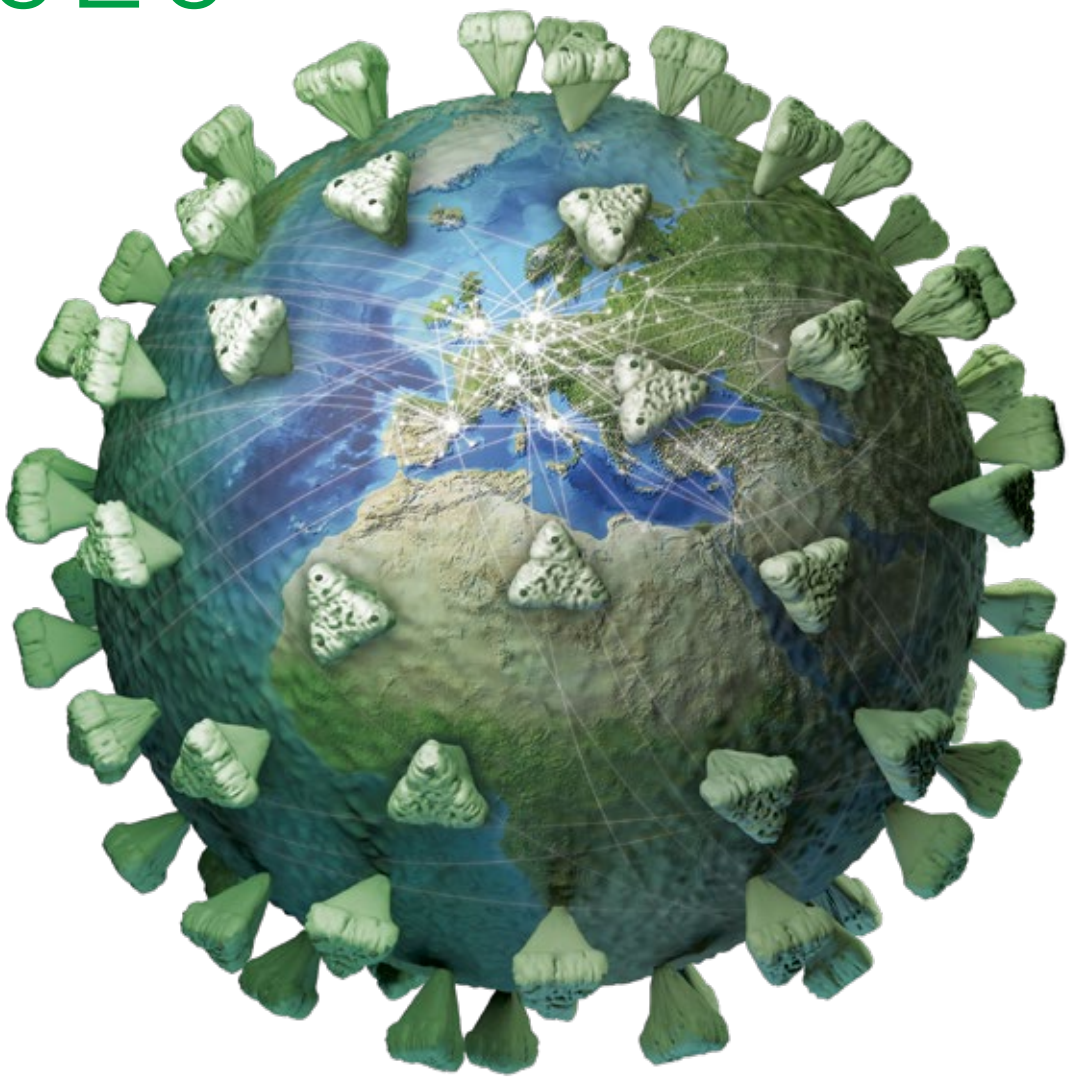
EMBL

Annual Report

2020



Collaborative discovery in challenging times

Collaborative discovery in challenging times

This image of SARS-CoV-2 has been combined with the globe and a representation of EMBL's network of collaborations, showing how our work and discoveries have continued throughout the COVID-19 pandemic.
Design team/EMBL

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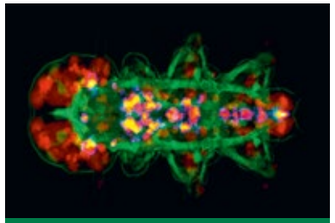
EMBL was set up to promote molecular biology across Europe, and to create a centre of excellence for training Europe's leading young molecular biologists. To accomplish this, EMBL pursues five missions.



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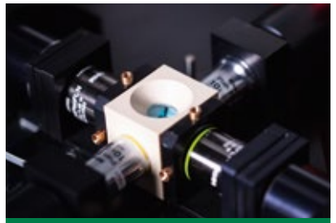

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Foreword

For all of us, 2020 was a year of unprecedented challenges. I am proud of EMBL's rapid and effective action to ensure the safety of our staff and to join the global response to the COVID-19 pandemic. Our work to establish the European COVID-19 Data Platform supported scientists in rapidly sharing and analysing data on the pandemic. We conducted numerous projects to understand the biology of the SARS-CoV-2 virus and advance the development of testing methods, treatments, and vaccines (pp. 5–11). The pandemic demonstrated once again the value to our member states of the technologies EMBL has developed to allow automated and remote access to our structural biology facilities, and several other facilities have now implemented systems for remote access to allow safe operations on site. These initiatives have helped us continue our vital work of supporting scientific research across Europe and around the world, as well as providing advice and guidance to member state governments and policymakers.

EMBL has always carried out research that benefits society, and it is gratifying to see how research by members of the EMBL community as far back as the 1970s laid the groundwork for vaccine technologies that are helping us out of the current crisis (p. 10). As these examples show, fundamental research not only enables us to deal with present concerns, but also equips us with knowledge and tools that can be applied to unforeseen challenges in the future.

Despite the pandemic, our preparations have continued for the next EMBL Programme, *Molecules to Ecosystems*, which will begin in 2022. The new programme will advance our knowledge of the fundamental principles of life. By giving us a deeper understanding of life in the context of its environment, which is where life really happens, this programme will also inform solutions to global challenges such as climate change, pollution, loss of biodiversity, and the spread of antimicrobial resistance. It will help us to understand more about the causes of pandemics and how we might be able to prevent their most serious effects. Collaborations across EMBL's member states will be an essential part of the programme, as we bring together institutes and disciplines to create a new era of life science research in Europe, with resulting societal, economic, and health benefits.

We knew that 2020 would be a year of change for EMBL as an organisation, but the COVID-19 pandemic has in some ways helped to accelerate that process. We will seek to maintain the benefits of new ways of working that the pandemic has imposed on us. Regular efficient communication by videoconference has provided new opportunities for connecting people across the organisation, and the transition to virtual events has significantly expanded the reach of our courses and conferences (p. 43). Two areas where we also made significant progress in 2020 are sustainability (p. 71) and equality, diversity, and inclusion (p. 69), and we have begun to develop long-term strategies in both of these areas. We also reaffirmed our commitment to the San Francisco Declaration on Research Assessment (DORA) and will ensure that EMBL implements fair and responsible processes for recruitment, performance assessment, and promotion.

I truly admire the effort and dedication of staff across EMBL, and no more so than over the past year. They have done everything necessary to ensure that we could remain both operational and safe. Our swift and assured response to the coronavirus pandemic leaves me in no doubt of our ability to deliver on our aims in the next EMBL Programme and to provide the knowledge and tools needed to solve challenges of global importance.

Edith Heard, FRS
Director General

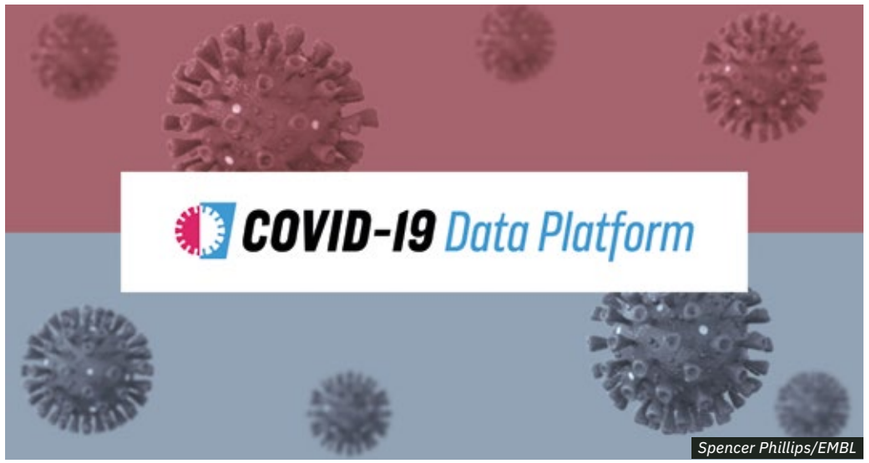
Challenging times

EMBL's role in the global response to COVID-19

The COVID-19 pandemic has demonstrated that a global crisis can only be fought by collaboration and open science, with rapid sharing of data and knowledge. EMBL responded swiftly to the pandemic by launching new initiatives and repurposing facilities to provide various research and support services. Our research groups and scientific service teams immediately joined forces with external collaborators to share and analyse COVID-19-related data, develop new testing methods, study the molecular mechanisms of coronavirus infection, and aid the development of treatments and vaccines. EMBL's open, collaborative approach to science enabled us to play an essential role in Europe's response to the pandemic.

Tracking and monitoring

Open data infrastructure, such as the data resources at EMBL's European Bioinformatics Institute (EMBL-EBI), was essential for the scientific community to rapidly share data and findings about the novel coronavirus, SARS-CoV-2. A focus of EMBL-EBI's efforts in 2020 was making such data easily accessible to the international research and healthcare communities, to accelerate research and support the development of diagnostics, therapeutics, and effective vaccines. EMBL-EBI promptly set up the European COVID-19 Data Platform: a collaborative space for the rapid sharing and analysis of COVID-19-related data. The platform helps scientists, public health authorities, and health practitioners work together and share data and knowledge in a way that is open, sustainable, and smart.



Spencer Phillips/EMBL

EMBL-EBI and partners launched the COVID-19 Data Platform to help scientists, public health and healthcare professionals to tackle the coronavirus pandemic.

The COVID-19 Data Platform consists of three connected components:

- SARS-CoV-2 Data Hubs, which organise the flow of SARS-CoV-2 sequence data and provide comprehensive open data sharing for the European and global research communities. In 2020, EMBL-EBI supported the setup of 16 national data hubs.
- The Federated European Genome-phenome Archive, which provides secure, controlled-access sharing of sensitive COVID-19-related datasets from patients and research subjects.
- The COVID-19 Data Portal, which enables researchers to access and share relevant COVID-19 datasets and tools, spanning genomics, proteins, biochemistry, imaging, literature, and more.

At the end of 2020, the COVID-19 Data Platform contained more than half a million data records and the COVID-19 Data Portal had received more than 3.6 million web requests from more than 114,000 users in 175 countries. During the year, EMBL-EBI also supported Italy, Japan, Norway, Poland, Spain, Sweden, and Turkey in setting up their own national portals to enable secure data sharing and to galvanise national efforts. The COVID-19 Data Platform was set up with the support of the European Commission, ELIXIR (a research infrastructure for biological data, of which EMBL is one node), and the European Open Science Cloud (p. 64).

COVID-19 in numbers

COVID-19 DATA PORTAL

The COVID-19 Data Portal, part of the European COVID-19 Data Platform, brings together relevant COVID-19 datasets and tools. The portal is synchronised with COVID-19-related data held in EMBL-EBI's data resources, and includes gene sequences, protein structures, expression data, compound screens, biochemistry, and scientific publications.

3.6 million web requests to the COVID-19 Data Portal from **114,000** users in **175** countries

COVID-19 GRANTS

EMBL is carrying out fundamental research to support the global fight against the COVID-19 pandemic. EMBL's Grants Services team has enabled EMBL scientists to secure additional funding for COVID-19 research.

€7.3 million secured for COVID-19 research projects

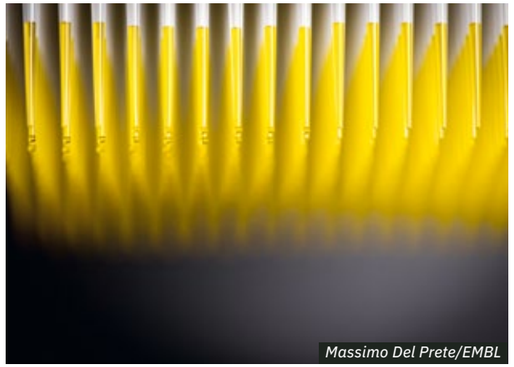
The importance of tracking viral sequence data over time and around the world was underscored in the final months of 2020 by the emergence of the novel SARS-CoV-2 B.1.1.7 lineage. On behalf of the COVID-19 Genomics UK Consortium, scientists in the Gerstung Group and collaborators analysed the increasing prevalence of the novel strain using data collected during the lockdown in England from November to December 2020.[1] Their analysis confirmed that B.1.1.7 is significantly more transmissible than previous variants and indicated that lockdown measures applied until then were insufficient to contain its spread. Upon request, the scientists involved have provided support to governments and policymakers in EMBL member states.

Developing new testing methods

At the start of the pandemic, testing large numbers of potentially infected individuals posed significant challenges for health authorities and diagnostic labs. Testing capacities for sensitive PCR methods were limited, and reagent shortages caused further problems.

A team of EMBL scientists from the Genome Biology Unit, the Protein Expression and Purification Core Facility, the Genomics Core Facility, and collaborators set out to develop a new testing method. They have established a robust protocol for detecting SARS-CoV-2 using next-generation sequencing, called multiplexed SARS-CoV-2 quantification (McQ), which can process more than 5,000 samples in parallel.[2] The test has been automated and optimised to use almost exclusively non-proprietary buffers and enzymes. This drastically reduces the cost of testing and avoids reagent shortages, making McQ accessible to a wider range of institutions worldwide. In the future, McQ could help scientists and clinicians to regularly test large portions of the population.

Another approach for detecting SARS-CoV-2 infections was developed by Heidelberg's Center for Integrative Infectious Disease Research, the Heidelberg Collaboratory for Image Processing, EMBL's Kreshuk Group, and EMBL's Centre for Bioimage Analysis. They developed a microscopy-based assay for the semi-quantitative detection of



EMBL scientists used liquid-handling robots to automate and speed up coronavirus testing.

1. Vöhringer H *et al.* (2020) Lineage-specific growth of SARS-CoV-2 B.1.1.7 during the English national lockdown. Virological.org, published online 30 December
2. Vonesch SC *et al.* (2020) McQ – An open-source multiplexed SARS-CoV-2 quantification platform. medRxiv. DOI: 10.1101/2020.12.02.20242628

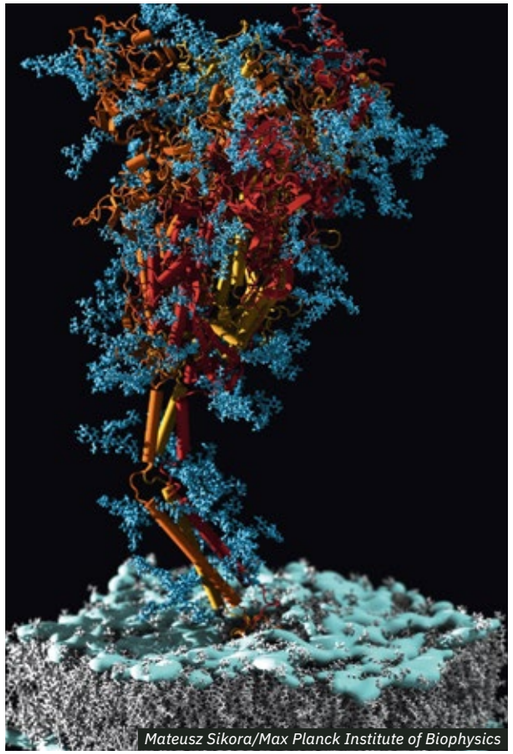
SARS-CoV-2-specific antibodies in human blood samples.[1] The detection method was applied in a study commissioned by the state government of Baden-Württemberg,[2] the results of which informed the state government's decisions on reopening kindergartens and elementary schools.

Understanding the virus

EMBL's historic contributions to the development of cryo-electron microscopy and X-ray imaging have been at the heart of many studies around the world to understand SARS-CoV-2 and the changes it causes in infected individuals. A key feature of the virus is the spike protein on its surface, which enables the virus to bind to certain cell types and infect them. The spike protein is also at the centre of vaccine development, as it triggers an immune response in humans.

The Beck Group and collaborators, including members of EMBL's Genomics Core Facility and Cryo-Electron Microscopy Service Platform, have used cryo-electron tomography and molecular dynamics simulations to analyse the spike protein in its natural environment, on intact viruses.[3] They observed an unexpected level of flexibility within the protein, which may allow it more freedom of movement as it searches for a receptor on the host cell. They also found a protective coat of sugar-like molecules attached to the spike protein, which helps to hide it from antibodies. These findings have important implications for the development of vaccines and therapeutics.

EMBL's Schwab Team and Electron Microscopy Core Facility (EMCF), with collaborators at Heidelberg



Model of the SARS-CoV-2 spike protein, with its protective coat of sugar-like molecules (cyan).

1. Pape C, Remme R *et al.* (2021) Microscopy-based assay for semi-quantitative detection of SARS-CoV-2 specific antibodies in human sera. *BioEssays* 43:2000257. DOI: 10.1002/bies.202000257
2. Tönshoff B, Müller B, Elling R, Renk H, Meissner P *et al.* (2021) Prevalence of SARS-CoV-2 infection in children and their parents in southwest Germany. *JAMA Pediatrics*. DOI: 10.1001/jamapediatrics.2021.0001
3. Turoňová B, Sikora M, Schürmann C *et al.* (2020) In situ structural analysis of SARS-CoV-2 spike reveals flexibility mediated by three hinges. *Science* 370(6513):203–208. DOI: 10.1126/science.abd5223

University Hospital, have used a range of state-of-the-art imaging techniques to observe the changes in cell structures that occur after SARS-CoV-2 infection.[1] At EMBL, a team of 15 electron microscopists and several other scientists worked to complete the project in record time, aided by volume electron microscopy and a workflow for high-throughput transmission electron microscopy developed in the EMCF.[2] The result was an unprecedented repository of 3D structural information showing the effects of SARS-CoV-2 inside cells. The team has made this information freely available to the scientific community via the Electron Microscopy Public Image Archive (EMPIAR) at EMBL-EBI. This will support the global effort to understand how SARS-CoV-2 interacts with cells, and to develop new therapies to reduce viral replication and disease severity.

Supporting vaccine development

EMBL's past and current activities have played an important role in the development of vaccines. At EMBL Hamburg, there is an extensive collaboration between the Svergun Group and German biotech company BioNTech, which was the developer of the first approved COVID-19 vaccine based on messenger RNA (mRNA). Delivering mRNA into cells is challenging, because unprotected mRNA injected into the body is rapidly broken down before it can be taken up by cells. To protect it from damage, scientists must develop ways to package it into tiny particles known as nanoparticles.

To analyse the molecular structure of nanoparticles carrying mRNA, BioNTech used EMBL Hamburg's beamline P12, which is dedicated to small-angle X-ray scattering (SAXS), a technique for studying the molecular structure of particles in solution. This enabled studies of the structure, behaviour, and delivery efficiency of nanoparticles made of lipids, or a combination of lipids and biopolymers, under various conditions. Three papers on these SAXS studies were published in 2020, including EMBL scientists as authors.[3,4,5]

1. Cortese M *et al.* (2020) Integrative imaging reveals SARS-CoV-2-induced reshaping of subcellular morphologies. *Cell Host & Microbe* 28(6):853–866. DOI: 10.1016/j.chom.2020.11.003
2. Schorb M *et al.* (2019) Software tools for automated transmission electron microscopy. *Nature Methods* 16(6):471–477. DOI: 10.1038/s41592-019-0396-9
3. Siewert CD *et al.* (2020) Hybrid biopolymer and lipid nanoparticles with improved transfection efficacy for mRNA. *Cells* 9(9):2034. DOI: 10.3390/cells9092034
4. Nogueira SS *et al.* (2020) Polysarcosine-functionalized lipid nanoparticles for therapeutic mRNA delivery. *ACS Applied Nano Materials* 3(11):10634–10645. DOI: 10.1021/acsanm.0c01834
5. Uebbing L *et al.* (2020) Investigation of pH-responsiveness inside lipid nanoparticles for parenteral mRNA application using small-angle X-ray scattering. *Langmuir* 36(44):13331–13341. DOI: 10.1021/acs.langmuir.0c02446

ALUMNI IMPACT

Advancing vaccine technologies

Some of the most prominent COVID-19 vaccines have been developed thanks to key technologies and discoveries made by EMBL alumni

Improved adenovirus vectors

EMBL alumnus Angelo Raggioli is Head of Vectorology at ReiThera, an Italian company whose COVID-19 vaccine candidate, GRAd-COV2, is currently in clinical trials. GRAd-COV2 builds on the work of three other Italian EMBL alumni – Riccardo Cortese, Alfredo Nicosia, and Alessandra Vitelli – whose research has focused on using a harmless type of virus called an adenovirus as a vector for carrying a genetic message into human cells.

While working on a human adenovirus-based vaccine against the hepatitis C virus, Riccardo and his colleagues found that the vaccine's effect was weakened in people previously exposed to adenovirus. This prompted the idea of using a chimpanzee adenovirus as a vector, since it would be less likely to be recognised and destroyed by the human immune system. The research continued at Okairos, a company Riccardo founded with Alfredo and two other colleagues, leading to the first simian adenovirus vectors to enter clinical trials in humans. This approach is now widespread in vaccine development. A chimpanzee adenovirus is used in the Oxford–AstraZeneca COVID-19 vaccine, while GRAd-COV2 uses a vector based on a gorilla adenovirus.

Protein nanoparticles

Finnish scientist Kai Simons came to EMBL Heidelberg in 1975 with two members of his group, Ari Helenius and Henrik Garoff. Together they carried out research on Semliki Forest virus. They used detergents to break up the virus and produce protein micelles – essentially, small droplets made up of the viral spike protein – that elicited an immune response. When the researchers used this preparation to vaccinate mice infected with Semliki Forest virus, they found that it was remarkably effective in small doses at fully protecting the mice from the virus.

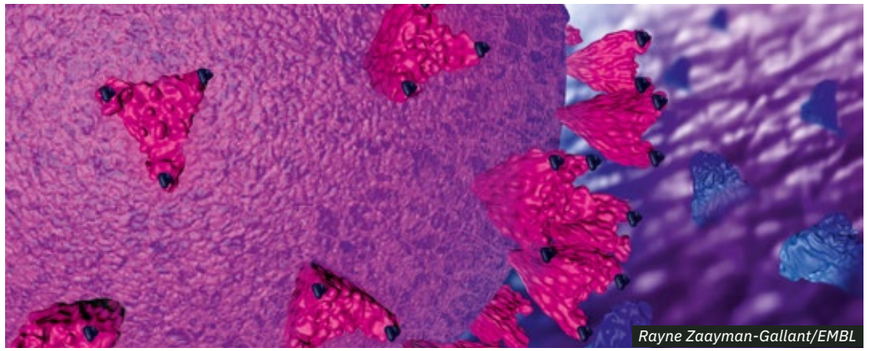
This was a completely new way to make vaccines, but the group's results – published in *Nature* in 1978 – attracted no interest in the vaccine field at the time. It has taken until now for their full potential to be realised, with US biotechnology company Novavax building on Kai's research to produce protein nanoparticles for its COVID-19 vaccine. The company reported in January 2021 that this vaccine had an 89% efficacy rate in a phase III clinical trial in the UK.

Developing treatments

The development of COVID-19 vaccines has been key to protecting uninfected members of the population. However, another essential strategy is the search for effective antiviral treatments that help to protect infected people against severe disease.

An international team of researchers, including the Beltrao Group at EMBL-EBI, has analysed how SARS-CoV-2 hijacks the proteins in human cells. They investigated the interactions between viral and human proteins and identified those human proteins that physically associate with proteins carried by SARS-CoV-2.[1] Another study involving the Beltrao Group has shown how SARS-CoV-2 shifts its host cell's activity to promote its own replication and to infect nearby cells.[2] In these projects, the researchers identified pharmacological agents that have the potential to be repurposed for treating COVID-19. Among these, 26 compounds are now being tested in clinical trials.

The Löw Group and collaborators, including EMBL's Protein Expression and Purification Core Facility and Svergun Group, have explored a novel approach for diagnosis or treatment of SARS-CoV-2 infection.[3] They studied nanobodies: small antibodies that have been found in certain types of animals, such as camels and llamas, which are promising tools for combating viruses due to their high stability and small size. Technological advances now enable rapid selection of synthetic nanobodies, called sybodies, in the lab. The scientists identified and structurally analysed sybodies that bind to SARS-CoV-2's spike protein and prevent the virus from infecting cells *in vitro*. They improved the binding strength of the selected sybodies by generating derivatives, increasing the binding efficiency more than 300-fold. Sybodies have the potential to be used as treatments for COVID-19 and as tools in diagnostic tests. The team has developed a protocol for rapidly identifying sybodies that could neutralise specific viruses. This provides a valuable tool for combating emerging viruses in future.



Rayne Zaayman-Gallant/EMBL

The Löw Group and collaborators have identified a synthetic mini-antibody (black) that might stop the SARS-CoV-2 spike protein (magenta) from binding to the human protein ACE2 (blue).

1. Gordon DE, Jang GM, Bouhaddou M, Xu J, Obernier K, White KM, O'Meara MJ, Rezelj VV *et al.* (2020) A SARS-CoV-2 protein interaction map reveals targets for drug repurposing. *Nature* 583(7816):459–468. DOI: 10.1038/s41586-020-2286-9
2. Bouhaddou M, Memon D, Meyer B, White KM, Rezelj VV, Correa Marrero M, Polacco BJ, Melnyk JE, Ulferts S, Kaake RM, Batra J *et al.* (2020) The global phosphorylation landscape of SARS-CoV-2 infection. *Cell* 182(3):685–712. DOI: 10.1016/j.cell.2020.06.034
3. Custódio TF *et al.* (2020) Selection, biophysical and structural analysis of synthetic nanobodies that effectively neutralize SARS-CoV-2. *Nature Communications* 11(1):5588. DOI: 10.1038/s41467-020-19204-y

Improving our response to emerging pandemics

On 3 July 2020, more than 600 participants on four continents came together for the virtual EMBL Conference 'SARS-CoV-2: Towards a New Era in Infection Research'. Within just a few weeks, the organisers had succeeded in putting together a day-long conference that featured scientific talks from world-renowned experts in fields such as microbial pathogenesis, drug discovery, bioinformatics, and epidemiology. The speakers highlighted the importance of fundamental research, collaboration, and data science in containing the COVID-19 pandemic, and discussed opportunities to improve our response to epidemics and pandemics in the future.

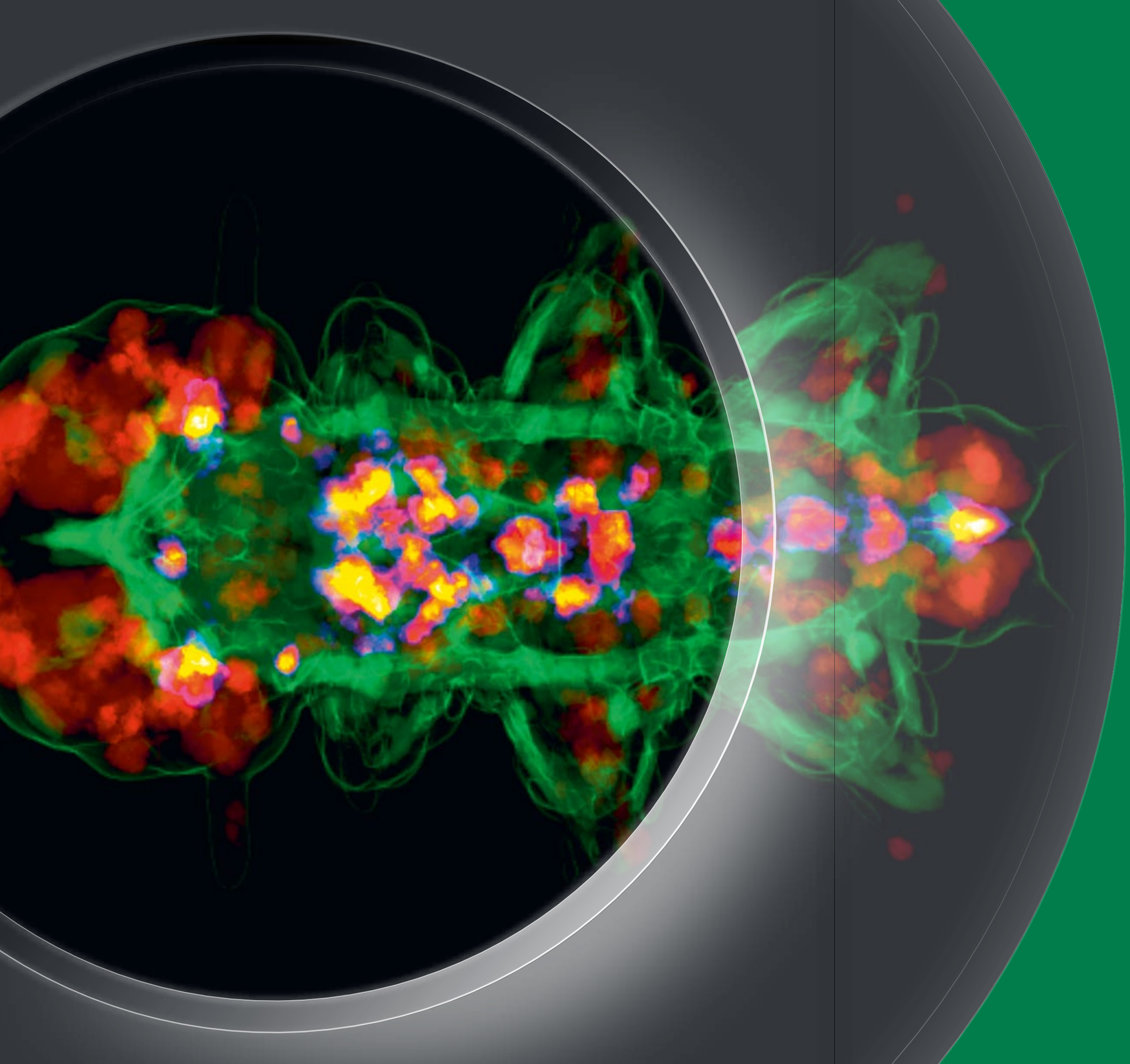
A recurring theme was the importance of collaboration in finding solutions to COVID-19. "It's obviously been a tragedy, this pandemic, but the silver lining for me was to see how fast we can move when we all work together," said conference speaker Nevan Krogan, Director of the Quantitative Biosciences Institute at the University of California San Francisco.

"And the challenge I think for us as scientists is to keep this infrastructure in place, keep this spirit in place when the dust settles on COVID-19, so we are more prepared for the next pandemic."

From the talks and the panel discussion that followed, a clear message emerged: there is an urgent need to better understand microbes and viruses, and their interactions with host organisms and with their natural surroundings. Interdisciplinary research and the development of novel tools are required to study a broad range of pathogens, to improve our ability to detect and trace infections, and to develop new drugs and vaccines.

The panellists also explored what we can do to better prepare for future pandemics, including building capacity and funding for fundamental research. Despite the urgency of fighting COVID-19, participants also emphasised that we should not neglect other pressing issues, such as the development of antimicrobial resistance and the effect of climate change on biodiversity and ecosystems.

Design team/EMBL



MISSION 1

To perform fundamental **research** in molecular biology

EMBL's overarching goal is to understand the molecular basis of life. Research at EMBL emphasises experimental and computational analyses of biological organisation, from molecules to organisms.

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Research

EMBL drives visionary research in molecular biology

Alongside EMBL's COVID-19 projects, research at our six sites has continued to make significant advances. These include early explorations of some of EMBL's new scientific directions as part of the next EMBL Programme, *Molecules to Ecosystems*, which will start in 2022. Below are some of the highlights from our research in 2020.

Pan-Cancer Analysis of Whole Genomes

EMBL scientists played a leading role in the Pan-Cancer Analysis of Whole Genomes (PCAWG) project: a collaboration of more than 1,300 scientists and clinicians from 37 countries, who have conducted the most comprehensive study to date of whole cancer genomes. PCAWG has significantly improved our fundamental understanding of cancer and marked out new directions for its diagnosis and treatment.

EMBL group leader Jan Korbel – now Head of Data Science for EMBL Heidelberg – is the initiator and one of the leaders of the project. EMBL's European Bioinformatics Institute (EMBL-EBI) stores all PCAWG data, and both EMBL-EBI and EMBL Heidelberg have carried out analyses and contributed software and scientific expertise. EMBL also coordinated the activities of participating national institutes, both in our member states and other parts of the world.

The Brazma and Stegle groups were among the leaders of a PCAWG study that analysed genomic and transcriptomic data from over 1,000 donors and more than 25 cancer types.[1] They created the largest catalogue to date of cancer-specific RNA alterations and proposed a new classification of gene fusions in cancer. The study greatly improved our knowledge of gene expression changes in cancer, opening avenues for identifying new cancer drug targets and therapies.

As part of PCAWG, the Korbel Group and collaborators developed a tool for the large-scale analysis of genomic data using cloud computing.[2] The main advantages of this tool, called Butler, are continuous system monitoring and the ability to take automated action to restart failed services or machines, making data processing 43% more efficient than with previous approaches. This dramatically reduces the time needed to execute large projects, and enables researchers to access a wide range of datasets while meeting stringent requirements for data protection.

The Korbel Group was also part of a collaboration that has conducted the most comprehensive genetic investigation to date of medulloblastomas,[3] which are among the most common malignant brain tumours affecting children. The scientists found hereditary causes for 40% of all cases of a certain subtype of medulloblastoma. In 14% of cases, they identified an inherited genetic variant that leads to errors in protein production. They predict that similar variants could be a previously underestimated cause of cancer.

1. PCAWG Transcriptome Core Group, Calabrese C, Davidson NR, Demircioğlu D, Fonseca NA, He Y, Kahles A, Lehmann K-V, Liu F, Shiraishi Y, Soulette CM, Urban L *et al.* (2020) Genomic basis for RNA alterations in cancer. *Nature* 578(7793):129–136. DOI: 10.1038/s41586-020-1970-0
2. Yakneen S *et al.* (2020) Butler enables rapid cloud-based analysis of thousands of human genomes. *Nature Biotechnology* 38(3):288–292. DOI: 10.1038/s41587-019-0360-3
3. Waszak SA, Robinson GW *et al.* (2020) Germline Elongator mutations in Sonic Hedgehog medulloblastoma. *Nature* 580(7803):396–401. DOI: 10.1038/s41586-020-2164-5

Gene regulation mechanisms and dynamics

EMBL integrates advanced methods in genomics with a range of computational, cell biology, and imaging approaches to understand how gene expression is regulated in time and space, and how this affects processes in development and disease.

The Heard Group and collaborators, supported by EMBL's Genomics Core Facility, have revealed a crucial role for the protein SPEN in the process of X-chromosome inactivation,[1] in which female mammalian embryos silence gene expression on one of their two X chromosomes. Together with the *Xist* long non-coding RNA, SPEN targets and silences active genes on the X chromosome by interacting with their regulatory regions. As soon as silencing is achieved, SPEN disengages from genes. As well as revealing more about the molecular basis of X-chromosome inactivation, the study provides insights into gene silencing, with implications for disease.

The Noh Group, with support from collaborators in the Zaugg Group and at the University of Pennsylvania, has investigated the role of a histone protein called H3.3 in regulating gene activity.[2] They changed the amino acids at two specific locations in H3.3 from one type of amino acid to another, revealing that one of these changes impaired the process by which cells differentiate to become more specialised cell types. The study provides a better understanding of the role of such mutations in the development of diseases, including cancer.

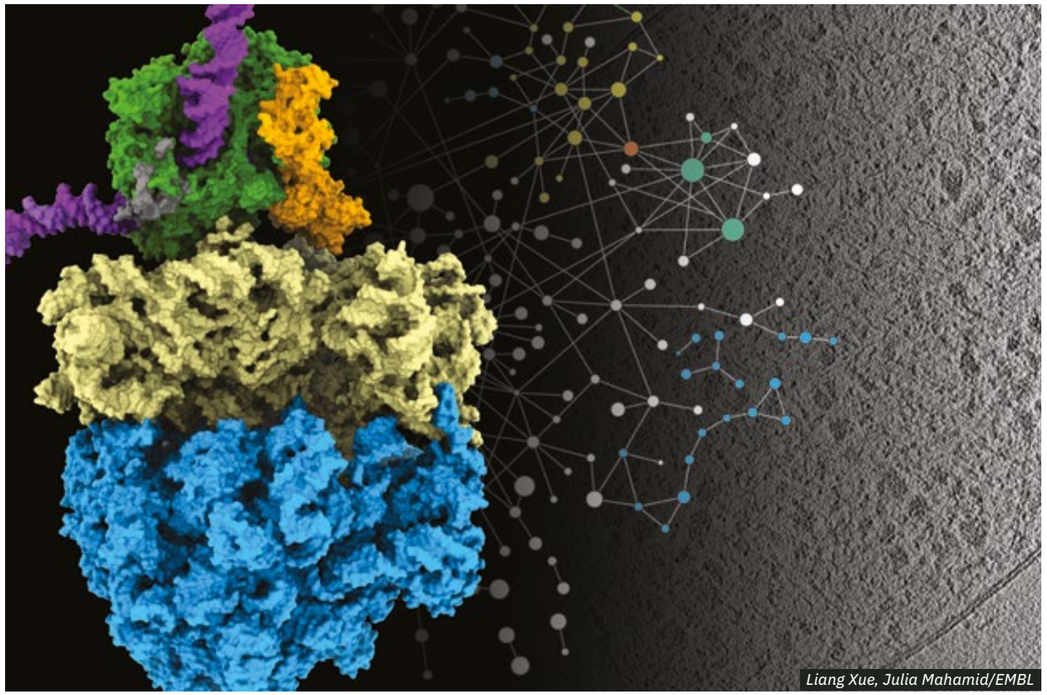
The PCAWG project involved large-scale analysis of genomic data using cloud computing.

1. Dossin F *et al.* (2020) SPEN integrates transcriptional and epigenetic control of X-inactivation. *Nature* 578(7795):455–460. DOI: 10.1038/s41586-020-1974-9
2. Gehre M *et al.* (2020) Lysine 4 of histone H3.3 is required for embryonic stem cell differentiation, histone enrichment at regulatory regions and transcription accuracy. *Nature Genetics* 52(3):273–282. DOI: 10.1038/s41588-020-0586-5

Molecular machines

EMBL's research brings together various technologies in structural biology and imaging to reveal the molecular processes at work inside cells. Alongside EMBL's established expertise in X-ray crystallography and cryo-electron microscopy (cryo-EM), EMBL is driving advances in cryo-electron tomography (cryo-ET), which is being developed by the Mahamid Group, supported by EMBL's Cryo-EM Service Platform. Cryo-ET builds on existing methods in cryo-EM, but – crucially – enables the observation of biological molecules in their natural context inside cells, providing important new insights.

The Mahamid Group and collaborators have combined cryo-ET with cross-linking mass spectrometry and computer modelling to produce the highest-resolution images ever obtained of *Mycoplasma pneumoniae*, a bacterium that causes a mild form of pneumonia.[1] They confirmed a decades-old hypothesis that, in bacterial cells, the processes of transcription and translation – which cells use to convert information from DNA to proteins – can be coupled together, with the molecular machinery for these processes interacting and forming a supercomplex. The researchers are planning a number of other studies



The Mahamid Group has studied the coupled molecular machines (left) responsible for transcription and translation in Mycoplasma pneumoniae. *These are accompanied by the protein interaction network from mass spectrometry (centre) and the cryo-electron tomography data (right) that the group used to model the structure.*

of molecular machines in bacteria, which could inform the development of new antibiotics.

The Beck and Kosinski groups and collaborators – including EMBL scientists from the Mahamid Group, the Electron Microscopy Core Facility, and the Cryo-EM Service Platform – have used cryo-ET to study the nuclear pore complex (NPC),[2] a ring-shaped complex of proteins that regulates the passage of molecules into and out of the cell's nucleus. They gained fundamental insights into the assembly of the NPC and the mechanisms by which it is broken down and replaced. Failures in NPC assembly lead to the death of the cell and have been linked to neurodegenerative diseases.

The Cusack Group has carried out a study on influenza polymerase[3] – a key enzyme of the flu virus. This enzyme transcribes the virus's genome, creating instructions that tell an infected cell to start manufacturing viral proteins. The scientists obtained a series of molecular snapshots of the complete transcription process, revealing in unprecedented detail how the polymerase works. The results will support the design of antiviral drugs, and can be extended to a range of other viruses, including Lassa virus and – more distantly – SARS-CoV-2. The study was supported by EMBL's Genomics Core Facility and Cryo-EM Service Platform, and by the X-ray beamlines in Grenoble, run jointly by the European Synchrotron Radiation Facility and EMBL.

The Marcia Group has collaborated with researchers from the Italian Institute of Technology to obtain some of the most detailed snapshots ever of the splicing process in cells:[4] a crucial step in using the genetic information stored in DNA to make proteins. The scientists used X-ray crystallography and computer simulations to study systems known as group II self-splicing introns, revealing the atomic details of the splicing process. Their findings have already sparked drug discovery efforts to inhibit splicing in pathogenic fungi. The type of splicing systems they studied also have potential applications as genome editing tools.

As part of a longstanding collaboration, the Wilmanns Group has worked with researchers at the University of Iceland to study a transcription factor,[5] a type of molecule that binds to specific DNA sites and regulates the expression of genes. The transcription factor they studied is called MITF, and is a key member of a family of transcription factors that selectively partner with each other in very precise ways. The scientists revealed that this high level of selectivity results from MITF's molecular structure, adding to our knowledge of how gene expression is regulated. MITF plays a key role in the development of melanoma – the most dangerous form of skin cancer – so understanding how it works could be crucial to treating the disease.

1. O'Reilly FJ, Xue L, Graziadei A *et al.* (2020) In-cell architecture of an actively transcribing-translating expressome. *Science* 369(6503):554–557. DOI: 10.1126/science.abb3758
2. Allegretti M, Zimmerli CE *et al.* (2020) In-cell architecture of the nuclear pore and snapshots of its turnover. *Nature* 586(7831):796–800. DOI: 10.1038/s41586-020-2670-5
3. Wandzik JM, Kouba T *et al.* (2020) A structure-based model for the complete transcription cycle of influenza polymerase. *Cell* 181(4):877–893. DOI: 10.1016/j.cell.2020.03.061
4. Manigrasso J, Chillón I *et al.* (2020) Visualizing group II intron dynamics between the first and second steps of splicing. *Nature Communications* 11(1):2837. DOI: 10.1038/s41467-020-16741-4
5. Pogenberg V *et al.* (2020) Mechanism of conditional partner selectivity in MITF/TFE family transcription factors with a conserved coiled coil stammer motif. *Nucleic Acids Research* 48(2):934–948. DOI: 10.1093/nar/gkz1104

Cellular and multicellular dynamics

To understand the development of complex living systems, it's necessary to understand how cells respond to internal and external cues to organise themselves in time and space. A key area of interest at EMBL is the segmentation clock: a group of genes that set up coordinated, oscillating patterns of gene expression that tell structures in the developing embryo where to form.

The Ebisuya Group and collaborators have created a system for studying the segmentation clock within a tissue grown *in vitro*. With this model, they found that the segmentation clock ticks at a slower rate in humans than in mice.[1] They showed that this is due to differences in the cellular environment, which cause biochemical reactions to take place more slowly in human cells. Another study involving the Ebisuya Group has explored how errors in the segmentation clock cause a hereditary disorder of the vertebrae known as spondylocostal dysostosis (SCD).[2] The researchers reproduced SCD-like abnormalities using cell lines established from patient samples. This will help them to identify further mutations that cause SCD.

By bringing together EMBL expertise in RNA sequencing and light-sheet imaging, scientists in the Neveu and Hufnagel groups, EMBL's Genomics Core Facility, and the University of Padua School of Medicine have created the first complete description of early development accounting for every cell in an embryo.[3] They studied a marine organism known as a sea squirt, creating a 'digital embryo' that maps the gene expression and morphology of every cell as the embryo develops from a single cell to the 64-cell stage. The digital embryo is a rich publicly available resource for investigating the molecular mechanisms that instruct the patterning of entire organisms, and it represents a leap forward in the emerging field of developmental genomics.

Microbial ecosystems

Scientists at EMBL use bioinformatics, computational biology, and a range of experimental approaches to study how communities of microorganisms interact with each other, with host organisms, and with their environment. An important area of research is the human gut microbiome – the ecosystem made up of all the microorganisms in the gut – which has wide-ranging impacts on human health and disease.

An international team of scientists led by the Finn Group has created a database of all known bacterial genomes and proteins from the human gut microbiome.[4] This resource, encompassing more than 280,000 microbial genomes and 625 million proteins, was made possible by the unparalleled computational resources and expertise at EMBL-EBI. All the data are freely available, enabling researchers to gain important insights and develop new therapeutic applications. The team plans to expand this resource to include microbial genomes and proteins from other biomes, such as human skin, soil, and marine environments.

1. Matsuda M *et al.* (2020) Species-specific segmentation clock periods are due to differential biochemical reaction speeds. *Science* 369(6510):1450–1455. DOI: 10.1126/science.aba7668
2. Matsuda M, Yamanaka Y *et al.* (2020) Recapitulating the human segmentation clock with pluripotent stem cells. *Nature* 580(7801):124–129. DOI: 10.1038/s41586-020-2144-9
3. Sladitschek HL *et al.* (2020) MorphoSeq: Full single-cell transcriptome dynamics up to gastrulation in a chordate. *Cell* 181(4):922–935.E21. DOI: 10.1016/j.cell.2020.03.055
4. Almeida A *et al.* (2021) A unified catalog of 204,938 reference genomes from the human gut microbiome. *Nature Biotechnology* 39(1):105–114. DOI: 10.1038/s41587-020-0603-3

The Patil Group and collaborators have revealed how a team of microbes is required to make the fermented milk drink known as kefir.[1] By combining advanced methods in metabolomics, transcriptomics, and mathematical modelling, they showed that the dominant species of *Lactobacillus* bacteria found in kefir grains cannot survive on its own in milk. However, when lactic and acetic acid bacteria and yeasts work together – feeding on each other's metabolites in the kefir culture – they each provide something the other needs. This shows how interspecies interactions can lead to stable coexistence.

The Savitski Team and Typas Group, supported by EMBL's Proteomics Core Facility, have used a technique known as thermal proteome profiling, developed by team leader Mikhail Savitski, to systematically map gene function in *E. coli* bacteria on an unprecedented scale.[2] Their work provides important insights into the interactions and functions of each protein, including hundreds of less well-understood proteins. The study also shows the value of the EMBL Interdisciplinary Postdocs (EIPOD) initiative, which enabled the lead author to carry out this project by combining expertise from the Savitski Team and Typas Group.

Organisms in their environment

Throughout their lives, from single-celled embryos to mature adults, organisms are exposed to constantly changing environments. Research groups at EMBL are helping to reveal the complex interplay between organism and environment, and its effects on development, evolution, and behaviour.

The Ikmi Group and collaborators, supported by EMBL's Advanced Light Microscopy Facility, have shown that the number of tentacles grown by the sea anemone *Nematostella vectensis* depends on the amount of food it eats.[3] Using a combination of genetic, cellular, and molecular approaches and analysing more than 1,000 growing *Nematostella* polyps, the scientists found that tentacle progression occurs in a feeding-dependent manner. *Nematostella* is the first animal species shown to grow entirely new limbs in response to food.

The Crocker Group and collaborators have performed an extensive study in fruit flies of a specific developmental enhancer[4] – a region of DNA that controls where, when, and how strongly genes are expressed. The group used a robot to handle fly embryos and worked with EMBL's Advanced Light Microscopy Facility to develop an automated microscope pipeline to study more than 700 unique, randomly generated mutations of the enhancer. They found that the density of regulatory information in the enhancer was much higher than expected, placing constraints on how the animal can evolve. In the future, such studies on enhancers will help scientists to understand more about how animals adapt to fast-changing environments, for example under conditions of climate change.

1. Blasche S, Kim Y *et al.* (2021) Metabolic cooperation and spatiotemporal niche partitioning in a kefir microbial community. *Nature Microbiology* 6(2):196–208. DOI: 10.1038/S41564-020-00816-5
2. Mateus A *et al.* (2020) The functional proteome landscape of *Escherichia coli*. *Nature* 588(7838):473–478. DOI: 10.1038/s41586-020-3002-5
3. Ikmi A *et al.* (2020) Feeding-dependent tentacle development in the sea anemone *Nematostella vectensis*. *Nature Communications* 11(1):4399. DOI: 10.1038/s41467-020-18133-0
4. Fuqua T *et al.* (2020) Dense and pleiotropic regulatory information in a developmental enhancer. *Nature* 587(7833):235–239. DOI: 10.1038/s41586-020-2816-5

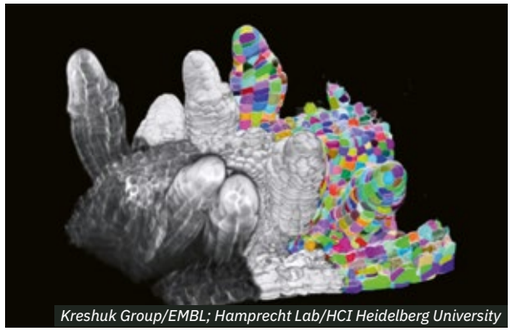
The Gross Group, supported by EMBL's Genetic and Viral Engineering Facility, has investigated the neuronal mechanism behind defensive behaviour in mice, to better understand how our brains make fight or flight decisions in conflicts over territory, mates, or food.[1] The scientists identified a specific area of the brain within the hypothalamus that encodes both spatial and threat cues to drive location-specific defensive responses. Their results provide insights into the regulation of emotions like fear and aggression, and suggest a novel role for the hypothalamus as a region that integrates sensory and contextual information, processing the level of threat and adapting survival behaviours to a changing environment.

Machine learning

Artificial intelligence is playing an increasingly important role in biology, with machine learning algorithms accelerating progress in areas such as image analysis and bioinformatics. Machine learning is applied in various research groups at EMBL, and new methods are actively being developed by the Kreshuk Group and others.

The Birney Group and collaborators have investigated the function of the complex mesh of muscle fibres, called trabeculae, lining the inner surface of the heart.[2] They applied deep learning algorithms to analyse MRI scans from the UK Biobank database, and used a combination of physical modelling, observational epidemiology, and genetic tools to show that trabeculae are essential for heart function, with differences in their shape having a clear impact on heart disease. This finding solves a longstanding question in cardiac physiology and could be used to improve diagnosis of a variety of human heart disease conditions.

The Kreshuk Group and collaborators have developed an open source software pipeline called PlantSeg,[3] which analyses images of plant tissues and segments them – identifying the boundaries of individual cells within the tissue. PlantSeg enables the most accurate and versatile analysis of plant tissue development to date, and can be applied to study tissue development in diverse contexts or under changing environmental conditions. The underlying machine learning algorithm could also be retrained for use on animal tissue. PlantSeg adds to the successful open source software developments supported by EMBL, such as ilastik, which enables non-experts to access and use machine learning algorithms to advance their research.

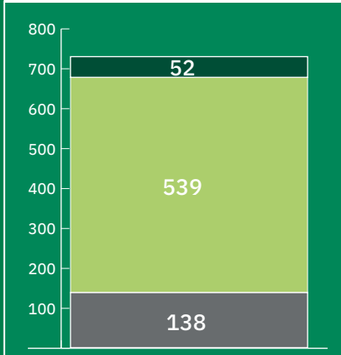


The Kreshuk Group has developed a new open source software pipeline for accurate and versatile analysis of plant tissues.

1. Krzywkowski P *et al.* (2020) Dynamic encoding of social threat and spatial context in the hypothalamus. *eLife* 9:e57148. DOI: 10.7554/eLife.57148
2. Meyer HV, Dawes TJW, Serrani M *et al.* (2020) Genetic and functional insights into the fractal structure of the heart. *Nature* 584(7822):589–594. DOI: 10.1038/s41586-020-2635-8
3. Wolny A, Cerrone L *et al.* (2020) Accurate and versatile 3D segmentation of plant tissues at cellular resolution. *eLife* 9:e57613. DOI: 10.7554/eLife.57613

Publications and grants in numbers

SCIENTIFIC PUBLICATIONS



EMBL's research groups and scientific service teams produce hundreds of scientific publications each year. In keeping with EMBL's collaborative spirit, the majority of our publications are produced in collaboration with scientists in EMBL member states or associate member states.

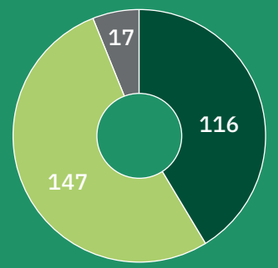
- By EMBL
- By EMBL in collaboration with organisations in member or associate member states
- By EMBL in collaboration with organisations in non-member states

Total 729

GRANTS IN NUMBERS

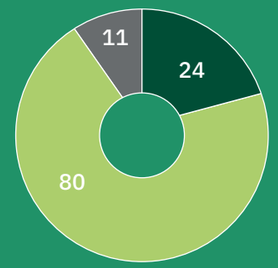
We currently depend on external grants to advance our research, our technical and service infrastructure, and our training and outreach activities. These grants complement EMBL's member state funding, enabling us to support the activities of scientists in EMBL member states and beyond.

ACTIVE RESEARCH GRANTS



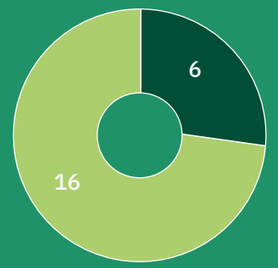
Total 280

ACTIVE INFRASTRUCTURE GRANTS



Total 115

ACTIVE TRAINING AND OUTREACH GRANTS



Total 22

- EMBL
- EMBL in collaboration with organisations in member or associate member states
- EMBL in collaboration with organisations in non-member states

New group leaders

Meet the group leaders who joined EMBL in 2020

Gautam Dey

I'm interested in the evolution of the cell's nucleus. Using a combination of approaches, we aim to understand the reasons for the startling diversity in the way the nucleus is organised in various organisms. Our research, with its mix of evolutionary biology, genomics, and cell biology, is interdisciplinary almost by definition. That makes it a perfect fit for EMBL. Some of our work will involve non-traditional microbial systems, pushing tools for electron and particularly light microscopy to their limits. We're looking forward to productive collaborations with the Advanced Light Microscopy Facility, the Electron Microscopy Core Facility, and hopefully soon with the new EMBL Imaging Centre.

Olivier Duss

My lab is interested in how RNA interacts with proteins. While we understand protein structures fairly well, we don't have that same understanding of how RNA folds and performs cellular functions. Using a technique called single-molecule fluorescence microscopy, along with structural biology and other approaches, we can gain a detailed understanding of RNA function, setting the stage to manipulate RNA for therapeutic purposes. We will study the folding of RNAs from different organisms, such as the bacterium that causes tuberculosis. This may ultimately reveal ways to make the bacterium less harmful or even kill it, without affecting other, beneficial microorganisms in the body.

Anna Erzberger

Living matter self-organises across scales of time and space that range from molecules to organisms. For example, as an embryo develops, its cells construct complex organs to carry out specific functions. My group uses theoretical tools from physics to explore the foundations of this cellular and multicellular organisation, helping to track molecular communication and measuring the ways cells make this happen. We work with experimental colleagues, using condensed matter theory to study this self-organisation that builds life. Armed with this knowledge, we hope to explain and predict the behaviour of a diverse range of systems, from cellular organelles to entire organs, as they develop.

Nicoletta Petridou

My group focuses on a particular developmental time period, corresponding to the onset of morphogenesis – the process in which a tissue or organism develops its shape. We study zebrafish embryos and combine methods from embryology, live quantitative imaging, and biophysics with theories from statistical mechanics. Currently, we're focusing on understanding how the structural properties of tissues are regulated in space and time by the underlying biochemical signals, and what their role is in changing cell identity. If you consider that all of us were once an amorphous mass of cells, it's mind-blowing to think about how these processes operate, with a precision that is able to shape us into fully functional organisms.

Sinem Saka

Our group strives to develop new molecular tools and methods to increase the density of data and depth of information that we acquire from our experiments, and to enhance our knowledge of cellular biology. By integrating imaging with multiple complementary techniques for single-cell analysis, we hope to understand the visible manifestations of a cell's state and how spatial features in biology contribute to the function and organisation of subcellular compartments, cells, and tissues. As we interface with and integrate multiple technologies, EMBL's core facilities will be tremendously important to push our research forward. Similarly, I have no doubt that the general collaborative atmosphere at EMBL will spark many new ideas and open new research avenues.

MISSION 2

To offer vital **services** to scientists in EMBL member states and around the world

The scientific services provided by EMBL include data, structural biology, and imaging services, as well as state-of-the-art core facilities.

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Scientific services

EMBL provides access to advanced technologies, infrastructure, and data resources

EMBL's scientific services, combined with our scientific and technical expertise, enable fundamental research that is essential to solving global societal challenges. EMBL's unique portfolio of integrated scientific services provides researchers from our member states and around the world with access to a broad range of world-class infrastructures and resources through a single Europe-wide partner.

Bioinformatics services

EMBL's European Bioinformatics Institute (EMBL-EBI) is a global hub for open data resources and tools for the life sciences. These are essential for scientists, industry, and the public. By offering open access to EMBL-EBI's bioinformatics services for data storage, sharing, and analysis, EMBL provides critical resources and tools that tens of millions of scientists use every day. This enables new discoveries worldwide.

One essential part of EMBL-EBI's work in 2020 was to develop and run the European COVID-19 Data Platform (p. 5). EMBL-EBI's data resources also prioritised SARS-CoV-2 data submissions, doubling efforts to get new data rapidly into the public domain. Many resources set up dedicated areas and tools for coronavirus research:

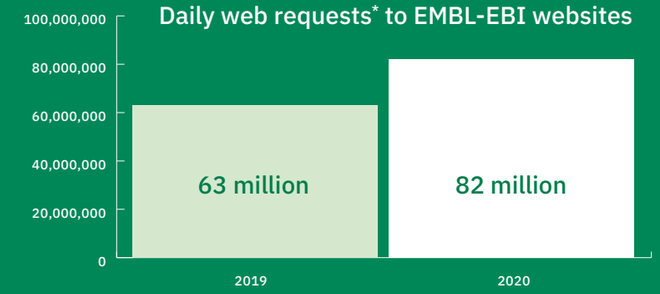
- Europe PMC, an open science platform for scientific literature, made full-text COVID-19 preprints freely available, ensuring that new scientific findings would be easily discoverable.
- Ensembl set up a dedicated SARS-CoV-2 genome browser, enabling researchers to explore the complete genome of the virus.
- The protein resources UniProt and the Protein Data Bank in Europe set up dedicated areas on their websites to facilitate finding and analysis of coronavirus data.

Alongside this major cross-institutional effort to support COVID-19 research and data sharing, which dominated 2020, EMBL-EBI launched many databases to explore new data types. These include the eQTL Catalogue, a valuable resource for gene expression data, and the Genome Targeting Catalogue, a repository of experiments using the genome editing tool CRISPR–Cas, which enables researchers to find experiments on any gene of interest.

EMBL-EBI data services in numbers

USAGE OF EMBL-EBI DATA RESOURCES

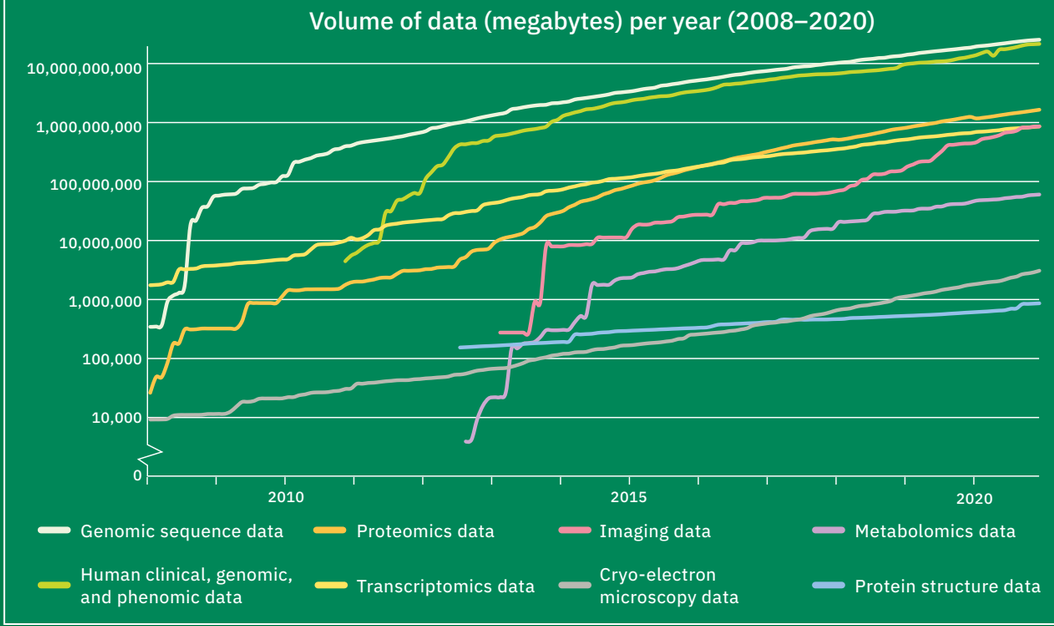
EMBL-EBI maintains the world's most comprehensive range of freely available and up-to-date molecular data resources. Developed in collaboration with scientists worldwide, these open databases, tools, and software can be accessed by anyone around the world.



* A web request is defined as any time a user or computer algorithm asks for information on our webpages using HTTP. Requests may retrieve an entire webpage or just a single piece of information from an EMBL-EBI data resource.

DATA GROWTH BY EMBL-EBI SERVICE

The scientific community has continued to submit data to EMBL-EBI's databases throughout the COVID-19 pandemic. Over the course of the year, data deposition for human clinical, genomic, and phenomic data grew by half, and the volume of cryo-electron microscopy data doubled.



ALUMNI IMPACT

Florent Cipriani

Retired
Head of Instrumentation Team
and Senior Scientist at EMBL, 1991–2020

Florent Cipriani has been a pioneer of instrumentation development in structural biology, creating ingenious inventions with worldwide impact. The EMBL environment has enabled Florent's team to collaborate closely with the research community to understand their needs, develop innovative technologies, and take these innovations through rapid cycles of design and testing.

When the first high-brilliance, third-generation synchrotron source opened at the European Synchrotron Radiation Facility (ESRF) in 1994, it created many new opportunities for X-ray crystallography. However, it also posed technological challenges, such as the need to align protein crystals only thousandths of a millimetre in size with an X-ray beam that was similarly narrow. To solve this problem, Florent worked with Tassos Perrakis – then a staff scientist at EMBL Grenoble – and the current Head of EMBL Grenoble, Stephen Cusack, to develop a first-generation micro-diffractometer, which allowed automated and precise positioning of crystals in the beam. The concept was patented, and subsequent versions are now in use at synchrotrons around the world.

Alongside this instrument, Florent created a first-generation automated sample changer to accelerate the process of exchanging crystals for analysis. This robot made it possible to load up to 50 crystals to be exposed, in turn, to the X-ray beam. The latest version of the sample changer, FlexHCD, has a capacity of 368 crystals.

These innovations have enabled more efficient use of scarce X-ray beamtime, and have improved data quality and facilitated structure determination on ever-smaller crystals. They have also set the stage for a complete automation of the structure determination process. Florent has worked closely with other technology-oriented groups at EMBL Grenoble and with the ESRF Structural Biology Group, merging technological innovation with software developments. One achievement was to completely automate data collection on one of the structural biology beamlines, MASSIF-1. A second example is the joint development with the Márquez Team of the CrystalDirect robot (p. 54), which led to the development of automated crystallography pipelines. A CrystalDirect robot will soon be incorporated directly into MASSIF-1, in effect putting a crystallisation facility and a synchrotron in every lab, no matter where it's located in the world.

Structural biology and imaging services

EMBL offers an extremely wide range of services in structural biology and imaging, including macromolecular crystallography, small-angle X-ray scattering, and electron and light microscopy, as well as services for sample preparation and characterisation.

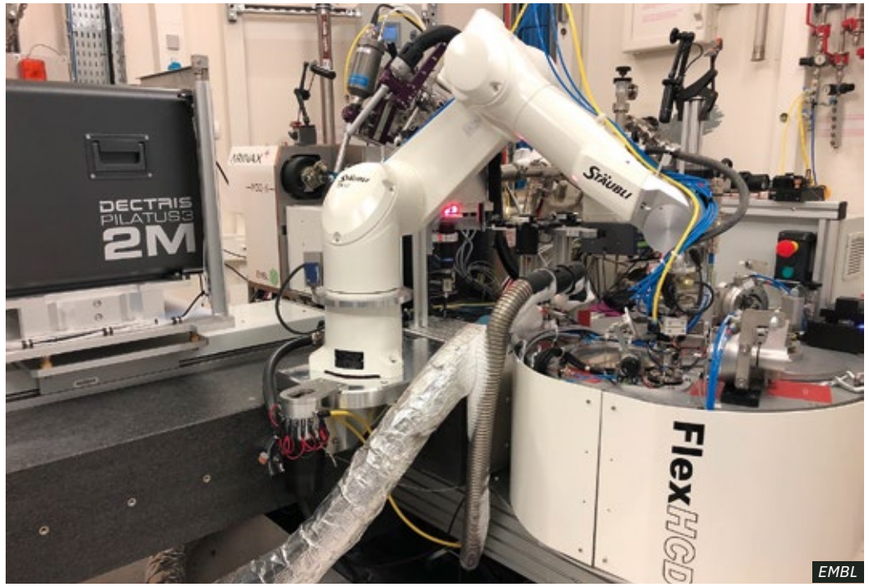
Grenoble structural biology services

EMBL Grenoble collaborates with the European Synchrotron Radiation Facility (ESRF) in building and operating state-of-the-art X-ray and high-end cryo-electron microscopy beamlines, and provides access to high-throughput crystallography and fragment screening pipelines at its High-Throughput Crystallisation (HTX) Facility.

The structural biology beamlines run jointly by EMBL Grenoble and the ESRF resumed user operations on 25 August 2020, following completion of the ESRF Extremely Brilliant Source (ESRF-EBS) – the world's first fourth-generation high-energy synchrotron.

Among the upgrades to these beamlines, there was a significant refurbishment of MASSIF-1 – the world's first autonomous beamline. Together, the ESRF-EBS and MASSIF-1 upgrades will substantially increase the speed of data collection and the quality of data collected, and will provide greater operational integration with the HTX Facility. Between the reopening and the end of the year, more than 5,500 samples were automatically processed on MASSIF-1, including around 500 for research relating to COVID-19.

The HTX Facility provides efficient remote access to fully automated protein-to-structure pipelines. High-throughput crystallisation, automated crystal



The MASSIF-1 experimental hutch.

harvesting and cryo-cooling, and diffraction data collection are integrated into a continuous workflow operated online via the Crystallographic Information Management System. During the shutdown period for the ESRF-EBS upgrade, the HTX Facility continued operations, sending crystal samples prepared in Grenoble for analysis at other European synchrotrons, such as the PETRA III beamlines supported by EMBL Hamburg.

Hamburg structural biology services

EMBL Hamburg operates two beamlines for macromolecular crystallography (MX) and one for small-angle X-ray scattering (SAXS) at DESY's PETRA III synchrotron, and an associated Sample Preparation and Characterisation (SPC) Facility.

After an initial closure in March, EMBL's beamlines at PETRA III reopened for COVID-19-related research projects in May, and for all projects in June. The majority of experiments were performed remotely, with users mailing in their samples and controlling experiments with the standard graphical user interface via an internet connection.

Several projects at the beamlines and in the SPC Facility were dedicated to COVID-19-related research. At EMBL's SAXS beamline, P12, these included a collaboration with EMBL's Löw Group (p. 11) and three collaborative papers published with scientists from Johannes Gutenberg University Mainz and BioNTech (p. 9). EMBL's MX beamlines, P13 and P14, were used for a crystallographic screening to identify potential drugs that could inhibit SARS-CoV-2's main protease – an enzyme crucial to the virus's life cycle. Up to the end of 2020, scientists from the SPC Facility had contributed to five coronavirus research projects, including measurements of how strongly potential drug molecules bind to SARS-CoV-2 proteins. This supports the identification of drug treatments for coronavirus infections.

The SPC Facility received funding in 2020 for a project to improve the stability of membrane proteins for cryo-EM studies. The funding, shared with scientists from the University of Copenhagen, was awarded as part of the EU's Hanseatic League of Science (HALOS) project, which aims to build collaborations between research institutes in Hamburg and south-west Scandinavia.

Advanced Light Microscopy Facility

To enable continued service provision in 2020, the Advanced Light Microscopy Facility (ALMF) established systems for remote control of its microscopes. This enabled training, support, and data acquisition while minimising physical contact. Members of the ALMF worked in collaboration with the German bioimaging community to develop guidelines for safe operation of imaging facilities during the COVID-19 pandemic.[1]

The ALMF provides image analysis services in collaboration with EMBL's Centre for Bioimage Analysis (CBA). In 2020, the CBA co-initiated the Network of European Bioimage Analysts (NEUBIAS) Academy: a series of more than 20 webinars on image analysis, with more than 40,000 views on YouTube.

Cryo-Electron Microscopy Service Platform

The Cryo-Electron Microscopy (Cryo-EM) Service Platform continued to provide services to external users throughout 2020, with users generally mailing in their samples and controlling data collection remotely. During the closure of the Heidelberg site in spring, the Cryo-EM Service Platform was open for COVID-19-related research projects only, for which services were provided free of charge. This enabled EMBL scientists and collaborators to determine the *in situ* structure of the SARS-CoV-2 spike protein in record time (p. 8).

Electron Microscopy Core Facility

The Electron Microscopy Core Facility began a collaboration with EMBL's Mahamid Group and Leica Microsystems in 2020, to develop workflows for cryogenic correlative light and electron microscopy (cryo-CLEM) and cryogenic focused ion beam scanning electron microscopy (cryo-FIB-SEM). These techniques use flash-frozen samples, making it possible to avoid other types of physical or chemical preparation that can damage or distort samples. This enables biological structures to be imaged close to the way they appear in nature.

Mesoscopic Imaging Facility

For several years, the Mesoscopic Imaging Facility (MIF) at EMBL Barcelona has collaborated with scientific instrument manufacturer Bruker to develop the multi-view single-plane illumination microscope (MuVi SPIM) platform. Among several improvements made to the technology in 2020, the collaborators implemented a temperature stabilisation system. This enabled a project at the MIF to study zebrafish development at precisely controlled temperatures.

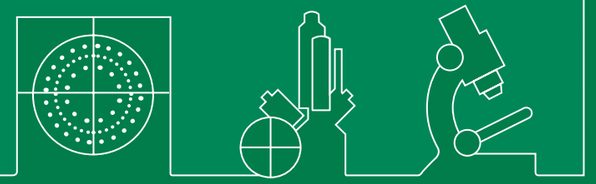
Microscopy Facility

In 2020, the Microscopy Facility at EMBL Rome began a collaborative project with EMBL Rome's Histology Service (p. 38) to establish a platform for spatial transcriptomics using sequential fluorescence *in situ* hybridisation (seqFISH), which makes it possible to spatially map gene expression. This helps scientists to understand how cells function and organise themselves within a tissue.

STRUCTURAL BIOLOGY AND IMAGING SERVICES IN NUMBERS

EMBL provides a range of structural biology and imaging services to the scientific community. These enable measurements across scales, from atomic snapshots of moving proteins to molecules within cells, tissues, or organisms. EMBL Grenoble and EMBL Hamburg provide services via synchrotron beamlines, and EMBL Barcelona, EMBL Grenoble, EMBL Heidelberg, and EMBL Rome enable member state scientists to access cryo-electron microscopy and advanced light microscopy techniques.

4,783
on-site user visits, mail-in samples, and remote user access sessions*



* This figure is affected by the shutdown of the ESRF–EMBL beamlines in Grenoble, which was required for the upgrade to a fourth-generation synchrotron, the ESRF Extremely Brilliant Source. The beamlines reopened in August 2020.

1. Dietzel S, Ferrando-May E *et al.* (2020) A Joint Action in Times of Pandemic: The German BioImaging Recommendations for Operating Imaging Core Facilities During the SARS-Cov-2 Emergency. *Cytometry Part A* 97(9):882–886. DOI: 10.1002/cyto.a.24178

EMBL Imaging Centre

The EMBL Imaging Centre will provide researchers with access to cutting-edge imaging technologies, which integrate methods from electron and light microscopy across scales. The Imaging Centre project has been enabled by the German government and by generous donations from private supporters, including the Boehringer Ingelheim Foundation and HeidelbergCement.

Recruitment of the first Imaging Centre staff took place in 2020, including team leaders Timo Zimmermann and Simone Mattei (see opposite), application specialists and engineers, and a scientific service support manager.

The Imaging Centre teams will integrate and expand the current activities of EMBL's Cryo-EM Service Platform, which will seamlessly link to the latest super-resolution technologies. These include a MINFLUX super-resolution microscope – the first time this technology has been offered as an open access service anywhere in the world. The microscope will enable scientists to image inside whole cells with a spatial resolution better than 10 nanometres in all three dimensions. In addition, the teams are already bringing into service EMBL-developed techniques for 3D stochastic optical reconstruction microscopy (STORM) and novel workflows for cryo-electron tomography, in close collaboration with EMBL research groups. With these interim services and preparatory activities, the Imaging Centre teams will be ready to provide high-level bespoke project support for researchers from around the world when the Imaging Centre opens in 2021.

EMBL Imaging Centre façade.

New team leaders

Meet the new team leaders driving technology development and service provision for the EMBL Imaging Centre

Timo Zimmermann

Team Leader, Light Microscopy

The idea of the EMBL Imaging Centre is to offer external researchers timely access to instruments that are not yet widely available. We will provide the highest-resolution technologies and other advanced methods, with a strong focus on connecting to the electron microscopy side of the Imaging Centre through correlative light and electron microscopy – or CLEM – and cryo-CLEM approaches. I'm also creating a research team to work on new microscopy techniques in the fields of super-resolution and cryo-fluorescence microscopy.

Cryo-fluorescence microscopes are still technically limited and very far away from the resolution of electron microscopes. Super-resolution methods could improve the resolution further and allow better correlation, but they require a lot of light to produce the desired improvements, at the risk of destroying fine structural details through heating and ice crystal formation. Imaging facilities pose very fulfilling, diverse challenges.

Simone Mattei

Team Leader, Electron Microscopy

The Imaging Centre is not just a new concept for EMBL; it's a new concept for Europe as well. It will be focused on external users, and it offers amazing potential for building connections and boosting collaboration. One of the great things about the centre is that we can interact closely with EMBL's research groups and develop the new methods required to answer their challenging biological questions.

Cryo-electron microscopy is an incredibly powerful tool, but we're still in the early stages of working out the best ways to harness it. By developing pipelines that allow sample preparation to be as automated as possible, we can increase throughput and really speed up our work. This has lots of benefits, for example when screening hundreds of molecules during the process of drug development. That level of work really needs an efficient system, and that's why what we're developing with the new EMBL Imaging Centre could open so many doors.

Multi-omics services

EMBL supports researchers in performing functional omics analyses, enabling the study of genes, proteins, and other molecules.

Genomics Core Facility

Throughout 2020, the Genomics Core Facility continued to provide services to scientists in EMBL's member states. Scientists from the facility were authors on 16 papers published by member state scientists, including a study revealing the limitations of current nanopore sequencing methods.[1] The facility was also involved at an early stage in EMBL's coronavirus research activities, for example in the development of a new testing protocol (p. 7).

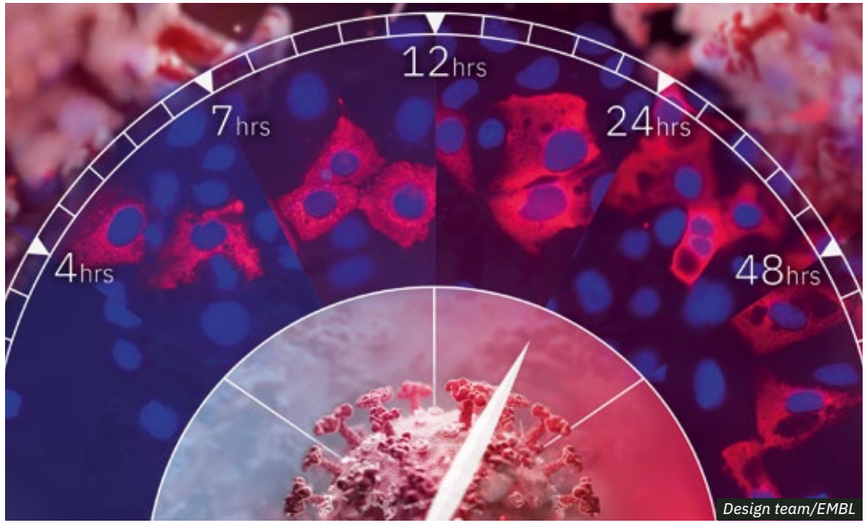
Metabolomics Core Facility

The Metabolomics Core Facility (MCF) has strengthened its collaborations with relevant networks in Europe by participating in the Core for Life Metabolomics Work Group and in standardisation efforts for metabolomics led by Phenome Centre Birmingham, UK. The MCF has also begun a collaboration with Universität Hamburg and Université Paris-Est Créteil on the CO-PROTECT project, which aims to identify favourable combinations of antibiotics to prevent the emergence of multidrug-resistant bacteria.

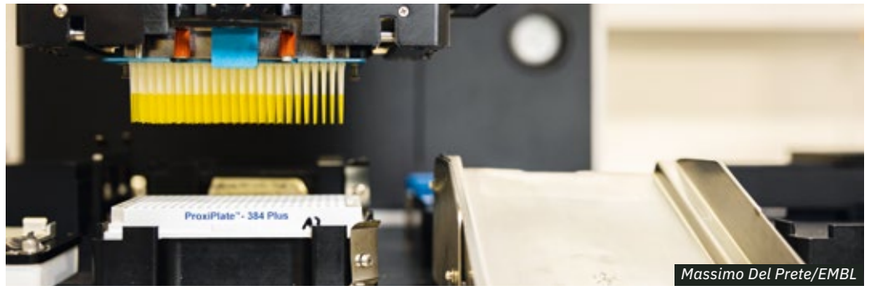
Proteomics Core Facility

The Proteomics Core Facility (PCF) has played a key role in a study of how SARS-CoV-2 infection alters the thermal stability of the host proteome, which led to the identification of potential drug targets for treating infection.[2]

The PCF has continued to support research at EMBL and in our member states. The facility has established a cross-linking workflow for structural



The Proteomics Core Facility has studied how SARS-CoV-2 infection alters the thermal stability of the host proteome.



Liquid-handling robots are used in a collaborative study between the Chemical Biology Core Facility and Heidelberg University Hospital, to measure levels of SARS-CoV-2 antigens in blood samples.

characterisation of proteins, which gained widespread attention in 2020 and is now being used by many research groups across Europe.

Flow Cytometry Core Facility

In 2020, the Flow Cytometry Core Facility (FCCF) formed a collaboration with opto biolabs, a start-up company producing illumination devices for optogenetics, which is a technique that uses light to control the activity of cells expressing light-sensitive receptors. The collaboration aims to develop a system to combine optogenetics with cell sorting. The FCCF is currently testing a prototype system produced by EMBL's Mechanical Workshop.

Chemical biology services

Chemical Biology Core Facility

In 2020, the Chemical Biology Core Facility (CBCF) worked with collaborators from Heidelberg University Hospital on a study measuring levels of SARS-CoV-2 antigens in blood samples from patients in the Heidelberg area. This allowed an estimation of viral infection rates and will help to inform public health strategy.

To prepare for research projects in the next EMBL Programme, and with a view to providing tools for scientists to explore the impact of environmental chemicals on various life forms, the CBCF acquired stocks of more than 1,000 pesticides and measured them into vials for future experiments. Although many of these chemicals are highly toxic, they could be prepared safely using the CBCF's well-equipped chemistry laboratory. A number of future studies will investigate the characteristics of these pesticides, ranging from their activity in cells to their effects on whole ecosystems. These studies will be carried out in close collaboration with EMBL member states, and will include institutes that specialise in chemical biology and toxicology.

1. Courtine D *et al.* (2020) Long-read only assembly of *Drechmeria coniospora* genomes reveals widespread chromosome plasticity and illustrates the limitations of current nanopore methods. *GigaScience* 9(9). DOI: 10.1093/gigascience/giaa099
2. Selkrig J, Stanifer M, Mateus A, Mitosch K, Barrio-Hernandez I, Rettel M *et al.* (2021) SARS-CoV-2 infection remodels the host protein thermal stability landscape. *Molecular Systems Biology* 17:e10188. DOI: 10.15252/msb.202010188

In vivo gene editing services

EMBL Rome's facilities offer a range of sophisticated gene editing services to scientists and play a key role in supporting the site's research in epigenetics and neurobiology.

Gene Editing and Embryology Facility

When EMBL Rome reopened after the first lockdown in Italy, members of the Gene Editing and Embryology Facility (GEEF) rapidly began work on a COVID-19-related project. They are creating a new transgenic mouse line that has a modified version of the protein ACE2 – the protein that SARS-CoV-2 binds to in humans, enabling the virus to infect cells. The project involves subtly editing the mouse version of the gene so that the protein it produces is like the human version at critical points where it interacts with SARS-CoV-2's spike protein.

Supported by virtual meetings, the GEEF's collaborations continued unaffected in 2020, and new multi-institute projects were initiated. The facility is currently running collaborative transgenic mouse projects with institutes in Rome, Bologna, Genoa, Milan, Siena, and Turin. The GEEF also made progress on its large-scale project to produce a 'zoo' of transgenic mice with various epigenetic modifications, which is nearing completion.

Genetic and Viral Engineering Facility

The Genetic and Viral Engineering Facility (GAVEF) has continued work on a collaborative project with the GEEF that aims to improve genome editing technologies by using viruses to deliver CRISPR genome editing systems into embryos. The GAVEF will also participate in EMBL's new collaborative partnership with the Life Sciences Center at Vilnius University, the VU LSC–EMBL Partnership for Genome Editing Technologies (p. 62). The partnership will focus on developing viral delivery of novel CRISPR–Cas systems for gene editing and modifications, enabling the study of fundamental biological processes as well as the applied use of potential therapeutics.

EMBL

The Sample Preparation and Characterisation Facility at EMBL Hamburg reopened in May to support scientists working on COVID-19 research.


Kinga Lubowiecka/EMBL

Scientists in the Protein Expression and Purification Core Facility produced several proteins relevant to studies of SARS-CoV-2.

Sample preparation services

EMBL offers various services for isolating biological samples of interest and preparing them for further analysis or experimentation. In addition to the High-Throughput Crystallisation Facility in Grenoble (p. 30) and the Sample Preparation and Characterisation Facility in Hamburg (p. 31), these facilities include the Histology Service at EMBL Rome and the Protein Expression and Purification Core Facility at EMBL Heidelberg.

Histology Service

The Histology Service is working to combine expansion microscopy, in which tissues are infiltrated with hydrogel to enlarge them for analysis, with the use of DNA-conjugated antibodies. This will make it possible to acquire super-resolution images of changes in genome structure in response to epigenetic modifications.

Protein Expression and Purification Core Facility

The Protein Expression and Purification Core Facility (PEPCF) contributed to various COVID-19-related research projects in 2020, in collaboration with research groups at EMBL and externally. The facility produced a range of enzymes to enable the development of new coronavirus testing methods, and made the relevant constructs and protocols freely available to the scientific community.
Using PEPCF's platform for protein expression in mammalian cells, set up in 2019, researchers were able to express and purify several proteins relevant to studies of SARS-CoV-2. These were used in projects aiming to combat the virus and develop new diagnostic tests.

MISSION 3

To **train** scientists, students, and visitors at all levels

EMBL's PhD and postdoctoral research programmes provide world-class training for scientists in a collaborative and interdisciplinary environment.

EMBL's courses and conferences cover a diverse range of topics and bring together experts to share new ideas and techniques, foster collaborations, and develop strategies to drive future research.

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Training

EMBL trains scientists, students, and visitors at all levels

Internal training

The Internal Training team provides EMBL pre- and postdoctoral fellows with a broad portfolio of training and career development opportunities to help them reach their professional goals. Since the start of the COVID-19 pandemic, recruitment and training activities have been conducted virtually. This has brought some benefits by making activities at specific EMBL sites accessible to fellows at all sites, and has increased EMBL's reach in the wider scientific community.

EMBL International PhD Programme

The EMBL International PhD Programme (EIPP) is international and diverse, currently hosting 227 students of 48 nationalities. Of these, 68% are from EMBL member states, and around 80% of graduates of the programme remain in EMBL member states after graduation, contributing to research and innovation in those countries.

Despite the challenges of the COVID-19 pandemic, the summer recruitment and predoc course – both of which were held virtually – received very positive feedback. The EIPP also successfully extended its network of partner universities by signing an agreement with Pompeu Fabra University (UPF) in Barcelona. In February, thanks to the generous financial support of the Friends of EMBL (p. 78), part two of the first EMBL Corporate Winter School for PhD students was held at EMBL's European Bioinformatics Institute (EMBL-EBI), following a successful first part at EMBL Heidelberg in September 2019. The course provided key insights into careers in the research and development sector in industry and start-ups.

EMBL INTERNATIONAL PHD PROGRAMME

The EMBL International PhD Programme recognises potential and trains students from EMBL member states and beyond. The programme gives PhD students the best starting platform for a successful career in science.

* Some graduations were delayed due to the COVID-19 pandemic.

EMBL Postdoctoral Programme

In 2020, EMBL welcomed the first cohort of postdocs supported by EIPOD4: the newest iteration of the EMBL Interdisciplinary Postdocs (EIPOD) initiative. EIPOD4 receives funding from the Marie Skłodowska-Curie Actions COFUND programme. To reach the widest possible pool of applicants, EIPOD4 is advertised globally, and the 20 new fellows in 2020 come from 14 countries. EIPOD fellows work on interdisciplinary projects involving two or more EMBL groups. Depending on their research interests, they may also involve external partners from academia, industry, or clinical practice. Six external partners from academia and one from industry will contribute to research projects carried out by the new cohort.

EMBL Fellows' Career Service

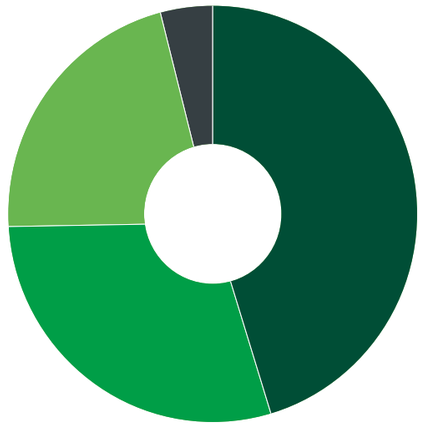
The pandemic has had a major impact on the next generation of scientists. EMBL's career advisors immediately rose to the challenge of providing advice to fellows considering their future plans at this time. The EMBL Fellows' Career Service celebrated its first anniversary in September 2020 and now offers an expanded portfolio of activities. These have also been delivered in virtual formats, enabling the service to bring together PhD students and postdocs from all of EMBL's sites. In 2020, a total of 138 individual career guidance sessions were held, and a survey of fellows showed that 100% would recommend a career guidance session to their peers. The annual EMBL Career Day was offered as a webinar series, allowing more people outside EMBL to attend. The Career Service organised 11 webinars covering academic and non-academic careers, which attracted more than 2,000 attendees, 85% of them from EMBL or our member states. Four new career workshops were developed, including

EMBL POSTDOCTORAL PROGRAMMES

EMBL welcomes talented postdoctoral fellows via several entry streams, including the EIPOD programme, which promotes multidisciplinary and multisectoral research in collaboration with national academic institutes, industry, and hospitals.

58
new postdocs in 2020

237
postdocs in 2020 in total*



51
postdocs leaving in 2020

* Does not include former PhD students finalising their projects via a bridging postdoc contract.

Oana Stroe/EMBL

Part two of the first EMBL Corporate Winter School for PhD students was held at EMBL-EBI in February.

one on interview skills in collaboration with life science company Eppendorf, a member of EMBL's Corporate Partnership Programme. Over the course of the year, the Career Service held 26 career workshops – 23 in virtual format – which were attended by more than 250 EMBL scientists in total.

External training

EMBL enables training, knowledge sharing, and continuing professional development for scientists from around the world via our international Course and Conference Programme and Scientific Visitor Programme. These activities are complemented by EMBL's educational programme, the European Learning Laboratory for the Life Sciences, which offers professional development to science teachers and aims to spark curiosity in primary and secondary school students about scientific research.

Course and Conference Programme

The COVID-19 pandemic was transformative for EMBL's courses and conferences. It created unprecedented challenges for EMBL's on-site training in 2020, at a time when scientific exchange between institutes and across borders was more important than ever. Changes were therefore made rapidly to ensure that as many events as possible could go ahead. Within weeks of the first lockdowns in Europe, EMBL was able to organise a virtual EMBL Conference 'SARS-CoV-2: Towards a New Era in Infection Research' (p. 12), which gathered together leading experts in infectious disease as well as policymakers. The conference was free and open to all.

The shift to virtual events not only enabled the Course and Conference Programme to continue, but also had clear benefits in terms of the number of scientists able to attend. The total number of attendees at EMBL's courses and conferences in 2020 was more

ARISE: training the next generation of research infrastructure scientists

EMBL's mission to train the next generation of scientists includes not only PhD students, postdocs, and group leaders, but also technology and research infrastructure scientists. In December 2020, EMBL began accepting applications for the ARISE fellowship programme. ARISE is the first long-term preparatory programme of its kind, and will train a diverse group of engineers, computer scientists, mathematicians, and others to develop and run research infrastructure.

"ARISE will offer a way for technology developers to acquire expertise needed to run research infrastructure in the life sciences, and a structured way to gain know-how previously handed down in a random way on the job," says Tanja Ninkovic, the ARISE programme manager, who designed and will implement this offering. "This programme aims to provide a more robust backbone to the research infrastructure so central to research and development."

Over five years, EMBL will train 62 fellows to become future leaders in technology development and to take senior positions in life science research infrastructure, in either academia or industry. Participants will represent diverse STEM disciplines, backgrounds, and interests, setting the stage for an expansive learning environment in which they will benefit from the knowledge of the instructors and other programme participants. Together, fellows will expand their expertise to better understand the practicalities of infrastructure, management, and regulatory issues, as well as the finer points of technology development and an overview of trends in the life sciences.

"There simply hasn't been training in any systematic way for research infrastructure scientists, and that was a trigger that made us realise EMBL could fill this need," says Peer Bork, a bioinformatician, Director of EMBL Heidelberg (Scientific Activities), and ARISE programme director. "There's nothing comparable to ARISE. New technology will keep coming and so will the need for infrastructure to support it. Its time is now."

ARISE partner organisations – representing both academia and industry – will support the core fellowship training with long- or short-term secondments at their sites. This offers fellows exposure to different approaches to infrastructure, as well as experiences that will prepare them for positions as senior scientists or leaders of research infrastructure in a variety of sectors.

By 2025, ARISE fellows will take up roles across industry, healthcare, academia, and other sectors. This is likely to be a boon for EMBL's member states.

than 30% higher than in 2019. Among the highlights of the programme was the virtual EMBO | EMBL Symposium ‘Organoids: Modelling Organ Development and Disease in 3D Culture’, which was attended by more than 850 people.

Established meetings were also successfully transitioned to virtual formats, with the 14th edition of the biennial EMBL Conference ‘Transcription and Chromatin’ attended by more than 750 people, compared to 430 in 2018. The EMBL Conference ‘BioMalPar XVI: Biology and Pathology of the Malaria Parasite’ was attended by almost 400 people; nearly double the number of attendees in 2019.

To meet the challenge of teaching practical courses virtually, both EMBL Heidelberg and EMBL-EBI developed virtual learning platforms. EMBL-EBI’s webinar programme and online tutorials provided immediate training opportunities for the research community. A total of 44 webinars took place in 2020, with 1,978 participants – almost four times as many as in 2019. EMBL-EBI’s online tutorials, available through the Train Online portal, were accessed from 545,000 unique IP addresses. As part of a larger project to make training content more accessible, interoperable, and reusable, EMBL-EBI redesigned all its online tutorials, webinars, and forthcoming live virtual courses, in preparation for the full relaunch of its training website early in 2021.

Although not all courses were suitable for conversion to virtual format, the new EMBL eCampus and EMBL-EBI’s one-stop online course handbooks provided an interactive platform that allowed participants to learn from experts, ask questions, and network with fellow participants. Through externally funded projects, EMBL-EBI trainers also delivered several other live virtual training events as part of the BioExcel, CABANA, and Global Alliance for Genomics and Health initiatives.

EMBL’s courses and conferences became accessible from home in 2020.

External training in numbers

The COVID-19 pandemic had a significant impact on EMBL’s on-site training. EMBL rapidly adapted to provide online training, enabling EMBL courses and conferences to be delivered to a greater number of people. EMBL’s Scientific Visitor Programme, which includes long-term visitors, has continued to train scientists throughout the COVID-19 pandemic.

COURSES AND CONFERENCES

9,912 participants from **101** countries attended courses and conferences hosted by EMBL sites

74% of participants were from EMBL member or associate member states

COURSES

26 on-site and virtual courses

100% of courses rated as **‘very good or excellent’** by the majority of participants

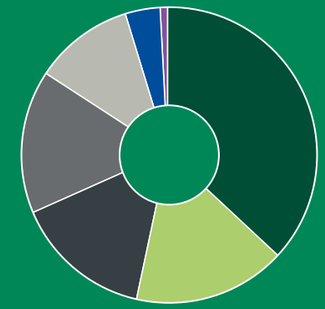
CONFERENCES

19 on-site and virtual conferences

94% of conferences rated as **‘very good or excellent’** by the majority of participants

SCIENTIFIC VISITORS

603 visitors



- 223 Master’s students and trainees
- 99 Visiting predoctoral fellows
- 91 Visiting postdoctoral fellows
- 95 Visiting researchers
- 67 Visiting technical experts
- 24 Visiting group leaders
- 4 Non-scientific visitors

78% of visitors from EMBL member states

ALUMNI IMPACT

Asifa Akhtar

Vice President of the Biology and Medicine Section, Max Planck Society; Director of the Chromatin Regulation Department, Max Planck Institute of Immunobiology and Epigenetics, Freiburg, Germany
Postdoc at EMBL, 1997–1999; Group Leader at EMBL, 2001–2009

EMBL alumna Asifa Akhtar is the first international female Vice President of the Max Planck Society, and is one of the recipients of the 2021 Leibniz Prizes – Germany's most prestigious awards in science.

Asifa is interested in the X chromosome and epigenetics: the factors outside the DNA code that control how our genes are expressed. In most mammals – including humans – females have two X chromosomes, while males have one X and one Y. To avoid getting a harmful double dose of certain genes, female mammals silence gene expression on one of their X chromosomes. Fruit flies deal with the same issue in the opposite way, with males doubling gene expression on their single X chromosome. In this way, epigenetic processes help to equalise the dosage of genes between the sexes.

A key part of Asifa's work involves an enzyme called MOF, which increases gene expression by chemically modifying the proteins that help to package the DNA. To her surprise, Asifa and her group discovered that MOF is located not only in the nucleus, where most of the cell's DNA is stored, but also outside the nucleus in the mitochondria, which generate the cell's energy. This discovery opened up a completely new area of research, revealing links between the cell's metabolism – in which mitochondria play a key role – and the processes of gene regulation at work in the nucleus.

In 2018, a neurodevelopmental syndrome in an infant patient led Julien Thevenon, a clinician from Université Bourgogne Franche-Comté in France, to connect rare medical cases and get in touch with Asifa. Her group soon found that mutated forms of a protein called MSL3, which was already implicated in this syndrome, failed to associate with MOF, leading to reductions in the expression of important developmental genes. Understanding more about this process could ultimately help scientists to find a cure for this syndrome, now known as Basilicata–Akhtar syndrome, which was a gratifying experience for Asifa.

"I always saw my work as important," she says, "but people relate to it differently when they hear about patients who are affected."

Scientific Visitor Programme

EMBL's Scientific Visitor Programme enables visiting scientists at all career levels to benefit from new technologies and state-of-the-art equipment in EMBL's laboratories and core facilities, and helps visitors to establish collaborations with scientists across EMBL's six sites.

Although the travel restrictions imposed as a result of the COVID-19 pandemic limited the number of new visitors to EMBL in 2020, those currently visiting were able to continue collaborating with research groups across EMBL's sites via virtual meetings, or in person where possible.

ELLS provides hands-on professional development courses for science teachers, as pictured here prior to COVID-19 lockdowns.

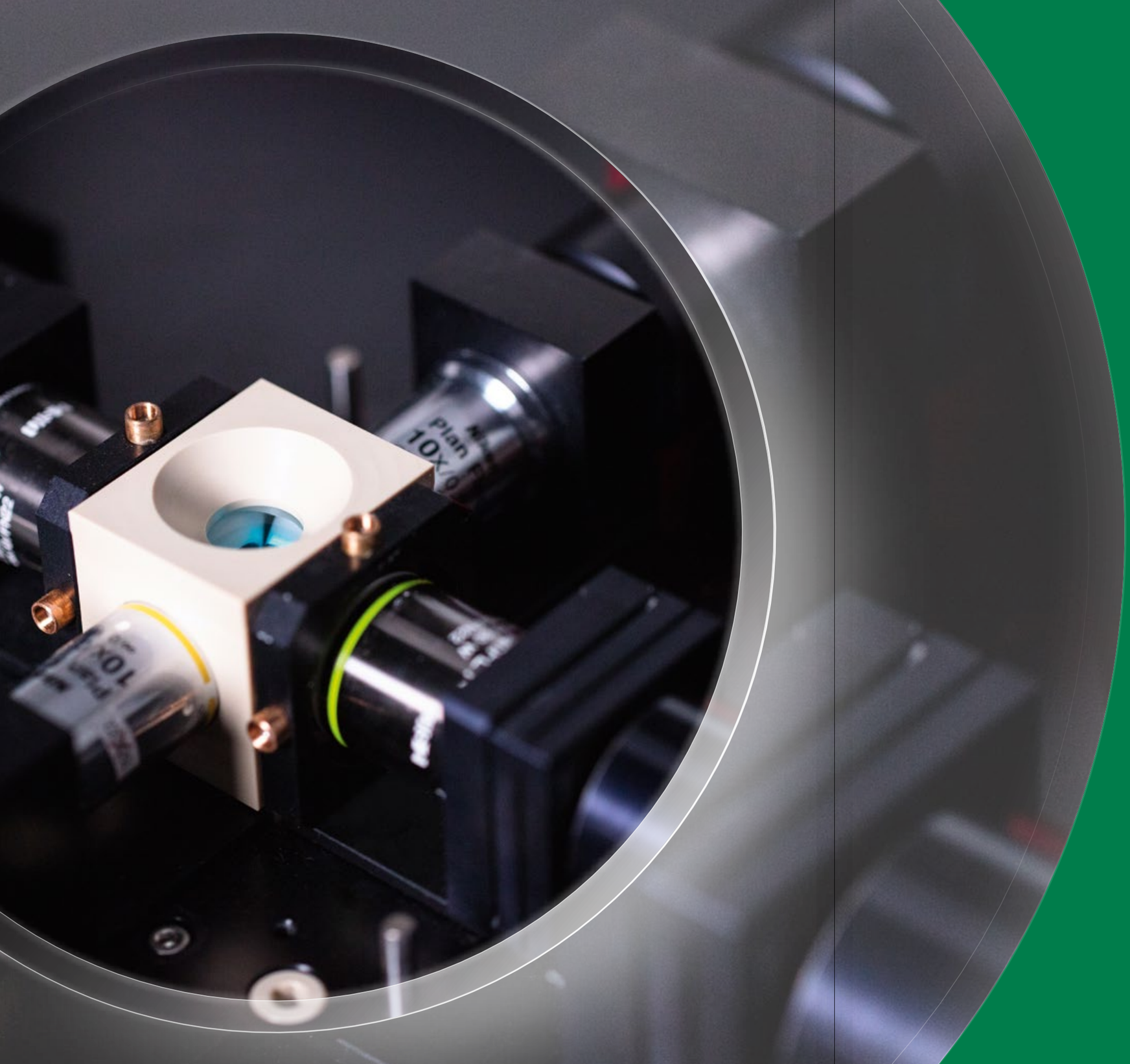
European Learning Laboratory for the Life Sciences

EMBL's educational programme, the European Learning Laboratory for the Life Sciences (ELLS), carried out science engagement activities that reached 245 high-school teachers and more than 1,298 students from 39 countries in 2020.

In the first few months of the year, ELLS welcomed three school groups to EMBL Heidelberg. After COVID-19 lockdown measures were imposed in March, ELLS focused on developing new online science education activities to continue supporting educators and young learners. ELLS subsequently launched a programme of virtual school visits, enabling 121 secondary school students to take virtual tours of EMBL.

During the year, ELLS organised four practical courses to provide continuing professional development for science teachers. ELLS also helped the NCSR Demokritos Institute of Nuclear and Particle Physics in Athens to organise a course on molecular biology techniques for 19 local teachers. In the autumn, ELLS launched a virtual LearningLAB, 'Introducing your microbiome', in partnership with the Communications team at EMBL-EBI. This course lasted five weeks and involved 89 participants from 25 countries.

ELLS supported the implementation of the SySTEM 2020 initiative, which aims to promote science literacy and education of children and teenagers across Europe in science, technology, engineering, art, and maths. As part of SySTEM 2020, ELLS engaged with more than 60 young learners in Germany and helped to develop a toolkit to support science educators in creating meaningful and inclusive science learning activities and programmes outside the classroom.



MISSION 4

To engage in **technology transfer** and **industry relations**

Scientists at EMBL seek innovative ways to answer biological questions, frequently developing new technologies and methods as part of the process, in close collaboration with industrial partners.

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Innovation and translation

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

Innovation and commercialisation activities

EMBL's technology transfer arm, EMBLEM, manages the process of translating EMBL's fundamental research into practical applications, making the discoveries, technologies, and methods developed at EMBL commercially available.

Despite the COVID-19 pandemic, EMBLEM had a very successful year in 2020 and supported EMBL in developing and expanding strategic partnerships with industry at various levels. Two spin-off companies were incorporated in 2020: Borea Therapeutics and Veraxa Biotech.

In collaboration with former EMBL Rome group leader Paul Heppenstall and the investment company Sofinnova Telethon, the spin-off company Borea Therapeutics was incorporated in Trieste in December. This spin-off will leverage the potential of a novel platform technology developed by Paul at EMBL Rome, which improves the use of adeno-associated virus (AAV) as a vector for delivering genes into cells. The new method is based on chemically modifying the protein shell – or capsid – of AAV, with the aim of developing next-generation viral vectors for targeted delivery of genes to specific cells or tissues.

In December, Veraxa Biotech was incorporated in Zürich to create a premium partner for the biopharmaceutical industry for accelerated drug development. Two existing EMBL spin-offs were merged into Veraxa: Velabs Therapeutics, based on the microfluidics technology developed by the Merten Group, and Araxa Biosciences, based on a protein engineering technology platform developed by the Lemke Group. The new company combines Velabs' functional antibody screening platform with Araxa's technology for developing highly specific antibody–drug conjugates or radioisotope analogues. Veraxa Biotech aims to characterise more drug candidates much faster and with higher specificity than was previously possible in the preclinical phase.

Public–private partnerships

Collaborations between EMBL and industrial partners for the EMBL Imaging Centre (p. 33) have made major steps forward in 2020. The Imaging Centre operates with a model of open innovation, bringing early-stage industrial imaging technology development closer to applications in life science research. Based on a long-term framework collaboration agreement with Leica Microsystems, several joint technology development projects began in 2020. A research collaboration agreement was made with Thermo Fisher Scientific to explore novel technologies for combining correlative live-cell subcellular mass spectrometry imaging with metabolomics. Under the agreement, EMBL group leader Theodore Alexandrov will develop new methods for direct coupling of imaging systems with mass spectrometers, with the aim of providing live-cell imaging, subcellular desorption, and *in situ* omics capabilities. Progress has also been made on an existing project with ZEISS and a new project with Abberior Instruments.

EMBL's collaboration with pharmaceutical company GSK builds on the close interaction between EMBL and Cellzome, an EMBL spin-off company located on the Heidelberg campus and acquired by GSK in 2012. The collaboration involved 10 projects in 2020, with six postdocs, three members of EMBL's core facilities, and one PhD student working jointly across EMBL and Cellzome. The third EMBL–GSK Science Day was held in July, this time conducted virtually. A new call for project proposals was opened during the event, with the aim of supporting joint research projects for discovering new molecular targets and biomarkers, especially using omics techniques. Nine proposals were submitted under this call, of which five have been approved for funding.

Innovation and translation in numbers

EMBL's innovation and translation activities include industry collaborations, public–private partnerships, forums for knowledge exchange, invention disclosures, and the creation of spin-off companies. EMBL's technology transfer arm, EMBLEM, plays a key role in enabling these activities.

EMBLEM IN NUMBERS

€11,783,000
income

404
licence and collaboration agreements concluded

30
inventions disclosed

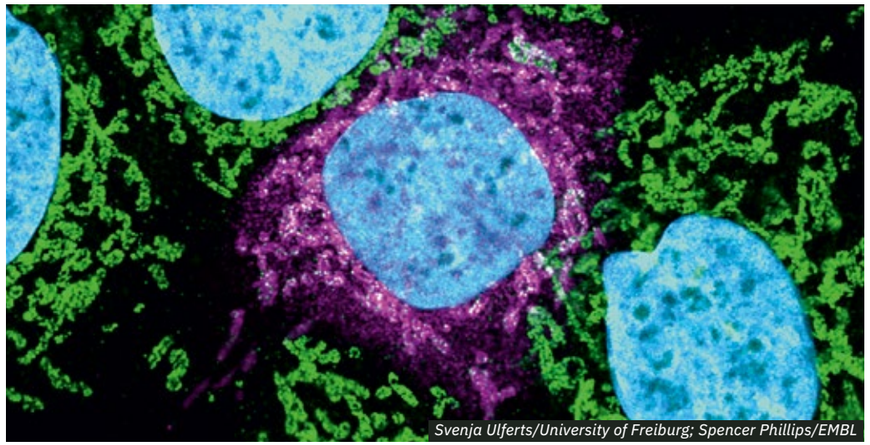
4
priority patent applications filed

19
patents granted

EMBLEM and PreOmics, a developer of innovative technologies for mass spectrometry-based sample preparation, have entered into an exclusive licensing agreement for EMBL's proprietary SP3 technology. This high-throughput technology for sample preparation in proteomics was developed in the lab of former EMBL group leader Jeroen Krijgsveld. SP3 enables ultrasensitive, rapid, unbiased, and flexible preparation of samples.

The public–private partnership Open Targets, which includes EMBL, the Wellcome Sanger Institute, and pharmaceutical companies GSK, Bristol Myers Squibb, and Sanofi, uses human genetics and genomics data to identify and prioritise drug targets. In 2020, the partnership entered its sixth year. In response to the COVID-19 pandemic, Open Targets established virtual ways of staying connected, including 15 training sessions for 475 participants across nine countries. Despite delays caused by lab closures, the Open Targets Validation Lab began its first experiments to validate oncology targets.

Bioinformatics projects at Open Targets were able to continue, with some rapidly shifting towards COVID-19-related work. Open Targets integrated data from its platform into the European COVID-19 Data Platform (p. 5), and the Open Targets Genetics Portal was used to provide insight into susceptibility to SARS-CoV-2 infection. A particular highlight was the analysis of human genetics factors: this resulted in contributions to a paper in *Science*,[1] which also included work from the Beltrao Group at EMBL's European Bioinformatics Institute (EMBL-EBI), and a letter in *The New England Journal of Medicine.*[2] Nine papers authored by Open Targets scientists were published in 2020, and the Open Targets Platform attracted more than 55,000 users.



Svenja Ulferts/University of Freiburg; Spencer Phillips/EMBL

Open Targets and the Beltrao Group contributed to a paper in Science, *which involved studies of interacting human (green) and coronavirus (pink) proteins to identify drug targets common to three coronavirus strains.*

1. Gordon DE, Hiatt J, Bouhaddou M, Rezelj VV, Ulferts S, Braberg H, Jureka AS, Obernier K, Guo JZ, Batra J, Kaake RM, Weckstein AR, Owens TW, Gupta M, Pourmal S, Titus EW, Cakir M *et al.* (2020) Comparative host-coronavirus protein interaction networks reveal pan-viral disease mechanisms. *Science* 370(6521):eabe9403. DOI: 10.1126/science.abe9403
2. Karim M *et al.* (2020) Mining a GWAS of severe Covid-19. *The New England Journal of Medicine* 383(26):2588–2589. DOI: 10.1056/NEJMc2025747

ALPX: providing automated crystallography services to accelerate research

ALPX is an EMBL spin-off company that offers automated X-ray crystallography and makes its tools accessible online anywhere in the world. A robot may be at the heart of the enterprise, but it's the people who made the idea happen and who guide clients through projects to advance science and medicine.

ALPX accelerates the process of determining biological structures using X-rays. By understanding the structures of biological molecules, researchers can predict how potential drugs might interact with them. This enables the development of new medical treatments.

At the centre of ALPX is its CrystalDirect technology and Crystallographic Information Management System (CRIMS) software – both developed at EMBL. José Márquez and Florent Cipriani, two researchers at EMBL Grenoble, developed the technology that led to CrystalDirect: a robotic system that prepares samples and places them in the X-ray beam for analysis. CRIMS tracks experiments and results and makes them available to scientists in real time. The software also connects to multiple synchrotrons in Europe, providing researchers with remote access to automated data collection at a range of facilities.

ALPX shortens to a matter of days a process that previously took weeks or months, which significantly cuts research costs.

ALPX's Chief Executive Officer, Irina Cornaciu, explains that EMBL not only helped advance the science but also recognised the opportunity it held as part of a public–private enterprise serving the research community. EMBLEM helped to establish ALPX's business infrastructure and to build the acumen necessary for a professional service provider that addresses client needs.

"We have an ever-growing demand, thanks to clients who share their delight in obtaining better crystal structures at a record pace," Irina says. "We're still hands-on for many projects, providing that additional expertise, but CrystalDirect and CRIMS help us to support more projects efficiently and smartly."

Training and knowledge exchange

Corporate Partnership Programme

EMBL's Corporate Partnership Programme (CPP) serves as a hub for collaboration, bringing together EMBL's research and training communities with global leaders in industry. In 2020, the number of CPP members increased to 19, following the signing of an agreement with NetApp as a new Corporate Partner. NetApp is a global leader in hybrid cloud data services and data storage, protection, and management across all business sectors, and is a service provider to EMBL.

During the COVID-19 pandemic, continuing financial support from CPP members has helped the EMBL International Centre for Advanced Training (EICAT) to rapidly migrate practical training courses and scientific conferences to virtual platforms. In the process, EICAT has significantly extended its global reach and level of participation, and has provided an increased number of course and conference registration fee waivers and childcare support grants.

In 2020, the CPP provided funding for 349 fellowships for course and conference participants from 64 countries. CPP members contributed to the organisation, training, or laboratory supplies for six courses held in 2020. In addition, 129 industry scientists from CPP member companies participated in EMBL conferences.

Massimo Del Prete/EMBL

The Corporate Partnership Programme's annual event in February 2020 brought together the EMBL research and training community with partners from industry for an evening of science and networking.

EMBL-EBI Industry Programme

The EMBL-EBI Industry Programme is a subscription-based programme for global companies that make significant use of EMBL-EBI's data and resources. Members of the Industry Programme team responded to the challenges of the COVID-19 pandemic by making their activities fully virtual. Working with partners from industry, the team reshaped meeting and workshop agendas to adapt them to a virtual format, and used digital engagement tools to maximise involvement and participation.

The team successfully delivered three quarterly meetings and six knowledge-exchange workshops for Industry Programme members in 2020. Compared with in-person meetings held in 2019, the average number of workshop participants doubled. A total of 756 industry delegates, from all 25 of the Industry Programme's member companies, attended the workshops.

Two new companies joined the EMBL-EBI Industry Programme in 2020: Eisai, a pharmaceutical company, and Lonza, a large contract development and manufacturing organisation (CDMO) that provides pharmaceutical and biotechnology products and services, and develops and manufactures specialised chemicals and composites. As a CDMO, Lonza represents a new sector for the programme.

To further increase engagement with the private sector, the Industry Programme team has set up a dedicated quarterly newsletter featuring updates on activities for Industry Programme members, and news about EMBL-EBI's research and data resources.

Jeff Dowling/EMBL

The EMBL-EBI Industry Programme delivered three quarterly meetings and six knowledge-exchange workshops for Industry Programme members in 2020.

MISSION 5

To coordinate and **integrate** European life science research

EMBL fosters international collaboration between scientific communities in Europe and around the world by playing a leading role in shaping scientific strategy and policy.

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Integrating European life sciences

EMBL fosters collaboration between scientific communities in Europe and around the world

In a year marked by a public health crisis and social isolation, staying connected to scientific communities in our member states and beyond was an important priority for EMBL. The COVID-19 pandemic highlighted the relevance of EMBL's collaborative science, shared research infrastructures, and open data. It also underlined the critical role that EMBL, as a pan-European institution, can play in delivering research, services, training, and technology development, and in helping to unite national efforts across Europe.

Member state relations

Throughout 2020, we engaged actively with our member states through multiple interactions to exchange ideas, share expertise, extend existing collaborations, and build new ones. A particular focus of discussions was the next EMBL Programme, *Molecules to Ecosystems*, which will bring many new collaborative opportunities and other benefits to member states when it begins in 2022.

To explore opportunities for collaboration as part of the next EMBL Programme, EMBL Director General Edith Heard and senior scientists from across the organisation participated in several joint workshops with representatives of the research communities in EMBL member states. A workshop with representatives from Switzerland was held in August, followed by workshops with representatives from Belgium and Iceland in October. The Iceland event was followed by a meeting between Edith Heard and Lilja Alfreðsdóttir, Iceland's Minister of Education, Science and Culture. Further joint workshops are planned with other EMBL member states.

EMBL and Germany engaged at many levels in 2020. In November, Edith Heard presented EMBL's future plans at an event at the German Bundestag, outlining how EMBL's activities will address global challenges such as pollution, loss of biodiversity, and the spread of antimicrobial resistance and infectious diseases. Edith also hosted a visit to EMBL Heidelberg by Theresia Bauer, Minister of Science, Research and Arts for the German federal state of Baden-Württemberg. Wolf-Dieter Lukas, State Secretary in Germany's Federal Ministry of Education and Research, visited EMBL Hamburg.

EMBL and France deepened collaborations, including discussions on the next EMBL Programme with the National Research Institute for Agriculture, Food and Environment (INRAE), the French National Institute

for Ocean Science (IFREMER), and the European Marine Biological Resource Centre. EMBL's European Bioinformatics Institute (EMBL-EBI) hosted a delegation from Inserm, France's national institute for health and medical research, to discuss bioinformatics knowledge transfer as France prepares for Plan France Médecine Génomique 2025: a national initiative to ensure that everyone has access to new technologies in genomic medicine by 2025. Additionally, EMBL signed new memoranda of understanding (MoUs) with two institutes in France: the Centre d'Immunologie de Marseille-Luminy and the Institute for Advanced Biosciences.

To explore areas of common interest relating to the next EMBL Programme, EMBL engaged with representatives from the UK's research councils, particularly the Biotechnology and Biological Sciences Research Council, Medical Research Council, and Natural Environment Research Council. EMBL-EBI also supported UK Research and Innovation (UKRI) with the development of the website 'Coronavirus: the science explained', which aimed to provide accessible and authoritative scientific information on the COVID-19 pandemic. The website was successfully handed over to the UKRI team in July 2020.

In April 2020, Edith Heard met representatives of the Italian Institute of Technology (IIT), with both EMBL and IIT agreeing to develop an institutional collaboration agreement to strengthen their existing ties. EMBL also began discussions with the Italian National Research Council (CNR) about deepening collaborative links through workshops and an MoU. Opportunities for even closer engagement between Italian scientists and EMBL will be provided by EMBL's amended Host Site Agreement with Italy, which was finalised and unanimously endorsed by the EMBL Council.

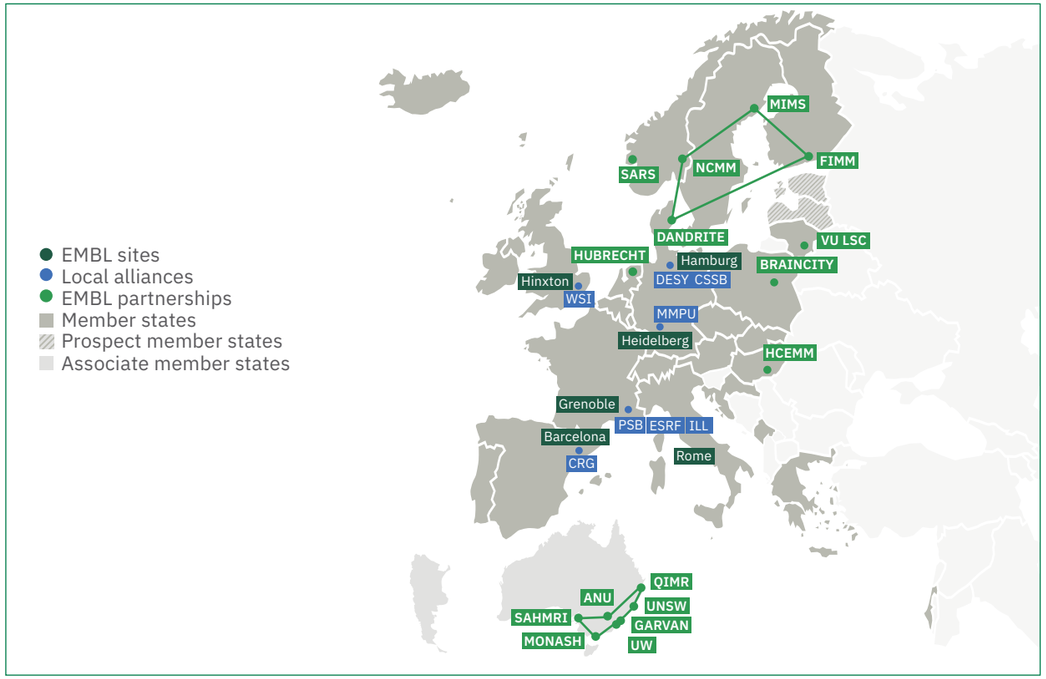
Edith Heard met representatives of the Spanish Ministry of Science and Innovation in October, and signed an MoU with the Spanish National Research Council (CSIC). CSIC's research in the life sciences covers topics such as sustainable development, climate change, precision and personalised medicine, agricultural and food science and

Theresia Bauer, Minister of Science, Research and Arts for the German federal state of Baden-Württemberg (left), met EMBL Director General Edith Heard during a visit to EMBL Heidelberg in February 2020.

technology, and healthy ageing. Many of CSIC's research areas therefore align closely with the scientific directions in the next EMBL Programme. The MoU with CSIC will stimulate scientific exchange and collaboration, ensuring greater connectivity, availability of scientific data, use of shared technology, and circulation of talent.

Hungary's Minister for Innovation and Technology, László Palkovics, visited EMBL Heidelberg to discuss research links between EMBL and Hungary, including the partnership between EMBL and the Hungarian Centre of Excellence for Molecular Medicine. Edith Heard met representatives of the Danish Ministry of Higher Education and Science, and discussed the next EMBL Programme with the leadership of the Nordic EMBL Partnership for Molecular Medicine and other senior stakeholders from the Nordic countries.

EMBL has been awarded funding from the European Commission for three Twinning projects with institutes in Portugal and the Czech Republic. These projects aim to foster knowledge transfer from leading European research institutes like EMBL, to enable new areas of expertise to be developed and sustained at other institutes. The projects are funded with €1 million each and will run for three years. EMBL's ties with Portugal were also strengthened by the renewal of the collaboration agreement with Fundação para a Ciência e Tecnologia, and by a new MoU with the Instituto Gulbenkian de Ciência.



EMBL partnerships

In September, a partnership was established between EMBL and the Life Sciences Center at Vilnius University (VU LSC) in Lithuania. The VU LSC–EMBL Partnership for Genome Editing Technologies builds on complementary scientific and technological strengths in the field of targeted genome modification. In close consultation with EMBL, VU LSC is setting up a partner unit based on the EMBL model, which will employ six high-level groups of international scientists and will pursue a collaborative research programme.

The annual conference of the Nordic EMBL Partnership for Molecular Medicine took place in October. The conference followed the announcement earlier in the year that the partnership had received a €210,000 NordForsk grant as part of the Nordic Research Infrastructure Hubs initiative, which aims to facilitate the development of world-leading Nordic research infrastructure environments. The funds will be used to train the next generation of specialists and research leaders in molecular medicine in the Nordic countries.

Representatives of EMBL and the Hubrecht Institute in Utrecht, Netherlands, met in October to discuss their research ambitions and plans. A shared commitment to continued joint activities was confirmed by the renewal of the partnership agreement for the EMBL–Hubrecht Partnership for Stem Cell and Tissue Biology.

Nora Lehotai/MIMS

Oliver Billker, Director of the Laboratory for Molecular Infection Medicine Sweden, speaks at the annual conference of the Nordic EMBL Partnership for Molecular Medicine.

Emmanuelle Charpentier: alumna of the Nordic EMBL Partnership

In October 2020, Emmanuelle Charpentier and Jennifer Doudna were awarded the Nobel Prize in Chemistry for developing a new method of genome editing using CRISPR–Cas. From medical therapy to fundamental research, CRISPR has wide-ranging applications and is used by research groups worldwide to address crucial questions in biology.

It was while working at the Laboratory for Molecular Infection Medicine Sweden (MIMS) – part of the Nordic EMBL Partnership for Molecular Medicine – that Emmanuelle published two key papers on CRISPR: one in *Nature* in 2011, and another, in collaboration with Jennifer Doudna, in *Science* in 2012.

Emmanuelle came to MIMS in 2009: one of three group leaders to join the institute during its first round of recruitment using the EMBL model. Previously, recruitment at the institute had focused on senior, well-established figures; by contrast, the EMBL model involves international recruitment of promising young group leaders on fixed-term contracts of nine years, who are provided with funding to support a small group, have opportunities to apply for further competitive funding, and are given scientific freedom and independence.

“The environment within the Nordic EMBL Partnership for Molecular Medicine was instrumental in helping us to achieve these results,” Emmanuelle said during an interview at EMBL in 2016. “Like scientists at EMBL, young researchers there receive the resources and space needed to pursue fundamental questions.”

EMBL’s Partnership Programme was established to promote scientific collaboration across the EMBL member states. The programme currently includes 12 partnerships: 11 in Europe and one in Australia. By establishing institutional and scientific interactions with EMBL, partner institutes become integrated into the extensive EMBL research network, providing fertile ground for new initiatives and projects. Partner institutes also gain increased international visibility, facilitating access to national, European, and international funding.

“Combining EMBL’s expertise with national research strengths, we help create centres of excellence that enrich the regional, national, and ultimately the European life sciences ecosystem,” says EMBL’s Head of International Relations, Plamena Markova. “The Nordic EMBL Partnership is the perfect example of how EMBL can bring together countries and build bridges for talent, ideas, and resources.”

“The environment within the Nordic EMBL Partnership for Molecular Medicine was instrumental in helping us to achieve these results.”

EU relations

Based on an MoU, EMBL maintains a close relationship with the European Commission (EC), as well as with key members of the European Parliament. In 2020, EMBL responded to multiple calls for public consultation from the EC, helping to shape the implementation of the next EU Framework Programme for Research and Innovation, Horizon Europe, and other important future policy programmes. At the end of the year, the Horizon 2020 Framework Programme came to an end. EMBL received 160 grants as part of Horizon 2020, totalling more than €137 million in funding.

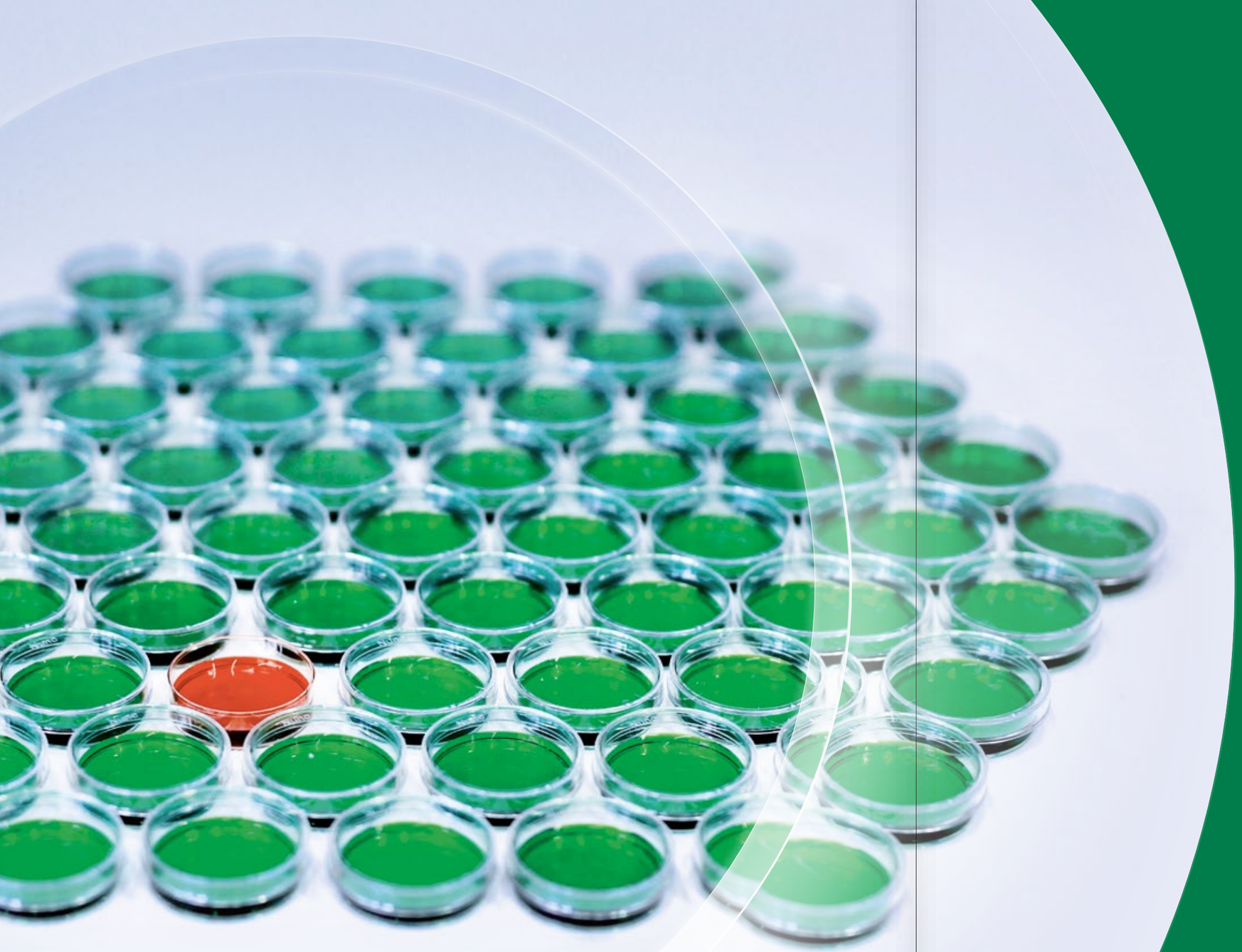
In December, Edith Heard and Jean-Eric Paquet, Director General for Research and Innovation at the EC, signed the 2021–2022 work plan, which defines areas of collaboration for that period. This was accompanied by a virtual meeting that allowed discussion of policy programmes on key topics relating to global challenges. The EC is currently working on the EU’s green transition, including the European Green Deal and the European Climate Pact, which aims to engage communities in action for the climate and environment. These initiatives resonate strongly with EMBL’s own work on sustainability and the research directions in the next EMBL Programme. The new work plan between EMBL and the EC aligns fully with these shared future directions.

An important EC initiative in which EMBL has a significant role is the development of the European Open Science Cloud (EOSC), which aims to unite access to research data and complementary services across scientific disciplines and borders. EMBL took part in many EOSC projects in 2020, including the deployment of the European COVID-19 Data Platform (p. 5) and ongoing work on the EOSC-Life and EOSC-hub projects. In November 2020, the EMBL Council unanimously approved EMBL’s application to become a member of the EOSC Association. Together with our partners, EMBL will continue to be an important player in shaping the future development of the EOSC.

European Research Infrastructures

In 2019, EMBL became the first intergovernmental organisation to join Instruct-ERIC, the European Research Infrastructure Consortium (ERIC) for structural biology. Instruct-ERIC is a pan-European distributed research infrastructure that makes advanced technologies and methods in structural biology available to users. In 2020, three of EMBL’s sites – Grenoble, Hamburg, and Heidelberg – were established as the 11th Instruct Centre.

The Euro-BioImaging ERIC completed its first year of operations at the end of 2020. Together with its nodes – including EMBL – Euro-BioImaging rapidly adapted in response to the COVID-19 pandemic and continued to facilitate research when institutions were facing complete or partial lockdowns. Euro-BioImaging shared best practice on safe user access during on-site visits, and developed new and existing schemes for providing remote user access to instruments and training.



Operations and engagement

EMBL's administrative and scientific operations teams provide the foundations for the five missions and enhance EMBL's activities and policies.

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Operations and engagement

Providing services to support EMBL's missions

Administration

The past year was very challenging, given the relatively limited resources and capacity that EMBL has in Administration, and the need to deploy these resources to deal with the COVID-19 pandemic. Members of EMBL's Administration teams played a vital role in coordinating our response. They developed a crisis management plan, setting out a structure of crisis management teams and a framework for determining crisis operation modes and stages of crisis, and for identifying risks. The plan also includes risk mitigation and recovery strategies. Crisis management teams were set up at each EMBL site, with a pan-EMBL team also meeting regularly to enable efficient flow of information around the organisation and to provide a coordinated response across sites.

EMBL's Human Resources team supported staff across EMBL through the transition to remote working and provided special leave for those who were unable to work due to childcare responsibilities or other reasons. Adjustments were made so that recruitment activities could continue in virtual formats and new starters could join their teams remotely.

Following a series of closures in March, EMBL's sites partially reopened in May. The Health and Safety Office implemented measures to ensure the health and safety of staff. All working spaces were reviewed and limits on occupancy were established to enable physical distancing to be maintained. Positive COVID-19 cases were followed up by tracing and informing contacts and by disinfecting rooms. Working spaces were rearranged and plexiglass screens were installed in various locations to reduce the possibility of viral transmission.

Despite the restrictions imposed as a result of the COVID-19 pandemic, the main construction phase of the EMBL Imaging Centre (p. 33) was completed at the end of 2020, on time and within budget. This was made possible by the close collaboration between EMBL Facility Management and the external architects, who together coordinated the work of many construction companies in line with COVID-19 safety rules. Facility Management also played an important role in coordinating the construction of a new building for GSK company Cellzome, which is located on the Heidelberg campus. At EMBL Barcelona, a new tissue culture room and microscope space were successfully completed.

The Purchase and Stores teams supported staff during the pandemic by monitoring the availability of goods and actively seeking alternatives where necessary, to guarantee continuity in the supply chain and ensure sufficient stocks of critical items, including masks and disinfectants. The teams also planned for the end of the Brexit transition period on 31 December. This included preparing for changes in customs regulations and potential disruptions to the supply of goods, as well as engaging in discussions with suppliers and carriers in the UK.

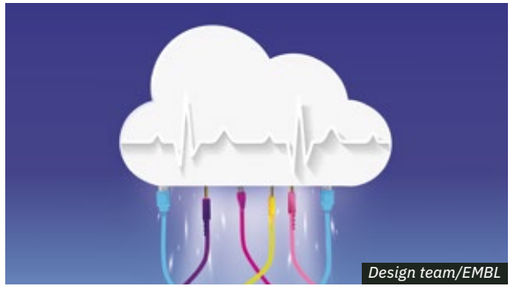
IT infrastructure and services

In 2020, EMBL made significant investments in upgrading the IT infrastructures at all sites to meet the needs of scientists and to secure an expansion of compute, cloud, and storage capabilities. In the Heidelberg compute cluster, high-performance file systems were set up to deliver data for analysis using graphics processing units at up to 1,600 gigabits per second. Network connections between the data centres at EMBL's European Bioinformatics Institute (EMBL-EBI) were upgraded to 100 gigabits per second, allowing performance to be maintained with ever-expanding data volumes.

Members of IT Services have continued their work on the EMBL Data Management Application: a software framework that will support EMBL's research groups by providing improved systems for organisation, tracking, and management of data. IT Services has collaborated closely with key stakeholders across EMBL to understand their requirements and workflows. This has resulted in preparatory work for pilot projects relating to data management and analysis in the areas of omics, imaging, and structural biology.

To support EMBL's long-term strategy of adopting a hybrid cloud approach to IT infrastructure provision, contract negotiations are in progress with leading public cloud providers. EMBL has established relevant internal policies and procedures for use of public clouds. This allows teams across EMBL to build workloads on internal cloud resources, such as the EMBL-EBI Embassy Cloud and the EMBL 3D Cloud, and to scale these out using public cloud capabilities, ultimately providing a foundation for the deployment of large-scale data analysis workloads needed to support EMBL's science.

All of these developments in EMBL's IT infrastructures and capabilities, driven by EMBL IT Services, enabled solutions for remote working to be swiftly put in place when lockdowns began in March. The IT departments at each site supported staff in setting up efficient systems for working from home. Technologies such as the EMBL 3D Cloud enabled scientists to conduct data analysis and visualisation remotely, and facilitated the transition of EMBL's Course and Conference Programme to virtual events. This enabled EMBL to rapidly adapt in response to the COVID-19 pandemic.



EMBL's IT infrastructure enables scientists to conduct data analysis and visualisation remotely.

Equality, diversity, and inclusion

EMBL's Equality, Diversity, and Inclusion (EDI) team continues to organise training and events to raise awareness of EDI issues, and contributes to the development of policies and strategy to create a more equal, diverse, and inclusive working environment at EMBL.

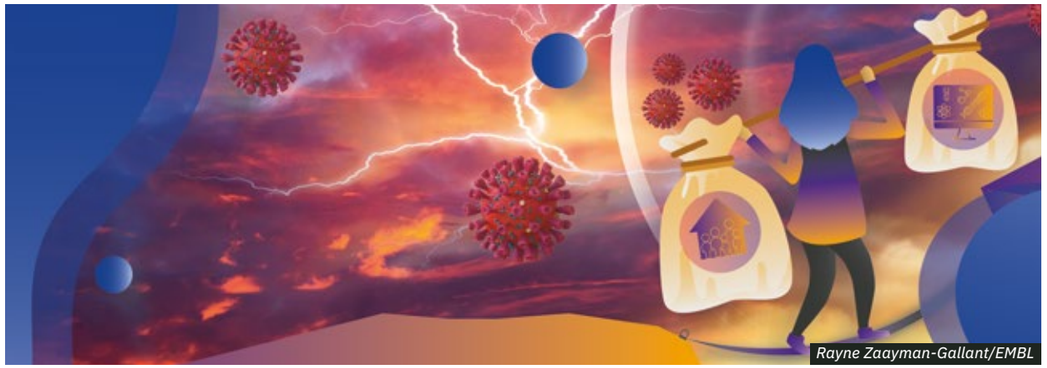
The EDI team has developed a new mentorship programme, Leadership and Excellence for Aspiring Postdocs (LEAP). Launched in spring 2020, LEAP is tailored to women postdocs at EMBL who want to pursue a career in academia. The programme features external mentors and one-to-one coaching and training. LEAP is funded by donations from the Friends of EMBL (p. 78) and supported by 70 members of the EMBL alumni community who have signed up as LEAP mentors.

EMBL has joined the Diversity Champions programme run by Stonewall, the largest LGBTQ+ charity in Europe. This is the leading employers' programme to help ensure that all LGBTQ+ staff are accepted in the workplace. Objectives for the first year include reviewing EMBL's current rules and regulations to ensure that they embed inclusion across the organisation, supporting our LGBTQ+ network to help grow and empower the community, and participating in Stonewall's Global Workplace Equality Index, which will function as a gap analysis tool to identify strategic objectives for the future. Stonewall's input will also help EMBL to develop systematic diversity policies and practices to attract and retain the best talent, benefiting the organisation as a whole.

EMBL's conference programme in 2020 included two virtual conferences on issues relating to EDI (see opposite). EMBL also hosted events to mark important dates including International Women's Day, Black History Month, LGBT History Month, LGBT Pride Month, and LGBTQ+ STEM Day.

EMBL's EDI Officers carried out numerous training activities in 2020, including EDI training for postdocs, as well as workshops on demand for various EMBL units and departments. The committee has identified ongoing training needs and will continue to provide input on EDI training at all levels of the organisation.

In early 2021, the EDI team commissioned an externally administered survey on perceptions of inclusion at EMBL. This will provide an important foundation for developing a long-term EDI strategy, and should usher in a new era of EDI at EMBL.



Rayne Zaayman-Gallant/EMBL

Challenges and solutions

EMBL hosted two highly successful virtual conferences in 2020 on issues relating to equality, diversity, and inclusion

The impact of COVID-19 on women in science

On 9 September, EMBL's conference 'The Impact of the COVID-19 Crisis on Women in Science: Challenges and Solutions' explored the disproportionate impacts experienced by women during the COVID-19 pandemic, for example impacts relating to employment issues, care responsibilities for children and elders, and domestic violence.

Speakers represented a diverse group of women scientists who provided insights into the effects of the COVID-19 pandemic on their work and future prospects. The conference also explored strategies for minimising the impact of the pandemic on women in science, highlighted tools and resources to support mental health, and examined the role of institutional leadership. Participants got involved through questions, tweets, and other interactions online, enabling them to share experiences and advice.

"Conferences like this will help bring to light gender-specific issues," said EMBL Director General Edith Heard, "helping us continue to grow and do a better job as leaders of scientific research organisations."

Gender roles in academia

From 13–15 October, EMBL co-hosted a conference 'Gender Roles and their Impact in Academia' with EMBO and the Howard Hughes Medical Institute. The conference brought together international experts in sociology, biology, psychology, education, and science policy to examine the causes of gender imbalances in academia and what can be done to overcome them.

A key strength of the conference lay in its interdisciplinarity and the conversations generated between science and the social sciences. The conference explored how biology and social structures shape gender roles, focusing on ways to achieve equal opportunities in the workplace and specifically in academia.

Preparations are ongoing for an expert analytic workshop to look in detail at measures for addressing the imbalances and their causes. A report for decision makers, consolidating findings from the conference and the workshop, is planned for the end of 2021.

Sustainability and Green EMBL

In 2019, the Green EMBL initiative was launched to make EMBL a greener, more sustainable organisation and to ensure that we play our part in responding to the environmental crises facing the world. A Green EMBL Working Group was set up, and in March 2020 EMBL recruited its first Environmental Officer to lead the initiative.

Headline figures

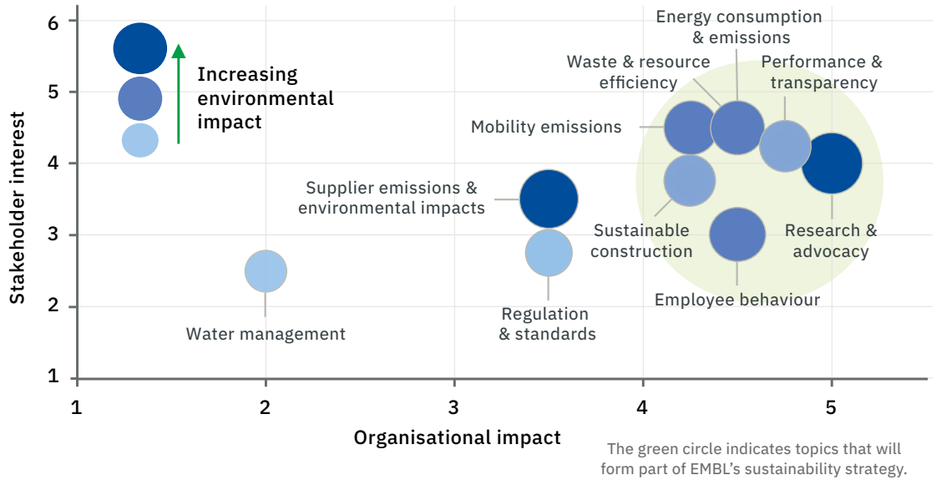
The COVID-19 pandemic caused operations across EMBL's sites to change dramatically. As activity levels reduced, so did our energy demand and therefore our carbon footprint. Compared to 2019, the carbon emissions associated with EMBL's energy use fell by 10% in 2020, while the emissions associated with the goods and services we purchase fell by 11%. The largest reduction, however, came from the emissions associated with air travel, which fell by 87%. The adaptability of EMBL staff in using online tools for virtual meetings and conferences enabled EMBL to carry out its collaborative activities despite the restrictions on travel and meeting in person.

Environmental materiality assessment

In 2020, EMBL completed a materiality assessment of the organisation's environmental impact. This assessment was carried out by an external consultancy that specialises in sustainability strategies.

The assessment involved a review of EMBL's operating environment, followed by interviews with a range of internal and external stakeholders. These interviews were used to score 10 environmental topics according to three criteria: the size of EMBL's impact, the financial and reputational impact on EMBL of managing these topics, and the interest shown by EMBL stakeholders in these topics. The results of the materiality assessment are shown below.

ENVIRONMENTAL MATERIALITY ASSESSMENT



Environmental strategy development

Based on the materiality assessment, EMBL has taken forward seven topics as priorities for the Green EMBL initiative. These are allocated to one of three workstreams, which will become the pillars of Green EMBL:

- Doing environmentally responsible research.
  Dedicated working groups are managing four operational topics: Energy Use and Emissions, Waste and Resource Efficiency, Mobility Emissions, and Sustainable Construction.
- Doing environmentally relevant research.
  The aim of the next EMBL Programme, *Molecules to Ecosystems*, is to achieve a fundamental understanding of life – including human life – in the context of populations and environments. This opens up many opportunities for EMBL to carry out environmentally relevant research.
- Promoting sustainable science.
  EMBL aims to be a European leader in sustainable science. This will require us to be transparent about our environmental impacts and to share information about our journey, encouraging other organisations to transition towards sustainability.

Behaviour change was also identified as a key topic that traverses these three pillars.

Green EMBL successes

In 2020, EMBL's first solar photovoltaic array was installed on the roof of the P1 car park on the Heidelberg campus. This array will generate enough electricity to save around 90 tonnes of CO_2 per year.

EMBL's Environmental Research Initiative (ERI) was launched in November 2020. To further support the research objectives of the next EMBL Programme through philanthropy, ERI will enable creative research across all EMBL sites to address society's environmental challenges and find innovative, impactful, and sustainable solutions. As part of its pilot phase, ERI has awarded funding to three new research projects at EMBL, made possible by the Friends of EMBL (p. 78) and other generous donors. The new research projects focus on tackling pollution caused by nanoplastics, pesticides, and artificial hormones.

The European Commission (EC) has launched the European Climate Pact, which aims to get people and organisations involved in climate action and building a greener Europe. EMBL's Environmental Officer, Brendan Rouse, was among the first group of EU Climate Pact Ambassadors: 181 people across Europe who were selected to promote the pact. In this role, Brendan will engage with scientific organisations not yet involved in climate action and will act as a bridge between the EC and those organisations and individuals who are keen to get more involved.


Kinga Lubowiecka/EMBL

The newly installed solar array at EMBL Heidelberg. It will generate around 200,000 kWh of electricity, saving around 90 tonnes of CO_2 annually.

Awards and honours

Celebrating individual achievements in 2020

EDITH HEARD

EMBL Director General

L'Oréal–UNESCO For Women in Science Award

Fondation L'Oréal and UNESCO

Doctor of Science *honoris causa*

University of Cambridge, UK

Senator of the Max Planck Society

Max Planck Society, Germany

GSCN 2020 Female Scientist Award

German Stem Cell Network

ALEX BATEMAN

Senior Team Leader

Vice President, ISCB

International Society for Computational Biology

PAUL FLICEK

Associate Director of EMBL-EBI Services

ISCB Fellowship

International Society for Computational Biology

EMBO Membership

EMBO

CAMILLE GOEMANS

Postdoctoral Fellow, Typas Group

L'Oréal–UNESCO For Women in Science Fellowship

Fondation L'Oréal and UNESCO

Eugène Yourassowsky Prize

Fonds de la Recherche Scientifique, Belgium

ALEXANDER AULEHLA

Group Leader and Senior Scientist

EMBO Membership

EMBO

MATTHIAS HENTZE

EMBL Director

RNA Society Lifetime Achievement Award

RNA Society

PRO SCIENTIA-Förderpreis

Eckhart-Buddecke-Stiftung zur Förderung der Medizinischen Grundlagenforschung

JUDITH REICHMANN

Research Scientist, Ellenberg Group

Paul Ehrlich and Ludwig Darmstaedter Prize for Young Researchers

Paul Ehrlich Foundation, Germany

MICHAEL ZIMMERMANN

Group Leader

Daimler and Benz Foundation Scholarship

Daimler and Benz Foundation, Germany

James B. Dougherty, MD Award for Scientific Merit

Lung Cancer Research Foundation, USA

CHRISTOPHER REINKEMEIER

PhD student, Lemke Group

International Birnstiel Award for Doctoral Research in Molecular Life Sciences

Max Birnstiel Foundation and Research Institute of Molecular Pathology, Austria

JOANNA WANDZIK

PhD student, Cusack Group

L'Oréal–UNESCO For Women in Science Fellowship

Fondation L'Oréal and UNESCO

AGNESE LODA

Postdoctoral Fellow, Heard Group

L'Oréal–UNESCO For Women in Science Fellowship

Fondation L'Oréal and UNESCO

YANNICK SCHWAB

Team Leader and Head of Electron Microscopy Core Facility

Mid-Career Scientific Achievement Award

Royal Microscopical Society, UK

JULIA MAHAMID

Group Leader

Early Excellence in Science Award

Bayer Foundation

Public engagement, communications, and outreach

By engaging with diverse audiences, EMBL's Communications team and Science and Society Programme share information about EMBL's activities and promote understanding and informed debate about science and its impacts on society.

Communications

EMBL expanded its communications function in 2020 with the creation of dedicated positions at EMBL's sites in Barcelona, Grenoble, Hamburg, and Rome, complementing the existing teams at EMBL Heidelberg and EMBL-EBI.

Throughout the year, the Communications team worked closely with EMBL's Director General, Chief Operating Officer, Health and Safety Office, and the heads of EMBL's sites to ensure that all staff were kept informed about the latest developments during the pandemic. This included updates to health and safety rules at each site, and information and advice on maintaining physical and mental health.

Media engagement activities led to EMBL being mentioned in the press 1,431 times in 63 countries in 2020. This included coverage by high-profile media outlets such as BBC News, Euronews, the *Financial Times*, *Le Monde, National Geographic*, and *The New York Times*, as well as increased coverage by top science and technology media outlets. EMBL's social media following also increased significantly in 2020, with the number of followers increasing by 34% on Twitter and 49% on LinkedIn over the course of the year.

A major ongoing project for the Communications team has been the development of the new embl.org website. This went live early in 2020 and has been progressively expanded, with a goal of switching entirely from the previous website to embl.org in 2021.

The past year saw the completion of a review of *Science in School*: a journal to support science teachers, produced by EMBL on behalf of our partners in the European Intergovernmental Research Organisation forum (EIROforum). Following the review, EIROforum agreed to continue *Science in School* as an online-only publication, and a new editorial team was recruited.

Science and Society

EMBL's Science and Society Programme seeks to create connections between EMBL, external stakeholders, and cross-sectoral experts by promoting analysis and discussion of the societal impact of scientific research. The COVID-19 pandemic brought an opportunity to explore new platforms for dialogue and debate, enabling the programme to examine the ethical, legal, and social implications of scientific research in virtual formats.

In 2020, the Science and Society Programme initiated a virtual seminar series on the theme of 'Infectious Disease and Society'. This examined not only COVID-19, but also other infectious diseases such as salmonellosis and malaria. The Science and Society Programme was also able to re-release a number of talks on infectious disease from its archive. All are available to view online, and the series is planned to continue until at least summer 2021.

In November, the EMBL Science and Society Conference took place virtually for the first time.

The conference, 'Our House is Burning: Scientific and Societal Responses to Mass Extinction', engaged a wide range of stakeholders, including policymakers, youth activists, and leaders of Indigenous groups. It was attended by more than 450 people, with the virtual format enabling the conference to reach people all over the world – not only those who would have been able to attend in person. The conference considered the impact of environmental changes on biodiversity, ecosystem services, and human well-being. It focused on potential solutions and types of action: from activism to political strategies, and from local grass-roots conservation groups to global youth movements. It also evaluated the application of various targeted intervention methods across data science, emerging technologies, sustainability solutions, and beyond.

The EMBL Science and Society Conference focused on threats to the natural world, such as climate change and loss of biodiversity.

ALUMNI IMPACT

Giorgia Guglielmi

Freelance science writer, Basel, Switzerland
PhD student at EMBL, 2011–2016

Giorgia Guglielmi spends most days researching and writing – not in the lab, but instead translating scientific discoveries so that anyone can understand and appreciate them.

"Over the past year, people have been hungry for reliable information about coronavirus testing, vaccines, treatments, and so on. This means that I've had much more work to do in covering COVID-related stories," Giorgia says. "But we shouldn't forget that there are other stories that need to be told, especially in the wake of the pandemic – for example, stories about health disparities, which largely affect people who are already marginalised by society."

Giorgia spent much of 2020 reporting on coronavirus testing, becoming increasingly aware that members of the public were confused about what different types of tests are for. This led her to write 'Rapid coronavirus tests: a guide for the perplexed'[1] for *Nature*, which examined the role that cheap, fast diagnostic kits can play in controlling infection rates.

It was at EMBL that Giorgia realised she could combine her passions for science and writing. "Being at EMBL and interacting with so many people from diverse backgrounds, I realised I could apply the skills I developed during my PhD to a number of different careers," she explains. "EMBL also helped me to develop a critical mindset: open-mindedness and healthy scepticism are key skills for my job."

Her follow-on curriculum in MIT's prestigious graduate programme in science writing has since led to steady freelance work as a science journalist, including bylines in *Nature*, *Science*, and *Scientific American*. In 2020, Giorgia received EMBL's John Kendrew Award, which recognises the role that communication plays in advancing science.

Giorgia views science communication as integral to public science literacy, but points out that those working in research also have a part to play. "Science journalists and communicators can convey scientific information in compelling, clear ways to help non-scientists understand the value and power of science," she says. "But researchers should also commit to sharing their knowledge and skills beyond the science community and participating in public debate. Then people might become a little less wary of scientists and a little more likely to embrace science and the scientific method."

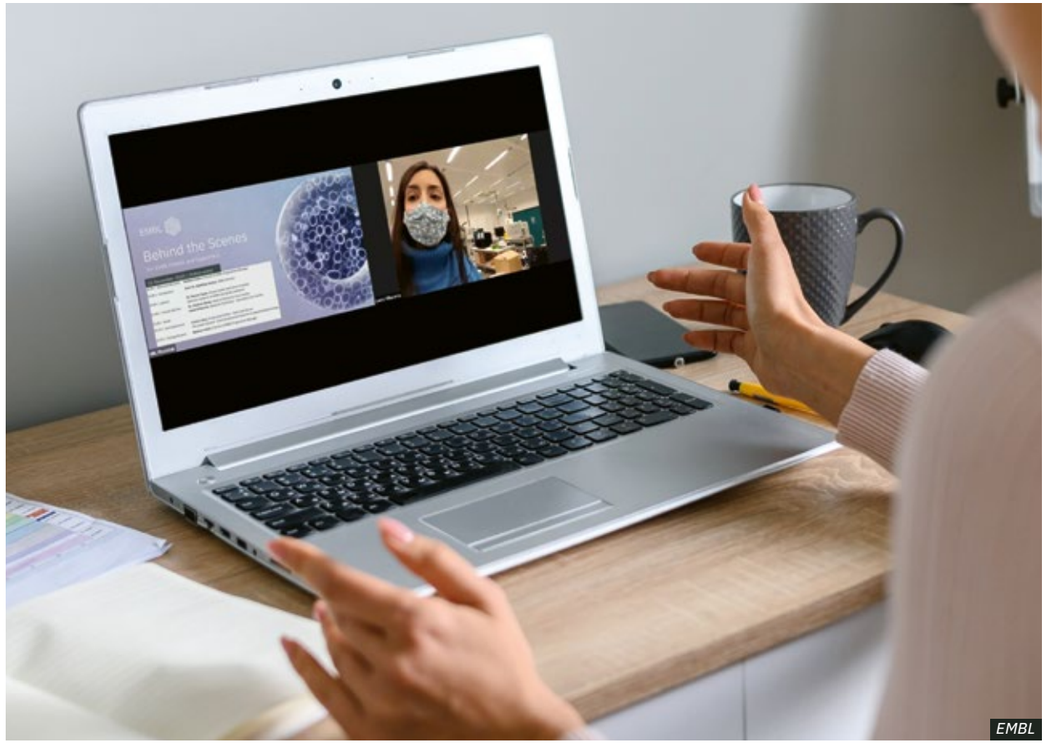
1. Guglielmi G (2021) Rapid coronavirus tests: a guide for the perplexed. *Nature* 590(7845):202–205. DOI: 10.1038/d41586-021-00332-4

Private support

Despite the uncertainties of 2020, EMBL continued to receive generous support from many individuals, companies, and foundations. Their donations enabled key projects that will advance science and aid the discovery of solutions to important societal challenges.

The Friends of EMBL are a community of individuals and businesses who support EMBL's work with annual donations. Two initiatives that were enabled solely by contributions from the Friends of EMBL were realised in 2020: the first EMBL Corporate Winter School for PhD students, and the LEAP mentoring programme (p. 69). Donations from the Friends of EMBL and others also support EMBL's Environmental Research Initiative (p. 72).

With the ongoing support of the Dieter Schwarz Foundation, the EMBL | Stanford Life Science Alliance continued its work to strengthen interdisciplinary, cross-border scientific cooperation. In 2020, the Life Science Alliance awarded the inaugural Bridging Excellence Fellowships, which enable postdocs to carry out collaborative projects at EMBL and Stanford.



Connecting with supporters of EMBL at a virtual 'Behind the Scenes' event in December 2020.

Alumni

In 2020, EMBL alumni played important roles in meeting the challenges of the COVID-19 pandemic, whether by carrying out research on the virus, advancing the development of treatments or vaccines, creating diagnostic kits, working in medical facilities, or in other ways contributing their resources, time, and expertise.

Despite the challenging circumstances of 2020, the use of technology to stay connected online made it easier for EMBL to reach alumni worldwide, strengthening connections with members of the community who would not have been able to join in-person events. In April, EMBL's Alumni Relations team launched 'Coffee with EMBL': a regular digital discussion forum for alumni and staff, bringing together members of the community to discuss their work and share their views and stories. The series gave a platform to a range of outstanding scientists and thinkers, and highlighted the impact of the alumni community in EMBL's member states and beyond. Nine 'Coffee with EMBL' events took place in 2020. Over the course of the year, 'Coffee with EMBL' brought together almost 700 participants from 278 cities in 51 countries.

A uniquely inclusive EMBL World Alumni Day took place in July, with alumni from across the globe joining online to catch up, share their research, and gain insights into plans for the next EMBL Programme from Director General Edith Heard.

The annual John Kendrew and Lennart Philipson awards, sponsored by philanthropist Roland Specker and EMBLEM (p. 51), respectively, delivered exceptional winners in 2020, whose work is highly relevant to the events of the year. The John Kendrew Award, which recognises excellence in science or science communication, went to Giorgia Guglielmi (p. 77) for her work as a science journalist, which has been more important than ever during the COVID-19 pandemic. The Lennart Philipson Award, which recognises outstanding contributions to translational research or technology development, went to John van der Oost for his contributions to our understanding of CRISPR–Cas: the genome editing tool whose developers, Emmanuelle Charpentier (p. 63) and Jennifer Doudna, were subsequently awarded the Nobel Prize in Chemistry.

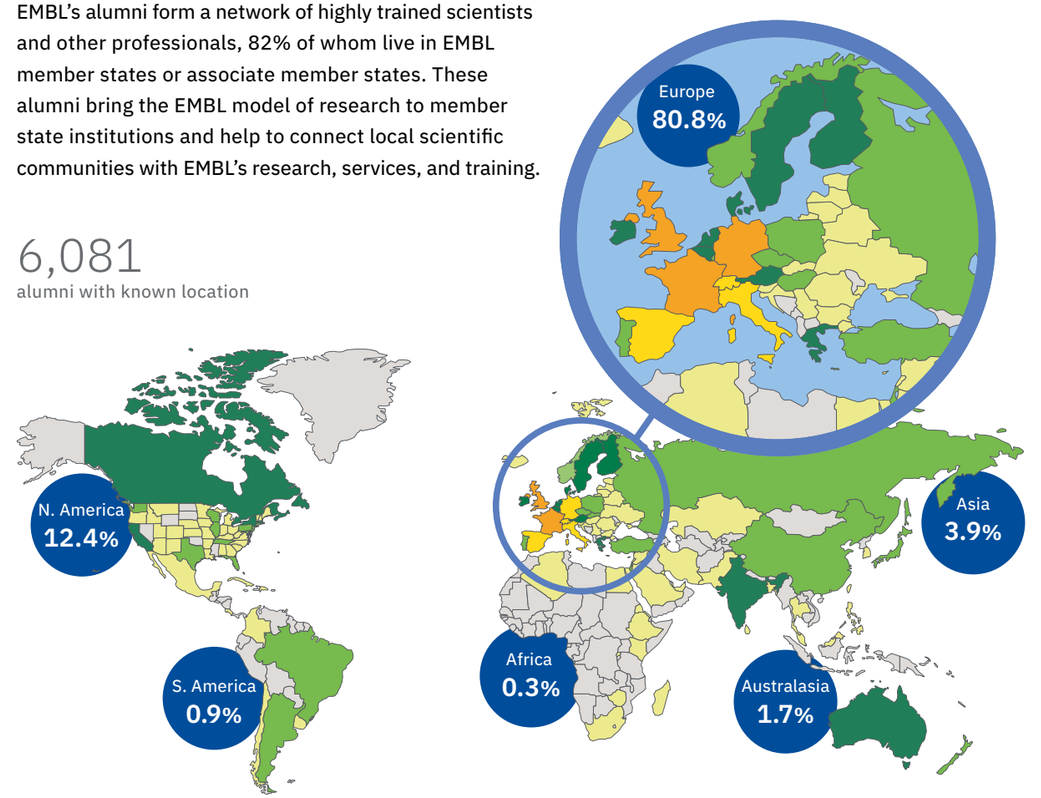
EMBL's network of alumni plays a vital role in advancing the life sciences in member states and around the world. With this in mind, EMBL collaborated with the Council for Advancement and Support of Education in October 2020 to deliver the first Advancement Summit for Life Sciences, supporting advancement professionals who work in life science institutes. Contributors included senior leaders from institutions across Europe.

Near the end of the year, the EMBL Alumni Association reached the milestone of 5,000 registered members, more than 180 of whom generously gave back to EMBL in 2020 by providing career support or written content, or by volunteering as speakers. A further 70 alumni mentors came forward to support the LEAP mentoring programme (p. 69).

EMBL ALUMNI IN NUMBERS

EMBL's alumni form a network of highly trained scientists and other professionals, 82% of whom live in EMBL member states or associate member states. These alumni bring the EMBL model of research to member state institutions and help to connect local scientific communities with EMBL's research, services, and training.

6,081
alumni with known location



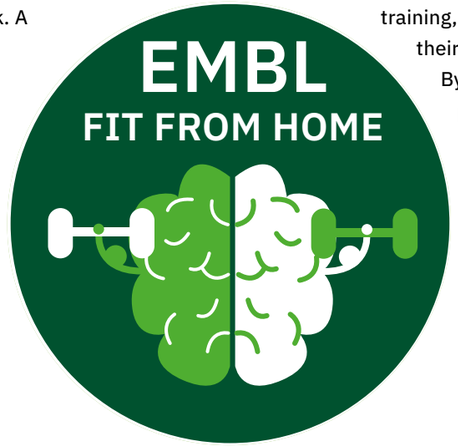
Staff Association

The Staff Association (SA) Committee has worked hard to maintain a high level of staff support during the COVID-19 pandemic. This has included regular meetings with senior management at each EMBL site to discuss issues relating to crisis management, as well as participation in pan-EMBL meetings to coordinate responses across sites. In particular, the SA focused on the issue of EMBL-wide staff welfare, paying special attention to mental health and morale. A major focus was communicating staff concerns to senior management and monitoring emerging issues through surveys and regular virtual meetings. Ensuring that EMBL staff can stay connected with their colleagues has been more important than ever during the pandemic, and the SA has played a vital role in providing channels for this.

Although in-person social events had to be cancelled, the SA has continued to maintain connections between staff through virtual clubs fairs and other virtual events. The SA also created a new range of activities for its members across all EMBL sites, including open forum chats on topics such as diversity at EMBL, sustainability projects, and activities during Mental Health Awareness Week. A series of 'Masterchef' events in which colleagues connected online to cook together, a 'Fit from Home' programme involving individual and team challenges, and various fitness classes run virtually by local instructors were also made available to all sites. The final event of the year was a virtual Winter Concert, which featured musicians from across EMBL and raised almost €4,800 for Whisper, a charity that runs a children's hospital and maternity unit in Jinja, Uganda.

During each meeting of the EMBL Council, the SA organises 'Meet the Delegates' sessions, in which EMBL staff have the opportunity to talk to council delegates. In 2020, the SA transformed the sessions for both the summer and winter council meetings into virtual events available to all EMBL sites; previously they had been limited to staff at the site where the council was meeting. This new opportunity enabled delegates to reach many more colleagues than usual, and feedback from both events was extremely positive. The SA is examining ways to increase staff participation in such events in future, possibly by continuing the virtual format.

The essential and highly valued personal contributions and commitment of SA representatives must be complemented by access to good training, to ensure that they can fulfil their role of supporting staff. By making access to virtual platforms available to staff working remotely, EMBL enabled the SA Committee to retain access to the necessary training courses in a virtual format.



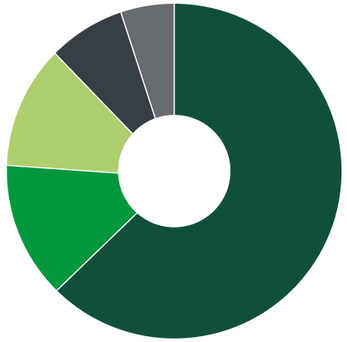
The Staff Association's online events to keep people connected have been warmly received by the EMBL community.

The SA's work to keep people connected and raise morale has been warmly received by the EMBL community. The events of the past year have led to new ways of connecting with colleagues and a partial mixing of personal and professional lives, as people share their experiences and new hobbies with each other, and invite people virtually into their home offices. Through all the challenges of 2020, these positive connections have made the EMBL community stronger and more collaborative than before.

Personnel statistics

EMBL's success depends on our greatest asset: our people. EMBL personnel are a diverse mix of scientists, scientific service staff, training and engagement specialists, and staff providing scientific, technical, organisational, and operational support.

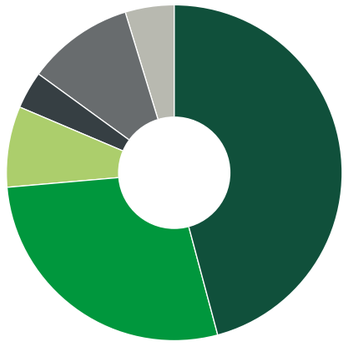
PERSONNEL CATEGORIES IN 2020



Total 1,911
in full-time equivalent (FTE)

- 1,203 Staff members
- 255 Postdocs
- 222 PhD students
- 140 Supernumeraries and ancillaries
- 91 Diploma students and trainees

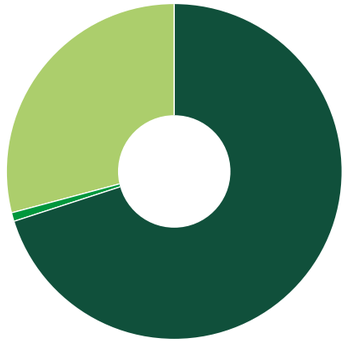
STAFF CLASSIFICATION IN 2020



Total 1,911
in full-time equivalent (FTE)

- 879 Research
- 530 Scientific services
- 147 Scientific or technical support
- 73 Training and outreach
- 195 Administrative support
- 87 General support

STAFF NATIONALITIES IN 2020

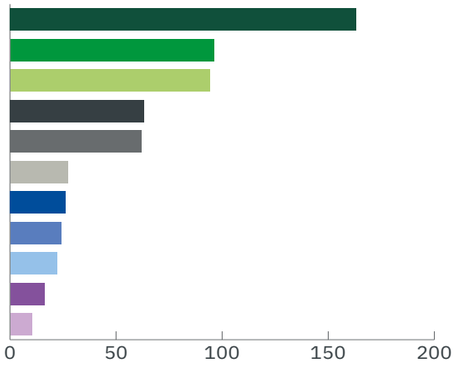


Total 1,911
in full-time equivalent (FTE)

- 1,343 EMBL member or associate member states
- 11 EMBL prospect member states
- 557 Non-member states

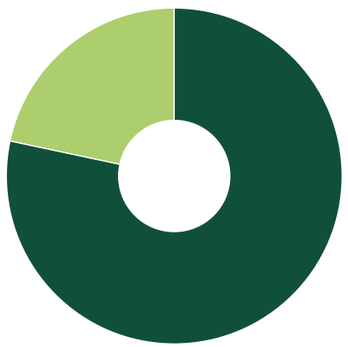
SCIENTIFIC VISITORS IN 2020

EMBL UNITS



- 163 EMBL-EBI
- 96 Core Facilities and Scientific Services
- 94 Structural and Computational Biology
- 63 Cell Biology and Biophysics
- 62 Genome Biology
- 27 Developmental Biology
- 26 EMBL Rome
- 24 Directors' Research
- 22 EMBL Hamburg
- 16 EMBL Grenoble
- 10 EMBL Barcelona

VISITORS' NATIONALITIES



- 473 EMBL member or associate member states
- 1 EMBL prospect member states
- 129 Non-member states

Total 603

Financial report

The COVID-19 pandemic has had a significant financial impact on academic research. During this exceptional year, EMBL took measures to guard against financial difficulties by implementing savings and mitigation measures to offset lost income and increased costs.

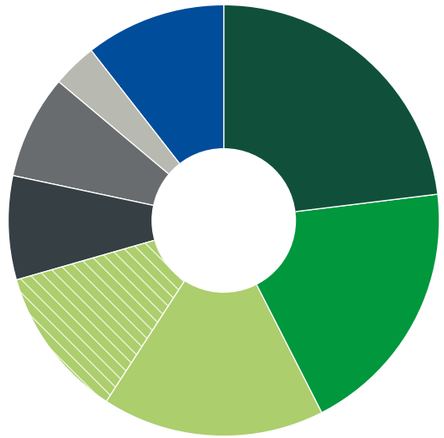
EMBL TOTAL INCOME IN 2020

€278 million

- 39% Member state contributions
- 11% Member state special contributions[1]
- 21% External grant funding
- 4% Other external funding[2]
- 25% Other receipts[3]

EMBL EXTERNAL GRANT FUNDING IN 2020

€59.0 million



- 23.2% NIH
- 19.4% Wellcome Trust
- 16.6% EC
- 11.4% ERC
- 7.8% BBSRC
- 7.8% BMBF
- 3.4% DFG
- 10.4% Other

1. Includes additional contributions from the UK government for the Technical Hub and European Data Centre on the EMBL-EBI campus, and from the German government for the EMBL Imaging Centre on the Heidelberg campus.
2. Includes ELIXIR member state contributions
3. Includes items such as contributions from EMBO, course and conference fees, internal tax, and income from the Heidelberg canteen, cafeteria, and guesthouses.

Member state contributions

	× €1,000	%
Ordinary contributions		
Austria	2,397	2.21%
Belgium	2,853	2.64%
Croatia	329	0.30%
Czech Republic	1,061	0.98%
Denmark	1,930	1.78%
Finland	1,411	1.30%
France	15,654	14.46%
Germany	22,410	20.71%
Greece	1,198	1.11%
Hungary	568	0.53%
Iceland	127	0.12%
Ireland	1,283	1.19%
Israel	2,100	1.94%
Italy	11,550	10.67%
Lithuania	110	0.10%
Luxembourg	233	0.22%
Malta	53	0.05%
Montenegro	15	0.01%
Netherlands	4,921	4.55%
Norway	2,461	2.27%
Poland	1,218	1.12%
Portugal	1,198	1.11%
Slovakia	265	0.24%
Spain	7,795	7.20%
Sweden	3,224	2.98%
Switzerland	4,476	4.14%
United Kingdom	17,393	16.07%
	108,233	100%

	× €1,000
Currency adjustment	
for sterling adjustments	(579)
Entry fees	
Hungary	124
Lithuania	66
Montenegro	4
Poland	733
Slovakia	100
	1,027
Associate member state contributions	
Argentina	1,495
Australia	2,860
	4,355
Additional contributions	
Germany	9,613
United Kingdom	14,707
	24,320

EMBL TOTAL EXPENDITURE IN 2020

Despite the challenges of the COVID-19 pandemic, EMBL continued performing research, providing services, and training scientists, with strong administrative support throughout the year.

€277 million

EXPENDITURE

- 62% Staff costs
- 32% Operating costs
- 6% Equipment expenditure, including depreciation

EXPENDITURE BY AREA OF ACTIVITY

- 33% Research
- 27% Scientific services
- 11% Scientific or technical support
- 7% Training and outreach
- 11% Administrative support
- 11% General support

Reviews of scientific and service units

EMBL Genome Biology Unit Review

The EMBL Genome Biology Unit was reviewed from 11 to 13 May 2020 by a panel of 12 international experts, including four members of the Scientific Advisory Committee (SAC). The review was chaired by Susan Gasser, Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland. The Chair of SAC Paul Nurse, EMBL Director General Edith Heard, the future Director of EMBL Heidelberg Peer Bork, EMBL Council Secretariat Michael Thompson, and Strategy and Analysis Officer Emma Steer attended the review as observers. Due to the COVID-19 pandemic and the resulting travel and physical distancing restrictions, the review was convened exceptionally via videoconference.

Evaluation summary

EMBL's Genome Biology Unit, headed by Eileen Furlong, comprises eight group leaders and one team leader, with one further group leader joining the unit later in 2020. EMBL Director Matthias Hentze is also thematically associated with the Genome Biology Unit. The unit encompasses a diverse range of interests associated with genome function, including the links between gene expression and DNA sequence variation, chromosome organisation, chromatin modifications, and protein expression and folding. Research topics include microbial genetics and virulence, human cancer and genome stability, genome folding and *Drosophila* development, and human neuronal differentiation.

The undeniable strength of the unit is its strong computational capacity, which includes the development and application of cutting-edge computational technologies to biology. It is clear that these essential tools impact the global research community.

The breadth of the unit's creative ideas, innovative approaches, and clear success is underlined by numerous significant publications, prestigious grants, nine patents, and two spin-out companies. The publications from the unit are characterised by their multidisciplinarity and a high degree of computational rigour, with an exceptional amount of collaboration both within and outside of the unit. There is also a palpable sense of excitement and enthusiasm for each other's research and findings, indicating a healthy environment of mutual respect. The panel praises Eileen Furlong in leading this unit, especially given the diversity of topics and approaches. Eileen Furlong has successfully encouraged members of the Genome Biology Unit to integrate their vast range of efforts into overlapping and synergistic studies of groundbreaking nature.

The panel would also like to highlight the generous contribution of the members of the Genome Biology Unit to the conceptualisation and writing of the upcoming EMBL Programme. The emphasis within the programme on ecological systems, microbial systems, and infection biology, as well as the cross-cutting theme of data sciences, clearly bear the mark of almost every member of the Genome Biology Unit's groups and team.


Kinga Lubowiecka/EMBL

Among the scientific achievements of this review period, the panel highlights the Pan-Cancer Analysis of Whole Genomes Consortium publications of Jan Korbel – a highly collaborative five-year effort that enabled a deep understanding of genome variation among individuals and individual cancers (p. 15). A collaborative study by Eileen Furlong and Oliver Stegle deployed population genetics to uncover the existence of extensive genetic epistasis within enhancer elements, and showed that the deleterious impact of large-effect variants are buffered by other variants within the same element attenuating their effects. In another collaborative study, with the Structural and Computational Biology Unit, Nassos Typas has developed one of the most comprehensive experimental frameworks to study the human gut microbiome and used it to monitor the impact of medication. A novel and powerful computational method that integrates different omics datasets to elucidate underlying biological processes that explain the data, Multi-Omics Factor Analysis (MOFA) was developed between the labs of Oliver Stegle and Wolfgang Huber. Thermal proteome profiling (TPP), a method to measure the thermal stability of proteins through mass spectrometry in high throughput, was pioneered by Mikhail Savitski to show the involvement of ATP in the stability of many proteins.

The panel noted that the number of open-ended contracts in the Genome Biology Unit is exceptionally high. However, the panel acknowledged that this is due to the strong computational approaches within the unit, which are considered essential to EMBL-wide research, and due to the outstanding quality of the scientists hired within the unit. Nevertheless, this represents a problem for the dynamic growth of the Genome Biology Unit, as there is little or no space or resources for further recruitment of young group leaders. The panel recommends that this should be remedied by redeployment of at least one senior group from the unit, as young hires are essential to future innovation.

The unit's balance between large-scale biology, consortium science, and model systems needs to be considered, particularly in the context of the upcoming EMBL Programme. The basis of large-scale biology is small-scale biology, and the molecular interactions that regulate genes are still at the heart of genome function. The panel recommends that this balance be maintained.

The panel felt that the percentage of pre- and postdoctoral fellows leaving without a paper is suboptimal, even though their mentoring is excellent. The experience of writing a manuscript and of dealing with peer review is integral to pre- and postdoctoral fellows' training and will enable them to be competitive for future positions. The Genome Biology Unit could better support the principles of DORA and open science by ensuring that students have experience of publishing methods or review papers earlier during their training at EMBL.

Continuing on the topic of DORA, the panel expects that successful Genome Biology Unit scientists should illustrate to trainees that the best science is not necessarily published in high-impact journals, but instead equip the next generation with the judgement and skills necessary for evaluating science based on content, in accord with the DORA principles.

Overall, the panel finds the current unit to be a harmonious, collaborative, and scientifically productive, internationally leading research unit.

Response to the panel's recommendations

I would like to thank the panel for their time and effort in reviewing the Genome Biology Unit, particularly given the virtual format the review had to take, due to the COVID-19 pandemic. I am very pleased to hear the extremely positive and enthusiastic evaluation of the unit, and I join the panel in warmly congratulating Eileen Furlong in successfully leading a highly motivated, multidisciplinary unit.

The Genome Biology Unit has been extremely productive over the review period, with a range of diverse scientific outputs that place it at the forefront of global life science research. The mix of computational and experimental research within the unit is key to this success, and the unit's highly collaborative and interdisciplinary atmosphere captures the essence of EMBL. These values will be further encouraged and prioritised as part of the next scientific EMBL Programme (2022–2026). Almost all Genome Biology Unit group and team leaders have been actively involved in the conception and writing of the new EMBL Programme, and I would like to praise them for being great assets to EMBL, at both the unit and the organisational level.

The panel noted a high number of open-ended contracts in the Genome Biology Unit. This is indeed unusual for EMBL, which prides itself on its nine-year turnover model, fostering early-career scientists and enabling EMBL to evolve constantly. I would like to reassure the panel on two matters. First, this is not a growing trend within EMBL: the Genome Biology Unit is an exception in hosting such a high number of open-ended contracts compared to other units. Second, it must be noted that all Genome Biology Unit scientists with open-ended contracts play an important role at EMBL, with EMBL-wide responsibilities. In the run-up to the next EMBL Programme, several of them participated very actively and will be involved in its implementation by being part of or even leading some of the new transversal themes, which will overlay the current unit structure and provide interactions and synergies between EMBL's six sites. This new organisation, which is currently being explored together with Peer Bork for EMBL Heidelberg, should free up some group leader positions in the unit to ensure the dynamic turnover of group and team leaders.

In response to the panel's second recommendation, the unit's future balance between large-scale biology, consortium science, and model systems will be carefully considered, particularly in the context of the new EMBL Programme. Indeed, one core philosophy of the new EMBL Programme, which will aim to explore life in the context of environments at different scales, is that an understanding of mechanisms at the molecular level in model organisms is essential for an understanding of large-scale biology. Eileen Furlong's own research, and her excellent track record in hiring talented individuals, gives me confidence that future group and team leaders in the unit will ensure this balance is maintained and will propagate out to further the aims of the new EMBL Programme.

Finally, on the topic of fellows and of publications: I fully agree with the panel's recommendation that students must have experience in publishing early on in their PhDs, and also that the best science is not necessarily published in high-impact journals. EMBL's training programme actively encourages students to think about and acquire the skills that they need, including writing and publishing, to help them embark on successful careers. However, I do not agree that there is pressure within the Genome Biology Unit, or EMBL in general, to publish only in high-impact journals. Indeed, as part of EMBL's own evaluation processes, which include this review, impact factor is not evaluated. Furthermore, through EMBL's active Open Science Working Group, which is co-chaired by one of the Genome Biology Unit's senior scientists, EMBL has been revising several of its internal policies to further encourage publication in open access journals, including practices that are in line with DORA principles. The points raised by the panel concerning DORA will be discussed at EMBL's next senior science management meeting.

In conclusion, I would like to warmly congratulate all members of the Genome Biology Unit for their outstanding contributions, as well as their enthusiasm and motivation, which fosters science and scientists of the highest quality across a diverse range of collaborative disciplines.

Professor Edith Heard, FRS
Director General

8 June 2020

EMBL Rome Unit Review

The EMBL Rome Unit was reviewed from 19 to 21 October 2020 by a panel of 14 international experts, including five members of the Scientific Advisory Committee (SAC). The review was chaired by James Briscoe, the Francis Crick Institute, London, UK. The Chair of SAC Paul Nurse, the Chair of Council Eiríkur Steingrímsson, EMBL Director General Edith Heard, Deputy Director General Ewan Birney, EMBL Council Secretariat Michael Thompson, and Strategy Officer Emma Steer attended the review as observers. Due to the COVID-19 pandemic and the resulting travel and physical distancing restrictions, the review was convened exceptionally via videoconference.

Evaluation summary

The EMBL Rome Epigenetics and Neurobiology Unit is headed by Interim Head of Unit Cornelius Gross, following Philip Avner's retirement in early 2020. The unit presently comprises five groups, with one further group leader joining the unit in 2021. Another affiliated group leader is based in the Cell Biology and Biophysics Unit at EMBL Heidelberg. The current research strategy, defined by Philip Avner in 2012, focuses on epigenetics and neurobiology with an ambition to bridge these two fields. The use of mouse genetics and genome engineering in the pursuit of these themes provides a technological focus and the opportunity for the unit to develop as a centre of excellence within Europe.

The quantity and quality of scientific output has remained strong, with notable contributions in both neurobiology and epigenetics. Scientists in the unit have been recognised by the award of competitive international grants, although more applications should be encouraged. The cooperative and interactive environment at EMBL Rome was noted by the panel, and provides a supportive atmosphere for training and mentoring.

For much of the review period, Philip Avner was the head of the EMBL Rome Unit, and under his direction the unit refocused its scientific strategy smoothly and efficiently. His dedication and skills enabled the current success of the unit and the collaborative and harmonious working atmosphere. Cornelius Gross has provided impressive stewardship in taking over interim leadership at a critical time. He commands the respect and trust of the other group leaders at the site and is clearly an asset to the unit and to EMBL more broadly. He has developed an impressive scientific vision for EMBL Rome that builds on the unit's scientific strengths and fits with the next EMBL Programme.

Among the scientific achievements of this review period, the panel highlights Cornelius Gross's important discovery of specific sets of territory cells in the mammalian hypothalamus and their contribution to integrating spatial and sensory cues to drive social behaviours (p. 21). Paul Heppenstall, who recently left the unit, developed a therapeutic strategy based on ligand-targeted ablation of pain neurons for mechanical allodynia – a painful sensation caused by innocuous stimuli like light touch. Research conducted by Matthieu Boulard identified sugar modifications as mediators of gene repression resulting from the epigenetic mark of DNA methylation. The panel also highlights the work of Jamie Hackett, who developed a ratiometric reporter of DNA methylation that led to the identification of *Dppa2* and *Dppa4* as key factors safeguarding against *de novo* DNA methylation and epigenetic silencing at lineage-associated genes.

The panel notes the impressive involvement of EMBL Rome members in the development of the next EMBL Programme. The science of the unit is well suited to the proposed transversal themes of the future *Molecules to Ecosystems* programme. For example, the unexpected gut–germline intergenerational interactions discovered by the Hackett Group provide exciting links with other EMBL sites on the Microbial Ecosystems theme. Additionally, EMBL Rome's proposal to develop its service capacity as part of the next EMBL Programme was encouraged by the panel. These services will include the new development and expansion of viral *in vivo* gene editing tools, thereby making these new tools available to the wider community. The ambitious idea of an innovative collaboration with EMBL Hamburg for sequential tissue ultrastructure and spatial transcriptomics was also considered as innovative and exciting.

The panel agrees that the interface between neurobiology and epigenetics is a distinctive and promising area, but recognises that these two fields are difficult to bridge or merge into one focus. Several options for strengthening or focusing the unit's scientific themes were discussed by the panel. Generally, it was felt that the best research themes will arise 'bottom up'.

The panel noted that EMBL Rome continues to suffer from a lack of critical mass, with only four to six groups on site at any time. Increasing the number of groups at EMBL Rome will benefit the scientific environment, financial efficiency, and international visibility of the unit. To achieve this, appropriate resources will be required. The panel also recommends that developing closer interactions with other institutes in Rome has the potential to increase the critical mass of EMBL Rome. Furthermore, closer interactions in a neuroscience and epigenetics network across EMBL and EMBL Partnerships can be beneficial.

The upcoming building refurbishment will address the severe structural deficiencies in the current building and the weak critical mass, and will support the development of the unit's interdisciplinary focus and integration into EMBL's new themes. Nevertheless, group leaders were worried about the disruption that the construction will bring, and the impact this may have on their research programmes. Similar worries were raised by the predoctoral fellows, who also mentioned the need for on-site family and medical support, advocated for more extensive safety training, and highlighted the pay gap between EMBL's German sites and EMBL Rome.

The panel recognises the progress made since the last review to improve mentorship and gender balance among group leaders at EMBL Rome. However, both will need to be further strengthened.

Overall, the panel finds the unit to be scientifically innovative and impactful, with a supportive atmosphere.

Response to the panel's recommendations

I would like to extend my thanks to the panel for their time and effort in reviewing the EMBL Rome Unit, particularly given the need to undertake the review in a virtual format. I was extremely pleased to hear all the positive and constructive discussions during the evaluation of the unit. I would like to extend my sincere congratulations to Philip Avner for his exceptional leadership and for successfully directing the unit through a refocusing of its scientific strategy. I would also like to congratulate and express my gratitude to Cornelius Gross for stepping up to guide EMBL Rome through a very critical time as Interim Head of Unit. Both are trusted leaders who have helped to create a collaborative and harmonious working atmosphere with exceptional scientific outputs.

The recognition by the panel of EMBL Rome's seamless integration into the next EMBL Programme is greatly appreciated. As was discussed during the unit review, EMBL Rome was very much implicated in the elaboration of this new programme. Indeed, some of the research highlights emphasised by the panel draw on areas of the next EMBL Programme, as well as being deeply rooted in molecular mechanistic questions, which is the essence of EMBL.

Alongside the panel, I also fully support the vision of EMBL Rome to enhance their external service capacity. These future services will prove to be vital for member state researchers who will gain access to use them.

In response to the panel's comments concerning the future focus of the unit, this will strongly depend on the interests and visions of the future Head of Unit. As the recruitment for this position is contingent on securing a new Host Site Agreement, EMBL is doing everything within the limits of the Italian parliamentary system to secure this new agreement as swiftly as possible.

I do agree with the panel's comments about the lack of critical mass within the unit, and I fully concur with the panel's suggestion to draw on EMBL Partnerships in an effort to better embed the scientists at EMBL Rome in the local community. EMBL is exploring new alliances and partnerships with institutes in the region to strengthen and cross-pollinate each other's scientific ideas. It is hoped that the resources available to each entity and shared within the partnership will enable mutually beneficial and productive scientific relationships. Securing the necessary and appropriate funds as part of the next Indicative Scheme will be vital in benefiting the scientific environment, financial efficiency, and international visibility of this unit.

The upcoming refurbishment of the unit will also address the lack of critical mass by providing an attractive and revitalised physical infrastructure. The much-needed refurbishment of the space will begin in 2022, and will be managed by a newly recruited project officer dedicated to this operation.

Neil Humphreys/EMBL

The concerns raised about the impact that the refurbishment may have on scientific activities are taken on board. EMBL management recognises the worries that the group leaders and other staff members within the unit may have concerning the construction, especially given the additional challenges that they are facing due to the ongoing pandemic. We will try to reassure staff about mitigation measures to minimise disruption and ensure that scientific activity can continue. Working closely with the Interim Head of Unit, the new Chief Operating Officer and I will continue to engage in a clear and open dialogue with all staff at the site, to allay fears and provide reassurance throughout the entire refurbishment process.

In response to points raised by the predoctoral fellows: unfortunately a kindergarten is not viable at EMBL Rome, given the small size of the unit, although alternative solutions are actively being investigated; the unit does in fact have a work doctor who performs regular medical visits; concerns expressed about safety training and awareness will be followed up; and on the topic of cross-site salary comparisons, the basic salary scales and allowances for personnel based at EMBL Rome are calculated according to the procedure of the Coordinated Organisations, as outlined in EMBL's Staff Rules and Regulations.

In response to the panel's comment on improving mentorship within the unit, I will be actively encouraging group leaders to take advantage of the expertise within other EMBL units. This will complement the already excellent mentoring ongoing within the EMBL Rome Unit, by taking advantage of the expertise of scientists from several relevant areas across EMBL.

I strongly agree with the panel's comments regarding the need to continue addressing the issue of gender balance within the unit. This topic is one that all of EMBL needs to address, and EMBL Rome has made significant efforts in this direction. I am confident that these efforts will continue and will be helped by new EMBL-wide recruitment guidelines, which will be implemented soon. The recent recruitment of Ana Boskovic at EMBL Rome, who will begin in 2021, is very welcome news, as she is both an excellent scientist and a very good fit for the unit.

In conclusion, I would like to congratulate Philip Avner and Cornelius Gross for their exceptional leadership, as well as the entire EMBL Rome Unit for a very successful review. The review highlights not only the scientific excellence of this unit, but also its collegial and harmonious spirit, which bodes well for even greater successes in the future.

Professor Edith Heard, FRS
Director General

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