synergy between EMBL and external research institutes of comparable standard in member and associate member states. While local partnerships with institutions at or near EMBL sites emerge largely from the benefits of sharing infrastructure and equipment, remote partnerships are aimed at implementing the successful EMBL operational model and

high scientific standards nationally, thus creating an interlinked system of excellent life science institutions.

The most recent EMBL Partnership, officially launched in September 2016 between EMBL and the Hubrecht Institute in Utrecht, brought the number of institutional partnerships to nine, with institutes in ten countries. Working at the interface between stem cell biology and tissue biology, the new partnership will leverage complementary strengths of the two institutes to study how human tissues and organs develop and are organised, advancing our understanding of a wide range of diseases, including heart degeneration, Alzheimer disease, diabetes and cancer.

The Partnership for Structural Biology (PSB), which brings together institutes on the EPN science campus in Grenoble, is one of EMBL's oldest partnerships. Since 2002, it has provided a framework for close collaboration and access to shared resources for researchers from EMBL, ESRF, the Institut Laue-Langevin, and the IBS. Confirming its success, the PSB was renewed for five more years in February 2016. The Unit for Virus Host Cell Interactions had come to its natural end in 2015 with the relocation of the IBS onto the EPN campus and was replaced in 2016 by a new cooperation between EMBL and the IBS termed the Federation de Recherche.

EMBL Director General Iain Mattaj (right) and Alexander van Oudenaarden, Director of the Hubrecht Institute, signed the agreement establishing the EMBL-Hubrecht Partnership for Stem Cell and Tissue Biology

Established in the same year as the PSB, the MMPU – a collaboration between EMBL and the Medical Faculty of the University of Heidelberg – focuses on translational research, aimed at bridging the gap between basic science and medicine. In February 2016, MMPU activities were reviewed by a panel of external experts, which found research carried out by the partnership to be of the highest international level.

Researchers from the MMPU were among nearly 200 participants to gather at EMBL Heidelberg for the EMBL Partnership Conference 'Perspectives in Translational Medicine' in June 2016. The second event of its kind, and the first hosted at EMBL, the conference enabled exchange of expertise, building of research networks, and new collaborations between EMBL and its partner institutes in the field of molecular medicine. In addition to the Heidelberg-based University Hospital and National Center for Tumor Diseases, these included the Centre for Genomic Regulation (CRG) in Barcelona, the University Medical Center Hamburg-Eppendorf, and four institutes within the Nordic EMBL Partnership for Molecular Medicine.

Further Broadening our Horizons

In recent years, EMBL has engaged in a successful collaboration with India, particularly in the field of structural biology. The cooperation between EMBL, the ESRF and the Indian Regional Centre for Biotechnology has greatly benefited the Indian research community by providing scientists

with access to the MX beamline BM14 in Grenoble. The beamline's time drew to a close in 2016, as it was decommissioned to make way for more advanced technologies. Building on the collaborative relationship that it enabled, EMBL and India are looking to identify and encourage new long-term cooperative activities in fields of common interest. Discussions with senior government officials and representatives of the Indian life science community were brought forward with a view to enabling India's associate membership in EMBL.

Building on the declaration of intent for scientific cooperation signed in 2015, intense discussions on future associate membership continued with the South African Department of Science and Technology. EMBL leadership and faculty participated in scientific and policy-oriented events supported by the department, including the International Conference on Research Infrastructures held in Cape Town in October 2016.

Finally, relations between EMBL and the Chinese scientific community further intensified over the year. In March 2016, a delegation including the Directors of EMBL-EBI visited six Chinese institutions with strong interests in bioinformatics, genomics and big data to promote EMBL's bioinformatics services and resources and to lay the groundwork for long-term strategic engagement. These resources were also successively showcased to the Vice Mayor of Chongqing during a visit to EMBL-EBI in September. Having established initial contact in 2015 with Tsinghua University, one of China's top research institutions, EMBL participated in a joint workshop in Beijing in May 2016 to identify and stimulate collaborations in areas of mutual interest.

EMBL representatives at the Tsinghua-EMBL Forum on Advanced Biological Technology that was held in Beijing in May 2016

EU Relations

Over the years, EMBL and the EC have established a strong relationship and are engaged in a broad collaboration based on a Memorandum of Understanding and the implementation of biennial work plans. January 2016 marked the start of a new extended programme for 2016–17, aligned with the strategic priorities of EMBL and the Commission. The new work plan addresses a number of key challenges, including analysing, storing and accessing research data; increasing interdisciplinarity and international cooperation in life science research and infrastructure; open access to scientific literature and data; sustainability and staffing needs; the promotion of gender equality; and the ever-increasing mobility and advanced training of researchers.

Before the EMBL-EC Annual Meeting took place in November, a visit to EMBL from European Commissioner for Research, Science and Innovation Carlos Moedas in April 2016 offered a further platform to discuss common goals and progress in these areas and to explore other opportunities for joint participation in events and initiatives.

EIROforum

EMBL is an active member of EIROforum, an organisation of eight intergovernmental research organisations operating in a wide range of disciplines – from particle physics, space science and biology to fusion research and neutron and photon science. EIROforum supports European science and international cooperation by facilitating interactions with the EC and other EU institutions as well as with national governments, industry and educators. In this context, EMBL participated in important events in 2016, as EIROforum presented its activities to the Research Working Party of the EU Council and participated in meetings on the sustainability and the socioeconomic impact of research infrastructures organised by the Organisation for Economic Co-operation and Development's Global Science Forum (OECD). Together with the other EIROforum organisations, EMBL participated in the consultation launched by the EC to gather views on the plans for a European Innovation Council, which led to the publication of a joint position paper in May 2016.

European Research Infrastructures

Building on its long-standing experience in the successful management and operation of distributed life science research infrastructures, EMBL has participated in the development of several biomedical projects on the European Strategic Forum for Research Infrastructure (ESFRI) roadmap, and has driven the establishment of the major transnational ESFRI

infrastructures Euro-BioImaging (EuBI) and ELIXIR. While EuBI provides open user access to state-of-the-art imaging technologies, ELIXIR is the pan-European infrastructure for the collection, archiving and integration of life science research data.

Following the successful conclusion of the Preparatory Phase I project in 2014, EMBL has coordinated the EC-funded EuBI Preparatory Phase II project since the beginning of 2016. The project aims to deliver the legal, financial, managerial and technical tools and procedures to start full operation of EuBI as a European Research Infrastructure Consortium (ERIC). In the first year of the project, the EuBI signatories, including 16 countries and EMBL, finalised and approved the statutes of the EuBI ERIC. Together with Finland as the future ERIC statutory seat, and Italy as the site for medical imaging coordination, EMBL will host the EuBI Hub for coordinating user access and training in biological imaging technologies, and EuBI's image data resources and tools for the provision of data services. As a major milestone, the EuBI Hub and node candidates began interim operation in May 2016, supporting over 40 user projects until December 2016 and providing access to 36 different imaging technologies.

EMBL also coordinates the EC-funded Global BioImaging project to extend EuBI's international collaboration and establish common services jointly with imaging infrastructure partners around the globe. In 2016, EMBL representatives visited partners in the Americas, Africa and Asia; organised an international workshop for imaging core facility staff with 80 participants from 6 continents; and ran two advanced training courses on facility and image data management at EMBL Heidelberg.

EMBL's integral role in facilitating the establishment of ELIXIR – coordinating its Preparatory Phase – has provided a strong foundation for the current rapid progress. ELIXIR continued to grow in size throughout 2016, becoming the ESFRI research infrastructure with the largest membership. Slovenia, Italy, Luxembourg, Ireland and Germany all joined during 2016, bringing the number of member countries to 20 by the end of the year. EMBL-EBI maintained its active role as the largest node in ELIXIR, supporting most of the new services launched in 2016 and embarking on several new projects involving national ELIXIR nodes. In its role as coordinator, ELIXIR continued to drive the implementation of the EC-funded grant ELIXIR-EXCELERATE, with EMBL-EBI at the forefront in developing a process to identify a set of core data resources that will form the bedrock for future long-term sustainability efforts.

EMBL also plays a key role in the other ELIXIR-coordinated project, CORBEL (Coordinated Research Infrastructures Building Enduring Life-science Services), which aims to create a common platform for the delivery of shared services from 11 ESFRI biomedical research infrastructures.

EMBL Alumni

7542
alumni

EMBL's alumni – which now number more than 7500 former students and staff members – are valuable ambassadors. They support EMBL and its missions in various ways, for example by facilitating collaborations with the countries and institutions in which they work. Alumni also form an integral part of EMBL's service to its member states, because after leaving EMBL they go on to enrich the national systems with the experience and training gained in EMBL's international, interdisciplinary and dynamic environment.

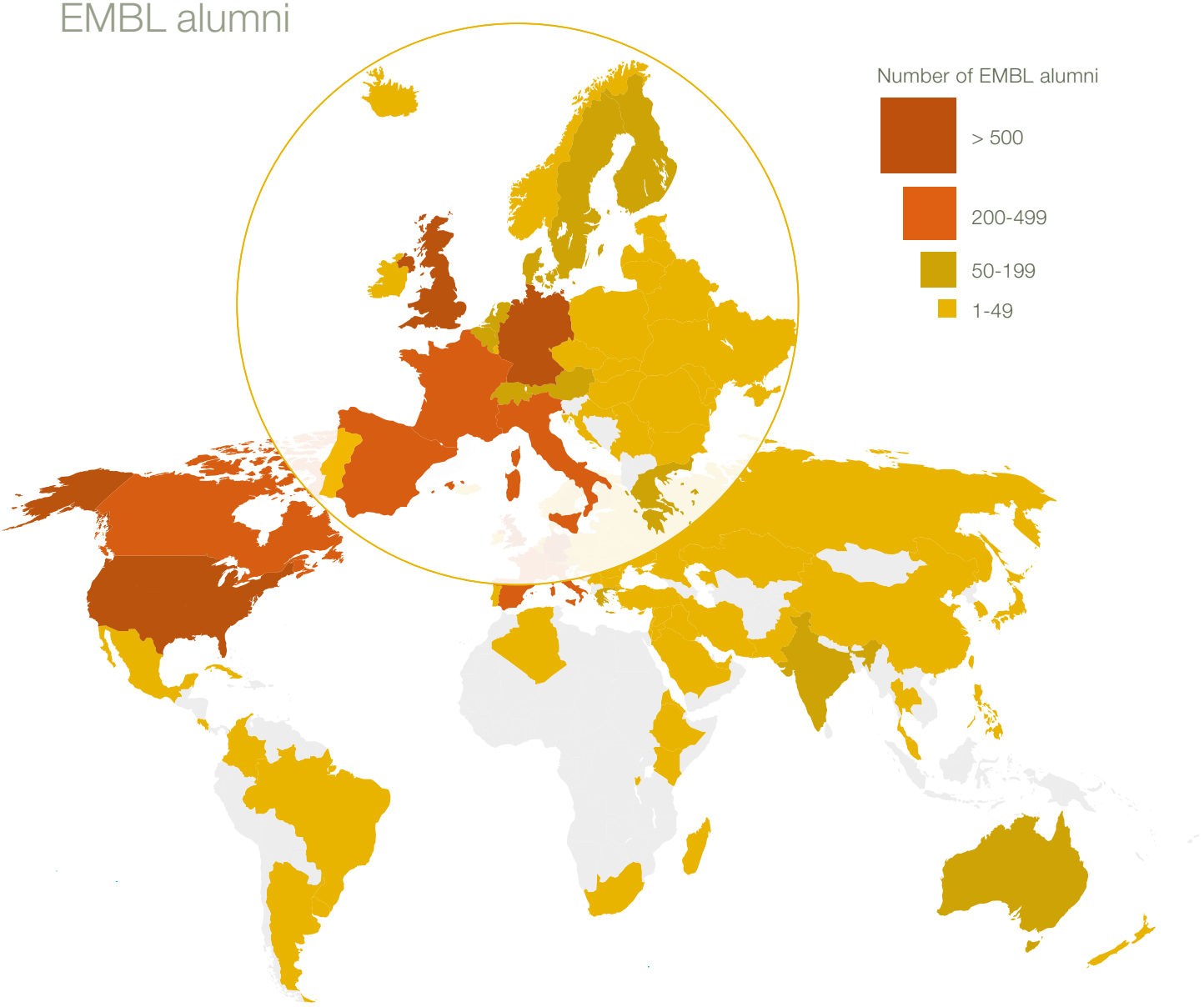
National meetings are organised in EMBL member and associate member states to strengthen the local alumni communities as well as EMBL's interactions with the scientific community in those countries. As non-EMBL scientists from the host countries are also invited, these meetings serve as a platform for scientists at national institutions to expand their networks and to learn about EMBL and its opportunities. Several such events took place in 2016, including at Cambridge University and at the CRG in Barcelona. The first 'EMBL in Italy' event, hosted by EMBL Monterotondo, took place at Sapienza University and attracted over 80 participants. The EMBL Pensioners' Coffee, a new annual event enabling EMBL pensioners to reconnect with EMBL and its ongoing developments, was launched in 2016 and held for the first time at EMBL Heidelberg in March.

'EMBL in Spain' event participants

The success of the alumni programme relies not only on support from EMBL, but most importantly on the enthusiastic engagement and work of alumni volunteers who contribute to events as hosts, speakers, advocates and sponsors. In 2016, in addition to representing EMBL at career fairs and organising national meetings, alumni supported EMBL's Alumni Relations in developing a proposal and laying the groundwork towards establishing a more structured Alumni Volunteer Programme, which is expected to launch in 2017. Along with promoting new initiatives for its alumni, EMBL also engages with external organisations to help connect the community of professionals who work in institutional alumni relations. In June 2016, EMBL hosted the 4th Central Europe Alumni Directors Summit in collaboration with the Council for Advancement and Support of Education – an international association that supports professionals working in alumni relations, fundraising, communication and marketing for educational institutions. The meeting served as a forum to explore and exchange best practices offered by research institutes.

EMBL's alumni relations programme benefits immensely from the dedicated support of the EMBL Alumni Association and its elected board members.

EMBL alumni



EMBL alumni in numbers

81%
of EMBL alumni work in member and associate member states

70%
work in academia

13%
work in industry

Following elections in 2015 and under the Chairmanship of Gareth Griffiths, former Group Leader in the Cell Biology and Biophysics Unit, the new board started work in January 2016, focussing on supporting EMBL's missions and further developing connections with alumni, member states, current staff and the general public.

Every year, the John Kendrew and Lennart Philipson awards, created to honour EMBL's first two Directors General, celebrate the work and achievements of EMBL alumni. The Lennart Philipson Award recognises outstanding contributions to translational research and technology development. Ernst Stelzer, a former EMBL Cell Biology and Biophysics group leader and now a professor at Goethe University in Frankfurt, was selected as the 2016 winner for his development and application of new light microscopy methods. The John Kendrew Young Scientist Award, which recognises excellence in science and science communication, was conferred to Jop Kind, a former PhD student in the Genome Biology Unit and now a group leader at the Hubrecht Institute, for his pioneering postdoctoral work on establishing novel technologies to map chromatin domains in single cells.

Administration

84

nationalities represented among EMBL employees

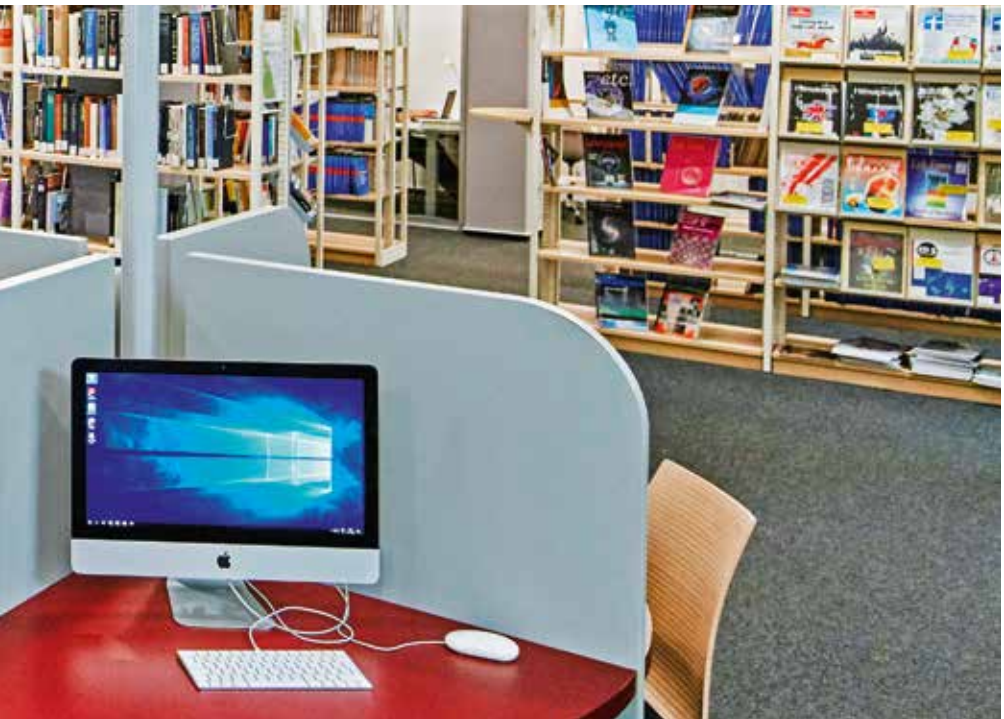
EMBL's Administration supports all of EMBL's missions by providing efficient services to EMBL staff across all sites, while constantly adapting its systems to EMBL's culture of cooperation and flexibility. In 2016, the Administration worked intensively on modernising EMBL's Staff Rules and Regulations, making them more coherent, consistent and user-friendly – with only minor modifications to staff entitlements and benefits. The updated Staff Rules and Regulations were approved by EMBL Council in November. Following important changes to EMBL's Pension Fund and the appointment by EMBL Council of a Pensions Advisory Board in 2015, the Administration also worked closely with the board members to develop a new investment strategy and follow the fund's development. In October 2016, a records specialist was recruited to support the Administration in implementing a tailor-made records and information management framework, with the aim to improve and streamline record-keeping practices and processes at EMBL and to liaise with the growing EMBL Archive.

EMBL's commitment to fostering and maintaining a culture that values and promotes diversity was reinforced with the creation of the EMBL Equality and Diversity Committee. An evolution of the previous Gender

Balance Committee, the committee aims to increase equality and diversity among EMBL personnel and to foster awareness and skills that promote these values at EMBL and beyond. The Equality and Diversity Committee achieved several goals over the year, including the introduction of measures to enhance the recruitment of female faculty, a training course in lab management for new group leaders, training for EMBL faculty in unconscious bias, and the creation of nursing rooms for staff across EMBL sites.

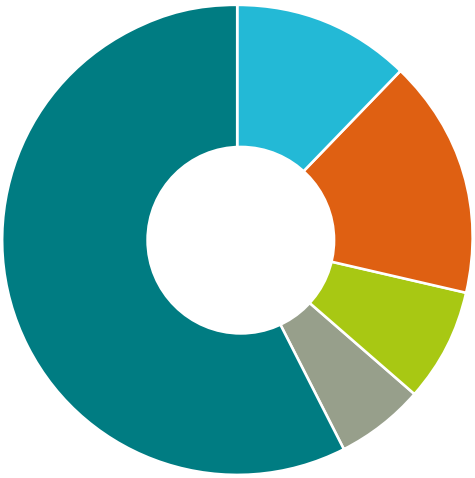
The Szílard Library at EMBL Heidelberg was reorganised and renovated to adapt it more to digital functions. The refurbished library was opened with an event for staff in May 2016. As building requirements constantly change in response to new research directions and technologies, other campus works – of varying scales and across EMBL sites – were also brought forward. Major projects that began in 2016 include the refurbishment of Hall 25e in Hamburg, which previously hosted the DORIS beamlines, and a building in Heidelberg to house a new high-end electron microscope that will complement EMBL's experimental imaging facilities. Construction of another building began at EMBL headquarters, which will host general services including the Staff Association, the Ombuds Office, the EMBL Archive, Facility Management and Technical Security. Finally, a new EMBL guesthouse opened in Heidelberg to supplement the two existing guesthouses in providing accommodation for newly arrived staff and visitors.

Supported by the Administration, and together with many other EMBL departments and clubs, the Staff Association coordinated a large number of events and initiatives in 2016 in the context of the EMBL Aid group. Established in late 2014, EMBL Aid is a platform for EMBL staff to engage in various fundraising and charitable activities, aimed particularly at supporting refugees living in the areas around EMBL sites. Support has included collections of clothes, bake sales, welcome events and Christmas parties, as well as training and other activities to help refugees find new jobs.



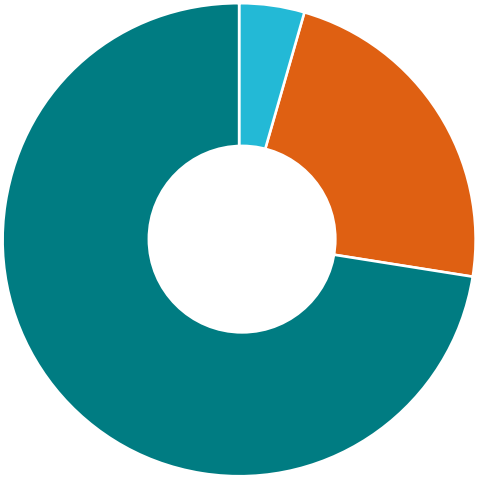
The refurbished Szilárd Library at EMBL Heidelberg

Personnel Statistics



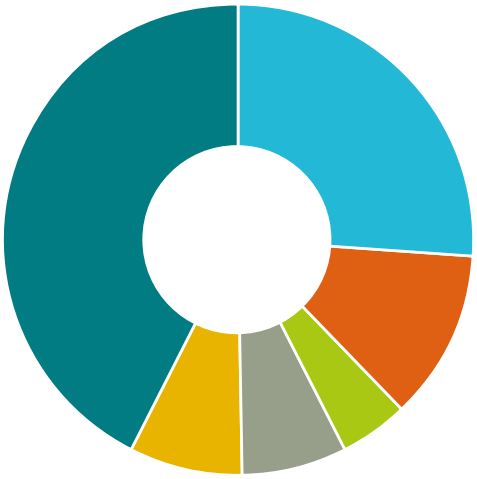
Personnel
in 2016 in FTE

958	Staff members
201	Predocs
273	Postdocs
131	Supernumeraries and ancillaries
98	Diploma students and trainees
1661	Total



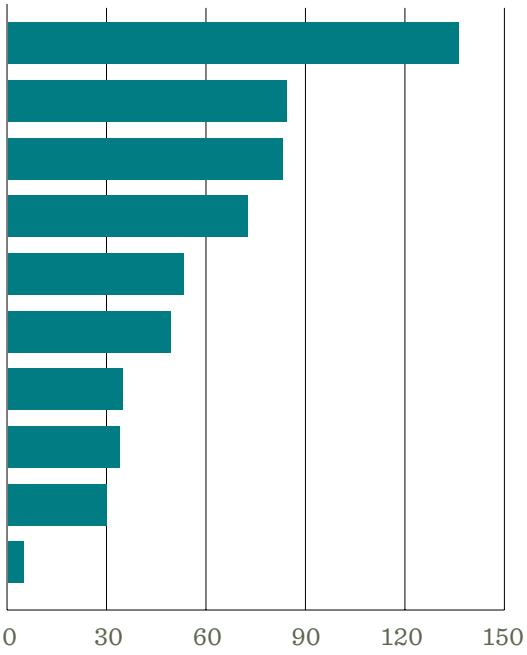
Staff nationalities
in 2016 in FTE

1208	EMBL member and associate member states
74	EMBL prospect member states
379	Non-member states
1661	Total



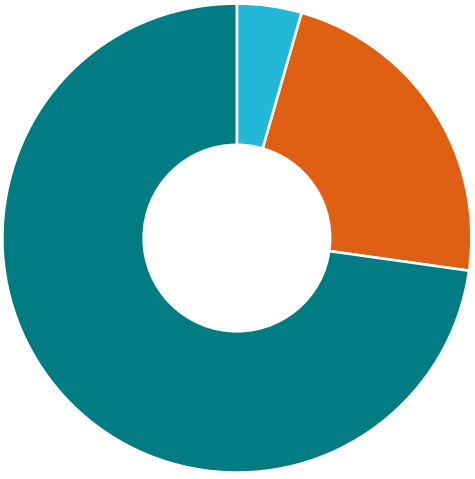
Staff categories of employment
in 2016 in FTE

710	Research
432	Scientific services
196	Scientific or technical support
78	Training and outreach
118	Administrative support
127	General support
1661	Total



Scientific visitors
in 2016

141	EMBL-EBI Hinxton
87	Structural and Computational Biology
86	Core Facilities
75	Genome Biology
55	Cell Biology and Biophysics
51	EMBL Monterotondo
36	EMBL Hamburg
35	Developmental Biology
31	Directors' Research
5	EMBL Grenoble
602	Total



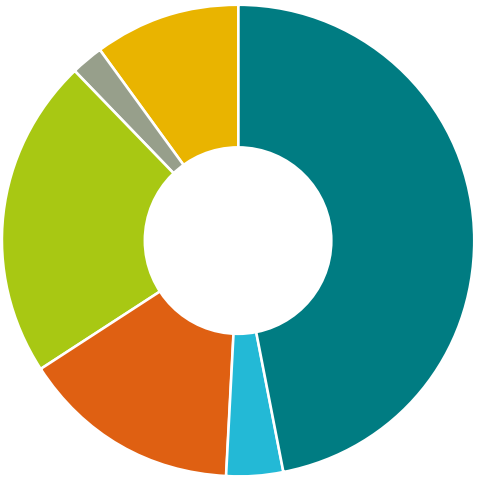
Scientific visitors' nationalities
in 2016

439	EMBL member and associate member states
26	EMBL prospect member states
137	Non-member states
602	Total

Financial Report

EMBL total income in 2016

€ 238 million

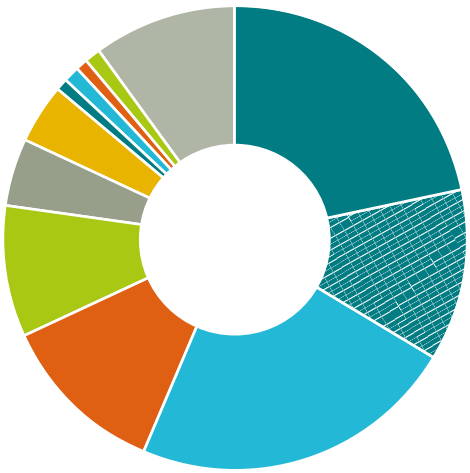


Income
in 2016

47 %	Member state contributions
4 %	Member state special contributions
15 %	Internal tax
22 %	External grant funding
2 %	Other external funding*
10 %	Other receipts**

EMBL external grant funding in 2016

€ 53 million

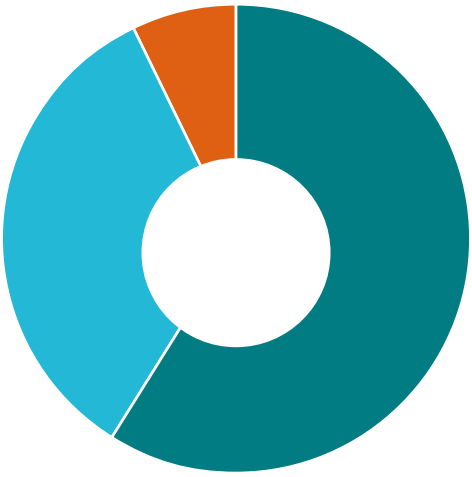


External grant funding
in 2016

22 %	EC	4 %	BMBF
12 %	ERC	1 %	MRC
23 %	NIH	1 %	Humboldt Foundation
12 %	Welcome Trust	1 %	ANR
9 %	BBSRC	1 %	HFSPO
5 %	DFG	10 %	Others

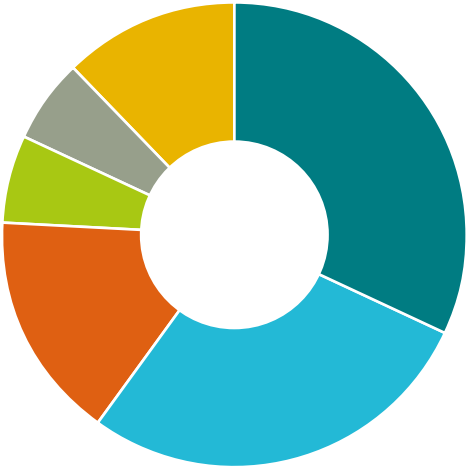
EMBL total expenditure in 2016

€ 235 million



Expenditure
in 2016

59 % Staff costs
34 % Operating costs
7 % Equipment expenditure incl. depreciation



Expenditure by area of activity
in 2016

32 % Research
28 % Scientific services
16 % Scientific or technical support
6 % Training and outreach
6 % Administrative support
12 % General support

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

Member state contributions

	2016 x € 1,000	%
Ordinary contributions		
Austria	2,433	2.3
Belgium	2,957	2.8
Croatia	336	0.3
Czech Republic	756	0.7
Denmark	1,888	1.8
Finland	1,468	1.4
France	17,220	16.3
Germany	21,593	20.4
Greece	1,741	1.6
Iceland	63	0.1
Ireland	1,133	1.1
Israel	1,353	1.3
Italy	12,721	12.0
Luxembourg	210	0.2
Malta	37	0.0
Netherlands	4,918	4.7
Norway	2,706	2.6
Portugal	1,290	1.2
Spain	8,924	8.4
Sweden	2,989	2.8
Switzerland	3,828	3.6
United Kingdom	15,099	14.3
	105,663	100%
Currency adjustment		
for Sterling contributions	1,228	
	1,228	
Entry fees		
Czech Republic	351	
	351	
Associate member state contributions		
Australia	2,647	
Argentina	903	
	3,550	
Additional contributions		
from United Kingdom	9,604	
from Germany	565	
	10,169	

Reviews of Scientific Units

Research and Service Units are evaluated every four years by members of the Scientific Advisory Committee and additional experts. The following section features summaries of the scientific reviews and presents the Director General's responses to the review reports.

EMBL Monterotondo Review

EMBL Monterotondo was reviewed on the 16 to 18 March 2016 by a panel of 13 experts, including four members of SAC and two observers from EMBL Council. The review was chaired by Denis Duboule, Federal Institute of Technology, Lausanne, and University of Geneva, Switzerland.

Evaluation Summary

EMBL Monterotondo has seen some important changes over the last review period, both in terms of staff turnover and of research themes. Traditionally, EMBL Monterotondo hosted research groups working on a wide variety of topics, yet all relying upon the mouse as a model system. This was associated with the role played by the Monterotondo campus on the European mouse biology scene, for example through the presence of the European Mouse Mutant Archive (EMMA). With the appointment of a new Head of Outstation, Phil Avner, the decision was taken to develop a narrower scientific focus and to utilise the EMBL entire environment to implement the use of the latest technologies involving mouse molecular genetics, genome editing, bioinformatics and imaging to help EMBL Monterotondo develop further its profile as a centre of excellence in the European landscape.

It was decided to focus on neurobiology, epigenetics and their interactions in the nervous system using in vivo approaches based on cutting-edge mouse genome modification techniques. Since the Head of EMBL Monterotondo is not a neurobiologist, an external committee with an advisory role was formed to help implement this ambitious programme. The review committee validated the feasibility and encouraged the development of a strong mouse-oriented neurobiology unit at EMBL Monterotondo.

Within this refocused research framework, two new Group Leaders have been recruited, following the departure of two Staff Scientists and one Group Leader and the relocation of another Group Leader to EMBL Heidelberg. Two further recruitments are planned that should bring the Monterotondo Outstation back to eight research groups during 2017.

The science carried out by EMBL Monterotondo has continued to be of a very high standard: the overall performance of the Unit was rated by the Review Panel as excellent in terms of the quality of its research. Part of this scientific excellence relies on the presence of strong core services, which overall have maintained and improved their service provision to the Unit over the period 2012–2016. Technical excellence, particularly in the area of genetic engineering and transgenesis, will continue to be an important asset in the context of the changing research focus of EMBL Monterotondo. In view of a potential moderate increase in the number of research groups at EMBL Monterotondo in the future, the Panel stressed the need for continued improvement in the management of the animal facility so as to better adapt to customer requests.

The Panel also recommended that training and outreach activities for the scientific community be redefined to better fit with the new thematic focus of the Unit, possibly also serving as a means to build or improve relationships with Italian institutes and the Italian community of researchers.

As the Head of EMBL Monterotondo, Phil Avner was congratulated for his smooth and efficient running of the Unit over the past four years. His management skills and commitment to the Unit's success were unanimously appreciated and his performance was rated as outstanding.

Response to the Panel's Recommendations

I would like to begin by thanking the Panel for their thorough review of the activities of the Monterotondo Outstation, as well as for their constructive feedback. Each of the Group Leaders under review received a detailed critique and helpful suggestions from the Panel. I agree with the evaluation that Phil Avner has performed in an outstanding way by shaping and driving forward the activities of EMBL Monterotondo through a crucial and very delicate phase for the Outstation, with very dedicated and useful support from Senior Scientist Cornelius Gross.

The strategic decision to move towards an increased focus on neurobiology and epigenetics was viewed very positively by the Panel. The requirement for a narrower focus to succeed as a small Outstation is an opinion that I completely share and thus I am very happy to acknowledge the endorsement of the Panel. It was pointed out that the Group Leader recruitments planned for the near future should be leveraged as an opportunity to acquire expertise in areas of neurobiology complementary to those currently represented within the Unit, while at the same time exploiting EMBL Monterotondo's strengths in genetic and epigenetic regulation and in the generation and use of genetically engineered mouse models. I note and agree with the Panel's recommendation, and trust that it will be possible to identify excellent candidates with the right profile in the upcoming rounds of recruitment.

The Panel also recommended that special attention be given to the establishment of a better balance between genders at the faculty level in order to correct the current situation, which is characterised by the absence of a single female Group Leader. Both I and the management of EMBL Monterotondo are very aware of this problem, which we consider of the utmost importance. Ongoing and future search committees will consider this issue very seriously, and specific approaches to identify and attract qualified women have been implemented.

While noting a more equal distribution of grants amongst the individual Group Leaders in the Unit relative to the previous review period, the Panel felt that the overall level of external funding obtained by the groups at EMBL Monterotondo was low. While I agree that it is desirable to raise more external funding I point out that there are almost no opportunities for Outstation Group Leaders to access Italian national funding schemes

and that the Health Directorate of the European Commission, previously a major supporter of health-related research utilising the mouse model, has essentially stopped funding such research. Thus, apart from the ERC funding schemes, where the Unit has been successful, there are in fact very few opportunities for external funding.

A major concern in previous reviews of EMBL Monterotondo has been the limited interaction between the Unit and the Italian scientific community. As noted by the Panel, the situation in this respect has improved to some extent over the last four years thanks to new programmes and activities specifically promoted by the Unit leadership. While acknowledging and strongly supporting these initiatives, the Panel recommended that efforts be further intensified to create new and strengthen existing links with the Italian research community and to ensure the successful integration of EMBL Monterotondo in the surrounding scientific landscape. Several useful suggestions were provided, which I will discuss and follow up on with the Unit leadership.

It was the opinion of the Panel that mentoring of young Group Leaders within the Unit should be strengthened. This is an element of concern, particularly for young Group Leaders who, due to the timing of their recruitment, only undergo a full review several years into their tenure at EMBL. Following very fruitful discussions with the Panel during the review, I have consulted with EMBL scientific leadership and decided to establish an additional mechanism to recruit external expert mentors to advise (rather than evaluate) young EMBL Group Leaders on their research and career strategies. A detailed plan regarding the frequency and format of such meetings is being developed by a committee chaired by Cornelius Gross.

Finally, the predoctoral fellows on site reported on a lack of communication with the management of the Unit. Although the review inadvertently identified this as an issue, whereas the fellows had in fact failed to bring items that were of concern to them to the attention of management through any of the multiple existing routes of communication (direct discussion with or e-mail to either local or central EMBL management, the PhD and postdoctoral programme managers, the EMBL Staff Association, the Ombudsperson, etc.), I will ensure that the local Outstation management actively pursues this matter.

Professor Iain W. Mattaj, FRS
Director General

6 May 2016

Genome Biology Unit Review

The Genome Biology Unit at EMBL Heidelberg was reviewed on 17 to 19 May 2016 by a panel of 16 experts, including six members of SAC. The review was chaired by Olli Kallioniemi, Science for Life Laboratory, Karolinska Institute, Stockholm, Sweden.

Evaluation Summary

Overall, the Genome Biology Unit was rated as outstanding based on the quality of its research and its contribution to integrated activities in European life science research. The quality and quantity of its scientific output during the review period was considered exceptional. The Panel was impressed by the breadth of expertise and achievements within the Unit, with scientific highlights ranging from yeast genome biology, functional biology of structural variants of the human genome, computational strategies, chemical biology, microbiology, cancer and microfluidics, just to mention a few of the areas of interest. The level of external funding attracted by the Unit, particularly in the form of ERC grants, and the excellent career progression of postdoctoral fellows and Group Leaders upon leaving the Unit were also noted. Overall, the Head of Unit, the Director General and EMBL as a whole were congratulated on having assembled a world-class capability for genome biology.

The intensity of multidisciplinary interactions within the Genome Biology Unit, with other parts of EMBL and with the external research community was highlighted as a specific strength of the Unit. Particularly, scientific and technological interactions with EMBL-EBI have increased significantly since the last review, as computational approaches have become more and more central to the Unit's research. In this context the Panel was impressed by the number of joint appointments with Genome Biology of faculty from other EMBL Units, which reflects a response to the recommendations of previous evaluations, such as the recommendation to increase computational capabilities in the Unit. Since the last review the leadership of the Genome Biology Unit, previously shared with Senior Scientist Lars Steinmetz, has passed solely into the hands of Eileen Furlong. In addition to this change in leadership, the Unit has undergone moderate changes over the past four years, with one Group Leader departing the Unit and two new Group Leaders being hired. The recent nomination of an additional Group Leader to a University professorship creates the opportunity for a further new recruitment in the near future.

While recognising the Unit as extremely successful, the Panel provided suggestions regarding its future and long-term positioning, particularly in view of global developments in the rapidly growing field of genome biology. The Unit was encouraged to articulate a clearer vision and mission for the future, potentially developing a more targeted focus in specific niche areas of genome research rather than maintaining the current, more general approach.

Response to the Panel's Recommendations

I wish to thank the Panel for their time and considerable effort in reviewing the Genome Biology Unit. I am extremely pleased with the very positive assessment of the Unit's activities and appreciate the Panel's constructive feedback and recommendations with a view to further improving the Unit's future profiling.

The review panel stressed the importance of continuing to (re)define the Unit's vision and to specifically leverage Group Leader recruitments to gradually develop a narrower profile for the Unit. It suggested this was preferable to an alternative strategy, to use recruitments to bridge specific gaps in capabilities and technologies in the Unit. Given the limits to the size of EMBL Units, only few such positions will in any case be available. I agree that this is a constructive recommendation. Upon discussing the matter with the Head of Unit, it was agreed that future Group Leader recruitments in the Unit will, as in the past, focus on hiring outstanding scientists across the spectrum of genome biology that complement and synergise with existing groups rather than re-filling gaps that arise as individuals leave.

Related to the previous point, and given the fact that much of the research carried out in the Unit involves high-throughput methods and considerable data production, a question discussed by the Panel was whether the Genome Biology Unit should recruit additional Group Leaders who engage in large-scale biology and consortium science or continue with a mix of "big" and "small" science. This topic is of strategic importance, not just for the profile of the Genome Biology Unit but for the entire organisation, as it links to the overall role and positioning of EMBL. I therefore agree with the Panel that this issue requires careful consideration and should be carefully discussed together with other EMBL Units. In this context, I have initiated and will continue to promote in-depth discussions within the organisation on the balance in EMBL science between large-scale, including consortium, projects and more mechanistic studies. Following these internal discussions, this topic will be the subject of discussion with SAC at the next annual meeting. At present, however, I see the issue as one that requires striking a good balance between the two approaches rather than selecting one or the other.

I note that the Panel feels that, while the Unit has a significant impact in a number of fields, it is less present at Genome Biology meetings themselves. In my view this is more a semantic rather than a real problem (some panel members discussed the possibility of renaming the Programme) but I will bring this matter up with the Unit leadership.

It was felt by the Panel that more attention could be paid to the career development of young Group Leaders, both by fostering research collaborations and by active mentoring. I have been assured by the Unit leadership that every effort is made to promote collaboration and a uniform integration of all faculty members in the Unit, and special attention is dedicated by the Senior Scientists in the Unit to advise more

junior colleagues. I also note that one of the two Group Leaders on the basis of whom this comment was formulated has recently obtained an appointment elsewhere that the panel rightly regarded as prestigious. Career development and mentorship of young Group Leaders are considered a priority in the organisation and have recently been the object of in-depth discussions among EMBL scientific leadership. In addition to strengthening internal mentorship EMBL is in the process of introducing an external mentorship programme, by which young Group Leaders will benefit from informal advice from an established colleague in their field on their research and career strategies. Eileen Furlong, Head of the Genome Biology Unit, is an active member of the working group that is active in developing a detailed proposal for the structure of this programme and is committed to its success.

Finally, an issue raised by the Panel in view of concerns voiced in particular by the predoctoral fellows regards the possibly excessive focus by Group Leaders in the Unit on publishing in the very limited number of journals of the highest impact, which may delay publication of results due to lengthy submission/revision/acceptance processes. This may become detrimental to PhD students (and to a lesser extent also to postdocs), whose chances to successfully compete for future fellowships and positions depend on obtaining publications during the period of their fellowship. Similar concerns have arisen in more than one EMBL Unit evaluation in recent years. Following recommendations from the Review Panels, I have repeatedly encouraged Group Leaders to discuss publication strategies openly and transparently with the members of their groups, and to balance the desirability of publishing in top journals with the need of fellows to publish in a timely manner. It is my intention to monitor closely that these recommendations are followed to avoid any adverse effects on fellows' career opportunities. In order to analyse and review the situation in the different Units, and to facilitate discussion with the review panels on this topic, it was decided that publication statistics for fellows will be provided to future review panels as part of the background documentation for Unit reviews. These will include detailed information on the number of predoctoral and postdoctoral fellows that have left the Unit over the last review period and their publication record during their time at EMBL and for a limited period (6-12 months) thereafter. In this way, more focussed attention can be brought to cases where fellows have had to leave prior to publication and the reasons for such cases be discussed on the basis of concrete information.

To summarise, I wish to congratulate the Unit on a very strong performance in the last review period. In particular, credit should go to Eileen Furlong and Lars Steinmetz for their initial decisions on how to shape the Unit and to Eileen for her continuing leadership success.

Professor Iain W. Mattaj, FRS
Director General

13 June 2016

Publisher
EMBL

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Design
Edenspiekermann, Amsterdam

Printed by
ColorDruck Solutions, Leimen

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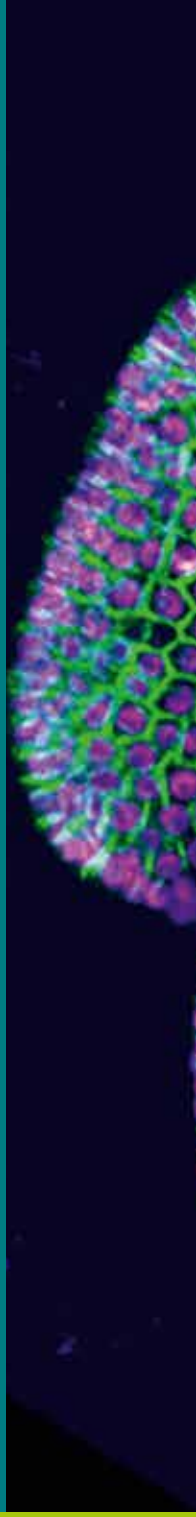

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