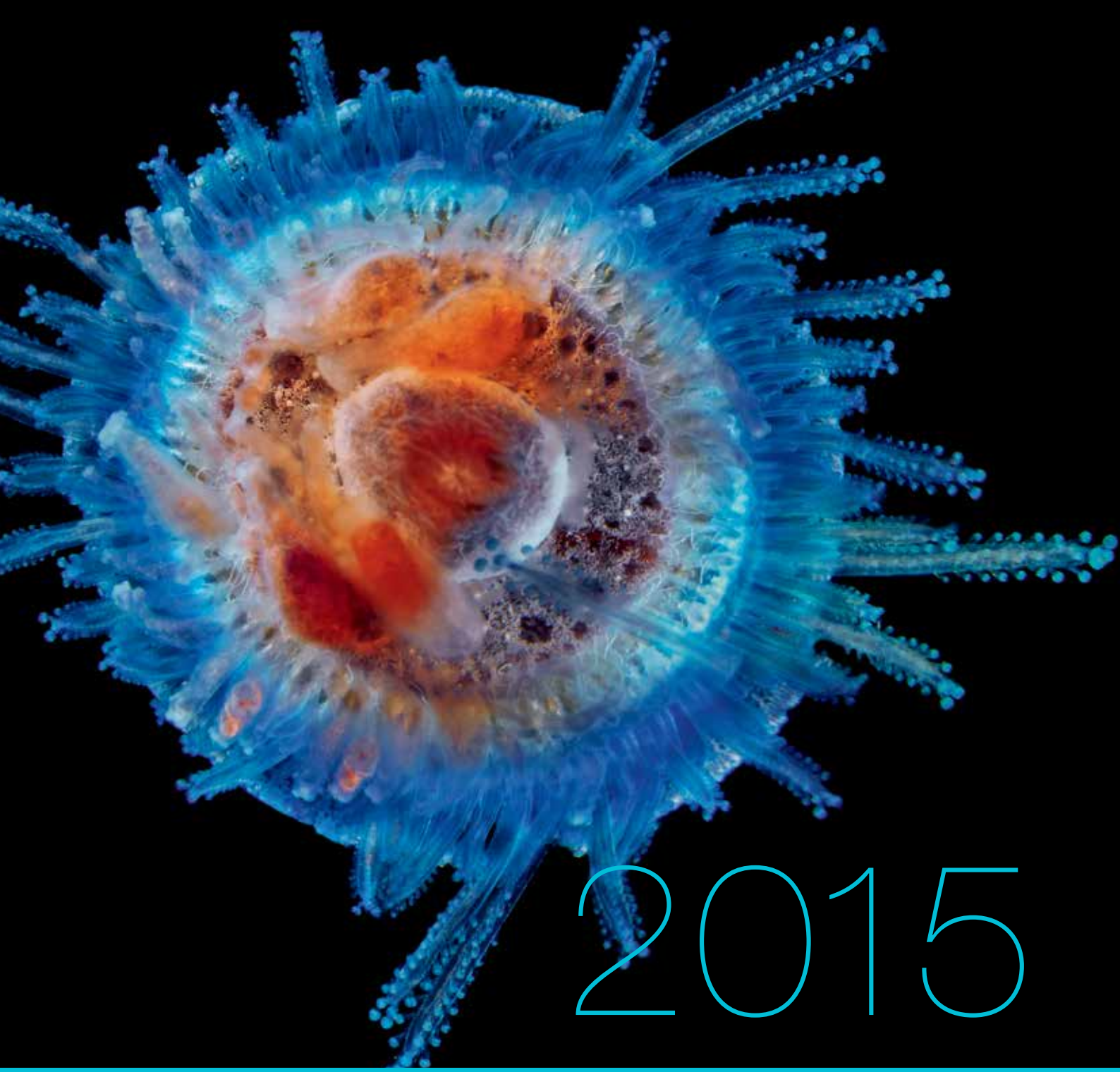


2015

Annual Report

EMBL

Cover image

Microscopic marine life – like this Cnidarian, Porpita *– came into sharp focus as a result of the TARA Oceans expeditions (photo C. Sardet/CNRS/TARA Oceans).*

Contents

Foreword

2015 was a year to prepare for new challenges ahead. Scientists from across EMBL contributed to the development of a strategic roadmap for 2017–2021 and the entire EMBL community will, I'm sure, drive its success. This ambitious plan will focus on our strengths in digital biology and on developing our services portfolio in a way that complements national activities and maximises value to member states.

The past year also saw some important changes in the EMBL leadership as Janet Thornton stepped down as Director of EMBL-EBI and we said goodbye to Administrative Director, Keith Williamson. I would like to pay tribute to their work and express my support and trust in their successors.

Janet's clear scientific vision, talent in recruiting and developing the best people, commitment to excellence and her passion for science led EMBL-EBI through an astonishing period of growth during her tenure. This was a growth in numbers, but also in the reputation and importance of EMBL-EBI to life-science researchers throughout the world. She is a role model for all of us in the scientific community, where women are sorely underrepresented at senior levels. Janet's legacy at EMBL-EBI has found the most capable stewards in Rolf Apweiler and Ewan Birney, who take over as Joint Directors.

Keith's extensive contributions to EMBL over the past 14 years were marked by collegiality, friendliness and a wry sense of humour. EMBL Administration is now in capable hands as Christian Scherf takes the baton from Keith, joining the EMBL family alongside many new colleagues who bring fresh energy and inspiration to us all.

Our incredible people bring the ideas, tenacity and infectious enthusiasm that enable EMBL's great science. I am confident that they will drive the realisation of our ambitious plans to lead basic life-science research into the era of digital biology.

Iain Mattaj

Research Highlights

"People here really try to answer the big questions, and I find that really inspiring!"

Kim Remans, Head of Protein Expression and Purification Core Facility

EMBL had its eyes fixed on the future in 2015 with scientists from across the organisation contributing to the vision that has been laid out in the next EMBL Programme, which defines EMBL's strategy and directions for 2017–2021. Under the theme "Digital Biology", the Programme illustrates how EMBL will build on its strengths to address major upcoming challenges in life-science research by: bridging scales of biological organisation through integrated imaging approaches; exploiting the wave of big data generated by new technologies; and reaping the benefits of molecular biology to understand and improve human health and well-being. After being reviewed and endorsed by EMBL's Scientific Advisory Committee, the draft EMBL Programme was presented to EMBL Council in November along with the Indicative Scheme, EMBL's indicative five-year budget. The approval of both documents by Council is expected at the end of 2016.

The following research highlights of 2015 are a preview of the digital biology research in which EMBL scientists will engage in the future.

Science dedicated a special issue to the results of the TARA Oceans expedition

Directors' Research

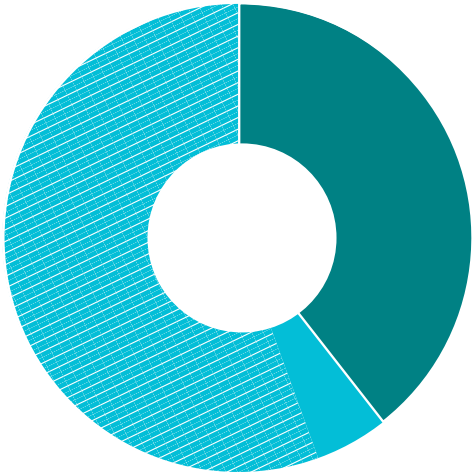
Eric Karsenti, former Head of EMBL's Cell Biology and Biophysics Unit and visiting scientist at EMBL, led an international, interdisciplinary team of scientists who comprise the TARA Oceans expedition. The team published an unprecedented and comprehensive view of microscopic ocean life in a special issue of the journal Science dedicated to the initial results from the project. This three-year sailing expedition around the globe aimed to shed new light on the relatively unknown world of plankton, analyse the effects of climate change on marine biodiversity and increase general awareness about environmental issues. The five research papers in the special issue of Science – along with the accompanying materials and underlying data – provide valuable resources to delve deeper into this underwater realm. These include a catalogue of 30 million new genes developed by Peer Bork's group, which indicates that at depths still reached by sunlight, temperature is the main factor that influences the composition of plankton communities – a result of obvious importance in the light of global warming.

Special issue: TARA Oceans. *Science*, 22 May 2015. Vol 348, Issue 6237

The group of Maria Leptin, the Director of EMBO, studies the very early processes of life. During development, the embryo of most animals – including humans – goes through a stage when cells on the embryo's surface must fold inwards to create layers of tissue that will give rise to muscles, bones and other organs. Using the multiview selective plane illumination microscopy (Muvi-SPIM) technique developed by Lars Hufnagel's group, Leptin's group showed that cells throughout the whole embryo play a part in this process, and that it is dependent on the mechanical properties of these cells such as their stiffness.

Rauzi M *et al.* (2015) Embryo-scale tissue mechanics during Drosophila gastrulation movements. *Nat Commun* 6:8677. doi: 10.1038/ncomms9677

Scientific Publications in 2015



273 By EMBL

422 By EMBL in collaboration with over 500 organisations worldwide

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

695 Total

EMBL-EBI

EMBL's European Bioinformatics Institute (EMBL-EBI) saw a change in leadership as Janet Thornton stepped down as Director after 14 years and former Joint Associate Directors Ewan Birney and Rolf Apweiler were appointed as Joint Directors in July. Ewan and Rolf now share the responsibility for all aspects of EMBL-EBI, including research, services, training, industry engagement and European coordination.

The 1000 Genomes Project, the most comprehensive fully open survey of human genetic variation ever performed, announced its final set of results in 2015. The project exceeded its original aim by studying the DNA of more than 2500 people rather than the 1000 originally envisaged, and has given unprecedented insights into the genetic differences that make each of us unique. Among its outcomes is the most extensive catalogue to date of structural variations, which are changes in large sections of a person's DNA sequence. Created by Jan Korbel's and Oliver Stegle's groups in a collaboration between EMBL Heidelberg's Genome Biology Unit and EMBL-EBI, this reference catalogue shows that a missing gene may be less problematic than one might think. In charting how structural variations vary in populations across the globe, the catalogue will help guide future studies of genetics, evolution and disease. But the 1000 Genomes Project's most important legacy lies in the methods and technological innovations that made the work possible and these are transforming how genetic and genomic research is carried out around the world.

1000 Genomes Project Consortium. (2015) A global reference for human genetic variation. *Nature* 526:68-74. doi: 10.1038/nature15393

Sudmant PH *et al*. (2015) An integrated map of structural variation in 2,504 human genomes. *Nature* 526:75-81. doi: 10.1038/nature15394

Sarah Teichmann led her group and colleagues at the Wellcome Genome Campus, the University of Cambridge, the University of Oxford and the

University of Edinburgh in publishing the Periodic Table of Protein Complexes. By offering a new way of looking at the enormous variety of structures that proteins can build in nature, postulating which ones might be discovered next, and predicting how entirely novel structures could be engineered, the Table provides a valuable tool for research into evolution and protein engineering.

Ahnert SE *et al*. (2015) Principles of assembly reveal a periodic table of protein complexes. *Science* 350:aaa2245. doi: 10.1126/science.aaa2245

EMBL Monterotondo

Neuropathic pain is a severely impairing, mostly chronic disease caused by a nerve lesion, but intact neurons adjacent to the lesion also play a part. Paul Heppenstall's group developed a new approach to clearly distinguish between damaged neuropathic neurons and "bystanders" by combining differential fluorescent neuronal labelling and fluorescence-activated cell sorting (FACS). This will help scientists to determine how each group of cells contributes to the disease.

Reinhold AK *et al*. (2015) Differential transcriptional profiling of damaged and intact adjacent dorsal root Ganglia neurons in neuropathic pain. *PLoS One* 10:e123342. doi: 10.1371/journal.pone.0123342

Structural and Computational Biology

In the field of structural biology, cryo-electron microscopy (cryo-EM) is becoming increasingly important. This is a type of electron microscopy in which samples are kept below freezing, which holds the structures in place and preserves their form. Recent technological developments are pushing the resolution of cryo-EM to a point where it can be used to determine the structure of molecules that crystallographers have been grappling with for years.

Christoph Müller's and Carsten Sachse's groups, for instance, used cryo-EM to determine the first high-resolution structure of RNA polymerase III, the largest and most elusive of the RNA polymerases that produce RNA from DNA. For Martin Beck's group, the technique has enabled them to obtain an ever-deeper view of the structure of the nuclear pore, which constitutes the gateway to the nucleus and is the largest protein complex in human cells.

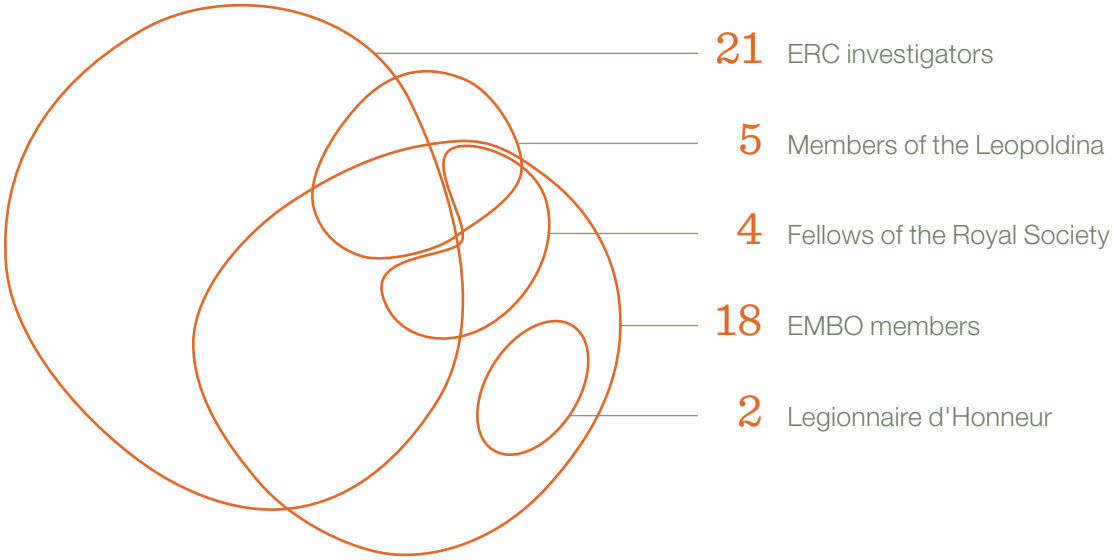
Hoffmann NA *et al.* (2015) Molecular structures of unbound and transcribing RNA polymerase III. *Nature* 528:231-6. doi: 10.1038/nature16143

von Appen A *et al*. (2015) In situ structural analysis of the human nuclear pore complex. *Nature* 526:140-3. doi: 10.1038/nature15381

Moving from molecules to whole organs, the Beck group also took a comprehensive approach to measure and compare just how ageing affects liver and brain cells in the rat. Together with collaborators at the Salk Institute and the University of California, Berkeley, they combined

Awards and honours

Excellent scientists in numbers



Award Highlights 2015

John Briggs
EMBO member

Detlev Arendt
EMBO member

Stephen Cusack
Fellow of the
Royal Society

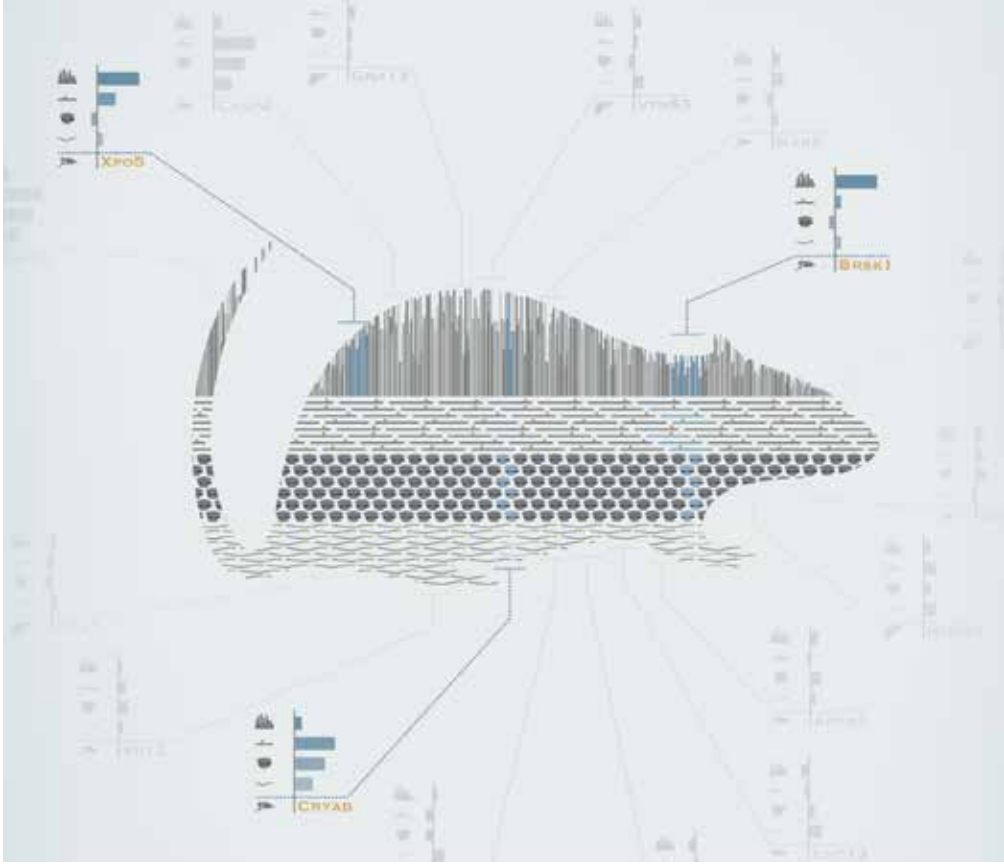
Jan Korbel
Member of the
Leopoldina

Sarah Teichmann
EMBO Gold Medal

Anne Ephrussi
Legionnaire d'Honneur

Eric Karsenti
CNRS Gold Medal

transcriptomics, proteomics and other approaches to tease out general ageing processes from those that are specific to each of these organs.
Ori A *et al.* (2015) Integrated transcriptome and proteome analyses reveal organ-specific proteome deterioration in old rats. *Cell Sys* 1:224-37. doi: 10.1016/j.cels.2015.08.012



The Beck group combined data from a variety of techniques to better understand how rats – and humans – age

From repairing damage to transporting materials, there are a number of tasks that require a cell to sense changes in the membranes that partition off compartments such as the nucleus, and in the membrane that encloses the cell itself. It does so through proteins that dock onto the membrane – but many of these proteins bind to lipids that occur in several membranes, so it was unclear how they "know" which particular membrane to bind to at a particular time. Anne-Claude Gavin's group developed a new approach to answering this question, together with the labs of Peer Bork and Jan Ellenberg. They found that lipids known as PIPs act as flags that say "This is the membrane" and a second lipid pinpoints further: "This is the section of membrane to bind to now."

Vonkova I *et al.* (2015) Lipid cooperativity as a general membrane-recruitment principle for PH domains. *Cell Rep* 12:1519-30. doi: 10.1016/j.celrep.2015.07.054

Cell Biology and Biophysics

Cryo-EM techniques have also enabled EMBL scientists to shed new light on endocytosis, the process by which cells engulf and "swallow" molecules. Marko Kaksonen led a cross-disciplinary team – including Carsten Sachse's and John Briggs' groups in the Structural and Computational Biology Unit and Rob Meijers' group at EMBL Hamburg, as well as the Protein Expression and Purification Core Facility and the European X-ray Free Electron Laser (XFEL) in Hamburg – in a study that showed that for the cell membrane to bend inwards to "swallow" materials, a group of proteins called clathrin adaptor proteins are essential.

Avinoam O *et al.* (2015) Endocytic sites mature by continuous bending and remodeling of the clathrin coat. *Science* 348:1369-72. doi: 10.1126/science.aaa9555

In the realm of light microscopy, Rainer Pepperkok's team and collaborators in the Molecular Medicine Partnership Unit (p. 31) developed a new approach that takes scientists a step beyond gene-sequencing studies, enabling them to pinpoint which rare genetic variants cause a disease. The method also allows researchers to draw meaningful conclusions from smaller sample sizes, which is especially important in the context of relatively rare diseases.
Thormaehlen AS *et al*. (2015) Systematic cell-based phenotyping of missense alleles empowers rare variant association studies: a case for LDLR and myocardial infarction. *PLoS Genet* 11:e1004855. doi: 10.1371/journal.pgen.1004855

EMBL Hamburg

Despite decades of considerable global research efforts, how *Mycobacterium tuberculosis* – the bacterium that causes tuberculosis – infects and survives in the human body is still largely a mystery. Matthias Wilmanns at EMBL Hamburg teamed up with the Sachse group in Heidelberg and various specialists across four European countries to tackle the issue. They focused their efforts on the bacterium's cell wall, which is a waxy protective layer that could enable the microbe to remain dormant in a patient for years, and as such is a potential drug target. They discovered that the cellular machine known as AccD1-AccA1 had been wrongly assumed to make the wall's building blocks. As it turns out, it is involved in the degradation of one of the building blocks used to make proteins instead.
Ehebauer MT *et al*. (2015) Characterization of the mycobacterial acyl-CoA carboxylase holo complexes reveals their functional expansion into amino acid catabolism. *PLoS Pathog* 11:e1004623. doi: 10.1371/journal.ppat.1004623

Scanning electron micrograph of Mycobacterium tuberculosis bacteria, which cause TB

Clostridium bacteria are involved in a variety of human diseases, like the *C. diff (Clostridium difficile)* infections which are becoming a serious problem in hospitals and healthcare institutes. Investigating viruses that infect *Clostridium* bacteria, Rob Meijers and collaborators provided insights into how viral enzymes degrade their cell wall, and could potentially be used to combat a range of infections.
Dunne M *et al*. (2015) Crystal structure of the CTP1L endolysin reveals how its activity is regulated by a secondary translation product. *J Biol Chem* 291:4882-93. doi: 10.1074/jbc.M115.671172

Developmental Biology

Anne Ephrussi's group, in collaboration with the Müller lab, determined the structure of two sections of the Oskar protein, which is known to be essential for fruit fly development. By enabling scientists to see how the different parts of the protein function, this advance could help to explain its role in healthy sperm and egg production and embryonic development, not only in fruit flies but also in other organisms as many animals – including humans – produce parts of the Oskar protein.

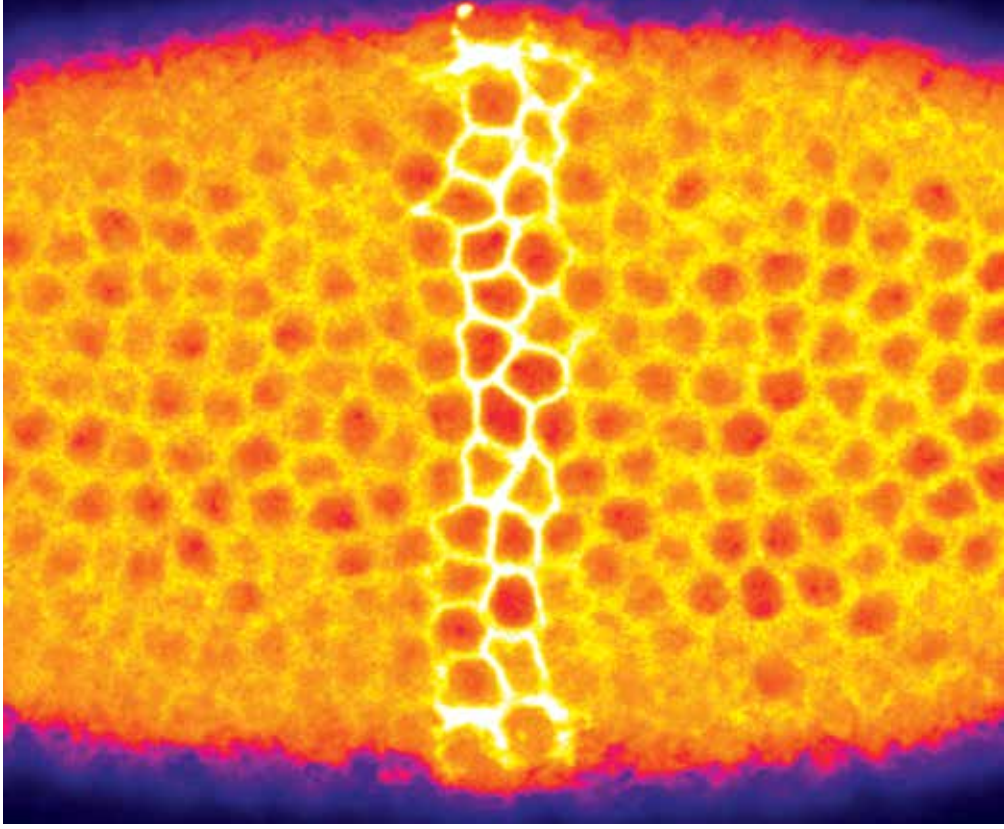


Image of a fruit fly embryo taken using a new microscopy technique that uses a laser to interact with cells

Jeske M *et al.* (2015) The crystal structure of the drosophila germline inducer Oskar identifies two domains with distinct vasa helicase- and RNA-binding activities. *Cell Rep* 12:1-12. doi: 10.1016/j.celrep.2015.06.055

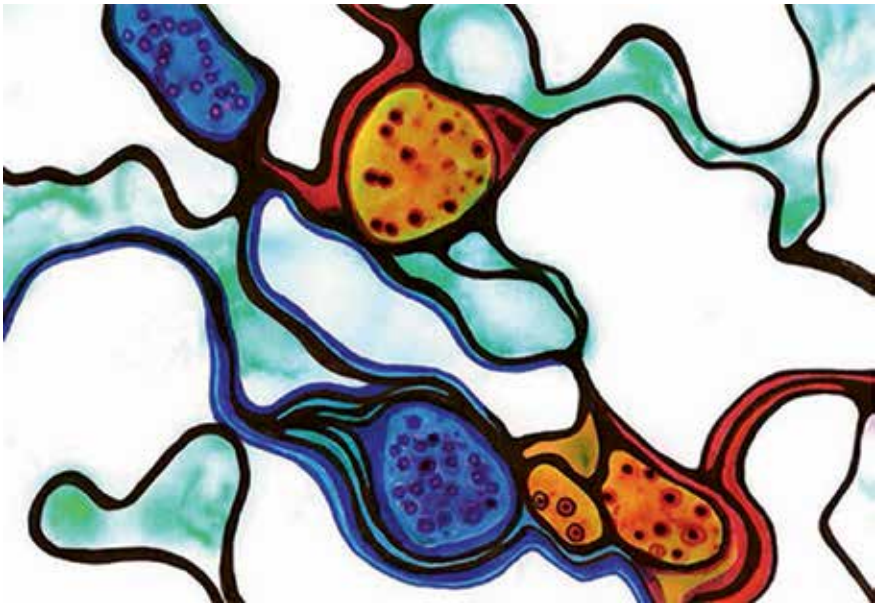
Thanks to a new technique that uses a laser as a remote control, Stefano De Renzis' group has identified a particular group of cells that are crucial for the tissue in a fruit fly embryo to fold inwards to form the animal's gut. They also showed for the first time that the shape in which cells are arranged determines the direction in which they contract.

Guglielmi G *et al.* (2015) An optogenetic method to modulate cell contractility during tissue morphogenesis. *Dev Cell* 35:646-60. doi: 10.1016/j.devcel.2015.10.020

Genome Biology

The T cells that help track down and eliminate disease-causing microbes must be able to distinguish between invaders and the body's own cells. As they mature, T cells travel from the bone marrow to the thymus, where they are trained not to react to markers called self-antigens that are produced by cells in the body. The "trainer" thymic cells thus need to express additional genes for the markers found in other tissues. Lars Steinmetz's groups at EMBL and Stanford University, working with Wolfgang Huber's group and collaborators at the German Cancer Research Centre (DKFZ), found that these "extra" genes are not random as they tend to be located close to each other in the genome.

Brennecke P *et al.* (2015) Single-cell transcriptome analysis reveals coordinated ectopic gene-expression patterns in medullary thymic epithelial cells. *Nat Immunol* 16:933-41. doi: 10.1038/ni.3246



Artistic impression of cells in the thymus expressing different combinations of genes

As part of another international team of researchers, scientists from the Korbel group identified key genetic specificities of an incurable subtype of acute lymphoblastic leukaemia (ALL), the most common form of cancer in children, as well as a small molecule that proved effective against the tumour cells in a drug-screening assay.
Fischer U *et al*. (2015) Genomics and drug profiling of fatal TCF3-HLF-positive acute lymphoblastic leukemia identifies recurrent mutation patterns and therapeutic options. *Nat Genet* 47:1020-9. doi: 10.1038/ng.3362

EMBL Grenoble

Stephen Cusack's group unveiled the first detailed 3D structure of the polymerase – the machinery that copies genetic material – of the La Crosse orthobunyavirus (LACV), a virus that can cause human encephalitis. LACV is in the same broad group of viruses as influenza and the findings show that the LACV polymerase has striking similarities to the influenza virus polymerase, the atomic structure of which was previously determined by the same team.
Gerlach P *et al*. (2015) Structural insights into bunyavirus replication and its regulation by the vRNA promoter. *Cell* 161:1267-79. doi: 10.1016/j.cell.2015.05.006

Thanks to a technique developed in their lab a few years ago, Imre Berger's group obtained the first experimental proof that the key cellular machine TFIID – a central regulator of human gene transcription – is formed from pre-assembled modules. These findings support the idea that first determining how the cell builds a complex can help to explain how it works.
Trowitzsch S *et al.* (2015) Cytoplasmic TAF2-TAF8-TAF10 complex provides evidence for nuclear holo-TFIID assembly from preformed submodules. *Nat Commun* 6:6011. doi: 10.1038/ncomms7011

Services

"The UniProtKB database is the engine that makes work on less-studied organisms possible. Our research programme would collapse without it."

Anonymous researcher, "The Value and Impact of the European Bioinformatics Institute" report

Bioinformatics Services

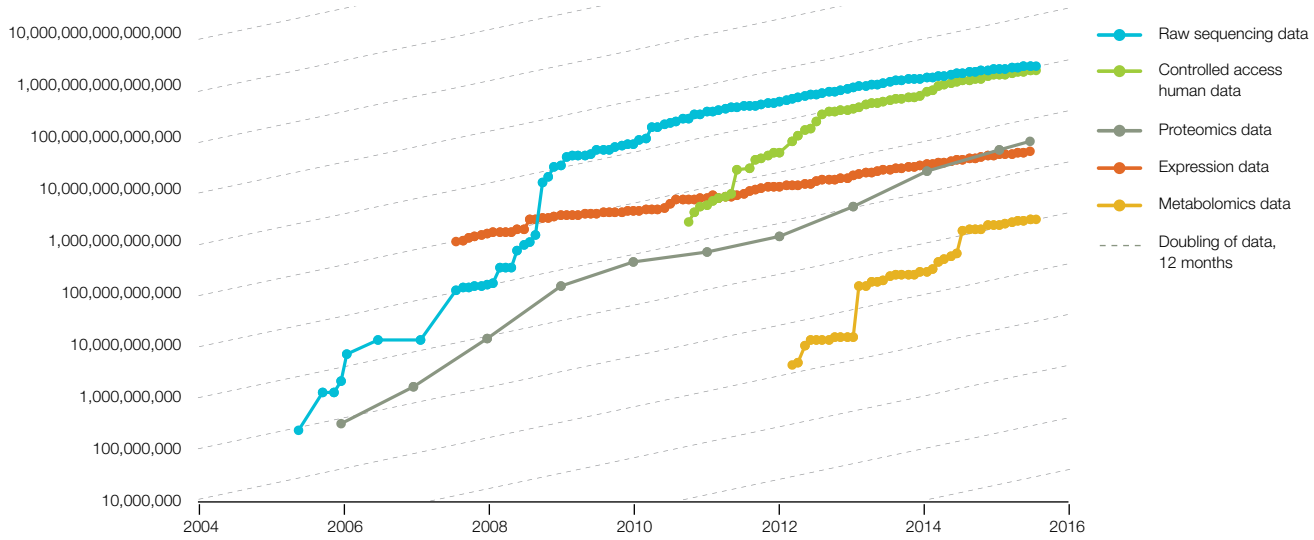
EMBL-EBI provides access to crucial biomolecular data for academic and commercial researchers throughout the world. While advances in life-science technologies enabled scientists to generate vast quantities of data on living systems, EMBL-EBI kept pace, with its storage capacity meeting demand and the use of its resources soaring to over 560 million requests a month on the ebi.ac.uk domain alone (see graph, p. 14). Here, we report on a selection of data resources in 2015; a comprehensive update can be found in the EMBL-EBI Annual Scientific Report.

Perhaps the most important legacy of the 1000 Genomes Project (p. 6), which wrapped up in 2015, is the methods and technological innovations that enabled the work, and transformed how genomic research is done around the world. More than 2500 datasets were generated through the project and these have been updated to reflect the latest human reference assembly, published and made available through Ensembl and the European Variation Archive (EVA).

The Genome-Wide Association Study (GWAS) Catalogue – originally developed by the National Human Genome Research Institute (NHGRI) in the USA and jointly curated by NHGRI and EMBL-EBI – helps researchers discover associations between DNA sequences and traits such as disease

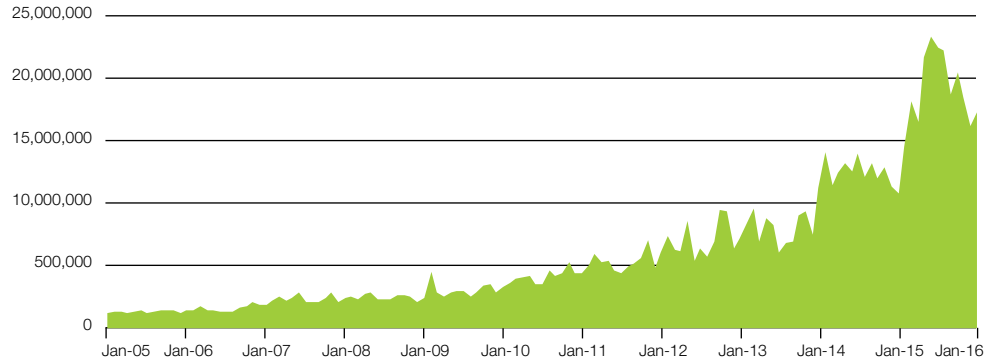
Growth of data by type

Volume of data (bytes)



Usage of EMBL-EBI Websites

Requests per day, 2005 through 2015



propensity. In 2015, the GWAS Catalogue moved to EMBL-EBI and was relaunched with a completely new scientific and technical infrastructure. The resource now provides enriched, ontology-driven search tools and improved visualisation of complex information.

The rapid, early sharing of pathogen surveillance data and related information is crucial during disease outbreaks, and in 2015 the European Nucleotide Archive (ENA) facilitated such sharing in the EU-funded COMPARE project. Working to provide the infrastructure needed to support sharing and analysis of incoming data from the consortium and beyond, EMBL-EBI developed new "Data Hubs" and established a cloud-compute environment. These and future developments will make it easier for researchers to track and rapidly share information about viruses such as influenza, Ebola and Zika.

To support the growing 3D electron microscopy user community, the Protein Data Bank in Europe (PDBe) launched a completely redesigned, interactive website. Its powerful search functionality and sophisticated tools for analysis optimise the resource for structural biologists, and its highly visual approach makes exploration of high-resolution structural data more accessible for users that are new to the field.

The IntAct database for molecular interactions launched the Complex Portal, a manually curated, encyclopaedic resource of macromolecular complexes from key model organisms, featuring an innovative graphical tool for visualising complex topology and stoichiometry.

EMBL-EBI offers comprehensive, high-quality data resources covering the full spectrum of molecular biology, including life-science literature through its management of Europe PubMed Central (Europe PMC). This is a publicly accessible literature resource that contains more than 3.5 million full-text research articles and was visited by users via over 10 million unique IPs in 2015. Europe PMC was also awarded continued funding from the Wellcome Trust, with participation from 26 other life-science funders, to support its development during the period 2016–2021.

A commitment to making biomedical data openly available for the benefit of the entire scientific community is the cornerstone of EMBL-EBI's activities. The value and impact of open data were underlined in 2015 by a large-scale externally performed analysis of the institute's impact. The report included a survey of over 4000 data service users, 45% of whom indicated that they "could neither have created nor collected the data they used themselves, nor obtained it elsewhere". The findings demonstrate the vital role of open, public data in life-science research and conclude that the sums invested in EMBL-EBI by the member states, the UK as EMBL-EBI's host country, and other funders produce a hugely beneficial return.

Structural Biology Services

EMBL provides vital services and facilities to the scientific community in its member states from its two structural biology Units in Hamburg and Grenoble, which operate integrated infrastructures for life-science applications using synchrotron radiation. In 2015, the beamlines for macromolecular crystallography (MX) and small angle X-ray scattering (SAXS), operated in close collaboration with the German Electron Synchrotron (DESY) and the European Synchrotron Radiation Facility (ESRF) in Hamburg and Grenoble respectively, jointly attracted over 3000 user visits. Beamlines at both sites are complemented by advanced facilities for biological sample preparation, characterisation and crystallisation. In addition, computational resources and software packages for structural data analysis developed at EMBL serve a rapidly growing community of several thousand users worldwide.

EMBL Hamburg and EMBL Grenoble participate in iNEXT, an initiative funded by the European Commission (EC) that was launched in 2015 to provide transnational access to state-of-the-art structural biology infrastructures for European scientists working in the area of translational research. In this context, the two sites offer access to services, expertise and user training across the entire structural biology workflow. The Electron Microscopy Core Facility and the Advanced Light Microscopy Facility at EMBL Heidelberg also participate in iNEXT and provide access to EM-based structure determination methods and advanced imaging services for validating structure-based predictions of biological function.

EMBL Hamburg

EMBL Hamburg has designed, built and 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. EMBL staff and scientists reconstructed and upgraded these beamline environments during the PETRA III shutdown from early 2014 to April 2015. The improved features of the MX beamlines P13 and P14 increase the accuracy for solving structures using small crystals and reduce the time required for high-quality data collection. The SAXS beamline P12 environment was redesigned and optimised to boost the intensity of the X-ray beam and enable rapid time-resolved scattering experiments. These enhancements were complemented by the implementation of an automated pipeline for purification, biophysical and X-ray analysis of bio-macromolecular solutions.

By offering beamline users protocols for sample optimisation and a suite of biophysical methods to best characterise their samples, the sample preparation and characterisation facility has enabled important breakthroughs in 2015, including ones by researchers without prior expertise in structural biology. The high-throughput crystallisation facility doubled its activity relative to previous years, preparing and imaging more than 1500 plates that could be remotely controlled through a web-based platform. A new service to crystallise membrane proteins using specialised crystallisation screens was introduced, which yielded the first successful X-ray structure of an integral membrane transporter protein in September.

In addition to maintaining and further developing research infrastructures, EMBL Hamburg engages in forward-looking co-operations with its key partners, including DESY, the European XFEL, the University Clinical Centre UKE, and the Centre for Structural Systems Biology (CSSB). As a consortium of nine research partners from northern Germany, the CSSB brings together structural biology, infection biology and systems biology approaches to uncover the mechanisms underlying infection and to discover more effective treatments against bacterial and viral pathogens. Under the leadership of Matthias Wilmanns, Head of EMBL Hamburg and Scientific Director of the CSSB, this joint initiative saw some key developments in 2015, as the Centre recruited new members to its faculty, held its first international symposium Systems in Infection Biology – from

Celebrating 40 years of EMBL Grenoble: Stephen Cusack (left), Head of Outstation, and EMBL Director General Iain Mattaj

Molecules to Organisms, and organised a Spring School that attracted PhD and postdoctoral fellows from across the world. In September, the CSSB also celebrated an important milestone with the topping out ceremony of its joint research building that is under construction on the DESY campus.

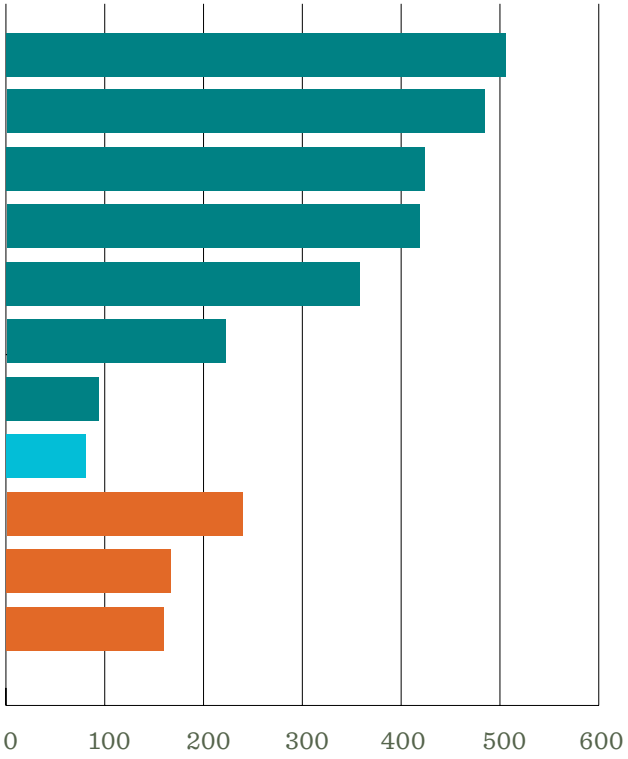
EMBL Grenoble

In June 2015, EMBL Grenoble celebrated four decades of successful service provision and scientific breakthroughs with its 40th Anniversary Symposium, which brought together staff, alumni, and facility users. Since 1975, EMBL Grenoble has been active in the design, construction, operation and development of synchrotron beamlines for MX and SAXS, as well as in the development of cutting-edge structural biology instrumentation.

User operation at the new MX beamline ID30B, operated by the EMBL-ESRF Joint Structural Biology Group, started in June 2015. This marked an important development in the services offered to EMBL's international user community. ID30B was the last structural biology beamline to be constructed within the ESRF Upgrade Programme Phase I and enables data collection from very small crystals. Since it became available, the ID30B beamline has enabled researchers to solve several new biological structures.

The first Massively Automated Sample Selection Integrated Facility-1 (MASSIF-1), inaugurated at the end of 2014, is a unique facility for the high-throughput, fully automatic characterisation and data collection of macromolecular crystals. In September 2015, less than one year after the beamline became operational, MASSIF-1 processed its 10 000th crystal, proving its remarkable efficiency and value to the scientific community. The CrystalDirect system for automated harvesting and crystal manipulation, recently developed at EMBL, also became available to the wider user community in 2015 at the High-Throughput Crystallisation Laboratory of EMBL Grenoble. The combination of the CrystalDirect and MASSIF technologies now enables EMBL to offer users a complete, fully automated and remotely operated MX workflow that provides a valuable tool for

Users of EMBL Beamlines
in 2014



504	ID23-1
486	BM29 SAXS
425	ID23-2
420	ID29
359	ID30A-3
222	ID30B
94	ID30A-1
81	BM14
240	P12 SAXS
167	P14
160	P13
3158	TOTAL

- Operated by ESRF with EMBL Grenoble
- Operated by EMBL, ESRF and the Indian Department of Biotechnology
- Operated by EMBL Hamburg (shutdown January–April and November–December 2015)

challenging crystallography projects, particularly in the context of structure-guided drug design.

Core Facilities & IT Services

By providing easy access to diverse cutting-edge technologies and accompanying expertise, EMBL's Core Facilities play a crucial role in enabling scientists from EMBL and its member states to achieve their ambitious research goals. EMBL's most recent facility, the Metabolomics Core Facility, provides a comprehensive infrastructure and service for the analysis of metabolites and lipids in several biological systems. Since it began with a pilot operation for internal users in October 2015, its services have been in high demand.

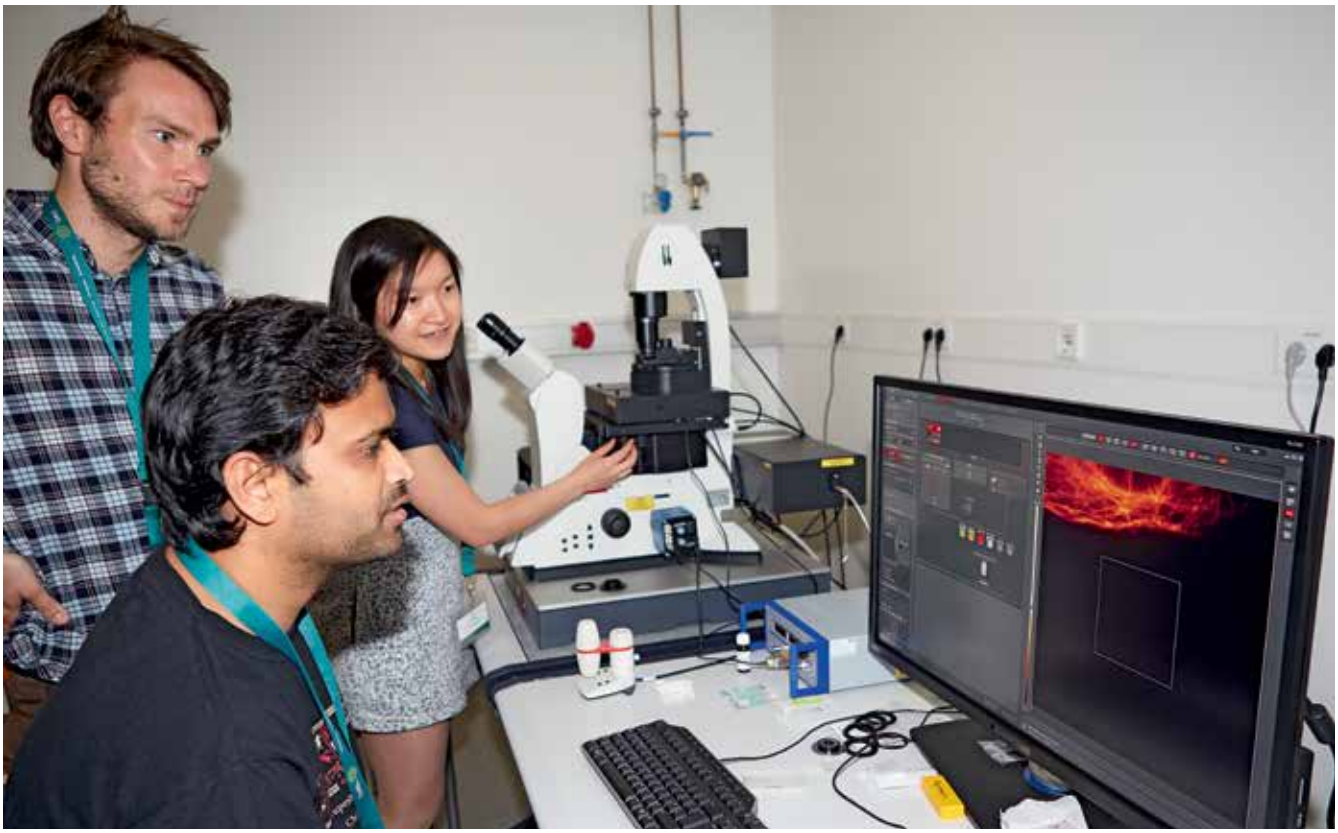
The Core Facilities contribute significantly to EMBL's training activities and organise internal and external training courses and workshops, often in collaboration with academic or industrial partners. In 2015, 18 internal and 18 international courses were organised by the staff of different Core Facilities. Prominent examples are the one-week Signalife course for international students, organised by the Genomics and Proteomics Core Facilities in collaboration with the University of Nizza, and the second EMBL Advanced Course on Super-Resolution Microscopy, jointly organised by the Advanced Light Microscopy Core Facility and its corporate partner, Leica Microsystems.

In addition to organising formal training activities, EMBL's Core Facilities staff share their expertise with users who visit the facilities to advance their research projects. The Christian Boulin Fellowships, established in honour of EMBL's former Director of Core Facilities and Services, were introduced as a new instrument to support young investigators from EMBL member states to visit the Core Facilities and learn the latest scientific techniques. In response to the first call in 2015, 11 Christian Boulin Fellowships were granted, which enabled visiting scientists from eight countries to visit five different Core Facilities.

As research in the life sciences becomes more and more data-driven, EMBL's IT services constantly strive to provide the best services and tools to researchers at EMBL. Recent efforts aimed at developing an EMBL-wide infrastructure to support large-scale management, analysis, visualisation and sharing of 3D imaging data represent only one example.

EMBL is a co-founder and the life-science flagship of Helix Nebula, a European consortium of over 40 academic and industry partners aimed at establishing a pan-European cloud infrastructure for science. In October 2015, EMBL hosted the Helix Nebula Data+ Workshop to explore with the EIROforum organisations (p. 33) and other research partners future models of cloud infrastructures to support big data analysis across different scientific domains. The new HNSciCloud project to build a hybrid public–commercial cloud platform for Europe's research communities received funding from the EC in 2015. In an effort led by EMBL-EBI, EMBL is participating in the new project with three use cases.

Participants of an EMBL advanced course on Super-Resolution Microscopy



Technology

Development and Transfer

"Being incubated at EMBL is a win-win situation: scientists have access to new technologies, and we can test and improve with our intended users."

Christoph Antz, CEO of EMBL spin-off Luxendo

Technology Development

EMBL has an extensive record of developing new biology-driven technologies, as our scientists frequently push the limits of technology to answer challenging biological questions. In addition to experimental technologies, EMBL is highly active in developing new bioinformatics and computational tools for life-science research. Many of the instruments and methods developed at EMBL are of benefit to the broader scientific community and are made available to the users of EMBL's bioinformatics and structural biology services or through EMBL's Core Facilities.

A traditional strength of EMBL lies in the development of novel tools and technologies for biological imaging. Prominent examples in 2015 were major advances in the area of light-sheet microscopy, a technology that enables scientists to observe living cells in three dimensions for extended periods of time at high resolution. Thanks to these newly developed techniques, which carry significant commercial potential (p. 22), EMBL scientists in Heidelberg were able to observe the initial phases of mouse embryonic development for the first time. Major technological progress was

also seen in the area of fluorescence correlation spectroscopy for the high-throughput analysis of protein dynamics in living cells.

In the field of synchrotron instrumentation for structural biology, development of the FLEX sample changer technology was finalised with the debut of the FlexED8 sample changer. Initiated in 2011, this technology is now on the way to commercialisation in collaboration with industry.
In 2015, EMBL was also involved in evaluating the performance of and further developing innovative DNA-sequencing technologies. In particular, the MinION™ – a new commercially developed handheld sequencing device – was evaluated by an open, international consortium co-ordinated by EMBL-EBI.

Technology Transfer

The transfer of discoveries and innovative technologies developed from basic research at EMBL to industry is facilitated by EMBL's commercial arm EMBLEM Technology Transfer GmbH. Established in 1999, EMBLEM currently manages a portfolio of close to 300 patents, copyrights and trademarks, which spans the life sciences and includes enabling technologies, instruments, molecular tools and techniques, as well as software programmes and databases. 2015 was a remarkably successful year for EMBL's technology transfer activities as two EMBL spin-off companies were created, and EMBLEM's annual income increased by 40% relative to the previous year.

Based on its long track record in the development of light-sheet microscopy, EMBL and EMBLEM have built up a strong patent portfolio covering key aspects of this technology. In October 2015, they launched the start-up company Luxendo, which will further develop and commercialise cutting-edge light-sheet microscopes, making them available to the global research

An example of the cutting-edge light-sheet microscopes that EMBL spin-off Luxendo will develop and commercialise

community. The company, initially hosted at EMBL headquarters, was co-funded by the EMBL Technology Fund II in Heidelberg and Life Science Partners (LSP) from Amsterdam.

Over the past few years, researchers at EMBL Hamburg have successfully collaborated and provided crucial services to industry partners in the field of SAXS-based structure analysis. Based on these successes, in November 2015 a founder team of EMBL scientists together with EMBLEM established the new company BIOSAXS GmbH. Initially located within EMBL facilities on the DESY campus, BIOSAXS will provide professional SAXS services as well as develop and commercialise hardware and software for structural biology applications.

Also in the area of structural biology, a formal collaboration was initiated between EMBL Grenoble and Roche Basel to explore structures of inhibitors bound to the full-length influenza polymerase, the enzyme that allows the virus to multiply in human cells. In 2014, scientists at EMBL Grenoble solved the structure of the enzyme and thereby paved the way for the design of new anti-influenza drugs. The collaboration with Roche leverages and complements earlier activities at EMBL Grenoble that led to the founding of the EMBL spin-off company Savira in 2009 to develop new therapies to fight influenza.

To stimulate exchange and future collaboration with industry, EMBLEM organises "EMBL Science Days", which bring together selected EMBL scientists and industry researchers on pre-defined topics. A meeting with the biopharmaceutical company AbbVie in March 2015 focused on technology platforms and applications, targets, drugs and biomarkers.

EMBLEM Technology Transfer in Numbers 2015

€ 8 300 000
Income

Discoveries & innovative technologies

43
Invention disclosures

318
Licence & collaboration contracts

19
Priority patent applications filed

19
Patents granted

Industry Relations

EMBL fosters mutually beneficial interactions with industry and small businesses in a variety of ways, ranging from strategic institutional programmes to less formal project-based collaborations. The Advanced Training Centre Corporate Partnership Programme (CPP) aims at enhancing long-term, effective relationships with industry partners in our member states, who benefit from access to the expertise of EMBL scientists and from opportunities to collaborate on the co-development of training, products and services. In February 2015, members of the CPP convened at EMBL Heidelberg for its annual event, which this year focused on big data and bioimaging. Over the course of the year, the CPP also facilitated bilateral meetings between EMBL scientists and corporate partners on topics of common interest including genomics and library preparation technology, IT services and infrastructure, and imaging technologies.

The EMBL-EBI Industry Programme helps industry to make the most of advances in bioinformatics by developing resources and services for the benefit of its members, and by hosting regular strategy meetings and member-driven workshops. The Programme, which has now grown to include 22 companies, welcomed Astex, part of Otsuka Pharmaceuticals, as a new member in 2015.

The Centre for Therapeutic Target Validation (recently renamed Open Targets), a public–private partnership between GlaxoSmithKline, the Wellcome Trust Sanger Institute (WTSI) and EMBL-EBI, was established in 2014 with the support of EMBLEM. Its aim is to leverage genome-scale experiments and analysis to validate therapeutic targets, and focus research into treatments for a wide range of human diseases. Following the interim directorship of Joint EMBL-EBI Director Ewan Birney, Jeffrey Barrett of the WTSI was appointed Director of the partnership in 2015. At the end of the year, the open-access, web-based Target Validation Platform was created to help scientists discover relationships between specific molecules and diseases, and thereby identify new therapeutic targets. At its launch, the new service provided evidence for more than 21 800 therapeutic targets spanning more than 8800 diseases and phenotypes, and registered over 9000 visits in its first six weeks of operation.

In the course of 2015, a number of events aimed at promoting dialogue with industry were hosted across EMBL sites, such as the BioBeat15 conference organised by EMBL-EBI together with the WTSI to explore the burgeoning opportunities for developing companies in the genomics sector. Another example is the industrial workshop organised by EMBL Hamburg in the context of the EU project BioStruct-X, which brought together synchrotron radiation facilities with pharma and biotech companies.

2
Spin-off companies

Training and Outreach

"My supervisor really understood my strengths and pushed me in the right direction."

Erica Valentini, PhD student, Svergun group

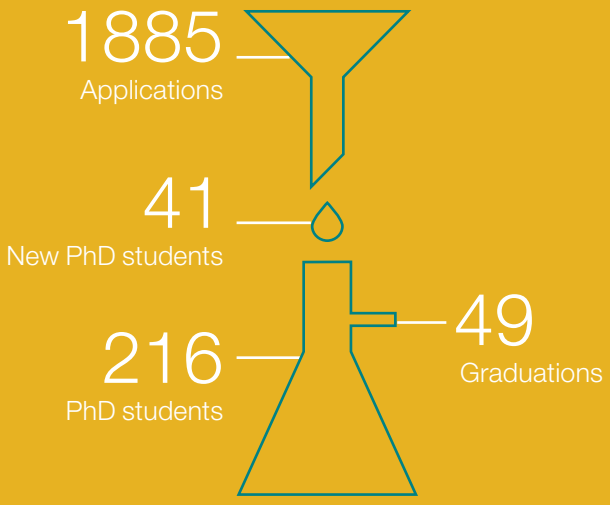
Internal Training

EMBL is proud to have influenced and contributed to the scientific development of several generations of young scientists, many now leaders in academia and industry. EMBL's competitive doctoral and postdoctoral training programmes build on our interdisciplinary and international scientific environment to provide fellows with an ideal starting platform for their career.

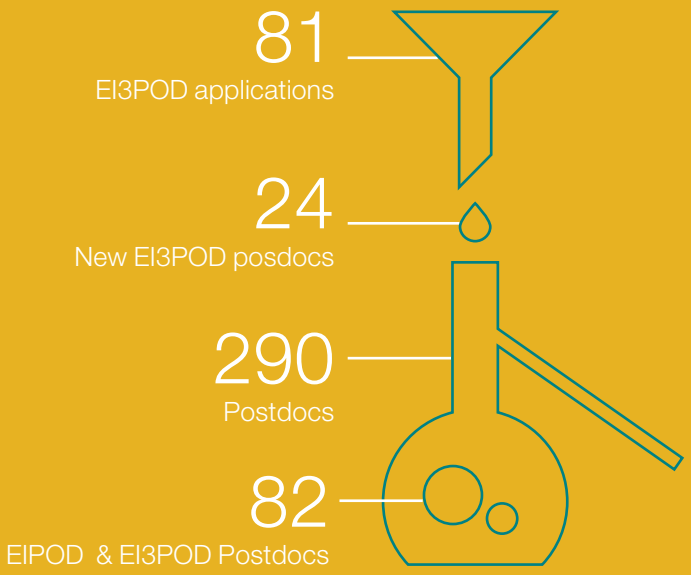
With a curriculum based on internationality, dedicated mentoring and research independence, the EMBL International PhD Programme (EIPP) strives to meet the highest standards for the education and training of PhD students in the molecular life sciences. To do so, the EIPP collaborates closely with national education institutions in EMBL member states,

Internal Training in Numbers 2015

EMBL International PhD Programme



EMBL Postdoctoral Programmes



for example by establishing partnerships with some of the most highly respected universities in different European countries. This allows PhD students at EMBL to obtain joint PhD degrees from the two institutions. In 2015, a new partnership for awarding joint PhD degrees was initiated with the Sapienza University in Rome, raising the number of EIPP partner universities to 25 European member state universities and the "Group of Eight" in Australia.

Since its inception in 2007, the EMBL Interdisciplinary Postdoctoral (EIPOD) Programme has fostered research projects involving two or more research groups with different expertise from across EMBL. After two rounds of successful funding in 2009 and 2012, the EIPOD Programme was awarded a third grant from the EC through its Marie Skłodowska-Curie COFUND Actions for the period 2015–2020. The new EI3POD Programme sees the addition of two further dimensions – "inter-institutional" and "inter-sectorial" – to its traditional interdisciplinary component. This should enable collaborations with other research institutes and with industry, fostering cross-institutional academic research, industry collaborations and the development of commercial know-how and entrepreneurship. The evolved programme also includes a training curriculum targeting non-scientific researcher skills – for example, research ethics, outreach, and gender in science – and offering dedicated career development support. The EI3POD Programme has already attracted close to 30 partners from academia and industry, including institutions in Argentina, Australia, the Czech Republic, Denmark, Finland, Norway, Spain, Sweden and the USA. The first call opened in July 2015 and 24 new fellows were selected.

External Training

EMBL's cutting-edge Course and Conference Programme welcomed nearly 6500 scientists to conferences and training courses at the Advanced Training Centre (ATC) in Heidelberg and the EMBL campuses in Grenoble, Hamburg, Hinxton and Monterotondo in 2015. Many exciting conferences took place in the ATC, among them nine EMBO|EMBL Symposia – the highest number in this prestigious series so far. A prominent example was the symposium The Non-Coding Genome, which registered 491 participants and filled the ATC to its maximum capacity. In November 2015, EMBL inaugurated its collaboration with Stanford University (p. 32) with the first EMBL|Stanford Conference entitled Personalised Health. The first joint EMBL-Wellcome Genome Campus (WGC) Conference Target Validation using Genomics and Informatics also took place at the Wellcome Trust Conference Centre in Hinxton in December. This new series of conferences, which will alternate between EMBL and the WGC, establishes a collaboration between the two institutions to provide the scientific community with world-class training in fields of common interest.

Among the 35 advanced courses held in the ATC training laboratories during 2015, the EMBO Practical Course Synthetic Biology in Action was a particularly successful example and the first course at EMBL Heidelberg to be filmed and made available for e-learning purposes, in collaboration with iBiology and EMBO. A FELASA-accredited course on mouse experimentation was also organised at EMBL Monterotondo and 20 different courses in bioinformatics were offered at EMBL-EBI.

Bioinformatics remains one of the most sought-after topics in training and to cater for this growing need, EMBL-EBI also organises a range of off-site training events, conference exhibitions and workshops, which reached over 7000 scientists in more than 20 countries in 2015. Train online, EMBL-EBI's web-based training resource, offered 19 new or updated courses and saw an impressive growth in the number of users, which increased to over 210 000 unique IP addresses in 2015. The online bioinformatics training was complemented by the launch of a new webinar series for users of EMBL-EBI services.

External Training in Numbers 2015

20 EMBL Conferences

56 EMBL Courses

6443 Participants across EMBL sites

Participants from **90** different countries,

over **73%** from EMBL member and associate member states

EMBL regularly involves industry partners in its training activities through the Corporate Partnership Programme (CPP) and the EMBL-EBI Industry Programme (p. 23). A consultation panel is organised annually with CPP members to explore collaborations in the area of scientific training. In 2015, EMBL's corporate partners supported the training of talented young scientists with 227 CPP fellowships and travel grants to attend 39 different EMBL conferences and courses.

Through the Visitor Programme, EMBL welcomed almost 600 visiting scientists from Europe and overseas to its laboratories and Core Facilities to collaborate on research projects and gain expertise in specific techniques.

Outreach

The TARA research vessel docked in London to host an event for life-science funders and policymakers

EMBL hit the headlines with two major scientific endeavours in 2015: TARA Oceans (p. 5) and the 1000 Genomes Project (p. 6). These explorations of, respectively, the world's oceans and what it means to be human captured the imagination of people around the world via mainstream media.

EMBL has continued to engage with people on social media, and the institute's scientists are increasingly joining the conversation on platforms such as Twitter. EMBL received many visitors in 2015, with almost 1000 visitors coming to Heidelberg alone. Coming from across the member states, the majority of visitors were university students, but film crews, reporters and school students also came to get to know EMBL.

2015 marked the first full year of the Friends of EMBL programme, which aims to bring people and businesses into closer contact with EMBL science and scientists. The programme launched Science Movie Nights, which comprise screenings of Hollywood blockbusters paired with commentary and discussion from young EMBL scientists. Friends of EMBL were also invited to an exclusive lunch with EMBL PhD students and to a Ladies Night organised back-to-back with the Science meets Business event by the Association of German Women Entrepreneurs.

EMBL's Science and Society Programme had a busy year, organising seminars and symposia in Heidelberg and Hinxton on topics ranging from the global spread of infectious diseases to the natural, cultural, and social foundations of human life. The annual EMBO|EMBL Science & Society Conference focused on the impact of innovative biotechnologies on society, particularly in the areas of human health and the environment.

Other highlights of outreach activities in Hinxton included a one-day event celebrating the contribution of Janet Thornton, on the occasion of her stepping down as Director of EMBL-EBI, and a large-scale event for entrepreneurs in genomics, BioBeat15 (p. 23), which took place under the auspices of the Wellcome Genome Campus' Sex in Science programme and

Young EMBL researchers discussing the science of the movie Jurassic Park during the Science Movie Night event for the public

featured key business leaders and entrepreneurs. An event for life-science funders and policymakers aboard the TARA research vessel in London provided an opportunity to showcase EMBL's key role in the life sciences to an influential audience, and to highlight the central role of EMBL-EBI in managing the data produced by large-scale, global scientific endeavours.

EMBL also organised an exciting programme targeted at students and educators. The European Learning Laboratory for the Life Sciences (ELLS) ran three practical courses for science teachers to gain hands-on experience in molecular biology experiments, including the two-day LearningLAB Structural biology – shining light onto the fabric of life, held at EMBL Grenoble. EMBL researchers also inspired and shared their experiences with hundreds of high school students in Croatia, Germany, Italy and Spain through the EMBL School Ambassador Programme. Science in School – the European journal for science teachers funded by EMBL and its EIROforum partners (p. 33) – launched a completely new website, a redesigned print journal and a new e-newsletter. The new website hosts short articles highlighting current events in a timely fashion. The Directors General of EIROforum decided in 2015 to extend the project's funding until 2020.

Private support

Private support for EMBL has continued to increase during 2015. EMBL appreciates the support it has received from individuals, businesses and foundations. These include contributions through the Friends of EMBL network and the ATC Corporate Partnership Programme.

In recognition of her accomplishments in fostering scientific excellence, the first honorary Friends of EMBL membership was awarded to Theresia Bauer, Minister for Science, Research and the Arts, Baden-Württemberg. Honorary membership of the Friends of EMBL is for life and is offered to persons who have made a difference in promoting the life sciences in EMBL member states and beyond.

Integrating Life Sciences

in Europe and Across the World

"Participating in EMBL will make a big difference to our research community."

Audronė Pitrėnienė, Lithuanian Minister of Education and Science

As Europe's only intergovernmental laboratory in the life sciences, EMBL plays a leading role in the integration of science initiatives and helps shape science policy and strategy in Europe by proactively engaging with its member states, with the broader scientific communities, and with European policy-making bodies. EMBL also builds links and fosters strategic cooperation with countries outside Europe to promote global integration in the life sciences.

Member State Relations

EMBL maintains strong relationships with the major life-science institutions in its member states. In 2015, EMBL and the Central European Institute of Technology (CEITEC) in the Czech Republic secured funding through the EC's Twinning instrument to foster collaboration and transfer scientific excellence in the field of medical genomics. Events in Prague and Brno were also organised jointly with the Czech Ministry of Research to raise awareness of EMBL's research, service and training opportunities among the Czech Republic's scientific leadership. With a similar purpose of promoting opportunities, particularly for young researchers, and in view of the upcoming ratification of Malta's membership in EMBL, a very successful workshop was organised at the University of Malta in November 2015. Finally, the cooperation with Luxembourg continued, with the Ministry for Higher Education and Research and EMBL issuing their annual joint call for collaborative research projects, which was this year awarded to EMBL scientist Peer Bork.

Lithuania became the fourth prospect member state, after Slovakia, Hungary and Poland.

To further develop and integrate Europe's wider life-science landscape, EMBL's prospect membership scheme gives non-member European countries the opportunity to participate in EMBL – under similar conditions as member states – for a period of three years prior to acceding to EMBL. After Hungary, Poland and Slovakia joined the scheme in 2014, EMBL actively engaged with their scientific communities. For example, EMBL and a consortium of partners from Hungary – the National Research, Development and Innovation Office (NKFIH), the University of Debrecen, the Biological Research Centre of the National Academy of Sciences, the University of Szeged and the Semmelweis University – were awarded Horizon 2020 Teaming funds by the EC towards the establishment of a new Hungarian Centre of Excellence in Molecular Medicine. The participation of EMBL management and senior researchers in a number of scientific conferences and visits to research institutes in Poland triggered fruitful discussions, which also led to the signing of a Memorandum of Understanding on scientific collaboration with the Nencki Institute – one of Poland's highest ranked scientific institutes. Scientific delegations from leading Slovakian institutions were hosted at EMBL over the course of 2015. EMBL will also enjoy closer collaboration with the Lithuanian research community in the future as this country became EMBL's fourth prospect member state in September 2015. Shortly after, the first visits of representatives from the University of Vilnius and other research institutes took place, with the aim of facilitating the rapid integration of Lithuanian scientists in EMBL's activities.

In 2015, Australia renewed its associate membership by signing on to the new EMBL associate membership scheme revised by the EMBL Council in 2013. Australia's membership in EMBL has been in effect since 2008 and was supported by a new round of national funding under the National Collaborative Research Infrastructure Strategy (NCRIS). EMBL and Argentina signed the associate membership agreement in early 2014, and have since spearheaded various collaborative actions to facilitate

the integration of their respective research communities. During 2015, with the support of the Argentinian Ministry for Science, Technology and Productive Innovation (MINCYT), six highly skilled young investigators conducted short-term visits to EMBL to initiate scientific collaborations and learn new techniques. EMBL faculty members participated in a bilateral structural biology workshop in March 2015 hosted by the Institute of Molecular and Cellular Biology of Rosario (IBR CONICET-UNR). In October, the EMBL-EBI Industry Programme brought together representatives of industry and academia in Buenos Aires for a two-day workshop focused on applications of biotechnology and genomics in healthcare, agriculture and livestock breeding, jointly organised with MINCYT and the Argentinean Chamber of Biotechnology (CAB).

EMBL Partnerships

EMBL's institutional partnerships are close cooperative affiliations with external research organisations in the member states, aimed at leveraging the EMBL model and the strengths of the partners to create an interlinked system of excellent life-science institutions.

The Molecular Medicine Partnership Unit (MMPU) in Heidelberg brings together the complementary expertise of EMBL and the University Hospital to bridge the gap between basic and medical research. After 13 years of productive collaboration, EMBL and the Medical Faculty of the University of Heidelberg renewed the successful MMPU agreement in June 2015 for ten more years.

Established in the same year as the MMPU, the Partnership for Structural Biology (PSB) in Grenoble unites EMBL, ESRF, Institut Laue Langevin (ILL), Institut de Biologie Structurale (IBS) – supported by the French Alternative Energies and Atomic Energy Commission, the French National Centre for Scientific Research (CNRS), and the University Joseph Fourier (UJF) – and the EMBL-CNRS-UJF Unit for Viral Host Cell Interactions (UVHCI) to provide a unique environment for state-of-the-art integrated structural biology. In view of the success of the PSB, the collaborating institutes extended the partnership agreement in 2015 for a further five-year period. Discussions were also initiated to establish a cooperation between EMBL Grenoble and the IBS upon expiry of the UVHCI agreement in 2015.

Following more than a decade of fruitful collaboration and exchange, EMBL's partnership with the Sars International Centre for Marine Molecular Biology in Bergen, Norway, was renewed for a further ten years.

Several meetings took place to explore possibilities for establishing EMBL partnerships in Ireland and the Netherlands with the leadership of Systems Biology Ireland and the Director of the Hubrecht Institute in Utrecht, respectively.

Matthias Hentze (left) and Andreas Kulozik, joint heads of the Molecular Medicine Partnership Unit in Heidelberg

Further Broadening our Horizons

Following meetings with the South African scientific community and government representatives in the previous year, in September 2015 EMBL signed a Declaration of Intent for strategic scientific cooperation with South Africa with a view to enabling its associate membership to EMBL in the future. First links were also established this year with the Chinese research community through a visit to EMBL of representatives from Tsinghua University, one of the country's top research institutions, to initiate relations and stimulate discussion in fields of mutual interest. EMBL enjoys a close collaboration with Stanford University through the EMBL–Stanford Life Science Alliance, which was initiated in 2014 and aims to foster synergies and facilitate exchange between the two institutions, with an initial focus on the areas of genomics, biological imaging and structural biology. EMBL and Stanford celebrated the launch of the Life Science Alliance with a special event in November 2015 during the first jointly organised EMBL|Stanford Conference on Personalised Health in Heidelberg.

EMBL's global dimension and impact was reinforced in 2015 as the EC brought EMBL to the attention of the Group of Senior Officials (GSO), mandated by the G8 Science and Technology Ministers to take stock and explore cooperation on Global Research Infrastructures (GRI). In October 2015, the official GSO report on GRIs featured EMBL in its list of selected research infrastructures of global interest.

EU Relations

EMBL engages in a broad collaboration with the EC based on a Memorandum of Understanding for the consolidation and further

development of the European Research Area. In November 2015, the new Work Plan for the implementation of the Memorandum of Understanding for the period 2016–2017 was signed. The Work Plan sets out future collaboration in specific areas of interest, leveraging synergies between the EMBL Programme 2017–2021 (p. 4) and EC research and innovation priority areas.

EMBL also continued developing strong relations with other European institutions as a member of EIROforum, which unites eight European intergovernmental research organisations. Under the EMBL chairmanship of the International Affairs Working Group, a policy paper on the long-term sustainability of research infrastructures was developed and published in January 2015. The document, which was presented to the Directorate-General for Research and Innovation of the EC and to representatives of the EU Council Working Party on Research, was also referred to by the Organisation for Economic Cooperation and Development (OECD) in the context of work on research infrastructures at the global level.

European Research Infrastructures

As a long-standing provider of European-scale research infrastructure, EMBL participates in several biomedical projects on the European Strategic Forum for Research Infrastructure (ESFRI) roadmap. For example, EMBL previously had a role in the preparatory phase of the Instruct project, which aims to provide European scientists with access to high-end structural biology infrastructure, and has now re-joined this project in 2015 with observer status.

After coordinating its Preparatory Phase I until 2014, EMBL continued to play a key role in Euro-BioImaging, the distributed European research infrastructure for open user access to state-of-the art imaging technologies. In 2015, the Euro-BioImaging Interim Board, consisting of 14 European countries and EMBL, took the fast track towards construction and operation of Euro-BioImaging as a European Research Infrastructure Consortium (ERIC). Euro-BioImaging will take shape as a distributed infrastructure with hubs and nodes. Over the course of the year, major progress was made in developing the statutes for the future ERIC, and the Euro-BioImaging hub and the first generation of node candidates were identified. Together with Finland as the statutory seat of the ERIC, and Italy as the site for medical imaging coordination, EMBL will host the Euro-BioImaging hub for coordinating user access and training in biological imaging technologies, and image data repositories and tools.

In September 2015, Euro-BioImaging was awarded EC funding for its Preparatory Phase II, to be coordinated by EMBL, to take the final steps required for the first user access by 2017. In addition, Euro-BioImaging received funding from the EC for the Global BioImaging project, also

coordinated by EMBL, which allows Euro-BioImaging to extend its international collaborations and establish common services together with imaging infrastructure partners in Argentina, Australia, India, Japan, South Africa and the USA.

EMBL also maintained its active involvement in ELIXIR, the pan-European infrastructure for the collection, archiving and integration of life-science research data. After leading the project during the preparatory and interim phases, ELIXIR is now an independent international consortium and since 2014, EMBL has contributed by providing core data services and hosting the ELIXIR hub at EMBL-EBI. Following the ESFRI and European Council decision to categorise ELIXIR as one of Europe's three priority new research infrastructures, ELIXIR was granted EC funding for the EXCELERATE project to accelerate the implementation of ELIXIR over a period of four years. EXCELERATE is co-ordinated by the ELIXIR hub and started in September 2015. At the same time, the Coordinated Research Infrastructures Building Enduring Life-science Services (Corbel) project received European funding to enable the delivery of shared services from 11 European biomedical research infrastructures, by harmonising user access to resources, unifying data management and creating common ethical and legal services. The Corbel project builds on the previous BioMedBridges project for developing a shared e-infrastructure among ESFRI biomedical research infrastructures, which concluded in 2015.

EMBL Alumni

"Being an EMBL alumnus means sharing the benefits of my stay at EMBL and its existence with the scientific community at home."

George Simos, Associate Professor, School of Medicine, University of Thessaly, Greece

Beyond the chance to pursue excellent research, EMBL offers a unique venue where young scientists from all over the world form durable friendships and collaborations that are truly pan-European. The distributed network formed by EMBL's over 7000 alumni is one of its greatest assets and a major benefit for our member states, as the skills and expertise that scientists acquire at EMBL are exported to national research systems when researchers leave to assume key positions in other institutes.

The EMBL Alumni Relations programme actively engages our growing body of alumni to support EMBL staff and alumni, helps recruit new talented young scientists to EMBL, and facilitates EMBL's international activities. The 40th anniversary celebrations across EMBL's five sites in 2014 and 2015 provided an exciting opportunity to further grow and strengthen relationships within EMBL's alumni community. Building on this, an impact survey was conducted in spring 2015 to capture the value of its alumni for EMBL. The survey, which enjoyed a remarkably high response rate, revealed a very positive picture of EMBL's alumni network: their activities and achievements, the extent to which these were influenced by their time at EMBL, and the various ways in which alumni support and contribute to the continued success of EMBL.

The EMBL alumni local chapter in Switzerland during the inaugural meeting in 2015

The active engagement of EMBL's alumni is evident by their enthusiastic participation in EMBL staff and alumni reunions, such as the 40th anniversary celebrations that took place at EMBL Grenoble in June 2015 (p. 17). Alongside these larger events, EMBL alumni also attend national Alumni Association meetings known as "local chapters", through which EMBL staff, alumni and their lab members expand their networks and explore collaborations and career opportunities within alumni labs in the member states and at EMBL. Such a scientific and networking event was organised alongside the EMBO Meeting in Birmingham in September,

EMBL alumni in numbers

7178
EMBL alumni

82%
of EMBL alumni work in member states

42%
have senior positions

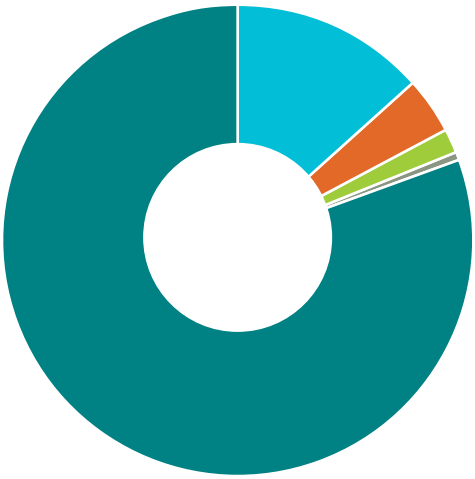
70%
work in academia

12%
work in industry

while one month later over 50 scientists convened in Leuven for an EMBL Benelux meeting involving speakers and participants from Belgium, the Netherlands and Luxembourg. 2015 also saw the inauguration of EMBL alumni local chapters in Denmark and in Switzerland, hosted by the University of Copenhagen and the University of Zurich, respectively.

The receptiveness of our alumni community also rests on the close and trusted relationship between EMBL, the members of the Alumni Association and its elected board, which plays a major role in supporting EMBL's Alumni Relations programme and activities. 2015 saw an important development as a new board was elected that will begin office in 2016.

EMBL takes pride in and celebrates the achievements of its alumni, sometimes long after their time at EMBL, through the John Kendrew and Lennart Philipson Awards, established in honour of EMBL's first two Directors General. The John Kendrew Award, which recognises excellence in science and science communication, was awarded in 2015 to Melina Schuh, former PhD student at EMBL and now Department Head at the Max Planck Institute for Biophysical Chemistry in Göttingen. She was selected for her remarkable scientific achievements in the field of mammalian oocyte maturation as well as for her active engagement in innovative science communication and outreach initiatives. The Lennart Philipson Award, inaugurated in 2015, celebrates outstanding contributions to translational research and technology innovation in the life sciences, and was conferred for the first time to Jacques Dubochet, former group leader at EMBL, for his revolutionary and enabling work in the field of cryo-electron microscopy that began in the late 1970s and spanned his entire career.



Alumni worldwide

80.7% in Europe
13.2% in the Americas
4.1% in Asia
1.6% in Oceania
0.4% in Africa

Administration

"We want to minimise bureaucracy so that scientists can focus on their science."

Keith Williamson, former EMBL Administrative Director

EMBL Administration delivers high-quality services to over 1600 personnel across all EMBL sites, allowing our staff to focus on doing their best work.

A major changing of the guard took place in EMBL's leadership in 2015 as Christian Scherf, former Administrative Director of the German Electron Synchrotron Facility (DESY), was selected to succeed Keith Williamson, EMBL Administrative Director since 2012. Christian Scherf, who upon joining EMBL in November worked alongside his predecessor to learn about EMBL's processes, will officially take up his duties as Administrative Director in the beginning of 2016. This handover followed another important recruitment in EMBL senior management when Roland Block took office as new Head of Human Resources at the beginning of the year.

The "EMBL Code of Conduct" was introduced in 2015 with the aim to preserve and actively promote the special culture of EMBL – based on diversity, openness and collaboration – by translating it into a set of guiding behavioural principles. These guidelines were conceived to minimise the emergence of conflict situations at EMBL, and were complemented by the recruitment of an Ombudsperson, who provides an independent, impartial and confidential service to help staff resolve potential conflicts by facilitating dialogue and discussion. To offer assistance to EMBL staff at all

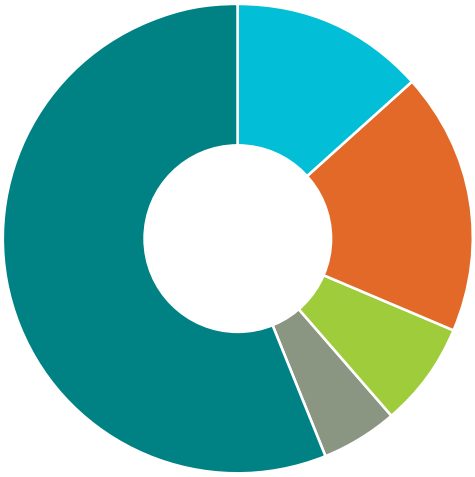
locations, the Ombudsperson supports and trains a network of volunteers from different EMBL departments. The first pilot workshops on conflict resolution were organised at various EMBL sites over the course of 2015. In 2015, a new committee was also established aimed at raising awareness of gender issues and promoting gender balance at EMBL. The committee, which includes a broad representation from all EMBL sites, various career stages, and scientific and support roles, will focus on four key areas – recruitment and employment, career development, organisation and culture, and evaluation and monitoring – with the goal of developing and implementing a Gender Equality Plan to help achieve gender parity at EMBL and beyond.

In line with its commitment to providing open and unrestricted access to published research, in June 2015 EMBL implemented an Open Access Policy aimed at making all EMBL publications widely and freely accessible. EMBL's policy follows major developments towards open access to scientific literature in its member states and conforms to the mandates of several major external funders of EMBL.

Finally, in an effort mainly driven by the EMBL Staff Association, and together with many other EMBL departments and clubs, the Administration engaged in a variety of activities to support refugees entering Europe in response to the political events that marked 2015. As one of numerous "refugee-welcoming organisations", EMBL also supported the EC's Science4Refugees initiative to help refugee scientists and researchers find suitable jobs in Europe.

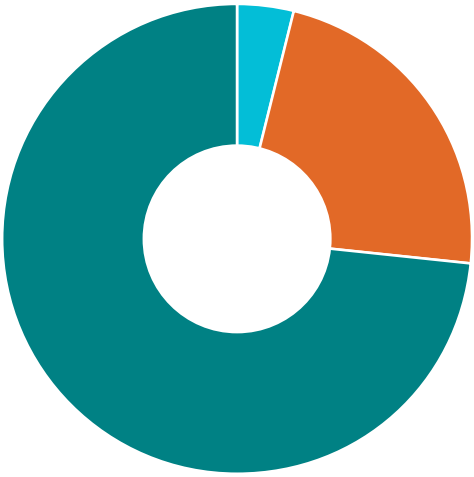
New EMBL Administrative Director Christian Scherf

Personnel Statistics



Personnel
in 2015 in FTE

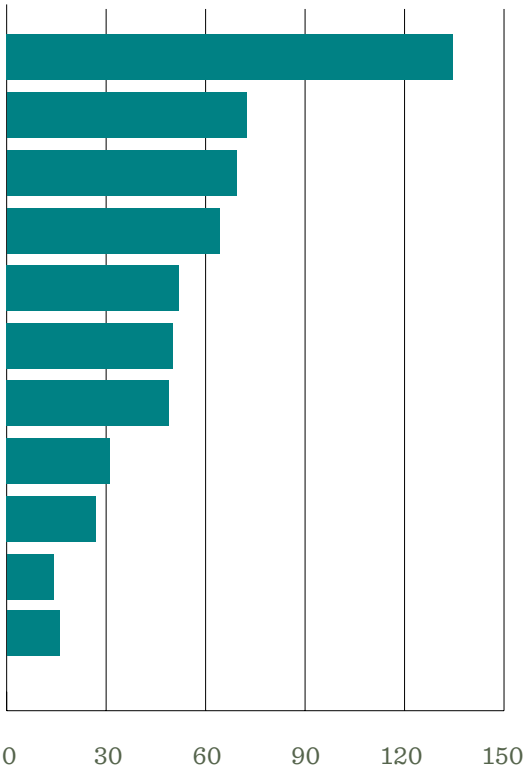
910	Staff
216	Predocs
290	Postdocs
118	Supernumeraries and ancillaries
81	Diploma students and trainees
1615	Total



Staff Nationalities
in 2015 in FTE

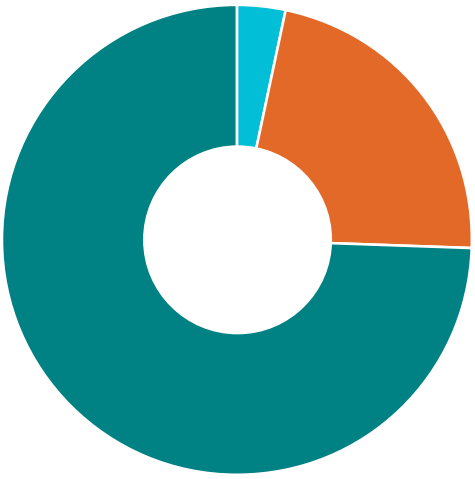
1188	EMBL member and associate member states
59	EMBL prospect member states
368	Non-member states
1615	Total

Visitors to EMBL Units
in 2015



134	EMBL-EBI Hinxton
72	Genome Biology
69	Core Facilities
64	Structural and Computational Biology
52	EMBL Monterotondo
50	Developmental Biology
49	Cell Biology and Biophysics
31	EMBL Hamburg
27	Directors' Research
14	EMBL Grenoble
16	Others
578	Total

Visitors' Nationalities



431	EMBL member and associate member states
18	EMBL prospect member states
129	Non-member states
578	Total

Financial Report

Income/expenditure statement

Income x € 1,000	2015	2014
Member state contributions		
— Ordinary contributions	102,035	99,692
- Currency adjustment for Sterling contributions	1,465	-151
- Entry fees	334	335
— Associate member state contributions	3,430	1,353
- Entry fees	–	1,245
— Additional contributions	9,636	9,937
Internal tax	36,597	31,992
External grant funding	54,669	45,146
Other external funding	3,267	2,480
Other income	19,404	17,768
Total income	230,837	209,797
Expenditure		
Staff costs	135,288	120,623
Operating costs	67,438	67,848
Equipment expenditure incl. Depreciation	14,519	13,702
Total expenditure	217,245	202,173
Surplus (deficit) for the year	13,592	7,624

External grant funding

	2015		2014	
	x € 1,000	%	x € 1,000	%
EC	11,678	21.4	13,556	30.0
ERC	7,021	12.8	5,920	13.1
NIH	12,458	22.8	8,629	19.1
Wellcome Trust	6,108	11.2	5,444	12.1
BBSRC	4,986	9.1	2,887	6.4
DFG	2,658	4.9	1,960	4.3
BMBF	2,402	4.4	2,165	4.8
MRC	589	1.1	459	1.0
EMBO	407	0.7	342	0.8
ANR	386	0.7	226	0.5
Humboldt Foundation	363	0.7	374	0.8
HFSPO	313	0.6	198	0.4
Others	5,300	9.7	2,986	6.6
Total	54,669	100%	45,146	100%

Other external funding

EMBL-EBI industry support	826		755
Elixir member state contributions	2,064		1,198
Other external funding	377		527
Total	3,267		2,480

EMBL total income 2015

€ 231 million

Member state contributions

	2015 x € 1,000	2015 %	2014 x € 1,000	2014 %
Ordinary contributions				
Austria	2,350	2.3	2,296	2.3
Belgium	2,857	2.8	2,791	2.8
Croatia	324	0.3	317	0.3
Czech Republic	730	0.7	715	0.7
Denmark	1,823	1.8	1,782	1.8
Finland	1,418	1.4	1,386	1.4
France	16,634	16.3	16,252	16.3
Germany	20,859	20.4	20,379	20.4
Greece	1,682	1.6	1,643	1.6
Iceland	61	0.1	59	0.1
Ireland	1,094	1.1	1,069	1.1
Israel	1,307	1.3	1,277	1.3
Italy	12,288	12.0	12,006	12.0
Luxembourg	203	0.2	198	0.2
Netherlands	4,751	4.7	4,642	4.7
Norway	2,614	2.6	2,554	2.6
Portugal	1,246	1.2	1,217	1.2
Spain	8,621	8.4	8,423	8.4
Sweden	2,887	2.8	2,821	2.8
Switzerland	3,698	3.6	3,613	3.6
United Kingdom	14,588	14.3	14,252	14.3
Total	102,035	100%	99,692	100%
Currency adjustment				
for Sterling contributions	1.465		-151	
	1.465		-151	
Associate member state contributions				
Australia	2,557		501	
Argentina	873		852	
	3,430		1,353	
Additional contributions				
from UK Government	8,409		9,130	
from Germany	1,227		807	
	9,636		9,937	

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 Hamburg Unit Review

EMBL Hamburg was reviewed on 24 and 25 February 2015 by a panel of 12 experts, including two members of EMBL's Scientific Advisory Committee (SAC) and two observers from EMBL Council. The review was chaired by Andrea Musacchio from the Max Planck Institute of Molecular Physiology, Dortmund, Germany.

Evaluation Summary

The quality of research, services and leadership of EMBL Hamburg were all ranked as outstanding. The environment at DESY, in which the outstation is embedded, has undergone substantial new developments since the last review in 2011, including the decommissioning of the old storage ring, DORIS and its replacement with PETRA III, the construction of the X-ray free electron laser (XFEL), which is underway, and plans for enhancing structural biology on campus. The outstation has been at the forefront of these developments. Main elements of novelty were the commissioning of macromolecular beamlines at PETRA III, the affiliation with the Centre for Structural Systems Biology (CSSB) and the development of plans to establish biological user infrastructure for sample preparation and characterisation at the XFEL. The Panel looks highly favourably on the latter development. The uniqueness of the Hamburg outstation will be further enhanced through its planned participation in the establishment of biological user facilities at the XFEL.

During the period of reference, the small angle X-ray scattering (SAXS) beamline P12 and the two macromolecular crystallography (MX) beamlines P13 and P14 were commissioned and are now ready for resumption of operation in April–May 2015. Impressive developments have been made regarding beamline instrumentation, which will configure the EMBL Hamburg outstation as an absolute world leader in the provision of SAXS and MX beamline time to end users. EMBL Hamburg has maintained its very high profile in the area of software development, with the ARP/wARP and ATSAS suites being clear, but not the only, showcases. These activities are world-class and contribute to the international stature and visibility of the outstation. There have also been very important contributions in structural biology research, such as the work on the Netrin-1/DCC complex and the elastic protein myomesin.

As Head of EMBL Hamburg with ultimate responsibility for all activities, Matthias Wilmanns has been very successful in developing the overall strategy and recruitment plan for the commissioning of the EMBL beamlines at PETRA III. At the same time, he has been working to increase the research profile of the outstation in structural biology, running a competitive research group, being very active and successful in critical

fundraising, and devoting a significant part of his time to the direction of the CSSB. Wilmanns' dedication to EMBL Hamburg is admirable. His national and international visibility represents a decisive asset for EMBL and for the viability of the outstation. However, given the increased range of duties of the Head, the Panel recommends delegation of specific responsibilities and accountabilities to other senior staff members and the establishment of effective structured mechanisms for the senior staff to support the Head in the increasingly complex environment.

Finally, providing adequate funding for access to services, including synchrotron beamlines and affiliated activities, is an absolute requirement for making the services offered by EMBL Hamburg available to the community at large. Due to decreasing European resources for transnational access, current funding for access to infrastructure is inadequate, and this is of course also true for the outstation. The Panel takes the occasion to urge the EMBL member states, through its Council, to dedicate appropriate consideration to this urgent and crucial problem.

Response to the Panel's Recommendations

I would like to begin by thanking the Panel for their thorough review of the activities of the Hamburg outstation. It is clear that they grasped the specificities of both EMBL Hamburg's range of activities, which are distinct from all other EMBL Units, and the considerable change in the local environment that has occurred over the four-year review period. I am very pleased that their overall opinion of the performance of the Hamburg outstation is so positive. I also acknowledge the suggestions that they made for further improvement, both to the individuals under review and to EMBL management as a whole. I will take up several of the general issues they raised here.

As pointed out by the Panel, the two main areas of focus in the four-year period were those recommended for priority in the last EMBL Hamburg review: continuation of the EMBL@Petra3 beamline project and participation in the creation of the CSSB. Although these have both been pursued very successfully, this led to an unusual pressure of work for the five people mainly involved in leading these activities – Matthias Wilmanns, Dmitri Svergun, Thomas Schneider, Rob Meijers and Stefan Fiedler. All were evaluated as having given outstanding performances by the Panel, an opinion which reflects my own. It is also gratifying that the collaboration between EMBL Hamburg and EMBL Grenoble on the beamline projects at both locations continues to function extremely well.

Looking forward, the stressful recent period underlined the need for some change in the organisation of the outstation leadership. The Panel recommended that some of the responsibilities currently in the remit of Matthias Wilmanns should be delegated to senior staff members. This will enable Matthias to devote more of his time to those activities where he is

most urgently required and establish a more collegial form of leadership. I have discussed this with Matthias and he plans, and indeed has already begun, to implement the changes suggested by the Panel.

As recommended by the Panel, it is clear that the four group and team leaders responsible for the implementation of EMBL@Petra3 should now be given the opportunity to both document what they have done during the project and also to pursue a greater level of research and research-related activity than was possible during the review period.

The Panel recommends timely planning for succession in the SAXS area as Dmitri Svergun, one of the world leaders in the SAXS field, is nearing normal retirement age. A plan was presented as part of the review documentation, which the Panel endorsed and EMBL intends to follow.
The Panel recommends to EMBL Council that the member states should consider funding access to the EMBL service facilities, in light of the reduction of support for structural biology infrastructure access that will occur during Horizon 2020. I will transmit this recommendation to EMBL Council and discuss it with them during preparation of the next Indicative Scheme.

In view of the progress toward the inauguration of the European XFEL in 2017, and the very promising results obtained from structural biology projects carried out at existing, smaller XFELs, the Panel strongly supported EMBL Hamburg's involvement in a consortium that will set up and run a sample preparation and characterisation facility for structural biology users of the XFEL. I support this initiative because of EMBL Hamburg's successful history of providing synchrotron-based services to the structural biology community. However, because the (long-term) staffing required has clear financial implications, I will have to discuss this with EMBL Council in preparing the next Indicative Scheme.

Two issues that need attention were raised by both predoctoral and postdoctoral fellows. The first concerns the need for an in-house course in crystallography and SAXS techniques. This course has normally been offered but because of the other pressing commitments referred to above, it was cancelled last year. It was always intended to reinstate the course and this will be done.

Several aspects of the mentoring of fellows, including encouragement to attend scientific meetings, preparing publications in a timely way and, for postdoctoral fellows, designating a second mentor with whom the postdoctoral fellow would regularly meet are not being uniformly carried out in a satisfactory manner. EMBL has policies and guidelines on mentoring, and I am following up to ensure that these are upheld uniformly in future.

Professor Iain W. Mattaj, FRS
Director General

28 April 2015

EMBL-EBI Services Review

On 26 to 27 March 2015 the review of the EMBL-EBI services took place. The Review Panel comprised 25 experts, including three members of EMBL's SAC and was chaired by Michael Snyder from Stanford University, USA. The Chair of EMBL Council attended as an observer.

Evaluation Summary

The EMBL-EBI provides a wide array of valuable informatics services to the world. The EMBL-EBI services have had enormous impact on both medicine and industry and EMBL-EBI has reached a status of international pre-eminence. The quality and utility of the services provided as well as EMBL-EBI's training programmes and contribution to integrated activities in European life-science research were all rated as outstanding.

Both the breadth and quality of the service activities are impressive, and the data are accessed by millions of people around the world. The services bring international recognition to both the EMBL and EMBL-EBI. Whereas a decade ago these services might for the most part have been viewed as useful "add-ons" to international efforts (with some exceptions), it is now clear that the EMBL-EBI services are often leading these areas in both the information provided and the innovative ways employed to manage, access, visualise, and utilise the data. There are a number of services/activities that are unique to EMBL-EBI (e.g. Ensembl, Pfam, ChEBI, Metabolights, EMDB) and they build valuable software tools that are used worldwide (e.g. ChEMBL). They also help establish standards used by the rest of the international community. Although the services are broad, there is an impressive amount of collaboration and integration across the different activities. In 2011, the major preoccupation seemed to be how to handle the deluge of data whereas now (although that issue remains present) scaling plans are in place and the challenges are very different, demonstrating the consolidation and maturity of the Unit.

The service division will continue its mission of archiving, managing, and integrating the vast amounts and diverse types of data. It will also continue its outstanding training. The Review Panel endorsed the new movement of the EMBL-EBI services towards providing linkage to the clinical arena by establishing standards/platforms and reaching out to biomedical institutes located in EMBL member states to link their medical informatics with EBI resources and to establish at EMBL-EBI reference data sets of relevance to clinicians. EMBL-EBI has the opportunity to make a huge impact in this area. Similarly, the move into imaging by preparing reference samples and interfacing with the broader community was enthusiastically endorsed as a potentially high impact area serving a large community and one of great strength in Europe.

Much of the success of EMBL-EBI is credited to its leader Janet Thornton, Director of the EBI, its two Associate Directors Rolf Apweiler and Ewan

Birney, and their predecessor Graham Cameron. Together, they are to be commended for transforming EMBL-EBI into a premier global bioinformatics centre. The Panel fully endorsed the recent designation of Ewan Birney and Rolf Apweiler as the new Joint Directors of EMBL-EBI.

Response to the Panel's Recommendations

For the second time, the EMBL-EBI services were reviewed as "clusters" of related data resources rather than being classified for review by the individual team leader responsible. The Review Panel members were satisfied that the format of the review, which also included evaluation of the technical support teams and the training activities, permitted evaluation of the diverse areas in sufficient depth for them to form firm conclusions. Given that this required a Review Panel of exceptional size (25), I would very much like to thank the Panel members and in particular the Panel Chair, SAC member Michael Snyder, for their excellent and efficient work and discussions and for the numerous helpful and insightful recommendations they provided. I note that the Panel recommended the generation of additional performance metrics and comparisons with other service providers for future reviews and I will discuss with my colleagues how these can best be generated. I also note here that this response does not include comment on the many valuable suggestions provided in the review sections on individual clusters. These will be brought to the attention of the cluster leaders and will be addressed by them together with EMBL-EBI's senior management. In my response I concentrate on more general issues.

The Panel noted that EMBL-EBI data services have attained a level of maturity in the provision of services and infrastructure that is of "industry standard". The data resources are all available 24/7 and major technical challenges such as the migration of all the resources from one commercial IT provider to another were accomplished with no unplanned downtime and a minimum of disruption. This has to be viewed against a background of exponential data growth. The Panel notes, in contrast to the situation at the last review in 2011, that a plan to deal with this growth in a cost- and personnel-effective way is in place provided sufficient funding is available. I agree with the Panel that this represents a major step forward in the professionalisation of EMBL-EBI service provision during the past four years. In my view, this speaks to a remarkable, broadly based, team effort and to the high quality of the overall leadership provided by Janet Thornton, Graham Cameron, Rolf Apweiler and Ewan Birney. I congratulate them and their many colleagues on this achievement.

Against this background I also find it gratifying that the Review Panel endorsed the recent decision to appoint Ewan Birney and Rolf Apweiler as Joint EMBL-EBI Directors when Janet Thornton steps down later this year. I note and agree with the Panel's recommendation that it is wise to use this opportunity to look closely at the overall leadership structure of EMBL-EBI and to make any necessary changes to accommodate past growth and prepare for predictable future developments. A plan to accomplish this

will be developed over the course of this year and will involve close prior consultation of all EMBL-EBI faculty with the Joint Directors.

Although dealing with the above-mentioned growth in data will remain a major task for EMBL-EBI in the upcoming period, it is by no means the only planned activity. The Panel endorsed the proposal for EMBL-EBI to work with biomedical institutes to provide the open access reference biomolecular datasets against which medical professionals can perform comparisons of confidential patient-derived data. I believe that this will be a crucial aspect of efficient precision medicine provision and an excellent opportunity for EMBL-EBI to work together with all of our member states in the individual way that will be required when dealing with medical data. The Panel also endorsed the plan for EMBL-EBI to work together with other experts to develop standards and methods for the construction and operation of imaging data resources. I find this to be a critical current challenge of considerable importance for the biomedical sciences and concur that EMBL-EBI's expertise means that it has a crucial role to play in this area.

The Panel noted that one of the two senior team leaders in the area of chemoinformatics had announced his imminent departure shortly before the review. I agree with their warning that it is urgent to provide stability in this important and rapidly growing area of EMBL-EBI's activity and have already, after receiving advice and input from the EMBL-EBI leadership, endorsed a plan to deal with the consequences of this recent decision in both the short and the longer term.

The Panel made some valuable recommendations regarding the organisation of data in EMBL-EBI resources. For example, in the future it will be beneficial to find additional ways of integrating condition-dependent and condition-independent data resources. A second suggestion is to find ways in which stable and transient protein complexes can be presented as such in the protein-structure databases. A final excellent recommendation is to see whether cell types, one of the fundamental units of biological organisation, can be used as an additional way of classifying datasets across EMBL-EBI.

EMBL-EBI engages in a considerable amount of training, which forms part of the overall EMBL International Centre for Advanced Training (EICAT). This was the first time we organised an external review of training activity, using EMBL-EBI training as a test case. The Panel was impressed by the range and quality of the training efforts aimed at teaching users of different levels of expertise how they can make better use of the data resources. The Panel praised those in charge of the training and noted that many individuals who are part of all the data resources participate in training. They recommend that we consider ways the training can be even better integrated into the thinking and organisation of the data service teams and I will work with my colleagues to follow up on this suggestion.

Finally, the Panel asked me to transmit two of their specific concerns to EMBL Council. The first is that they feel it is important that EMBL

Council realise that, although ELIXIR is a tremendously valuable project whose realisation will be of great future benefit, at the present stage it is an activity that increases, rather than decreases, the costs, workload and responsibilities of the EMBL-EBI service staff and leadership. The Panel considered that it is crucial that EMBL-EBI funders are aware of this.

The second is a more generic worry. EMBL-EBI depends significantly on external funds. Close to half of the total current EMBL-EBI funding is external. This level of funding reflects the tremendous effort put into raising resources by senior staff and also reflects the high regard in which the data resources are held by both funders and reviewers of funding proposals. The Panel points out, however, that external funding is never predictable and seldom stable. They see no alternative than to continue making use of it where possible to support EMBL-EBI activities, but feel that the member states have to be made aware of the potential danger of this source of instability for one of the world's most valuable and highly used collections of data resources.

Professor Iain W. Mattaj, FRS
Director General

5 May 2015

EMBL Developmental Biology Unit Review

EMBL's Developmental Biology Unit was reviewed on 6 and 7 May 2015 by a panel of 14 experts, including six members of SAC. The review was chaired by Pernille Rørth, until recently with A*Star in Singapore and currently in Copenhagen, Denmark.

Evaluation Summary

The Developmental Biology Unit is one of the world's leading centres for the study of developmental processes. It strikes a delicate balance between the diversity of biological problems and model systems used, and depth of investigation into fundamental principles, while retaining cohesion within the Unit. Despite having only eight investigators, the Unit manages this challenge excellently by means of extensive collaboration with other EMBL Units and Core Facilities.

Each of the Unit's investigators has mounted a strong, independent research programme. For example, more than half of the group leaders have been awarded ERC starting or advanced grants. The strong focus on mechanistic studies using genetic as well as other perturbations is a particular strength of the Unit and is one of the Unit's major contributions to the scientific and intellectual environment of EMBL.

The Developmental Biology Unit's contribution to training continues to be very significant. This includes EMBL-wide training: Anne Ephrussi has a long-standing leading role as Head of the EMBL International Centre for Advanced Training (EICAT) and Detlev Arendt heads up the very successful EMBL Postdoctoral Programme. In addition, there is strong scientific training within the Unit (predoctoral and postdoctoral fellows and young group leaders). The Panel did note some issues arising from pressure for top-level publications among fellows. Most of the group leaders in the Developmental Biology Unit have also served as lead organisers for major conferences at EMBL during the review period, showing a broad commitment to the development of their scientific fields.

As Head of Unit for the past eight years, Anne Ephrussi has done an outstanding job. She is internationally highly recognised for her own work. In addition, she has led the Unit successfully both by hiring a truly impressive set of innovative group leaders, who are now producing top-level science, by mentoring them and by providing a supportive structure in which they can interact productively with their colleagues. The junior group leaders were unanimously happy with the support they are given in the Unit and the collegial spirit. Apart from Anne Ephrussi and Detlev Arendt, the remaining six group leaders are expected to be replaced during the next review period, thus the upcoming four years will be one of change and new opportunities for the Unit. This should be exploited by recruiting

insightful and innovative scientists who will seize the possibilities of new technologies, utilise the unique collaborative EMBL environment and, most importantly, ask key biological questions to provide functional insights.

Overall, the Panel ranked the Developmental Biology Unit as outstanding in terms of its overall performance, the quality of its research and its contribution to the training and development of young scientists.

Response to the Panel's Recommendations

I would like to thank the Panel for their time and considerable effort in reviewing the Developmental Biology Unit, as well as for their constructive feedback. I am gratified by the highly positive overall evaluation of the Unit and would like to congratulate the Unit members and, in particular, the Head of Unit Anne Ephrussi. Beyond the excellent research of the Unit, several of its members show an additional level of commitment to EMBL and its community. As the report mentions, Anne Ephrussi and Detlev Arendt play vital roles in EMBL's training efforts and Alexander Aulehla is highly committed to his additional responsibilities as Head of EMBL's Laboratory Animal Resources.

The review report notes some issues around the publications strategy of groups in the Unit. In particular, the Panel was concerned that some PhD students graduated without a first author paper. This was deemed to result from a combination of the strict four-year duration of PhD studies at EMBL and the highly ambitious scientists in the Unit, including both group leaders and trainees. I acknowledge that there is a tendency for some EMBL groups (also beyond the Developmental Biology Unit) to focus perhaps too strongly on high-impact publications, which may lower the overall numbers of publications produced by a lab. This is largely due to a combination of science becoming more interdisciplinary, which usually lengthens the time a project takes, and the changing and ever-increasing requirements of journals for publication. However, this trend can have negative consequences for predoctoral and postdoctoral fellows, who need to produce first-author publications in order to apply for fellowships or to obtain independent positions. I will continue to encourage all EMBL group and team leaders to consider these issues and aim for balance in their publication strategies and to discuss these issues openly and transparently with the members of their groups and teams.

The Panel made useful specific recommendations regarding this topic, which we will consider carefully. For the predoctoral fellows these include rigorously enforcing thesis submission by the end of the fourth year of the PhD (which is the basis for a 6-month's contract extension beyond four years to finish a project or a publication), encouraging joint research efforts between members of a group to increase the likelihood of co-authorships and joint-first authorships, and discussion of publication strategies by the student's thesis advisory committee (TAC) at the end of the second and third years. Regarding the latter point, EMBL has recently revised its

guidelines to make the development of a publication strategy mandatory for the second-year committee meeting and a review of this strategy obligatory for the third year. Furthermore, SAC suggests a 3.5-year ad hoc TAC to further monitor thesis completion and preparation of publications. I will discuss this suggestion with EICAT and senior faculty.

The Panel also pointed out that it is important for fellows to take advantage of the large variety of meetings and networking opportunities available at EMBL, ranging from seminars and courses and conferences to fostering connections with both local and visiting group leaders. We actively encourage this participation and consider it an integral part of PhD and postdoctoral studies at EMBL.

In addition, the Panel noted that effort should be made to expose postdoctoral fellows to teaching experience, for example through the supervision of trainees, and to involve them in discussions with external visitors. Both of these recommendations are common practice in postdoctoral training at EMBL and should be followed wherever possible. We will continue to actively encourage the involvement of postdoctoral fellows in such activities but note that EMBL can only accommodate a limited number of trainee visitors.

Finally, the review report states that the contribution of the Developmental Biology Unit to integrated activities in European life-science research has not been discussed in detail. Although this may have been the case during the review, I would like to point out that the Unit is in fact very active in this area. This is particularly evident from the high number of major conferences organised at EMBL by group leaders of the Unit (e.g. EMBO|EMBL Symposia Complex Life of mRNA, Biological Oscillators: Design, Mechanism, Function, and Germline: Immortality through Totipotency) and illustrated further by the large number of scientific advisory and review boards of research organisations and funding bodies (e.g. ERC, EMBO, HFSPO etc.) on which members of the Unit regularly serve.

Professor Iain W. Mattaj, FRS
Director General

10 June 2015

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