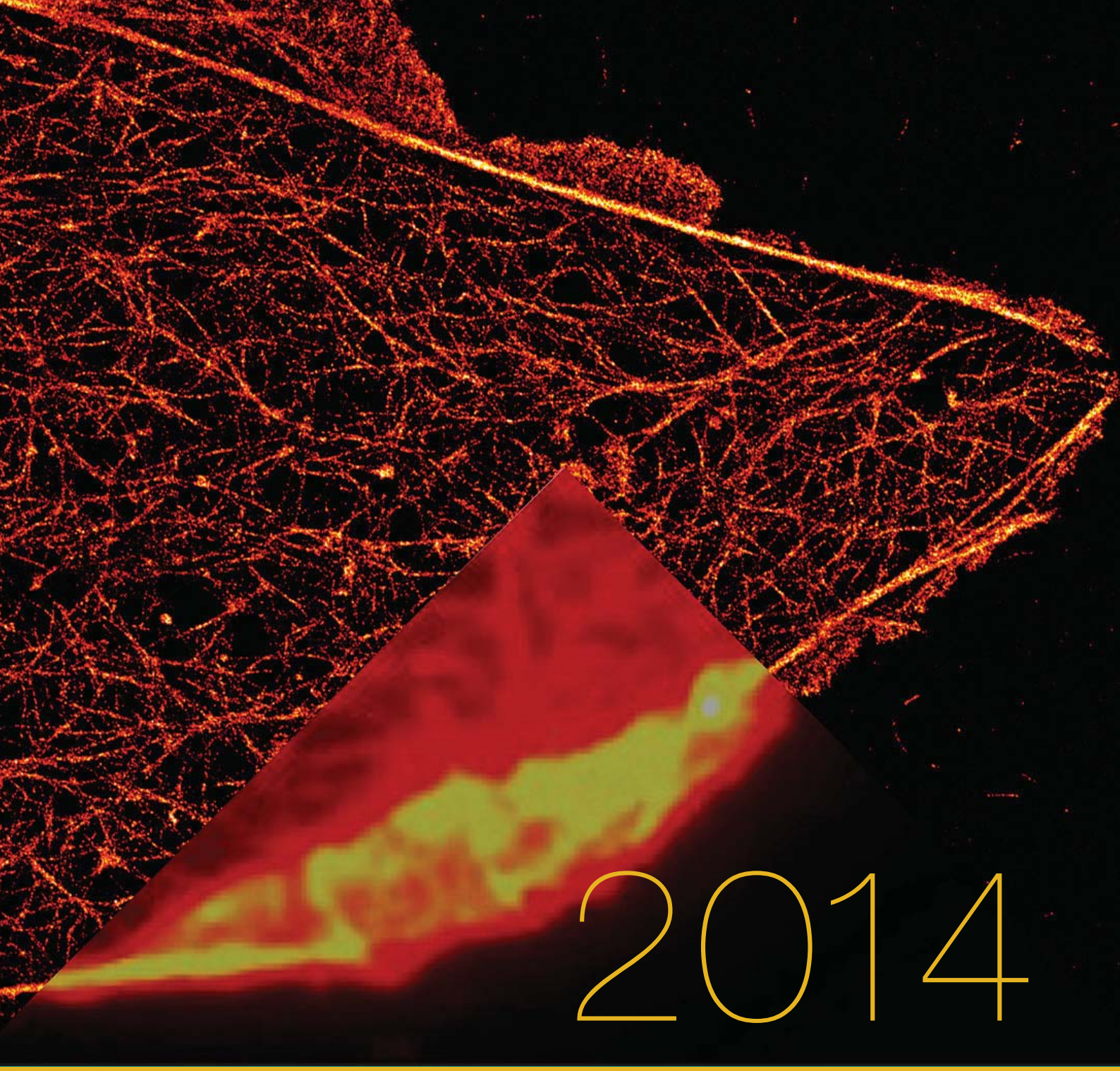


# 2014

# *Annual Report*

EMBL

***Cover image***

*Comparative imaging of an actin meshwork, by confocal and super-resolution microscopy (photo Jonas Ries).*

# Contents



**For your information**

We would like to inform our readership that the reporting period for the EMBL Annual Report has recently been changed to cover the full calendar year. Unlike previous editions, which featured events from June to May, this document will cover relevant developments that took place between January and December 2014.

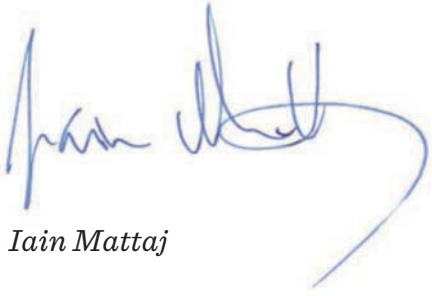
2014 – the year that marked EMBL's 40th birthday – has been an incredible year for us. Anniversary celebrations throughout the year saw tremendous engagement from the whole EMBL community – past and present – and offered an opportunity to look back on the Laboratory's many accomplishments.

2014 also marked a further historic development for EMBL: 15 years after the opening of our youngest outstation in Monterotondo, Italy, EMBL Council decided to establish a new, fifth outstation in Barcelona, Spain, which will be dedicated to Tissue Biology and Disease Modelling.

EMBL was founded 40 years ago to create a centre of excellence in molecular biology for Europe's most talented young scientists. Its founding principles – scientific independence, opportunity for creative young thinkers, interdisciplinarity and collaboration – have remained at the heart of the EMBL model until today. Despite its 'middle age', EMBL is still young at heart and enthusiastically active in pursuing its five missions: basic life science research, provision of services to the scientific community, advanced training, technology development and transfer, and the integration of life-science research in Europe.

2014 saw important advances in each of our missions. The excellence of the research carried out at EMBL is evident from the fact that nearly 30% of our research faculty now consists of ERC investigators. The EMBL-EBI biological data resources registered an average of 11 million web hits per day over the course of the year, representing an ever-growing user community. The opening of the new, fully automated MASSIF beamline at the ESRF, jointly operated with EMBL Grenoble, represents a milestone in the provision of cutting-edge services to the structural biology community. Welcoming over 6000 participants across its five sites, EMBL hosted its largest ever courses and conferences programme in 2014. Joining forces with industry, EMBL launched the Centre for Therapeutic Target Validation, a public–private partnership aimed at harnessing the power of 'big data' and genomic methods to accelerate drug discovery. In its effort to integrate life-science research throughout Europe and beyond, EMBL welcomed the Czech Republic as its 21st member state, Argentina as its second associate member state and Slovakia, Poland and Hungary as prospect member states.

These recent developments and its unique history make EMBL's story one of great achievement, a success that has been made possible by the work, energy and commitment of its incredibly talented people. Hence, I wish to conclude by thanking the people who have made EMBL what it is today, the people who continue to drive it forward, and those who contribute to spreading its impact worldwide. After looking back on EMBL's past we can look forward to the next 40 years with anticipation, excitement and pride.



*Iain Mattaj*

# Celebrating . . .

## 18 March

Prominent members of the local community in Heidelberg met EMBL scientists at the EMBL Annual Reception and learned about EMBL's science, past achievements and plans for the future.

Throughout the year, young EMBL scientists have shared their passion for the life sciences with the general public in the Sunday matinee 'More from Life' lecture series, which covered a variety of topics from human origins to the future of data storage in DNA.


## 12 June

Staff and alumni celebrated EMBL-EBI's 20th and EMBL's 40th anniversary with a day of inspiring talks and fun activities on the Wellcome Trust Genome Campus in Hinxton.

## 20 June

EMBL Monterotondo marked its 15th birthday – along with EMBL's 40th anniversary – with a symposium dedicated to the contribution of EMBL to European science.

## 2-3 July

Science, policy and politics came together at the EMBO-EMBL Anniversary Science and Policy Meeting in Heidelberg to mark the 50-, 45-, and 40-year histories of EMBO, EMBC and EMBL respectively. The event was attended by several European science ministers and ministry representatives as well as high-level EU representatives.

## 18-19 July

More than 1000 staff and alumni from around the world came together at EMBL Heidelberg to celebrate EMBL's 40th Anniversary Reunion, the central event in the anniversary year.

>>

# ...40 years of

## 25-26 July

Members of the public took the opportunity for a hands-on experience of EMBL science at a special Research Camp.

## 12 September

Local and national public figures attended a gala evening, featuring a panel discussion with Nobel Prize winners and alumni Christiane Nüsslein-Volhard and Eric Wieschaus, followed by dinner and entertainment. Germany's Minister for Education and Research, Johanna Wanka, delivered the opening address.

In the photo project DNA | Portraits by Horst Hamann, the renowned photographer took images of more than 170 current and former EMBL employees from over 40 nations to capture EMBL's unique history, culture and spirit.

# EMBL

## 31 October

EMBL Heidelberg hosted an unforgettable concert by Nik Bärtsch as part of the annual international Enjoy Jazz festival. Music, multimedia design and the remarkable architecture of the ATC building fused to create a unique atmosphere for the concert, which was reviewed in the press as the highlight of the festival.

## 27-28 November

EMBL Hamburg honoured its 40th anniversary together with its staff, alumni, and the external users of its structural biology platforms. The celebrations included a scientific symposium and a prestigious reception at Hamburg Town Hall.

## …and in 2015

The Grenoble outstation, founded in 1975, is preparing an inspiring programme to celebrate its 40th anniversary with EMBL staff, alumni and its user community in June 2015.

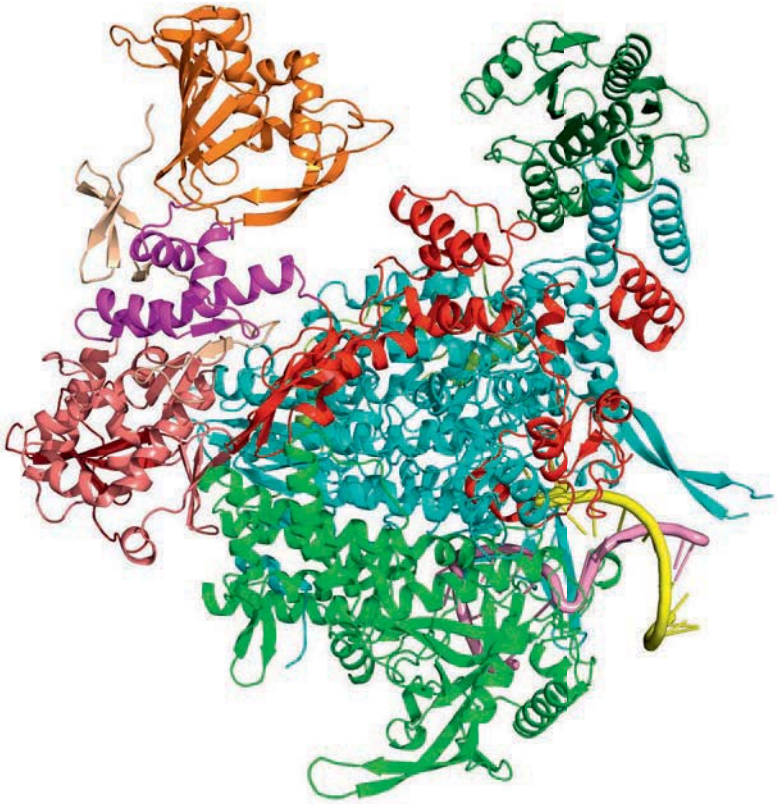
# Research Highlights

*For 40 years researchers at EMBL have been uncovering the basic principles and mechanisms of life.*

Research at EMBL integrates a broad range of disciplines and methods and navigates across scales – from molecules to organisms and beyond – to uncover the basic principles and mechanisms that regulate complex biological systems. The interdisciplinarity, breadth of research topics and culture of collaboration that have characterised EMBL's research over the past 40 years are illustrated by the following selected research highlights produced by EMBL scientists in 2014.

## EMBL Grenoble

After two decades of work – half of EMBL's history – Stephen Cusack and his group at EMBL Grenoble obtained the first complete structure of one of the key machines of the influenza virus: its RNA polymerase. The structure allows researchers to finally understand how the polymerase works as a whole, and how it can process the viral genetic material – RNA – in two different ways: either copying it for packaging into new viruses that can



*The Cusack group obtained the first complete structure of the influenza virus polymerase.*

infect other cells, or reading the instructions in the genetic material to make viral messenger RNA, which directs the infected cell to produce viral proteins. This work, which was carried out on one of the ESRF beamlines operated in collaboration with EMBL Grenoble, could prove instrumental in designing new drugs to treat serious flu infections and combat flu pandemics.

Pflug A *et al.* (2014) Structure of influenza A polymerase bound to the viral RNA promoter. *Nature* 516:355-60. doi: 10.1038/nature14008

Reich S *et al.* (2014) Structural insight into cap-snatching and RNA synthesis by influenza polymerase. *Nature* 516:361-6. doi: 10.1038/nature14009

Ramesh Pillai's group pinned down the function of Vasa, a protein that is crucial for keeping DNA healthy and viable from one generation to the next. Paradoxically, this protein safeguards DNA by protecting fragments of potentially harmful transposon RNA from being digested. The Pillai group, working with the Cusack group at EMBL Grenoble and Anne Ephrussi's group in the Developmental Biology Unit in Heidelberg, discovered that Vasa fastens around such fragments like a bracelet, and hands them over to the machinery that uses them as templates to produce complex enzymes that target transposon RNA for destruction.

Xiol J *et al.* (2014) RNA clamping by Vasa assembles a piRNA amplifier complex on transposon transcripts. *Cell* 157:1698-711. doi: 10.1016/j.cell.2014.05.018

## Genome Biology

Working with Stefan Pfister at the German Cancer Research Centre (DKFZ), Jan Korbel's group found that Group 3 medulloblastoma – a paediatric brain tumour with the poorest prognosis – is linked to a variety of large-scale genetic rearrangements that all have one thing in common: they bring a gene called GFI1B close to so-called 'super-enhancers'–

stretches of DNA that dramatically increase the activity of nearby genes.
Northcott PA *et al.* (2014) Enhancer hijacking activates GFI1 family oncogenes in medulloblastoma. *Nature* 511:428-34. doi: 10.1038/nature13379

Eileen Furlong's group found that, contrary to what was thought, enhancers find their targets long before they are activated during embryonic development in the fruit fly. This indicates that the whole system is primed in advance, ready to spring into action when needed. In work that drew on expertise from the Flow Cytometry Core Facility, the Genomics Core Facility, and Wolfgang Huber's group, they discovered that these genetic regulators act across long distances in the genome, in ways that are as complex as those seen in vertebrates.
Ghavi-Helm Y *et al.* (2014) Enhancer loops appear stable during development and are associated with paused polymerase. *Nature* 512:96-100. doi: 10.1038/nature13417

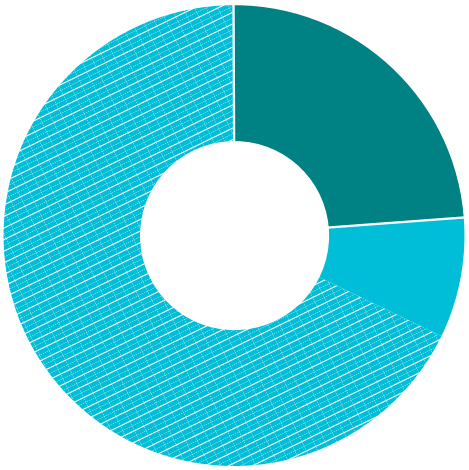
## Developmental Biology

François Spitz's group identified how a specific stretch of DNA controls distant genes to influence the formation of the face. In a study that helps to clarify the genetic causes of two of the most common congenital malformations in humans – cleft lip and cleft palate – they found that this stretch of DNA contains regulatory elements that control the activity of a gene called Myc, which sits far away on the same chromosome. Crucially, this control is exerted specifically in the cells that form the upper lip.
Vural V *et al.* (2014) Long-range enhancers regulating Myc expression are required for normal facial morphogenesis. *Nat Genet* 46:753-8. doi: 10.1038/ng.2971

Detlev Arendt's group found that one of the world's largest migrations is probably driven by melatonin, a hormone that governs sleep and jet lag in humans. The group discovered that melatonin governs the nightly migration of a plankton species – the marine ragworm Platynereis dumerilii – from the surface to deeper waters, indicating that the hormone's role in controlling daily rhythms probably evolved early in the history of animals.
Tosches MA *et al.* (2014) Melatonin signaling controls circadian swimming behavior in marine zooplankton. *Cell* 159:46-57. doi: 10.1016/j.cell.2014.07.042

In another study involving *P. dumerilii*, the Arendt group unexpectedly found that the notochord – a rod of cartilage that vertebrates have running lengthwise along the middle of their body, under their spinal chord – most likely evolved from a muscle. The EMBL scientists found that this worm has a group of cells with the same genetic signature as the vertebrate notochord. These cells form a muscle that is located in the same region of the body as the notochord, and most of the animal groups that sit between *Platynereis* and chordates on the evolutionary tree also have a similar, muscle-based structure in the same position. Taken together, the findings suggest that the notochord evolved much earlier than previously thought.
Lauri A *et al*. (2014) Development of the annelid axochord: Insights into notochord evolution. *Science* 345:1365-8. doi: 10.1126/science.1253396

# Scientific Publications in 2014

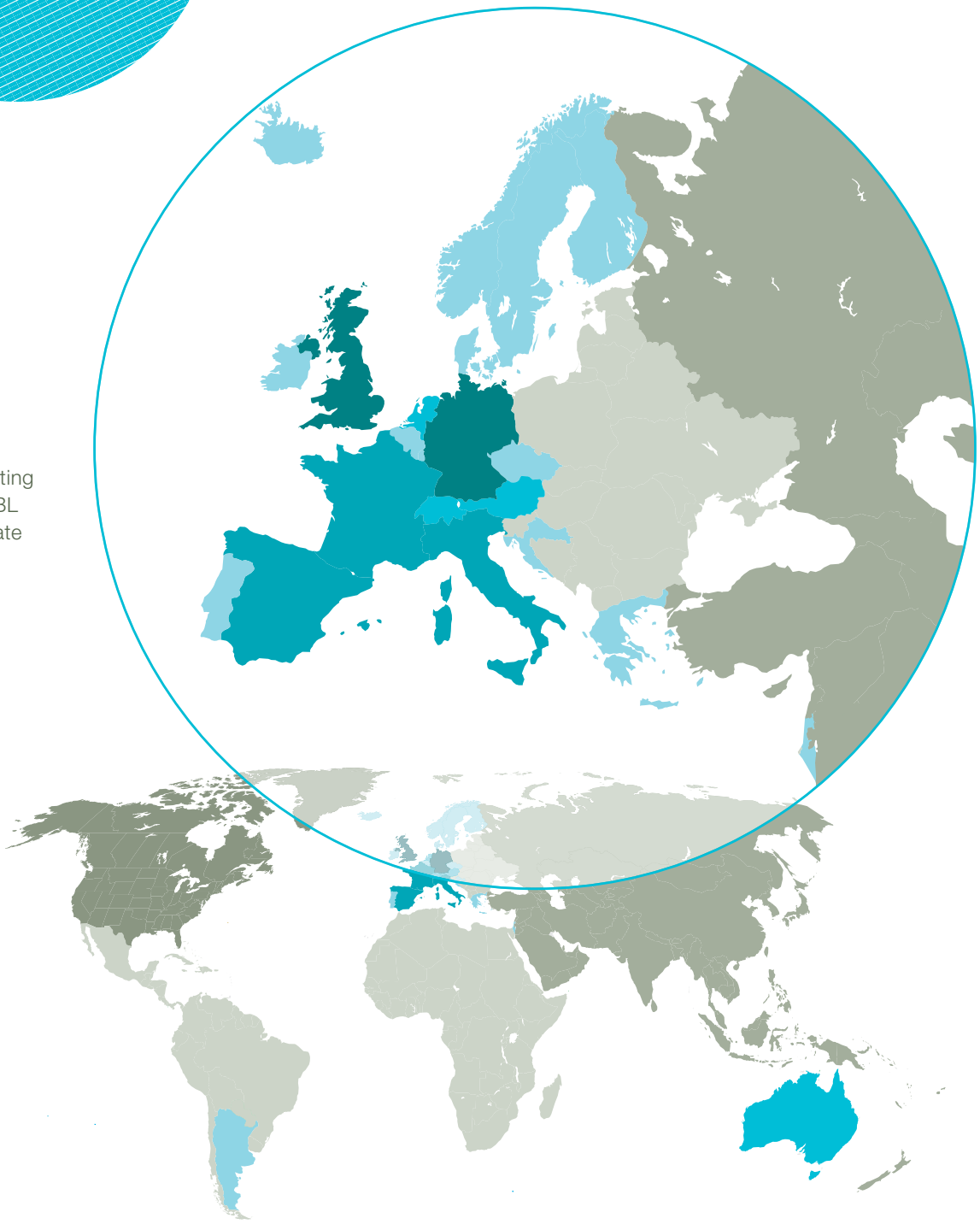


**155** By EMBL

**497** By EMBL in collaboration with over 580 organisations worldwide

**442** By EMBL in collaboration with organisations in member and associate member states

**652** Total



# ERC Investigators at EMBL

## *Consolidator Grants*


John Briggs


Edward Lemke


Sarah Teichmann


Ramesh Pillai

## *Advanced Grants*


Peer Bork


Detlev Arendt


Matthias Hentze


Lars Steinmetz


Christoph Müller


Stephen Cusack


Eileen Furlong


Cornelius Gross

## *Starting Grants*


Alexander Aulehla


Maja Köhn


Marcus Heisler


Christiane Schaffitzel


Pedro Beltrao


Martin Beck


Jan Korbel


Donal O'Carroll


Rocio Sotillo

*Newly awarded in 2014*

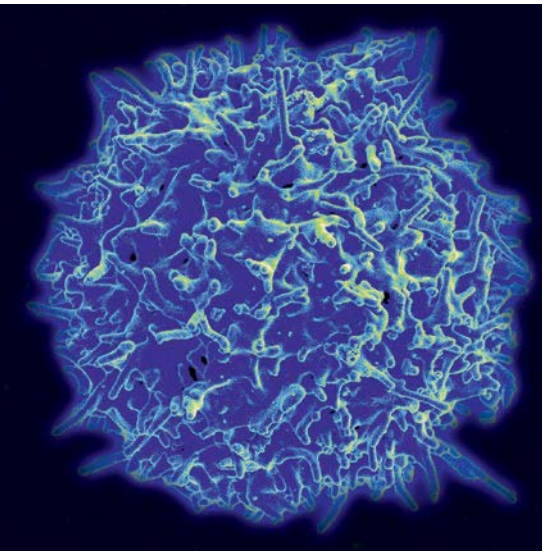
## EMBL-EBI

Paul Bertone and his group have resolved a long-standing challenge in stem cell biology by successfully 'resetting' human pluripotent stem cells to a fully pristine state, at the point of their greatest developmental potential. The study involved scientists from the UK, Germany and Japan and was led jointly by EMBL-EBI and the University of Cambridge. Taking a new approach, the scientists used reprogramming methods to express two different proteins, NANOG and KLF2, which reset the cells. These cells can be maintained indefinitely by inhibiting specific biological pathways, are capable of differentiating into any adult cell type, and are genetically normal. The discovery paves the way for the production of superior patient-derived cellular material for translational medicine. Reset cells mark a significant advance for human stem cell applications, such as drug screening of patient-specific cells, and are expected to provide reliable sources of specialised cell types for regenerative tissue grafts.

Takashima Y *et al.* (2014) Resetting transcription factor control circuitry toward ground-state pluripotency in human. *Cell* 158:1254-69. doi: 10.1016/j.cell.2014.08.02

Sarah Teichmann and her team, together with colleagues at the Wellcome Trust Sanger Institute, have discovered that some immune cells turn themselves off by producing a steroid. The scientists looked at Th2 immune cells during parasitic infection and could show for the first time that at a certain point, these cells produce a steroid called pregnenolone, which regulates their own proliferation. The steroid production by these cells is probably part of a more comprehensive mechanism to bring the immune system back into balance, and is thus an intrinsic component of this particular immune response. These findings, which have implications for the study of cancers, autoimmune diseases and parasitic infections, were made possible by the Single-Cell Genomics Center on the Wellcome Trust Genome Campus in Hinxton, which acts as a focal point for collaboration to accelerate the applications, methods and discoveries in single-cell genomics research.

Mahata B *et al*. (2014) Single-cell RNA sequencing reveals T helper cells synthesizing steroids de novo to contribute to immune homeostasis. *Cell* Rep 7:1130-42. doi: 10.1016/j.celrep.2014.04.011



*A healthy human T cell.*

## EMBL Hamburg

With the help of cutting-edge structural biology infrastructure operated by EMBL Hamburg, Rob Meijers and his group have uncovered how a single molecule can both attract and repel growing brain connections. They determined the 3D structure of netrin-1 bound to one of its receptors and found that an axon – a protrusion that grows out from one neuron to connect it to other neurons in the brain – can be attracted to or repelled by netrin depending on the receptors at the axonal tip. The work, which stemmed from a collaboration with the Harvard Medical School's Dana-

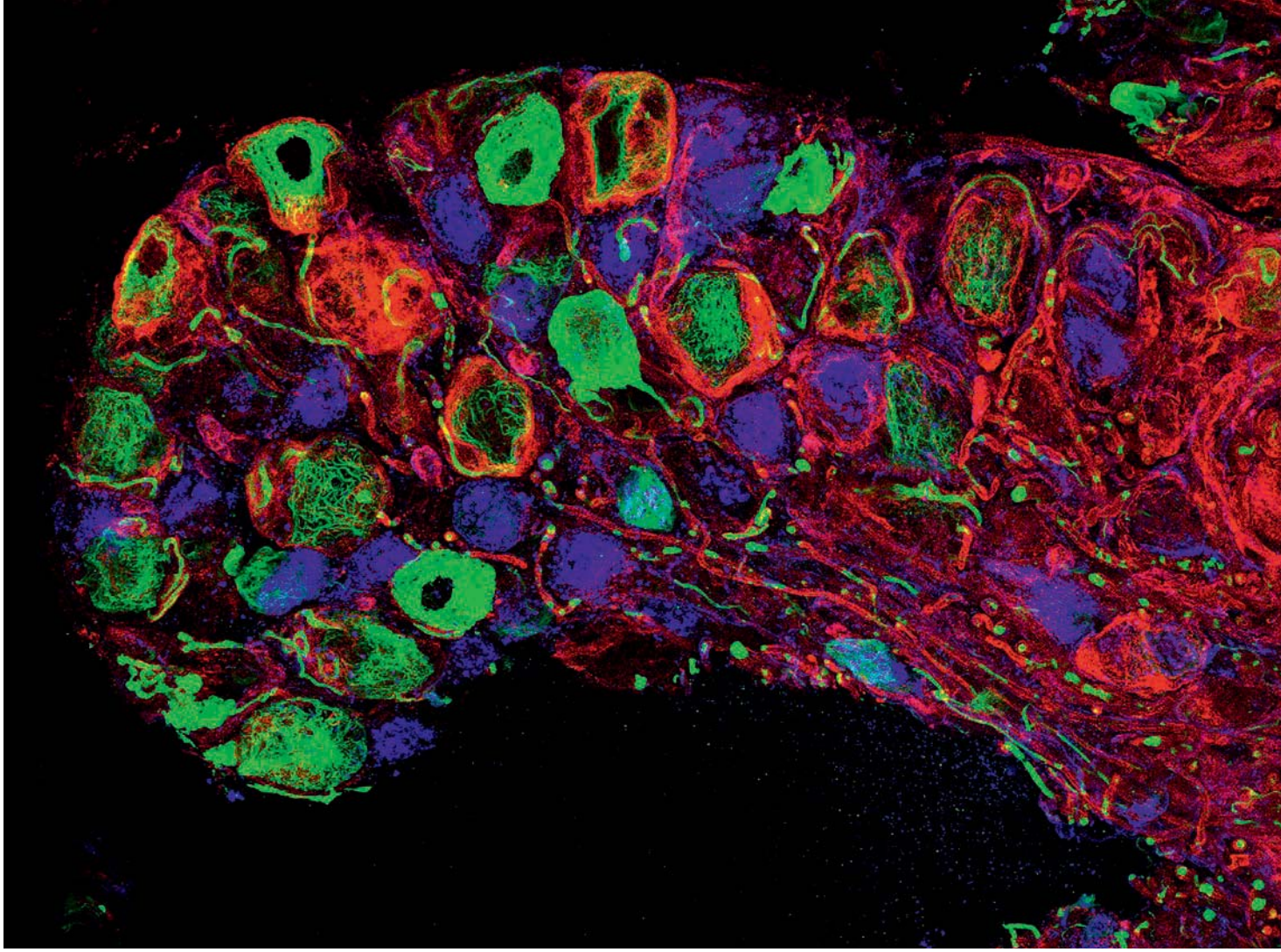
Farber Cancer Institute and Peking University, could have implications for cancer treatment: many cancer cells produce netrin to attract growing blood vessels for nourishment, whereas metastatic cancer cells are often no longer responsive to netrin.
Finci LI *et al*. (2014) The crystal structure of netrin-1 in complex with DCC reveals the bifunctionality of netrin-1 as a guidance cue. *Neuron* 83:839-49. doi: 10.1016/j.neuron.2014.07.010

In another study, the Meijers group has revealed how viruses called bacteriophages destroy the bacterium *Clostridium difficile*, which causes serious problems in hospitals and healthcare institutions because of its resistance to antibiotics. They discovered a structural switch that activates the enzymes involved, and could help engineer viruses to target specific bacteria.
Dunne M *et al*. (2014) The CD27L and CTP1L endolysins targeting Clostridia contain a built-in trigger and release factor. *PLoS Pathog* 10:e1004228. doi: 10.1371/journal.ppat.1004228

## Cell Biology and Biophysics

In a cross-Unit collaboration with Martin Beck's lab from the Structural and Computational Biology Unit, Christian Häring's group uncovered a fundamental mechanism ensuring that genetic material is equally distributed between daughter cells during the complex process of cell division. The EMBL researchers looked into how a protein complex called condensin forms rings around DNA to keep it from becoming tangled during cell division. They found that unlike many other DNA-binding sites, those on condensin do not recognise specific sequences of DNA and can bind anywhere on a chromosome. The team also found that when condensin binds DNA, the enzymatic portion of one of the condensin proteins is activated, which seems to open up the ring to allow the DNA to enter. The ring then closes, entrapping the DNA within the condensin ring.
Piazza I *et al.* (2014) Association of condensin with chromosomes depends on DNA binding by its HEAT-repeat subunits. *Nat Struct Mol Biol* 21:560-8. doi: 10.1038/nsmb.2831

Darren Gilmour's group found that cells in the developing zebrafish can combine to create a specific signal reservoir that enables them to communicate within a restricted group. This is the first time it has been shown that the way cells organise themselves influences their ability to communicate and the researchers propose that this strategy could be much more widespread, influencing processes such as wound repair, organ formation and even cancer.
Durdu S *et al.* (2014) Luminal signalling links cell communication to tissue architecture during organogenesis. *Nature* 515:120-4. doi: 10.1038/nature13852



*A bundle of nerves that relays information from touch receptors on the skin to the spinal cord and ultimately the brain, imaged with the new technique developed by the Heppenstall group.*

## EMBL Monterotondo

In collaboration with colleagues from the Italian Institute of Technology in Genoa and La Sapienza University in Rome, Cornelius Gross and his research team made an important step towards understanding neuropsychiatric disorders. Using genetically engineered mice, they showed that reduced functional brain connectivity and behaviours commonly linked to autism can be due to inefficient trimming of neuronal connections by cells termed microglia during development.

Zhan Y *et al.* (2014) Deficient neuron-microglia signaling results in impaired functional brain connectivity and social behavior. *Nat Neurosci* 17:400-6. doi: 10.1038/nn.3641

Thanks to an approach developed by Paul Heppenstall's group, scientists can now explore nerves in mice in much greater detail than ever before. The technique enables researchers to easily use artificial tags, which broadens the range of what can be studied and vastly increases image resolution. The technique, called SNAP-tagging, had been used for about a decade in studies using cell cultures but Heppenstall's group is the first to apply it to neurons in living mice. It has already enabled them to see structures that, until now, could only be speculated upon, such as nerves arranged around a hair on the skin.

Yang G *et al.* (2015) Genetic targeting of chemical indicators in vivo. *Nat Methods* 12:137-9. doi: 10.1038/nmeth.3207

## Director's Research

The Molecular Medicine Partnership Unit (MMPU) group jointly led by EMBL Director Matthias Hentze and Martina Muckenthaler from the Heidelberg University Clinic demonstrated for the first time in living organisms that the pancreas is most affected in a rare form of haemochromatosis caused by a small mutation in the iron transporter Ferroportin. A hereditary disease, heamochromatosis leads the body to store excessive amounts of iron, and is among the most common genetic disorders in northern Europe, affecting about 100 000 people in Germany alone.

Altamura S *et al.* (2014) Resistance of ferroportin to hepcidin binding causes exocrine pancreatic failure and fatal iron overload. *Cell Metab* 20:359-67. doi: 10.1016/j.cmet.2014.07.007

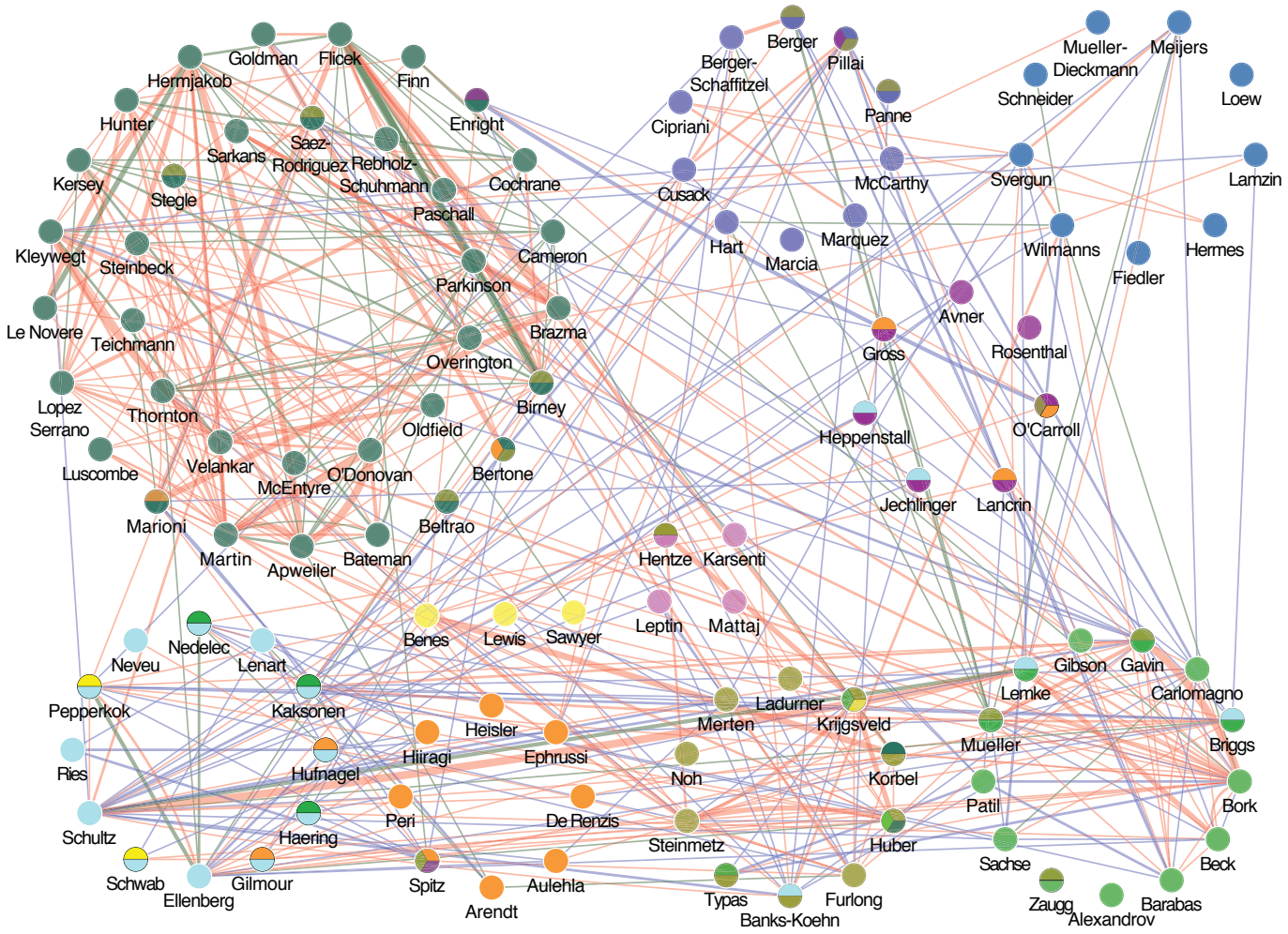
## Structural and Computational Biology

In two papers published in 2014, John Briggs and his group pushed the boundaries of our knowledge of the human immunodeficiency virus (HIV). Upon infection of a target cell, retroviruses such as HIV replicate to produce new immature viral particles, assembled from a medley of viral and cellular components. In May, the lab published a study in which they assembled several copies of a viral protein called Gag and showed how they come together in the immature form of the virus. A second study, published in November, revealed the first structure of the immature form of HIV at a sufficiently high resolution to pinpoint exactly where each building block sits in the virus. This unprecedented detail, which was obtained by optimising both the image data collection and analysis, revealed a surprise: those building blocks are arranged differently in HIV and the Mason-Pfizer Monkey Virus, even though both viruses use the same proteins for the same purpose. The results of this work are of great significance as, for instance, they provide the basis for investigating the mechanisms of drugs known to inhibit HIV assembly and maturation.

Bharat TAM *et al.* (2014) Cryo-electron microscopy of tubular arrays of HIV-1 Gag resolves structures essential for immature virus assembly. *Proc Natl Acad Sci* 111:8233-8. doi: 10.1073/pnas.1401455111

Schur FKM *et al.* (2014) The structure of the immature HIV-1 capsid in intact virus particles at 8.8 Å resolution. *Nature* 517:505-8. doi: 10.1038/nature13838

# Network of Internal Collaborations at EMBL




*The complexity of the network represents the intensity of collaborations between EMBL groups 2012 to 2014 as indicated by shared grants (78), publications (225) and EIPOD fellows (95). Each circle represents an EMBL group (indicated by the last name of the group leader).*

Scientific units & groups

- Cell Biology & Biophysics
- Core Facilities
- Developmental Biology
- Director's Research
- EBI
- Genome Biology
- Grenoble
- Hamburg
- Monterotondo
- Structural & Computational Biology
- Joint Appointments

Interactions

- EIPOD
- Publication
- Grant

Number of interactions

- > 5
- 2–4
- 1

# Services

*EMBL operates unique, world-leading research infrastructures that enable European researchers to achieve breakthroughs across many scientific disciplines.*

## Bioinformatics Services

EMBL provides bioinformatics services and infrastructures to the biomedical science community in its member states through EMBL-EBI, the world's leading source of biological and biomolecular data. In 2014, EMBL-EBI's biological data resources received an average of 11 million web hits per day from a growing user community of commercial and academic researchers throughout Europe and the world.

One of EMBL-EBI's public-facing data centres was moved within the UK in 2014 from London to Hemel Hempstead with no unscheduled downtime to any EMBL-EBI service, the result of a massive effort by all those involved.

In its continued endeavour to improve and expand its services to our member states, EMBL-EBI launched several new resources in 2014. Highlights include the new, open-access European Variation Archive (EVA) that facilitates the exploration of detailed information on genetic variation and the WormBase-ParaSite database that holds the largest collection of parasitic worm genomic data ever assembled. The latter was

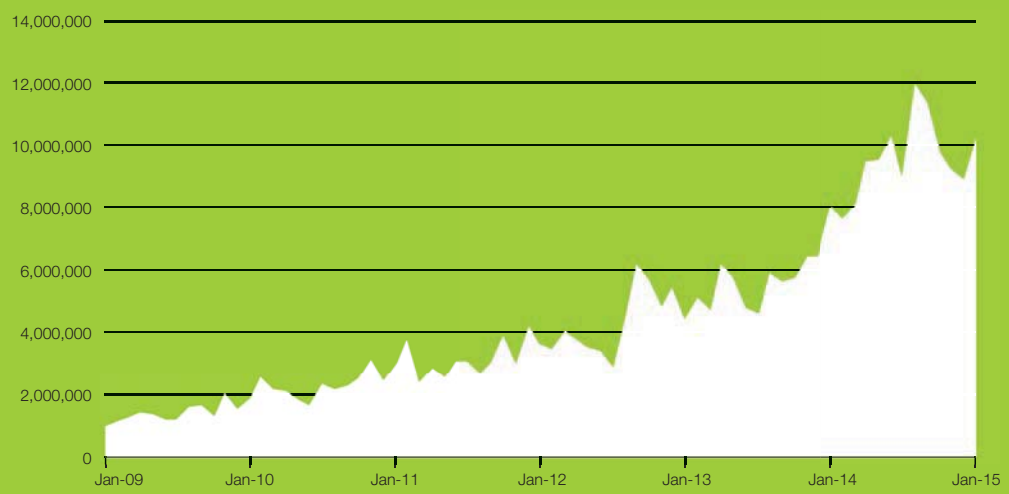
jointly developed by EMBL-EBI and the Wellcome Trust Sanger Institute to provide a fundamental resource for researchers dedicated to reducing the huge disease burden produced by these parasites. The goal of this research is to identify weaknesses in the worms through the use of the information in their genetic code.

As the world-wide Protein Data Bank welcomed its 100 000th structure deposition since its inception in 1971, the Protein Data Bank Team at EMBL-EBI are preparing to handle the increasing size and complexity of submitted data. As part of this effort they launched the Electron Microscopy Pilot Image Archive (EMPIAR), a new resource for raw, 2D electron microscopy images that enables researchers to take a closer look at the images used to build 3D molecular structures. The analysis of these extremely large datasets will drive the development of new and better validation methods, thus leading to better 3D structures.

The advances presented here represent a selection of newly introduced services, databases and tools at EMBL-EBI in 2014. More examples can be found in the EMBL-EBI Annual Report.

## Usage of EMBL-EBI Websites

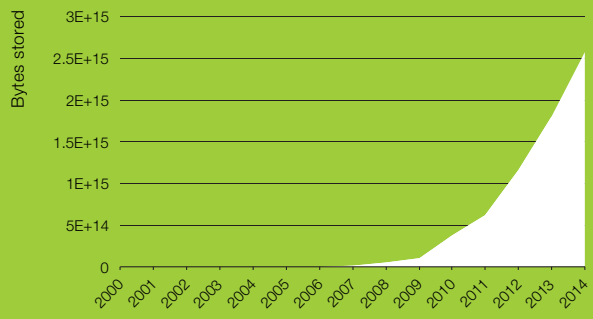
Requests per day, 2009 through 2014



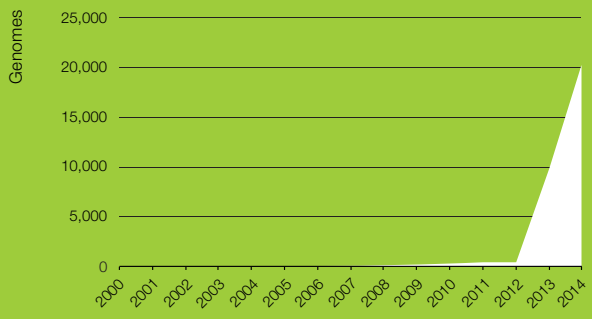

*At the end of 2014, we saw in excess of 11 million requests to EMBL-EBI services on an average weekday.*

# Growth of EMBL-EBI Resources

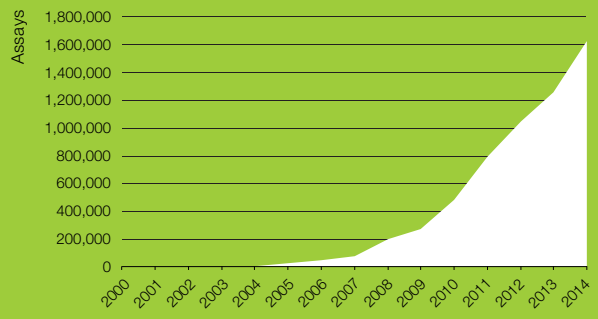
## Nucleotide sequence data (compressed)



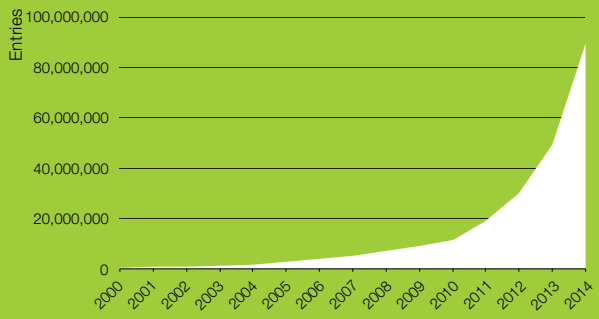

## Genomes (all species)



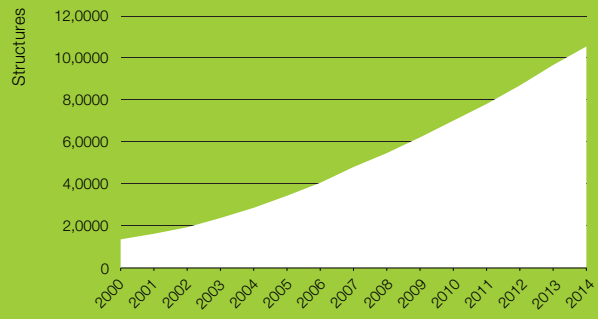

## Gene expression data



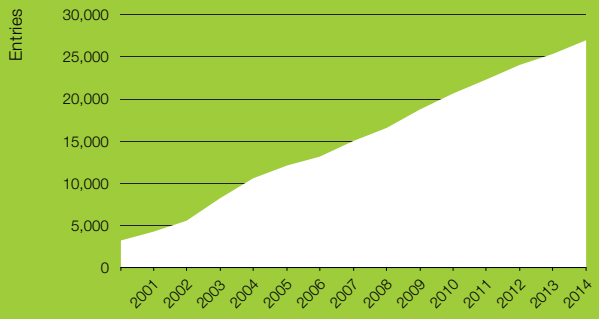

## Protein sequence data




## Macromolecular structures




## Protein families motifs and domains




*In 2014 our core data resources continued their unceasing growth. The cost of generating data continued to fall, which has a dramatic impact on EMBL-EBI databases as it enables researchers to generate more data. EMBL-EBI continues to develop and implement innovative data-storage methods.*

# Structural Biology Services

Structural biology has been at the core of EMBL's activities since its early days, when the pioneering work of Ken Holmes in Hamburg recognised the potential of using synchrotron radiation for life-science applications. Ever since, part of the Laboratory's mission has been to make these enabling technologies available to a broad international scientific community in its member states. Both EMBL Hamburg and EMBL Grenoble are ideally situated at powerful synchrotron sites and the European X-ray Free Electron Laser (European XFEL) is also under construction in Hamburg. Together with the German Electron Synchrotron (DESY) and the European Synchrotron Radiation Facility (ESRF) respectively, EMBL Hamburg and EMBL Grenoble provide X-ray-based research services in structural biology and jointly registered almost 2300 beamline user visits in 2014. Both sites have complemented their synchrotron-based facilities with a complete pipeline of structural biology services in sample preparation and characterisation, as well as data processing through the development of an impressive portfolio of computational services and software packages. Many of these stem from the close collaboration between EMBL Hamburg and EMBL Grenoble on the development of synchrotron instrumentation and methods for structural biology. 2014 marked the 10th anniversary of this successful cooperation, which was celebrated in April.

## EMBL Grenoble

In Grenoble, the ESRF has reached the peak of its Upgrade Programme Phase I, which entails the construction of five new beamlines, the refurbishment of many existing beamlines and major new developments in synchrotron radiation instrumentation. As part of this programme, the old macromolecular crystallography (MX) beamlines were shut down in 2014 and new beamlines have been built in collaboration with EMBL Grenoble teams.

A new era of automation has dawned at the ESRF in Grenoble with the opening of the first Massively Automated Sample Selection Integrated Facility (MASSIF) beamline in September 2014. MASSIF1, operated by the EMBL/ESRF Joint Structural Biology Group, offers a unique, fully automated service for sample evaluation and data collection from crystals of macromolecules, bypassing the need for users to physically come to the facility. In its first two months of operation, more than 2.3 million diffraction images were collected from 1422 samples – ranging from initial hits from crystallisation experiments to large-scale dataset collection for drug discovery programmes. Initial experiments have been very successful, with users complimenting the accuracy, efficiency and simplicity of the facility.

2014 also saw the continuation of a successful cooperation between EMBL Grenoble, the ESRF and the Indian Department of Biotechnology as the joint operation of the Collaborative Research Group beamline BM14, which provides beamtime and support to scientists from India and Europe, was extended for two more years.

# EMBL Hamburg

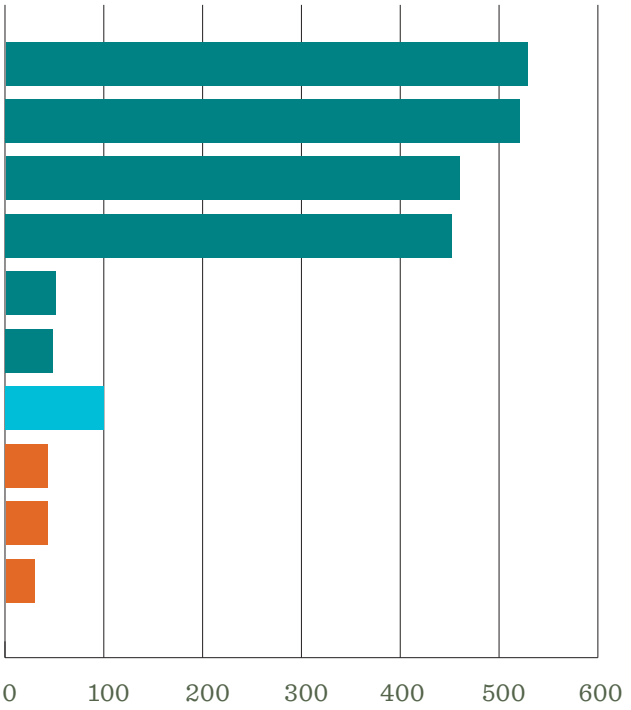
EMBL Hamburg operates three high-brilliance synchrotron radiation beamlines for applications in structural biology – one for small angle X-ray scattering (SAXS) and two for MX applications – at the synchrotron storage ring PETRA III. Despite extensive periods of shutdown between February and December 2014, several structures of unprecedented resolution have already been obtained by internal and external researchers using these beamlines.

Over the past few years, SAXS has grown rapidly as a powerful tool for biomolecular structure determination. In an attempt to meet the increasing demand and to share its world-leading expertise in the methodology, the SAXS group at EMBL Hamburg, led by Dmitri Svergun, organise the biennial EMBO Practical Course on Solution Scattering from Biological Macromolecules. 2014 saw the seventh iteration of the course, which took place for the first time in the EMBL building at PETRA III and, as in previous years, attracted attendees and speakers from around the world.

Hamburg will soon have a new technology highlight as the European XFEL – the most powerful free electron laser in the world – is currently under construction and is scheduled to start user operation in 2017. In line with EMBL's core service mission, EMBL Hamburg plans to make the next-generation infrastructure available to biological users. To this end, EMBL Hamburg coordinates the international XFEL Biological Infrastructure (XBI) user consortium, aimed at building and operating an integrated structural biology facility at the European XFEL to support users at each experimental stage of the structure determination pipeline.

*The European XFEL in Hamburg is scheduled to start operation in 2017. Underground constructions are already completed.*

## Users of EMBL Beamlines
in 2014




| | |
|---|---|
| 529 | ID23-1 |
| 523 | ID29 |
| 459 | BM29 SAXS |
| 454 | ID23-2 |
| 51 | ID30A-3 |
| 48 | ID30A-1 |
| 97 | BM14 |
| 43 | P13 |
| 42 | P12 SAXS |
| 29 | P14 |
| 2275 | TOTAL |

- Operated by ESRF with EMBL Grenoble
- Operated by EMBL, ESRF and the Indian Department of Biotechnology
- Operated by EMBL Hamburg (shutdown from February to December 2014)

# Core Facilities & IT Services

Cutting-edge technology, quality services, diverse expertise, and high user satisfaction characterise our shared research facilities. EMBL Heidelberg operates seven Core Facilities – for advanced light microscopy, chemical biology, electron microscopy, flow cytometry, genomics, protein expression and purification, and proteomics – which are a central component of EMBL's research network. These facilities are heavily used by scientists throughout EMBL, as well as researchers from our member states and beyond. In 2014 a total of over 1200 internal and external users benefited from EMBL's Core Facilities.

Thanks to the support of EMBL's Corporate Partnership Programme (page 28) EMBL launched a new kind of fellowship in 2014 to enable young scientists from EMBL member states to visit the EMBL Core Facilities to learn and use the latest scientific techniques. The Christian Boulin Fellowships have been established in commemoration of EMBL's former Director of Core Facilities and Services who sadly passed away on 27 April 2014, to honour his contribution to the infrastructure that supports European life sciences.

The services offered by the Core Facilities develop flexibly in response to changing demands and requirements in the scientific community.

For example, in the Chemical Biology Core Facility, a state-of-the-art medicinal chemistry lab has been installed and became operational in 2014. The laboratory, supervised by an experienced medicinal chemist, enables scientists to turn relevant hits identified by screening into active biomolecules, in order to explore their potential therapeutic applications. To support growing needs in the areas of metabolism and metabolites, the Laboratory has recruited an expert in imaging mass spectrometry who, in addition to heading a research team, will establish a new Metabolomics Core Facility that will become operational towards the end of 2015.

As life-science research is becoming increasingly data intensive, IT infrastructure and services have come to underpin almost all of EMBL's research activities and are at the heart of the Laboratory's large-scale bioinformatics service provision. The two largest EMBL IT facilities are in Heidelberg and Hinxton. IT capacities in Heidelberg support the needs of the Scientific Research Units and the Core Facilities and also provide central administrative IT services locally and to the outstations. By contrast, the Hinxton IT services are largely driven by EMBL-EBI's very large external services component, the need to produce the data resources behind these services, as well as to support the computational research groups in Hinxton. EMBL IT facilities at both sites support large-scale international research collaborations and participate in exploring and evaluating innovative large-scale IT solutions. For example, EMBL is a co-founder and life-science flagship of the 'Helix Nebula – the Science Cloud', a European consortium that brings together academia and industry with the aim of establishing a sustainable pan-European cloud infrastructure for science. EMBL's IT infrastructure is constantly challenged by extreme data growth – given the current growth rates, EMBL expects to store scientific data in the order of Exabytes by 2021 – and therefore engages in developing robust yet rapidly scalable high-performance IT solutions.

# Technology

## Development and Transfer

*New technologies and instrumentation developed at EMBL drive progress in life science research at the Laboratory and beyond.*

## Technology Development

EMBL has a long tradition and track record in technology development, which is intertwined with and complementary to EMBL's research and service activities. Engineers and technology developers are embedded in the EMBL Research Units and Core Facilities, and customise new instrumentation to researchers' needs. Many of the instruments and tools developed at EMBL are of benefit to the entire scientific community and are made available to the users of our services.

The Laboratory's pioneering role in developing new tools, and their value to the scientific community and its member states, is illustrated by a report published in the journal *Nature** in 2014 on the 100 most highly cited papers of all time, which include three methods papers produced at EMBL.

* Van Noorden et al. (2014) The top 100 papers. Nature 514(7524):550-3. doi: 10.1038/514550a

Although EMBL engages in technology development across a broad range of biological disciplines, some of its most prominent activities cluster around structural biology instrumentation, and computational and imaging technology. 2014 has been a productive year for imaging technology development and EMBL scientists have achieved important advances in the areas of functional imaging reporters, correlative light and electron microscopy and 3D super-resolution microscopy, among others. The importance of innovative imaging technologies in life-science research and medicine was underlined by the award of the 2014 Nobel Prize in Chemistry to three scientists, among them EMBL alumnus Stefan Hell, for the invention of super-resolution microscopy.

Another prominent example of technology development at EMBL, this time in the area of structural biology instrumentation, is CrystalDirect, an automated harvesting and crystal manipulation technology developed at EMBL Grenoble, which is currently being optimised for commercialisation in collaboration with industry. The combined use of this technology with the new highly automated MASSIF beamline at the ESRF (page 21) is a cornerstone in offering fully remote integrated crystallographic services.

# Technology Transfer

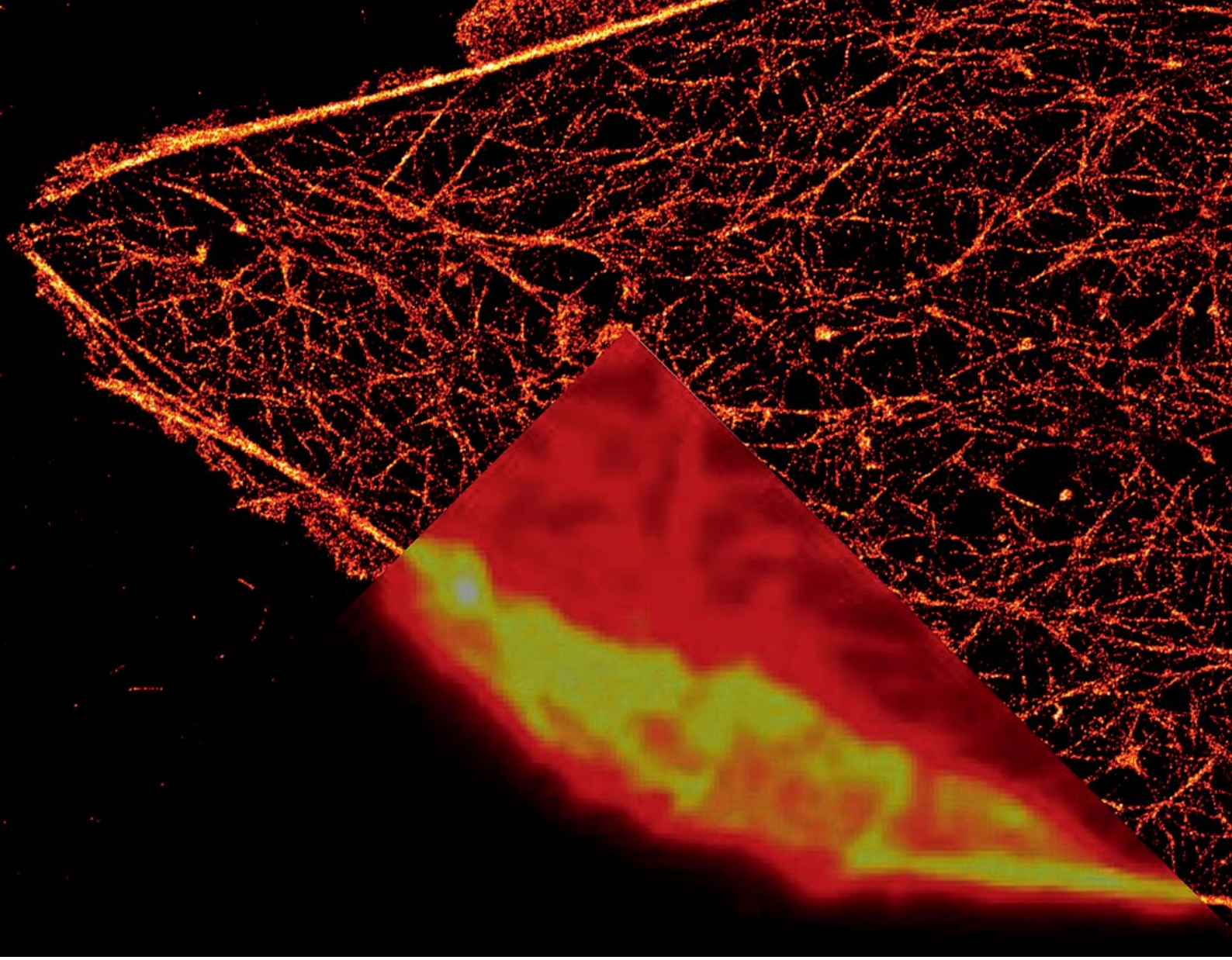
To facilitate the translation of basic research discoveries into practical applications and make new technologies and instruments developed at EMBL available to the broader scientific community and commercial

## EMBLEM Technology Transfer in Numbers 2014

| | |
|---|---|
| 35 | Invention disclosures |
| 269 | License & Collaboration Contracts Concluded |
| 15 | Priority Patent Applications Filed |
| 4 | Copyrights |
| 20 | Patents Granted |
| € 5 900 000 | Income |

## During its 15 years of operation, EMBLEM has registered

| | |
|---|---|
| over 550 | EMBL inventors |
| and more than 350 | commercial licensees |
| and has created 16 | start-up companies. |



*Zooming in on an actin meshwork: a comparison between confocal and super-resolution (stimulated emission depletion) microscopy demonstrates the stark difference in resolution.*

partners, EMBL engages in technology transfer through its commercial subsidiary EMBLEM Technology Transfer GmbH. EMBLEM's proactive technology transfer approach ensures the rapid commercial development of promising innovations while simultaneously securing the free dissemination of knowledge for basic research purposes. Established in 1999, EMBLEM celebrated its 15th anniversary in 2014 with a strong track record of successes and achievements, including a record income of nearly €6 million in 2014.

# Industry Relations

EMBL collaborates with industry and small businesses in a variety of ways, ranging from strategic institutional programmes to less formal project-based collaborations. These interactions provide industry partners in our member states with access to the expertise of our scientists, our infrastructure and our training events. They also ensure that EMBL's knowledge and technologies are broadly disseminated and thereby help to translate our fundamental research into tangible benefits for society.

The EMBL-EBI Industry Programme is the main way through which bioinformatics service teams interact with corporate partners, with dedicated meetings and expert-level workshops on topics prioritised by its members. The Corporate Partnership Programme (CPP), which has now grown to include 12 industry partners, contributes to advanced training at the Laboratory by supporting the development of innovative scientific events at the Advanced Training Centre (ATC) through various initiatives.

Two 'EMBL Science Days' were organised jointly by EMBL and EMBLEM in 2014. They brought together selected EMBL scientists and researchers from GlaxoSmithKline and Promega to foster exchange and future collaboration. 2014 also saw the launch of the Centre for Therapeutic Target Validation (CTTV), a joint venture between EMBL-EBI, GlaxoSmithKline and the Wellcome Trust Sanger Institute, with the aim of harnessing the power of 'big data' and genome sequencing to accelerate drug discovery to address a wide range of human diseases. The CTTV, which in 2014 was led by EMBL-EBI Joint Associate Director Ewan Birney for an interim period, represents the first success of EMBL's increased efforts to forge new strategic partnerships with industry.

*At the annual Corporate Partnership Programme meeting EMBL Director General Iain Mattaj highlights the Laboratory's accomplishments and future plans in his keynote speech to corporate partners.*

# Training and Outreach

*EMBL's diverse portfolio of training and outreach activities trains and inspires the next generation of stellar scientists and raises public awareness of life science research.*

## Internal Training

EMBL is a centre of excellence for training young scientists and has over its 40 years of history helped launch the careers of several thousands of life scientists, many of whom now have leading positions in academia or industry in our member states. EMBL trains doctoral and postdoctoral fellows in world-leading programmes as well as young principal investigators (PIs) who, for the first time, are independently leading their own research group or service team.

As one of the first such structured programmes in continental Europe, the EMBL International PhD Programme (EIPP) has a three-decade track record of serving as a role model for other major institutions across Europe (and beyond). EMBL's Dean of Graduate Studies, Helke Hillebrand, is regularly invited to participate in external advisory boards and PhD

## Internal Training in Numbers 2014

EMBL International PhD Programme

**1899** Applications

**52** New PhD students joining EMBL

**57** Graduations

**247** PhD students in total

EMBL Postdoctoral Programme

**104** EIPOD applications

**23** New EIPODs joining EMBL

**84** EIPOD postdocs

**262** Postdocs in total

*2014 EMBL PhD graduates*

programme committees across Europe. In 2014 she delivered the keynote lecture at the European conference 'Creating Career Opportunities for PhDs in Life and Health Sciences' organised by the Organisation for PhD Education in Biomedicine and Health Sciences in the European System (ORPHEUS). The EIPP welcomes over 50 new PhD students each year and hosts a total of about 230 PhD students at steady state.

Established in 2007, EMBL's Interdisciplinary Postdoc (EIPOD) Programme may not have quite as long a track record as the EIPP, but is not lagging behind in reputation. The Programme, which simultaneously associates postdoctoral fellows with two EMBL labs representing different skillsets, has been so successful that it has already been copied several times throughout Europe. Following the proven EIPOD model, EMBL has begun to establish further specialised training schemes together with national partners that place fellows at the interface between basic and clinical or wet-lab and computational research.

Every year EMBL organises a Career Day at which EMBL fellows as well as PhD students and postdocs from member state institutions can get information on career possibilities for scientists. The 2014 event was dedicated to the important topic of dual careers and attracted over 250 participants from 21 universities and research institutions in Germany, France, Switzerland and the UK.

# External Training

The EMBL International Centre for Advanced Training (EICAT) serves scientists across Europe with its cutting-edge Course and Conference Programme. The 2014 programme was the largest ever carried out at EMBL, and welcomed over 6000 participants to the ATC in Heidelberg and the EMBL campuses in Grenoble, Hamburg, Hinxton and Monterotondo. During the course of the year, several scientific symposia also complemented the celebrations for EMBL's 40th anniversary.

The '11th EMBL Conference: Transcription and Chromatin', which took place at the ATC in August 2014, registered a record attendance of 448 participants. Successful courses and workshops also took place at the outstations: for example, the EMBL workshop 'X-ray Radiation Damage to Biological Crystalline Samples' held in April 2014 at EMBL Hamburg, was attended by 78 scientists.

The EMBO | EMBL Symposia, now in their fourth year, have developed extremely well and are among the largest meetings of the Course & Conference Programme, illustrating the excellent collaboration between the two sister organisations. A prominent example is the EMBO | EMBL Symposium 'The Complex Life of mRNA', which was held in October 2014 and attracted 437 participants.

As the European training hub for bioinformatics, EMBL-EBI organises courses, off-site training events, conference exhibitions, career fairs and workshops, which together reached over 8000 scientists in 34 countries in 2014. EMBL-EBI's free web-based training resource Train online nearly doubled in the past year, increasing from 82 000 unique users in 2013 (based on unique IP addresses) to almost 133 000 unique IPs in 2014. 40 new courses were added to Train online in 2014.

EMBL training activities also involve its industry partners, and a variety of advanced training courses are organised in collaboration with world-leading companies such as those participating in the CPP (page 28). For example, 2014 saw the launch of a new course series on next-generation sequencing together with Illumina, the lead provider of this technology.

## External Training in Numbers 2014

**22** EMBL Conferences

**47** EMBL Courses

**6063** Participants across EMBL sites

Participants from **82** different countries,

over **75%** from EMBL member and associate member states

In 2014 EMBL launched a new EICAT Consultation Panel, comprising the founders and corporate members of the CPP, as a forum to explore training synergies with industry. EMBL-EBI's Industry Programme members also collaborate with EMBL to develop training that is particularly relevant to industry.

Importantly, EMBL's partners in the CPP also support the training of talented young scientists, particularly those coming from underfunded laboratories and countries: in 2014 a total of 147 CPP fellowships were awarded in the form of travel grants and registration fee waivers for EMBL advanced training events.

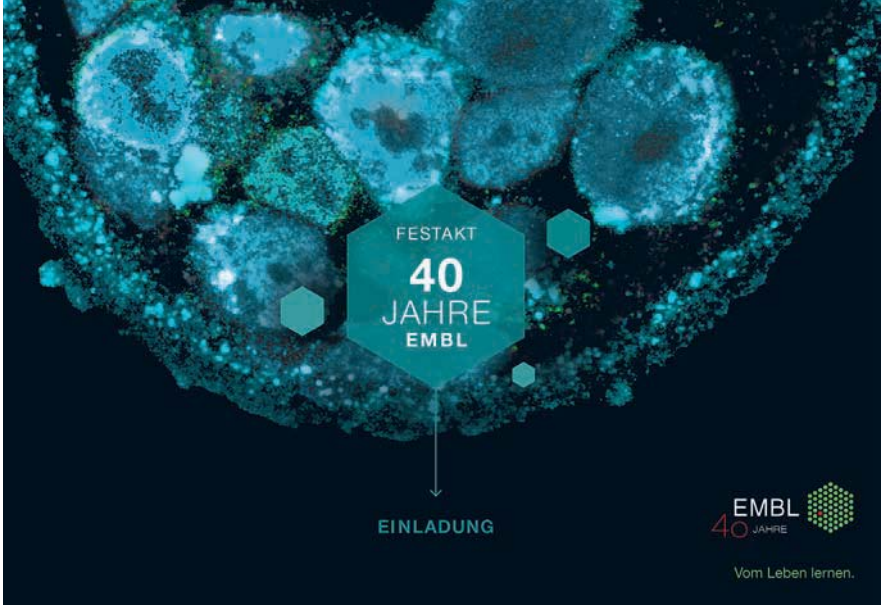
During 2014, EICAT built new and extended existing alliances, enabling for example the joint organisation of events at different sites to better serve the international scientific community. Alongside the long-standing partnership with the Cold Spring Harbor Meetings and Courses Programme, a new collaboration was established with the Wellcome Trust Scientific Conferences in 2014.

# Outreach

The anniversary year offered an excellent opportunity to raise public awareness and promote active engagement in EMBL and its missions. To this aim in 2014 the Laboratory initiated a pilot campaign in 2014 in Germany – as the host site of the EMBL headquarters – centered on a specially developed core theme to communicate EMBL's mission to the general public: 'Vom Leben lernen' ('Learning from life'). The EMBL Discovery Pages (www.embl.de/leben) were created as a campaign portal, to describe aspects of EMBL's research in an engaging and easily understandable way and to serve as a central 'landing page' for campaign-related activities.

Several outreach events for non-scientists were organised as part of this campaign in the course of 2014, starting with the EMBL Annual Reception in March. Scientific Sunday matinees, in which PhD students presented their research interests to public audiences were extremely popular, attracting close to 1400 visitors in five lectures between April and October 2014. 'Creativity' and 'the quest to understand life' as common denominators between the "arts" and "science" were highlighted in several events, including the photo exhibition "DNA | Portraits by Horst Hamann" with a vernissage and podium discussion on this topic, and a completely sold-out concert by the Swiss jazz musician Nik Bärtsch, hosted at the ATC within the widely renowned Enjoy Jazz festival. Finally, in September 2014 EMBL celebrated its 40th anniversary at a gala event with 180 distinguished invited guests, among them Germany's Minister for Education and Research, Johanna Wanka. An overview of these events can be found on pages 4-7.

2014 outreach events were complemented by EMBL's resource development efforts, geared towards building an active network of influential and philanthropic individuals to advise and support the institute. In this context,




EMBL launched "Friends of EMBL", which aims to provide an avenue for interested people to engage with the Laboratory.

A two-day EMBL Research Camp, organised by the European Learning Laboratory for the Life Sciences (ELLS), EMBL's programme for teacher training, took place in Heidelberg in July and allowed 20 members of the general public to gain hands-on experience in laboratory experiments. In addition, ELLS participated in a Design Thinking Challenge for university students to create innovative science education resources, which was presented in collaboration with the software company SAP at the world's largest IT trade fair CeBIT in Hannover in March 2014, and launched log2EMBL, an e-learning platform for science teachers.

Apart from organising EMBL-EBI's 20th anniversary celebrations, including a major event with staff and alumni, EMBL-EBI's External Relations team had a busy year strengthening the institute's social media presence and hosting several visits from high-level representatives of politics, science and the media.

EMBL's smaller outstations also raised awareness through outreach activities for local communities. In the context of this year's Fête de la Science in France, and in celebration of the International Year of Crystallography, EMBL Grenoble for example hosted 150 visitors at an Open Day organised jointly with the neighbouring Institut de Biologie Structurale.

EMBL's Science and Society Programme organised a highly successful EMBL | EMBO Joint Science and Society Conference with the title "Foods are us! On Eating & Becoming". The meeting, which focused on the impact food has on our body and mind and highlighted the biological and cultural processes through which food both defines and transforms human beings, attracted 400 attendees.

Finally, EMBL's Office of Information and Public Affairs revamped various EMBL publications in 2014, including the EMBL Annual Report and EMBLetc., which has evolved from a bi-monthly newsletter into a dynamic website, quarterly print magazine, and monthly e-newsletter.

# Integrating Life Sciences

## in Europe and Across the World

*EMBL interacts closely with the scientific communities in its member states, promotes the integration of European science initiatives and helps shape science policy and strategy in Europe.*

EMBL plays a leading role in promoting international cooperation in the life sciences in Europe and beyond. This is achieved through a number of different activities including hosting visitors at EMBL, establishing collaborations with excellent national research institutes, bringing communities together via scientific workshops and participating in important conferences.

## Member State Relations

Maintaining close relations and a dialogue with the scientific communities and government representatives in member and associate member states

*The accession of the Czech Republic to EMBL builds on a long-standing collaboration, fostered by numerous visits of Czech scientists and political representatives to EMBL.*

is of key importance to EMBL in pursuing its missions. At the same time, to further integrate the molecular biology community in Europe and beyond, the Laboratory constantly strives to establish new links with countries that are not yet part of EMBL. In 2014 EMBL has not only strengthened its relations with its member states, but has also taken important steps towards expanding its membership.

Building on a successful bilateral relationship and existing collaborations between EMBL and Czech scientists, the Czech Republic became EMBL's 21st member state in June 2014. Shortly after the inauguration of the membership, EMBL ran an ELLS LearningLab (page 33) at Charles University in Prague, co-organised with scientists from the Faculty of Science. EMBL has also made preparations to welcome Malta among its member states, as the country's formal application to join EMBL was endorsed in the 2014 Summer Council meeting and is awaiting ratification from the Maltese parliament.

*The Czech Republic became EMBL's 21st member state, and the Slovak Republic, Hungary and Poland joined the prospect membership scheme.*

Tailored to non-member European countries, EMBL's prospect membership scheme was established as a means to engage these countries in EMBL, with the aim to further develop and integrate Europe's scientific landscape in the life sciences and to harness the scientific talent and potential of all European states. By expressing an intent to accede to EMBL, prospect member states are given the opportunity, for a period of three years, to participate in EMBL and its training, and obtain access to services under the same conditions as member states as well as an observer status in the EMBL Council. After visits to several countries and discussions with their scientific communities and political leadership, Slovakia, Hungary, and Poland became prospect member states in the course of 2014.

After its revision in 2013, EMBL's new associate membership scheme has attracted the interest of several non-European countries. Building on a long-standing research relationship with Europe, Argentina became the first country to benefit from the new scheme in 2014. The agreement granting Argentina the status of EMBL associate member state was signed during a two-day inaugural and scientific event in April. Argentina's most recent events as a new EMBL associate member state included a bioinformatics training roadshow and an EMBL-EBI Industry Seminar. The events were followed by the launch of a short-term visitor programme, which in its first


*Intense scientific cooperation between EMBL and Argentina resulted in the country's accession to the new associate membership scheme.*

call for applications selected six postdocs and PhD students to conduct visits of up to three months to collaborate with EMBL scientists.

## EMBL Partnerships

EMBL institutional partnerships create a network of centres of excellence in Europe and beyond through close cooperative affiliations between EMBL and national institutions of comparable standard and international orientation. The Laboratory currently has nine partnerships including local ones with institutions located at or near EMBL sites, and remote partnerships located in member and associate member states aimed at implementing the EMBL model and high scientific standards nationally. One of EMBL's oldest partnerships is with DESY in Hamburg, enabling the exchange of complementary expertise in the construction and operation of research infrastructures for the benefit of the structural biology community. EMBL and DESY renewed their successful partnership and committed to another decade of collaboration during the celebrations for EMBL Hamburg's 40th anniversary in November 2014.

The EMBL Australia Partner Laboratory Network has also continued to develop and grow in 2014. In addition to providing strategic guidance towards the establishment of the Bioinformatics Resource Australia (BRAEMBL), EMBL has been providing continuous support and know-how for the recruitment of international talent at the partner institutions. New group leaders are being recruited at the node in the University of New South Wales, at the EMBL Australia hub at Monash University and at the South Australia Health and Medical Research Institute (SAHMRI) in Adelaide.

## Other Cooperations

In several member countries, links between EMBL and national research communities were intensified via formal collaboration agreements. 2014 saw several important milestones in the development of a new Centre for Structural Systems Biology (CSSB) in Hamburg. The CSSB is a joint initiative of nine research partners from northern Germany including three universities and six research institutes, one of them EMBL Hamburg. This interdisciplinary centre brings together state-of-the-art structural

biology, infection biology and systems biology approaches to investigate the underlying mechanisms of important pathogenic processes and discover more effective treatment options against bacterial and viral pathogens. After its official launch in early 2014 Matthias Wilmanns, Head of EMBL Hamburg, was appointed as the first Scientific Director of the CSSB. With the foundation stone ceremony on 28 August 2014, the new joint research building, which will house laboratories and offices for 180 scientists, also started to take shape. In April 2014 EMBL also committed to a strategic collaboration in research and training activities with the Hamburg University Clinical Center Eppendorf (UKE), one of the CSSB partners. This cooperation was strengthened by an agreement to jointly award PhD degrees. A formal collaboration was also initiated with the National Center for Tumor Diseases (NCT) in Heidelberg to address the application of high-throughput molecular technologies to study human cancer. In autumn 2014 EMBL and Systems Biology Ireland, an interdisciplinary centre conducting research in the fields of systems biology and systems medicine, signed a Memorandum of Understanding on promoting and supporting long-term scientific collaboration. Finally, in the context of a strong existing collaboration with Luxembourg's research community, EMBL and the Ministry for Higher Education and Research extended the joint calls for collaborative research projects with Luxembourg into 2015.

# Further Broadening our Horizons

In recent years, EMBL has established a fruitful collaboration with the Russian Foundation for Basic Research (RFBR), including the launch of two rounds of successful joint research projects. A new Memorandum of Understanding was signed by RFBR, EMBL and EMBO in early 2014 that aims to further this cooperation. Relations also exist with the Kurchatov Institute in Moscow, which received equipment from the decommissioning


*Signing ceremony for the extension of the joint calls for collaborative research projects with Luxembourg.*

of the DORIS beamlines in Hamburg, and which is also helping to establish the XBI at the European XFEL (page 22).

EMBL is also engaged in a successful collaboration with India in the field of structural biology. In December 2014 this saw a major development with the signing of a trilateral Statement of Intent between EMBL, ESRF and the Indian Department of Biotechnology aimed at enhancing strategic cooperation, with a view to enabling India's associate membership. In addition to supporting the exchange of scientific knowledge and enhancing the scientific capabilities of the respective research communities, this agreement provided a framework for the recent renewal of the joint operation of beamline BM14 at EMBL Grenoble (page 21).

In April 2014 EMBL and Stanford University (CA, USA) established the strategic EMBL-Stanford Life Science Alliance to intensify collaboration and exchange of researchers between the two institutions. The alliance aspires to address pressing global challenges in biomedical research, such as understanding common complex diseases, harnessing the potential of new high-throughput technologies, and driving forward the development of preventive and personalised approaches to medicine.

# EU Relations

By pursuing its missions, EMBL makes important contributions to the European Research Area (ERA). In view of this, the Laboratory engages in a broad collaboration with the European Commission (EC), based on an existing Memorandum of Understanding and implemented through biannual Work Plans. In 2014 EMBL worked intensely towards implementing the current Work Plan, which addresses areas of common interest such as research programming, e-infrastructures, mobility of researchers, technology transfer and international cooperation.
EMBL also maintains strong connections with the EC as a member of EIROforum, an organisation consisting of eight European intergovernmental research organisations. While chairing the Thematic Working Group for International Affairs, EMBL devoted significant efforts to the preparation of the EIROforum document on long-term sustainability of research infrastructures, to be published in early 2015.

# European Research Infrastructures

Based on its long-standing experience in operating European-scale life science research infrastructures, EMBL provides strategic advice and coordinates large research infrastructure projects on the European Strategy Forum on Research Infrastructures (ESFRI) roadmap.

Building on its unique expertise and track record in the management of microscopy facilities and international open-access user support, EMBL continues to play a key role in coordinating and implementing Euro-BioImaging, an ESFRI research infrastructure that will provide open user access to a complete range of state-of-the-art imaging technologies. Euro-BioImaging is a European Research Infrastructure Consortium (ERIC) that comprises a set of complementary, interlinked and distributed Nodes, where physical user access will take place, empowered by a strong Hub with a supporting and coordinating role.

The Euro-BioImaging preparatory phase I, administratively and scientifically coordinated by EMBL, was successfully completed in May 2014, with all major recommendations for the infrastructure implementation summarised in the Euro-BioImaging Business Plan. Since March 2014, 13 countries (Belgium, Czech Republic, Finland, France, Israel, Italy, Norway, Poland, Portugal, Slovakia, Spain, The Netherlands, United Kingdom) and EMBL have signed the Euro-BioImaging Memorandum of Understanding. These signatories form the Interim Board, which governs the interim phase of Euro-BioImaging.

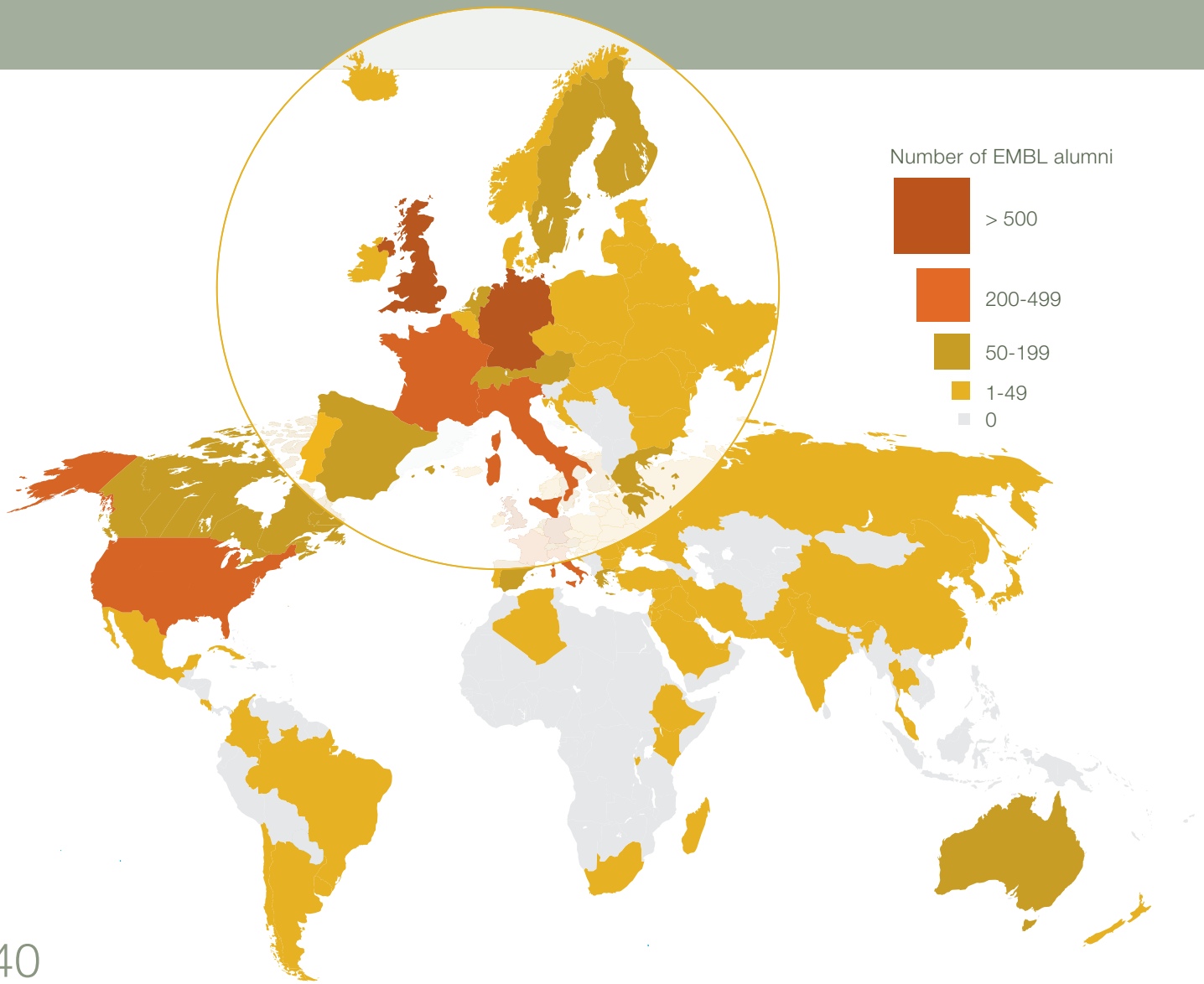
The key tasks of the interim board are now to prepare the submission of the Euro-BioImaging ERIC statutes to the EC, decide on the final governance structure, finance plan and user access policy, and decide on the location of the Euro-BioImaging Hub. After engaging in discussions with the interim board member states, EMBL has started to develop a joint proposal for the Euro-BioImaging Hub.

EMBL has also played a key role in ELIXIR, a research infrastructure that brings together national bioinformatics capacities with those of the EMBL-EBI to scale up the collective capability to archive, integrate, analyse and exploit the large datasets produced in modern life science research. After leading the development of ELIXIR during the preparatory and interim phases, today EMBL contributes to ELIXIR by providing core data services and hosting the ELIXIR Hub at EMBL-EBI. The project organisation and management, however, are now distinct from EMBL, as ELIXIR was established as an international consortium in 2014.

On behalf of ELIXIR, EMBL-EBI also coordinates the BioMedBridges project, aimed at improving access, security and interoperability between 12 biomedical sciences research infrastructures. In 2014 BioMedBridges partners provided a secure framework for sharing sensitive data ethically and legally and held a series of workshops to discuss the development of data standards for different scientific communities, opportunities for support from the European e-infrastructures, and tools to support researchers in issues related to sensitive data.

# EMBL Alumni

*Its over 6500 alumni act as ambassadors for EMBL and enrich the member states' national systems with the experience and training gained at the Laboratory.*



## EMBL alumni

80% of EMBL alumni work in member states

38% have senior positions

76% are in academia

13% are in industry

6690 alumni in total

3346 in Europe

557 in the America's

159 in Asia

65 in Australia

14 in Africa

2488 with unknown residence

Over the course of its four decades of history, EMBL has produced over 6500 alumni, 80% of whom have chosen to work in Europe and remain in research. EMBL alumni are valuable ambassadors for the Laboratory; they share their experiences of working in a unique international and interdisciplinary environment and often go on to successfully implement aspects of the EMBL model in member state institutions. Moreover, they continue to support EMBL in various ways, for example by raising awareness, sending young scientists to EMBL and facilitating collaborations and institutional agreements with the countries and the institutions in which they work.

EMBL's anniversary year saw tremendous alumni engagement, as more than 700 alumni joined celebrations in Hinxton, Monterotondo, Heidelberg and Hamburg, and over 100 alumni contributed as organisers, speakers and sponsors (for an overview of anniversary events at EMBL sites see page 4-7). EMBL alumni from the past four decades were also major contributors to the magazine "40 Years EMBL". A gift from the EMBL Alumni Association to EMBL, this magazine contains contributions from staff and alumni from the whole EMBL community and celebrates EMBL's 40th anniversary by documenting its relevance – past and present – for the European life sciences.

EMBL alumni organise national meetings, known as "local chapters", which have a catalytic effect on EMBL's interactions with scientists from the hosting member states. The 50th and 40th anniversaries of EMBO and EMBL and their impact in Austria were celebrated during the EMBanniversary, organised by EMBL alumni in Vienna in July 2014. In the autumn, the Greek and the Belgian alumni chapters organised similar scientific and networking events, at the annual Congress of the Hellenic Society of Biochemistry and Molecular Biology in Thessaloniki and at the VIB in Ghent, respectively.

EMBL has launched an ambitious project that relies on a vast community effort from its alumni: together with the Alumni Association, the Laboratory will build a web-based archive that preserves and makes visible EMBL's institutional history, its role in the history of molecular biology and its scientific impact worldwide. After a workshop held in January 2014 to share the underlying vision and discuss the plans with different stakeholders, the EMBL Archive has started to take shape, with the recruitment of an archivist and the launch of an online donations platform for material collections and funds in July 2014.

The EMBL Alumni Association celebrates the achievements and efforts of its alumni through the John Kendrew Award and the Lennart Philipson Award, created to honour EMBL's first two Director Generals. The 2014 John Kendrew Award, which recognises excellence in science and/or science communication, was awarded to Czech scientist Martin Jinek, former PhD student at EMBL and now Assistant Professor at ETH Zurich. The award acknowledges the impact of his work in the field of RNA-guided gene targeting on technology development and biotechnological innovation. The Lennart Philipson Award, which was launched in 2014, recognises outstanding contributions to translational research in human health and/or technology innovation in the life sciences, and will be awarded for the first time in 2015.

# Administration

*EMBL's administration supports all of the Laboratory's missions by efficiently handling all organisational aspects.*

The EMBL Administration supports EMBL's missions by handling administrative aspects so that EMBL staff can focus their activities in the areas of research, technology development, service provision, training or international integration. The activities of EMBL Administration span budgetary, financial and purchasing matters; human resources; grants and external funding management; facilities management; legal services; health and safety; and the development of administration IT systems.

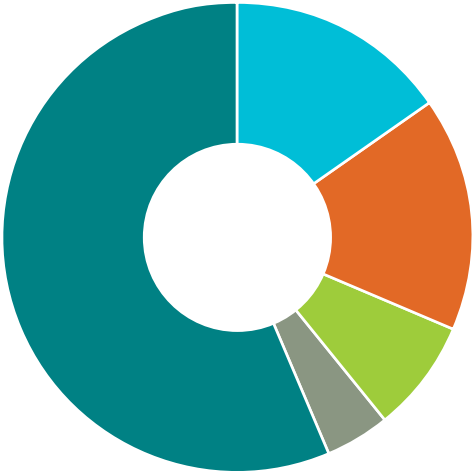
EMBL's Administration constantly works to upgrade and streamline its systems and procedures. In an effort to bring together commonly used administrative services into one simplified interface, an electronic time recording system was introduced in January 2014 and significant effort has been directed towards the implementation of a similar electronic system for leave recording.

In 2014 EMBL was awarded the European Commission's "HR Excellence in Research" badge in recognition of its efforts to implement the European Charter for Researchers and the Code of Conduct for Recruitment of Researchers and to improve employment, career development and working conditions of its scientists. EMBL has already substantially improved the working conditions of EMBL fellows, who are, as of January 2014, full members of the EMBL pension scheme. In addition, fellows are now entitled to the EMBL unemployment and accident at work insurance, and to allowances and benefits formerly restricted to staff members.

At the main Laboratory in Heidelberg a renovation of the building façade began in 2014 and will continue until the end of 2015. Major building works at other EMBL sites include the repair of buildings and the improvement of safety at Monterotondo and extensive input into the CSSB and European XFEL building projects in Hamburg to ensure that the needs of life scientists are reflected in the design of the facilities.

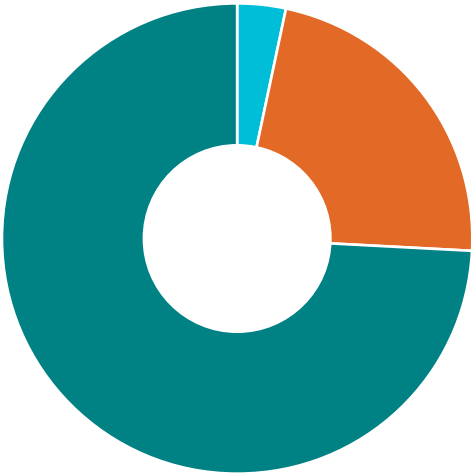
*The ATC as seen by Horst Hamann*

# Personnel Statistics



## Personnel
on 31 December 2014

| | |
|---|---|
| 919 | Staff |
| 247 | Predocs |
| 262 | Postdocs |
| 124 | Supernumeraries and ancillaries |
| 71 | Diploma students and trainees |
| 1623 | Total* |



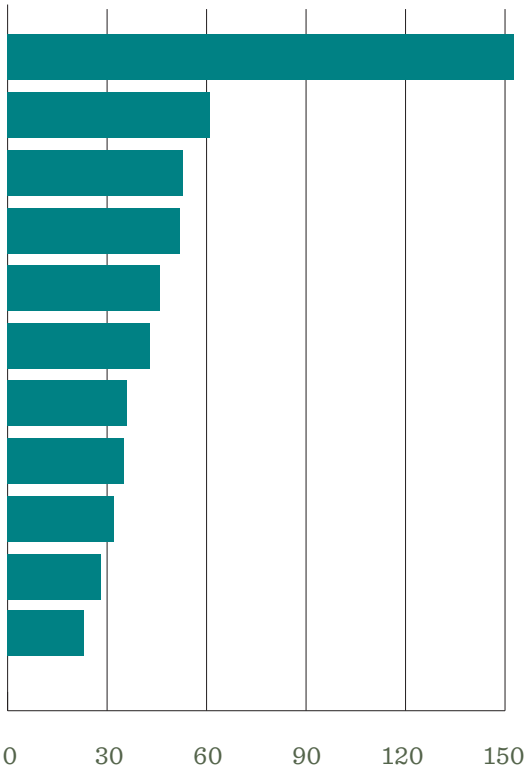
## Staff Nationalities

| | |
|---|---|
| 1205 | EMBL member and associate member states |
| 54 | EMBL prospect member states |
| 364 | Non-member states |
| 1623 | Total |

* Please note that as of 2014 the personnel statistics no longer include visitors to EMBL. Statistics for these are presented separately and refer to the entire calendar year (see page 45).

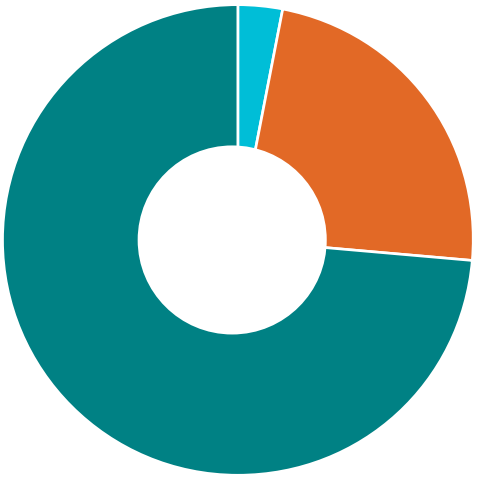
## Visitors to EMBL Units

during 2014




| | |
|---|---|
| 154 | EMBL-EBI Hinxton |
| 61 | Structural and Computational Biology |
| 53 | Genome Biology |
| 52 | Core Facilities |
| 46 | Cell Biology and Biophysics |
| 43 | Developmental Biology |
| 36 | EMBL Monterotondo |
| 35 | Others |
| 32 | EMBL Hamburg |
| 28 | EMBL Grenoble |
| 23 | Directors' Research |
| 563 | Total |

## Visitors' Nationalities



| | |
|---|---|
| 415 | EMBL member and associate member states |
| 16 | EMBL prospect member states |
| 132 | Non-member states |
| 563 | Total |

# Financial Report

## Income/expenditure statement

| Income<br>x € 1,000 | 2014 | 2013 |
|---|---|---|
| Member state contributions | | |
| — Ordinary contributions | 99,692 | 97,277 |
| - Currency adjustment for Sterling contributions | -151 | 189 |
| - Entry fees | 335 | |
| — Associate member state contributions | 1,353 | 501 |
| - Entry fees | 1,245 | |
| — Additional contributions | 9,937 | 22,457 |
| Internal tax | 31,992 | 29,871 |
| External grant funding | 45,146 | 40,160 |
| Other external funding | 2,480 | 1,923 |
| Other income | 17,768 | 14,044 |
| Total income | 209,797 | 206,422 |
| **Expenditure** | | |
| Staff costs | 120,623 | 113,772 |
| Operating costs | 67,848 | 72,875 |
| Equipment expenditure incl. Depreciation | 13,702 | 16,573 |
| Total expenditure | 202,173 | 203,220 |
| Surplus (deficit) for the year | 7,624 | 3,202 |

# External grant funding

| | 2014 | | 2013 | |
|---|---|---|---|---|
| | x € 1,000 | % | x € 1,000 | % |
| EC | 13,556 | 30.0 | 13,597 | 33.9 |
| ERC | 5,920 | 13.1 | 3,307 | 8.2 |
| NIH | 8,629 | 19.1 | 9,030 | 22.5 |
| Wellcome Trust | 5,444 | 12.1 | 5,447 | 13.6 |
| BBSRC | 2,887 | 6.4 | 2,422 | 6.0 |
| BMBF | 2,165 | 4.8 | 1,565 | 3.9 |
| DFG | 1,960 | 4.3 | 1,634 | 4.1 |
| MRC | 459 | 1.0 | 114 | 0.3 |
| Humboldt Foundation | 374 | 0.8 | 262 | 0.7 |
| ANR | 226 | 0.5 | 221 | 0.6 |
| HFSPO | 198 | 0.4 | 66 | 0.2 |
| Others | 3,328 | 7.4 | 2,496 | 6.2 |
| Total | 45,146 | 100% | 40,160 | 100% |

## Other external funding

| | | | | |
|---|---|---|---|---|
| EMBL-EBI industry support | 755 | 30.4 | 716 | 37.3 |
| Elixir member state contributions | 1,198 | 48.3 | 1,058 | 55.0 |
| Other external funding | 527 | 21.3 | 149 | 7.7 |
| Total | 2,480 | 100% | 1,923 | 100% |

# EMBL budget 2014

€ 210 million

# Member state contributions

| | 2014 | | 2013 | |
|---|---|---|---|---|
| | x € 1,000 | % | x € 1,000 | % |
| **Ordinary contributions** | | | | |
| Austria | 2,296 | 2.3 | 2,121 | 2.2 |
| Belgium | 2,791 | 2.8 | 2,617 | 2.7 |
| Croatia | 317 | 0.3 | 292 | 0.3 |
| Czech Republic | 715 | 0.7 | | |
| Denmark | 1,782 | 1.8 | 1,693 | 1.7 |
| Finland | 1,386 | 1.4 | 1,352 | 1.4 |
| France | 16,252 | 16.3 | 15,457 | 15.9 |
| Germany | 20,379 | 20.4 | 19,835 | 20.4 |
| Greece | 1,643 | 1.6 | 1,761 | 1.8 |
| Iceland | 59 | 0.1 | 88 | 0.1 |
| Ireland | 1,069 | 1.1 | 1,255 | 1.3 |
| Israel | 1,277 | 1.3 | 1,012 | 1.0 |
| Italy | 12,006 | 12.0 | 11,897 | 12.2 |
| Luxembourg | 198 | 0.2 | 224 | 0.2 |
| Netherlands | 4,642 | 4.7 | 4,514 | 4.6 |
| Norway | 2,554 | 2.6 | 2,335 | 2.4 |
| Portugal | 1,217 | 1.2 | 1,128 | 1.2 |
| Spain | 8,423 | 8.4 | 8,016 | 8.2 |
| Sweden | 2,821 | 2.8 | 2,675 | 2.8 |
| Switzerland | 3,613 | 3.6 | 2,646 | 2.7 |
| United Kingdom | 14,252 | 14.3 | 16,362 | 16.8 |
| Total | 99,692 | 100% | 97,277 | 100% |
| **Currency adjustment** | | | | |
| for Sterling contributions | -151 | | 189 | |
| | -151 | | 189 | |
| **Associate member state contributions** | | | | |
| Australia | 501 | | 501 | |
| Argentina | 852 | | | |
| | 1,353 | | 501 | |
| **Additional contributions** | | | | |
| from UK Government | 9,130 | | 7,052 | |
| from Germany | 807 | | 680 | |
| | 9,937 | | 7,732 | |

# 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 Core Facilities and IT Services Unit Review

On 26 to 27 March 2014 the review of the EMBL Core Facilities and IT Services took place. Fifteen international experts, including three members of EMBL's Scientific Advisory Committee, formed the Review Panel. The panel was chaired by Michael Snyder from Stanford University (CA, USA). Regrettably, Christian Boulin, the Director of Core Facilities and Scientific Services, was unable to participate in the review due to illness and he sadly passed away on 27 April 2014. Christian joined EMBL in 1976 and worked in a variety of positions until taking over the Core Facilities and Scientific Services leadership role under Fotis Kafatos. Christian will be remembered for his considerable effort in developing the Laboratory's Core Facilities over many years into their current excellent state. Christian was an ideal colleague, constructive, unselfish and committed to the success of everyone at EMBL. He incorporated the collaborative, good-humoured spirit that distinguishes the Laboratory and will be sorely missed by us all.

## Evaluation Summary

The EMBL Core Facilities and IT Services were created as a way to provide support to EMBL staff members. In the case of the Core Facilities, state-of-the-art technologies and equipment are provided to support EMBL researchers, and Core Facility staff with expertise in the use of the equipment and technologies are chosen with the role of supporting EMBL research and training staff members in the use of the Core Facilities. Where capacity permits, the Core Facilities also serve and advise external users from the member states. This function is much appreciated. IT Services in EMBL- Heidelberg have an even broader internal remit in that they provide access to all forms of IT service and support in their use to all members of staff in Heidelberg and Monterotondo. They also liaise with IT staff at the other three EMBL locations.

The panel rates the overall performance of the EMBL Core Facilities and IT Services as outstanding and congratulated Christian Boulin for moulding the EMBL Core Facilities over many years into their current excellent state. The panel praised the Core Facilities for clearly being one of the highlights of EMBL, supporting users, especially new researchers who use the facilities to get their research programmes up and running quickly. They considered the facilities a major attraction in recruiting outstanding faculty to EMBL.

All the Core Facilities offer advanced technologies to EMBL researchers and external users and all have kept pace with new developments. The quality of service was rated as outstanding in terms of number of users served and the quality of the service. The panel highlighted that the technologies and services offered by the Advanced Light Microscopy Facility (ALMF) and

Electron Microscopy Core Facility (EMCF) are rarely offered by other core facilities. The panel underlined the excellent interactions of the facilities with industry for obtaining and co-developing equipment and other support. The panel evaluation was supported by a user satisfaction survey carried out in late 2013, which showed that user satisfaction has generally grown since the last review, and stands at a very high level.

In addition to providing services, the facilities have an outstanding record of training, with most facilities offering numerous workshops, facility staff being involved in EMBL courses and facilities reaching out broadly to institutions in EMBL member countries. The facilities have increased the impact they have outside EMBL even more by being involved in networks such as the P4EU network initiative established by the Protein Expression and Purification Core Facility; the European Cytometry Network started by the Flow Cytometry Core Facility; and the support given to Euro-BioImaging.

The panel concluded that the Core Facilities function exceptionally well and all existing core facilities serve a useful purpose and should be maintained. They encourage EMBL and the Core Facilities to consider user fees for all users. The panel also recommended that all Core Facilities meet at least once a year with their user committee and that they should consider adopting a more formal process for horizon scanning of new technologies that might be worth adopting.

It was the second time that the IT Services in Heidelberg were included in the review and the first time that there was a dedicated sub-panel focused solely on IT services. The adjusted review format worked well. The IT infrastructure required to support data-driven research at EMBL is seriously challenged by high-throughput technologies in large-scale and interdisciplinary information biology projects. The IT Services perform extremely well, due in large part to the skills and commitment of the staff and efficient management. To maintain high quality service, the panel recommended EMBL to look into staffing, redundancy in skills, mechanisms for massive high-performance computing (HPC), storage and an upgrade of the EMBL data link to EBI and the rest of the network.

Finally, the panel made some recommendations concerning plans that need to be made to replace Christian Boulin as he was approaching retirement age.

## Response to the Panel's Recommendations

I wish to thank the panel for their extensive and detailed analysis of the Core Facilities and IT Services. I am very pleased with the strongly positive opinion of the performance of these crucial support functions and with the thoughtful recommendations on ways to further improve their performance and function.

I agree with the panel's opinion that Christian Boulin performed outstanding work in organising and leading these (and other) scientific support services for EMBL. The work of Christian and all his staff was evaluated very positively prior to the review by a large cross-section of users who participated in a web-based survey of the quality of service provided I note, and discussed with the panel, Christian's retirement towards the end of the next review period and the need for succession planning. Some preliminary discussion of this has already taken place and I value the panel's advice that it will likely be necessary to divide the future leadership into at least two sections, with the Core Facilities plus workshops forming one area and IT Services forming another.

Like many review panels before them, the panel is of the opinion that EMBL's staff turnover system may not be the best way to organise some aspects of our activity. I, however, disagree strongly with their recommendation that fixed term staff contracts should not be applied in the Core Facilities and IT Services. Their success and performance (and other EMBL Service Units) is ample evidence that the EMBL fixed-term contract model does not inhibit us from setting up excellent support services and we will continue with its use to the benefit of the member states.

Recommendations are made by the panel to increase staffing levels in two areas; to make user feedback and horizon scanning of new technologies more formal; and to introduce a transparent user fee system for all Core Facilities. I will discuss these issues with the Unit leadership and, where appropriate, with Council in preparing the next Indicative Scheme.

The panel, while acknowledging the very high level of performance of the staff, recommends that change is required in the overall organisation of the IT Services to increase its robustness to staff illness and turnover. They recommend following more closely some 'industry standard' organisational protocols to achieve this, as well as increasing the cross-training of staff members in each other's tasks. I believe this is a wise recommendation and will follow this up with the leadership of the Unit.

The panel recognises that EMBL Heidelberg and Hamburg do not have high capacity links to the German data network. They point out that this is already essential and will only become more of a problem for the function of these parts of EMBL as time goes on. We are already discussing this topic with the German Ministry for Education and Science, who are sympathetic to our needs, and will continue to work with them until a suitable solution is achieved.

*Professor Iain W. Mattaj, FRS*
Director General

28 April 2014

# EMBL Structural and Computational Biology Unit Review

The Structural and Computational Biology (SCB) Unit at EMBL Heidelberg was reviewed on 7 and 8 May 2014 by a panel of 17 international experts, including seven members of EMBL's Scientific Advisory Committee. The review was chaired by Ron Milligan from the Scripps Research Institute (CA, USA).

## Evaluation Summary

The quality of the research, training, and leadership of the SCB Unit were all ranked as outstanding. The review panel concluded that the Unit is one of the strongest such programmes worldwide, which is supported by the fact that many of their publications appear in top-notch journals. The strengths of the Unit include an outstanding infrastructure, high complementarity within the Unit, groups that cover a considerable range of disciplines and a high level of collaborative activity within and outside the Unit and overall high productivity. The Joint Heads of Unit Peer Bork and Christoph Müller have provided strong management and leadership in advancing a unified vision, in determining Unit composition, in supporting instrumentation acquisition, and in providing strong mentorship of younger colleagues and an outstanding environment in which the group leaders can thrive. The panel also congratulated the Unit and EMBL for the stimulating working environment it has created for PhD and postdoctoral fellows.

SCB employs a broad range of complementary approaches and expertise to study the structural and functional organisation of molecular networks. It is characterised by a rather unique combination of approaches, including multi-resolution structural biology approaches ranging from molecules to cells, proteomics, and computational systems biology. These disciplines synergise in non-traditional ways and enable the groups to reach into entirely new areas. Where groups have collaborated, as for example in the Mycoplasma pneumoniae systems biology project, the results have been remarkable and stand out worldwide.

A considerable commitment in electron microscopy (EM), nuclear magnetic resonance (NMR), biological instrumentation and computational facilities has been made since the last review in 2010. Of particular note was the installation of an FEI Titan Krios Electron Microscope and direct detector in a specially built facility. This state-of-the-art addition in EM has brought EMBL to the forefront of molecular microscopy. The panel notes, however, that there is a need to invest and upgrade further the instrumentation for electron tomography, storage capacity and CPU. Future plans to add an additional group leader in computational

biology and to support a Metabolomics Core Facility were viewed very positively. In addition, the panel highlighted the need for access to analytical ultracentrifugation and to upgrade the internet linkage of EMBL Heidelberg. Finally, the panel recommended recruiting an NMR group leader to replace Teresa Carlomagno when she leaves, if a candidate of suitable quality can be identified.

In summary, the panel considers that the SCB Unit continues to push the technical boundaries in both computational and structural biology, and is almost unique worldwide in its ability to deploy large-scale computational, -omics and structural approaches in an integrated fashion that allows problems in systems biology to be addressed in a comprehensive manner.

## Response to the Panel's Recommendations

I begin by thanking the panel for this Unit review and for their detailed report, the overall conclusions of which are very positive. Each of the group and team leaders under review received a detailed critique, and many helpful suggestions were included in the report. The panel attributes the success of the Unit in considerable part to the efforts of the Joint Heads of Unit Christoph Müller and Peer Bork. I agree with the evaluation that both have performed in an outstanding way.

Prior to the review I had specifically asked the panel whether, in their opinion, the technology coverage of the Unit was too broad. The Unit reaches from computational biology through multiple structural techniques to systems biochemistry and methods development. Although the Unit is large by EMBL standards, this is still a considerable range to cover. The panel clearly felt that the current structure is a great strength, fostering as it does interdisciplinary and multi-disciplinary projects within the Unit and involving many extra-Unit collaborations inside and outside EMBL. They felt that the way the Unit is organised has contributed to it becoming a leading centre for such studies. I am very happy to acknowledge their opinion.

Although not included in the report, the panel discussed – as have prior review panels of other EMBL Units – the slow loss of expertise in biochemistry that is happening not only in EMBL but also in many other life science research institutions. This is particularly important because structural biology projects often require parallel complex biochemical purification or reconstitution experiments. As I have already stated elsewhere, EMBL will strive to retain this expertise but it is evident that very few current group leader applicants have the requisite training.

The panel points out that the SCB Unit is very technology dependent and thus requires continuous investment in equipment that is often expensive. They suggest several areas in which investment will be required, including

the 10 GBit/s network link that was already discussed in the context of the recent IT Services review. I thank them for their advice and specific recommendations and will take them up with the Unit leadership and with Council as and when appropriate.

I note the panel's very positive opinion of the research that has resulted from the major investments made in high-resolution EM equipment during the past and current review periods. I believe that EM-based research on both molecular- and cellular- scale problems at EMBL is currently in a very active phase and will try to maintain this strength. As the panel points out, expensive investment is also required to do this.

The panel was made aware that the single group leader who specialises in NMR, Teresa Carlomagno, and who has performed outstandingly well, will reach the nine-year limit in the near future and already has obtained an excellent position elsewhere. They strongly recommend retention of NMR expertise in the Unit beyond Teresa's departure and we will take this advice into account when seeking a replacement.

Computational methods have become pervasive in all EMBL Heidelberg Units and in the vast majority of the individual groups. This often leads to the situation in which a group has one or a few research fellows who use computational methods that are outside the expertise of their group leader. The panel praises the SCB Unit for its role in developing solutions to the resulting problem of isolation and lack of mentorship through the leadership of EMBL Centres by some group leaders and the organisation of both Bio-IT in Heidelberg and regular semi-formal meetings with other computational biologists in Heidelberg. These are all open to Heidelberg staff and the Centres are also open to staff from other EMBL Units. I thank my colleagues for these efforts. I feel they have created promising model solutions that can be copied elsewhere to what is a widespread problem.

*Professor Iain W. Mattaj, FRS*
Director General

23 May 2014

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