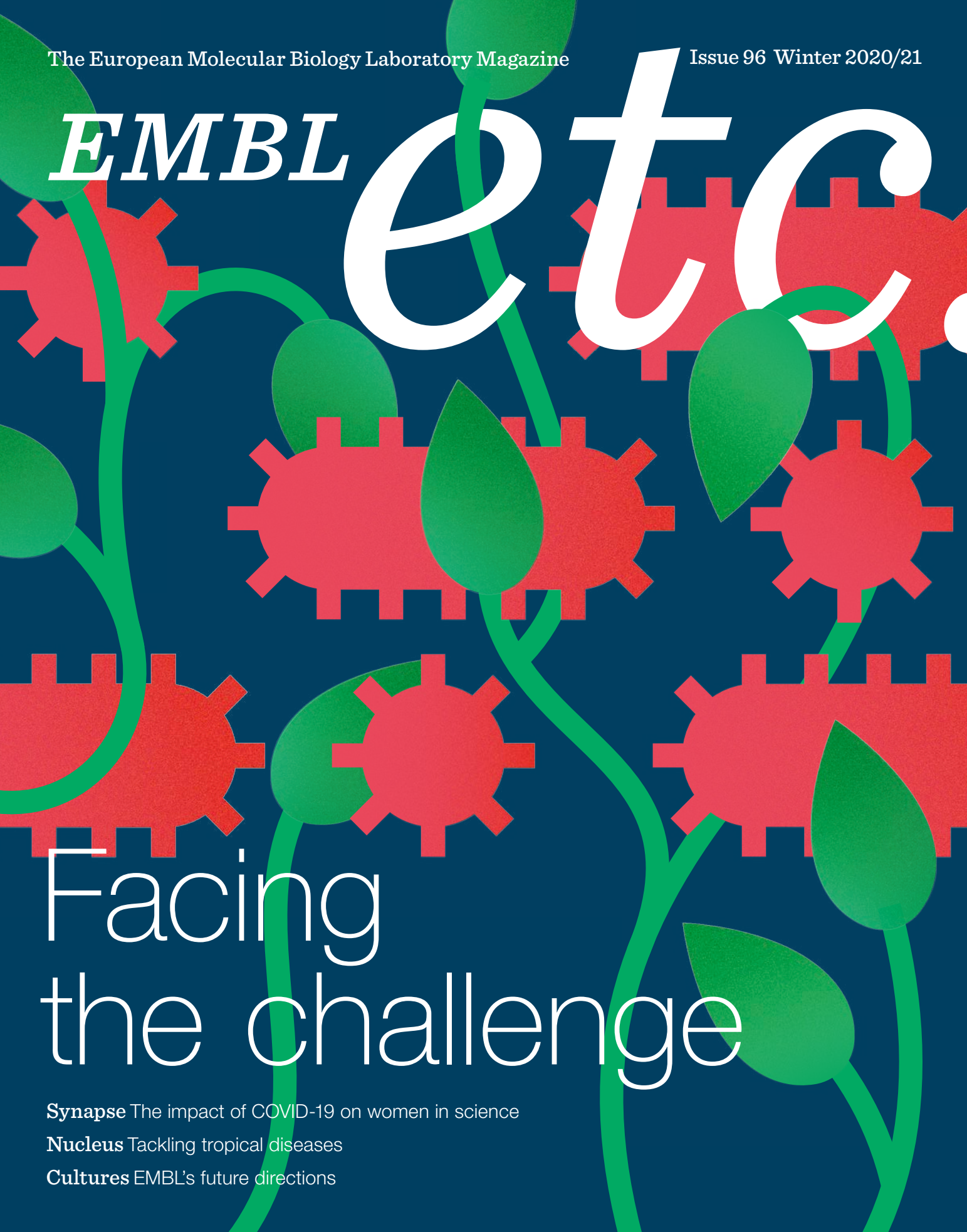
The European Molecular Biology Laboratory Magazine

Issue 96 Winter 2020/21

EMBL etc.



Facing the challenge

Synapse The impact of COVID-19 on women in science

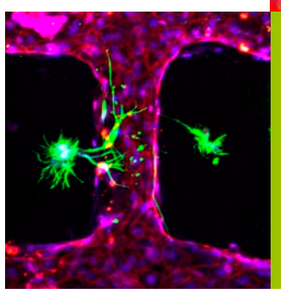
Nucleus Tackling tropical diseases

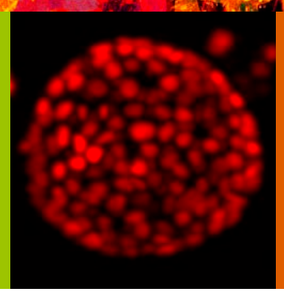
Cultures EMBL's future directions

Contents

Nucleus

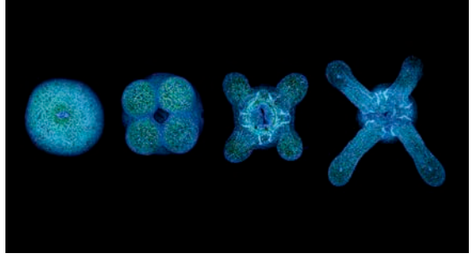
Feature stories





Synapse

News stories



Cultures

EMBL community stories

Alumni

MASSIMO DEL PRETE/EMBL

Editorial

For all of us, this has been a year of unexpected challenges. The coronavirus pandemic has significantly changed our daily lives, compelling us to find new ways to stay in contact and support one another from a distance. At EMBL, the response to the pandemic has continued, including the identification of a mini-antibody that shows potential as a future treatment for COVID-19 (p. 7).

EMBL's training teams – both internal (p. 32) and external – have faced the challenge of rapidly moving their training offerings online. This has opened up EMBL courses and conferences to larger and more diverse audiences, including many people who would not have been able to attend training on site. In this issue, we report on a conference examining the impact of COVID-19 on women in science (p. 6), and share insights from EMBL's annual Science and Society Conference (p. 18).

COVID-19 is only one of many challenges to human health being tackled at EMBL. Members of the EMBL community are carrying out research on the parasites that cause malaria and sleeping sickness (p. 22), while scientists from EMBL and Stanford have found that a drug used for treating acne might work as a treatment for a leading cause of heart failure (p. 10).

We also report on technological challenges, as members of EMBL's Mahamid group tell us about their work to develop cryo-electron tomography: an imaging technique that can show the structures of molecules inside cells (p. 26). This same technique has helped to reveal the structure of SARS-CoV-2's spike protein, providing details of the process by which the virus binds to cells and infects them (p. 5).

There's no doubt that the winter will bring additional challenges in our fight against COVID-19, and the pre-existing challenges – including other infectious diseases, climate change, and loss of biodiversity – have not gone away. At such times, the value of scientific discovery is made clearer to us than ever. It is only by pursuing knowledge, focusing our efforts, and working together across borders that we will understand the full complexity of these challenges and find new and enterprising ways to overcome them.

Edward Dadswell
Editor

Publisher
European Molecular Biology Laboratory

Managing editor
Edward Dadswell

Editors
Mehrnoosh Rayner
Tom Furnival-Adams

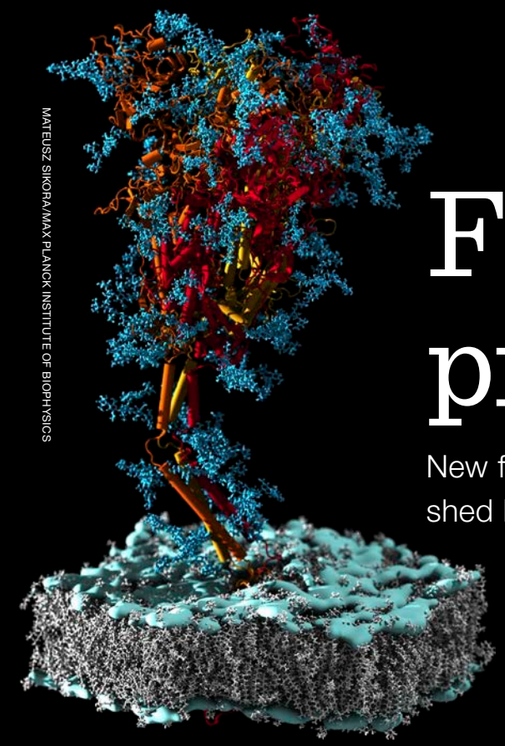
Design
Designyard

Printed by
ColorDruck Solutions

Contact
news@embl.de

Cover illustration
Aleksandra Krolik

embl.org/news



MATEUSZ SIKORA/MAX PLANCK INSTITUTE OF BIOPHYSICS

Flexible and protected

New findings on SARS-CoV-2 protein shed light on virus's ability to infect cells

BY MATHIAS JÄGER

At the start of a COVID-19 infection, the coronavirus SARS-CoV-2 docks onto human cells using the spike-like proteins on its surface. The spike protein is at the centre of vaccine development because it triggers an immune response in humans. A group of scientists in Germany, including members of EMBL Heidelberg, the Max Planck Institute (MPI) of Biophysics, the Paul-Ehrlich-Institut, and Goethe University Frankfurt, have focused on the surface structure of the virus to gain insights they can use for the development of vaccines and effective therapeutics to treat infected patients.

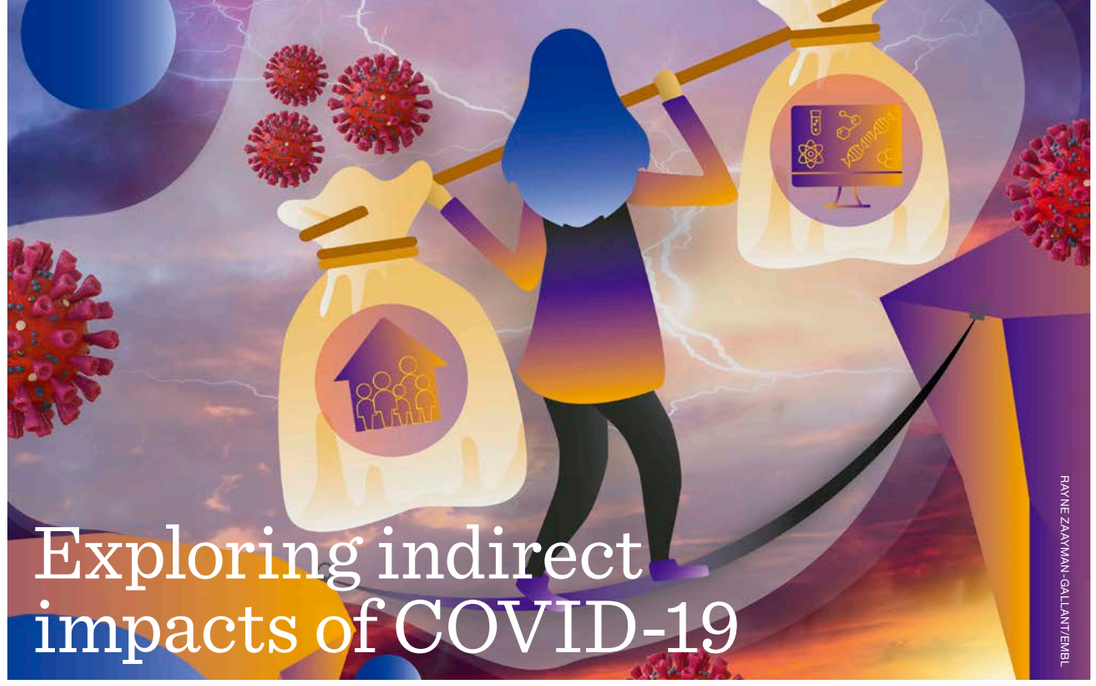
The team analysed the molecular structure of the spike protein in its natural environment, on intact virions, and with near-atomic resolution. The results were surprising: the data showed that the globular portion of the spike protein, which contains the receptor-binding region and the machinery required for fusion with the target cell, is connected to a flexible stalk. "The upper spherical part of the spike has a structure that is well reproduced by recombinant proteins used for vaccine development," explains Martin Beck, EMBL group leader and a director of the MPI of Biophysics. "However, our findings about the stalk, which fixes the globular part of the spike protein to the virus surface, were new."

"The stalk was expected to be quite rigid," adds Gerhard Hummer, from the MPI of Biophysics and the Institute of Biophysics at Goethe University Frankfurt. "But in our computer models and in the actual images, we discovered that the stalks are extremely flexible." By combining molecular dynamics simulations and cryo-electron tomography, the team identified three joints that give the stalk its flexibility.

"Like a balloon on a string, the spikes appear to move on the surface of the virus and thus are able to search for the receptor for docking to the target cell," explains Jacomine Krijnse Locker, group leader at the Paul-Ehrlich-Institut. To prevent infection, these spikes are targeted by antibodies. However, the images and models also showed that the entire spike protein, including the stalk, is covered with chains of glycans – sugar-like molecules. These chains provide a kind of protective coat that hides the spikes from neutralising antibodies: another important finding on the way to effective vaccines and medicines.

Turoňová, B, Sikora, M, Schürmann, C *et al. Science*, 18 August 2020. DOI: 10.1126/science.abd5223

(Above) Model of the spike protein, with its coat of protective glycan chains (cyan).



Exploring indirect impacts of COVID-19

EMBL hosts virtual conference 'The impact of the COVID-19 crisis on women in science: challenges and solutions'

BY IVY KUPEC

On 9 September, EMBL hosted a virtual conference to discuss the indirect impacts of the coronavirus pandemic on women in science. As one of the speakers noted, the pandemic has been a torrential storm. But individual differences in people's ability to weather this storm ultimately come down to a long list of factors like work and family responsibilities, available support, and career stage.

Before the event even began, it was clear the topic resonated with women in science, who accounted for 88% of the more than 1,300 people – of 75 nationalities – who registered. Participants got involved with questions, tweets, and interactions on multiple Slack channels, where they could swap stories and advice.

The conference followed an article published in *The Lancet* in August, which reported on COVID-19's indirect impacts on women. Despite the World Health Organization's calculation that, in its European region, men account for 57% of deaths from COVID-19 and 70% of admissions to intensive care, women have experienced disproportionate, unique, and plentiful indirect impacts, such as employment issues, care responsibilities for children and elders, and increases in domestic violence. For women in science, these distinctions are revealed in additional ways.

The conference began with personal stories from female scientists of various backgrounds, perspectives, and experiences. Their stories had several common themes, such as the need to be flexible, to prioritise and accept the balance between competing family and work needs, to find ways to still network and interact with other scientists to minimise isolation, and to look for opportunities created by the new work environment.

Geneviève Almouzni, from the French National Centre for Scientific Research (CNRS) and Institut Curie, shared COVID-related career strategies, especially for leadership, such as advocating for extensions of deadlines, being flexible with teams, and making accommodations for parent scientists or others facing unique pandemic-related challenges.

EMBL Director General Edith Heard and Ana Maria Franchi, President of Argentina's National Council for Scientific and Technical Research (CONICET), discussed how organisations might address the indirect impacts felt by such a large part of the scientific research community.

"We have to be proactive and pre-emptive," Edith said. "Conferences like this help bring to light gender-specific issues, helping us continue to grow and do a better job as leaders of scientific research organisations."

VIEW THE TALKS ONLINE:
bit.ly/embletc-96-wis-covid

A synthetic mini-antibody to combat COVID-19

Scientists screen hundreds of synthetic mini-antibodies, identifying one that might stop SARS-CoV-2 from infecting human cells

BY DOROTA BADOWSKA

Nanobodies, small antibodies found in camels and llamas, are promising as tools against viruses due to their high stability and small size. Technological advances now allow for rapid selection of synthetic nanobodies, called sybodies.

EMBL Hamburg's Löw group searched through existing sybody libraries to find sybodies that could block SARS-CoV-2 from infecting human cells. They tested the selected sybodies, with one called sybody 23 turning out to be particularly effective.

To test if sybody 23 could neutralise a virus, a different virus – called a lentivirus – was modified such that it carried SARS-CoV-2's spike protein on its surface. Sybody 23 successfully disabled the modified virus *in vitro*.

The results of this project hold out the promise of a potential way to treat COVID-19. In future work, the scientists will perform further analyses to confirm whether sybody 23 could be an effective COVID-19 treatment.

The project was led by EMBL Hamburg, together with collaborators from the Centre for Structural Systems Biology (CSSB) in Hamburg, and Karolinska Institutet, Sweden.

Custódio, TF *et al. Nature Communications*, 4 November 2020. DOI: 10.1038/s41467-020-19204-y

Funding to predict the risk of infectious disease outbreaks

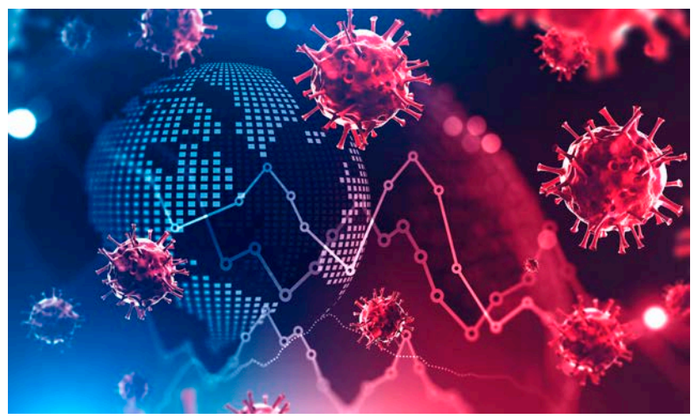
Better surveillance and prediction tools are needed to identify outbreaks earlier and anticipate their impact

BY OANA STROE

The Versatile Emerging infectious disease Observatory (VEO) project is a consortium of 20 research partners including EMBL's European Bioinformatics Institute (EMBL-EBI), which aims to develop a smart detection system for infectious disease outbreaks. The researchers will use laboratory research, field studies, and big data research to monitor and analyse various sources of information. VEO has recently received €15 million in funding from the European Commission's Horizon 2020 Programme to start its research.

By linking and analysing various sources of information, the scientists involved in the project hope to identify and classify the risk of disease outbreaks earlier. This will also allow researchers to generate clear information about the potential impact of the outbreak faster, and to develop a warning system.

"The VEO consortium builds on the work of the COMPARE project, a multidisciplinary research network that aims to bring together relevant data to help identify, contain, and mitigate emerging infectious disease and foodborne outbreaks," explains EMBL-EBI group leader Guy Cochrane. "By exploring the most likely scenarios, we are preparing ourselves for potential future outbreaks."



A precise new tool for cancer research

'Mini organs' help to clarify how cells turn cancerous, potentially shedding light on ways to stop tumour growth

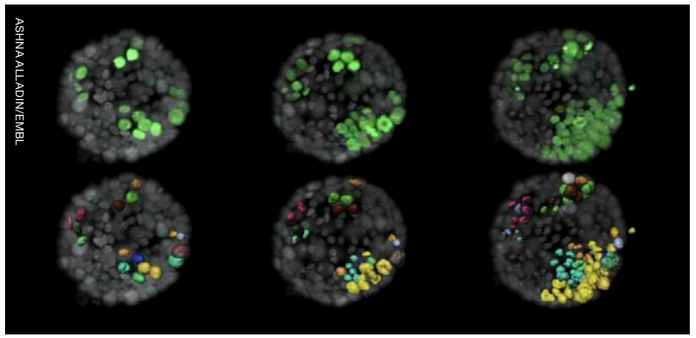
BY IVY KUPEC

Scientists in EMBL's Jechlinger group have created a new, realistic 3D testbed to help them study cancer cells as they first form.

This could potentially allow interventions to stop tumour development.

By creating 'mini organs', or organoids, from healthy mouse breast tissue and employing laser light-sheet technology to steadily monitor cell growth, researchers were able to track, study, and even determine a tipping point when cells that express oncogenes (cancer-causing genes) turn cancerous. The hope is that this work could lead to new strategies for approaching breast cancer treatment.

"We've now created a robust platform to explore cell deficiencies and a way to realistically study response to treatments at the cellular level," says EMBL group leader Martin Jechlinger. "If we know about deficiencies already tested in these systems, we can potentially more accurately flag risk groups for better medical care, in much the same way that identifying genes like BRCA1 and BRCA2 – which are found mutated in breast cancer – has informed medical decisions. Where this could potentially lead is quite exciting."



Tumour cells (green) among normal cells (grey) grow and encroach on the organoid structure, as shown in the progression in these snapshots. In the lower panel, it's possible to identify new cells that arise from a single cell of the same colour.

Alladin, A, Chaible, L *et al. eLife*, 21 July 2020. DOI: 10.7554/eLife.54066

An organoid cell atlas to enhance biomedical research

EMBL-EBI is one of eight partners in the new EU-funded HCA|Organoid consortium

BY OANA STROE

Organoids are groups of cells grown in laboratories. They can be useful tools for biomedical research, but they are restively new and there are many unanswered questions about how they work.

To address some of these questions, researchers are planning to create a specialised Organoid Cell Atlas, which will foster the production, quality control, dissemination, and utilisation of single-cell data for human organoids. By creating well-characterised *in vitro* models of human organs, this resource could enable translational research on rare genetic diseases, complex multifactorial diseases, and cancer.

The HCA|Organoid project is one of six pilot actions funded by the EU Horizon 2020 Framework Programme, which will be European contributions to the Human Cell Atlas (HCA) project. HCA is an ambitious global initiative striving to advance biomedical research and therapy using single-cell technologies. The HCA|Organoid consortium comprises eight partners, including EMBL's European Bioinformatics Institute, and will receive €5 million in EU funding.

Bock, C *et al. Zenodo*, 30 August 2020. DOI: 10.5281/zenodo.4001718

Genome sequencing accelerates cancer detection

Researchers have developed a statistical model that uses genomic data to predict the risk of developing cancer of the oesophagus

BY OANA STROE

Oesophageal cancer often develops from a condition called Barrett's oesophagus. Existing monitoring and treatment methods are very intrusive, with patients often undergoing burdensome procedures to ensure no cancer is missed.

Researchers have now developed a statistical model that uses genomic data to accurately predict whether a patient with Barrett's oesophagus has a high or low risk of developing cancer.

Researchers at EMBL's European Bioinformatics Institute (EMBL-EBI), the University of Cambridge, and collaborators sequenced genomes from biopsies collected from patients with Barrett's oesophagus. The researchers used the data to look for differences between patients who were ultimately diagnosed with cancer and those who were not. The data were used to develop a statistical model measuring each patient's individual risk.

This approach allows patients at greatest risk to be treated immediately, rather than conducting repeated biopsies until early signs of cancer are found. Patients with low risk and stable disease can be monitored less frequently. Overall, the authors estimate that monitoring can be reduced for 50% of patients with Barrett's oesophagus.

Killcoyne, S, Gregson, E *et al. Nature Medicine*, 7 September 2020. DOI: 10.1038/s41591-020-1033-y

Artificial intelligence finds patterns of mutations and survival

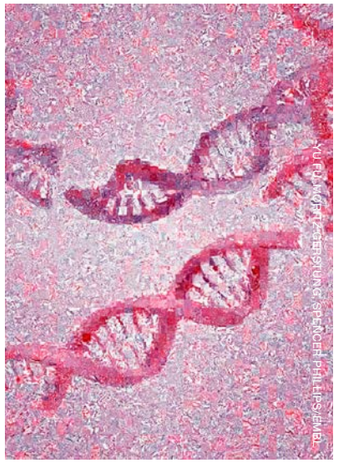
AI applied to tumour microscopy images detects patterns of 167 different mutations and predicts patient survival in 28 cancer types

BY MEHDI KHADRAOUI

Researchers at EMBL's European Bioinformatics Institute (EMBL-EBI) and collaborators have developed an artificial intelligence (AI) algorithm that uses computer vision to analyse tissue samples from cancer patients. The algorithm can distinguish between healthy and cancerous tissues, and can also identify patterns of more than 160 DNA and thousands of RNA changes in tumours. The study highlights the potential of AI for improving cancer diagnosis, prognosis, and treatment.

"Clinicians use microscopy slides for cancer diagnosis all the time. However, the full potential of these slides hasn't been unlocked yet. As computer vision advances, we can analyse digital images of these slides to understand what happens at a molecular level," says Yu Fu, a postdoc in EMBL-EBI's Gerstung group.

Computer vision algorithms are a form of AI that can recognise certain features in images. Fu and colleagues repurposed such an algorithm to distinguish various cancer types from healthy tissue. They showed that this algorithm can also be used to predict survival and even patterns of DNA and RNA changes from images of tumour tissue.



Fu, Y *et al. Nature Cancer*, 27 July 2020. DOI: 10.1038/s43018-020-0085-8

Fighting cardiovascular disease with acne drug

Researchers from EMBL Heidelberg and Stanford University show that a drug already used to treat acne is a potential treatment for a leading cause of heart failure

BY MATHIAS JÄGER

Dilated cardiomyopathy (DCM) affects 1 in 250 people, and is a leading cause of heart failure. Researchers at EMBL and Stanford University studied a single family with inherited DCM to understand the cause of their disease. By looking for differences in the genomes of family members, they found a mutation (P633L) in a gene coding for a protein called RBM20, which was disease causing.

The researchers used a combination of patient-derived cells and genome-edited cells to demonstrate *in vitro* that this was the pathogenic mutation. They then searched for compounds that might work as treatment options, using the open databases at EMBL's European Bioinformatics Institute (EMBL-EBI).

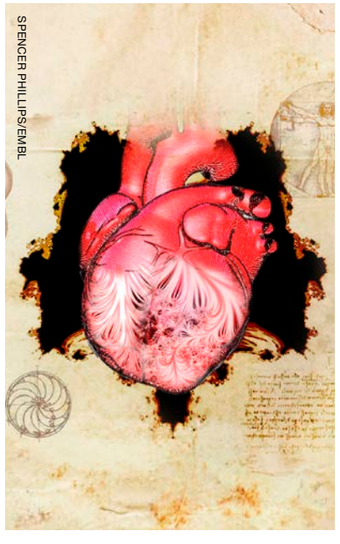
The team identified a chemical called all-trans retinoic acid (ATRA) as a potential treatment. ATRA is a drug used for the treatment of acne and a type of leukaemia called acute promyelocytic leukaemia.

"This is a promising result in approaching RBM20-deficient DCM," says EMBL and Stanford scientist Lars Steinmetz. "In addition, the general approach and the strategy we used in this study could work for a number of other dominant diseases."

Briganti, F, Sun, H *et al. Cell Reports*, 8 September 2020. DOI: 10.1016/j.celrep.2020.108117

New clues to a 500-year-old mystery about the human heart

Scientists show that muscular structures first described by Leonardo da Vinci are essential for heart function



SPENCER PHILLIPS/EMBL

BY MEHDI KHADRAOUI

A group of researchers, including scientists from EMBL's European Bioinformatics Institute (EMBL-EBI), have investigated the function of a complex mesh of muscle fibres that line the inner surface of the heart. Their study shows how the shape of these muscles impacts heart performance and heart failure.

In early development, the heart grows an intricate network of muscle fibres called trabeculae, which form geometric patterns on its inner surface. These are thought to help oxygenate the developing heart, but their function in adults has remained unknown since the 16th century, when Leonardo da Vinci first sketched trabeculae and their snowflake-like fractal patterns.

The researchers used artificial intelligence to analyse 25,000 MRI scans, along with associated heart morphology and genetic data. They discovered that the shape of trabeculae affects the performance of the heart. To confirm this, they analysed genetic data from 50,000 patients and found that different fractal patterns in these muscle fibres affected the risk of developing heart failure.

Further research on trabeculae may help scientists better understand how heart diseases develop and explore new approaches to treatment.

Meyer, HV, Dawes, TJW, Serrani, M *et al. Nature*, 19 August 2020. DOI: 10.1038/s41586-020-2635-8

SAMUEL PAZICKY/EMBL

How deadly parasites glide into human cells

New insights into the gliding movements by which the parasites causing malaria and toxoplasmosis invade human cells

BY DOROTA BADOWSKA

In biological terms, gliding refers to the type of motion in which a cell moves along a surface without changing its shape. This form of movement is unique to parasites from the phylum Apicomplexa, such as *Plasmodium*, which causes malaria, and *Toxoplasma*, which causes toxoplasmosis.

The gliding motion relies on the proteins actin and myosin. In Apicomplexa, myosin interacts with several other proteins, which together form a complex called the glideosome. Understanding the exact mechanism by which the glideosome works could aid the development of drugs to prevent its assembly, stopping disease progression.

A group of scientists led by EMBL Hamburg's Christian Löw analysed the molecular structure of essential light chains (ELCs), which are glideosome proteins that bind directly to myosin. Their study shows that ELCs work like molecular stilts, accelerating the parasite's gliding movements.

"*Plasmodium* passage through the skin is the first stage of human infection," says Maria Bernabeu, a group leader at EMBL Barcelona researching vascular dysfunction in cerebral malaria. "The advantage of targeting *Plasmodium* at that stage is that only about a hundred parasites are present. Understanding the parasite's gliding motility might help to develop drugs or vaccines that target *Plasmodium* before it multiplies."

Pazicky, S *et al. Communications Biology*, 13 October 2020. DOI: 10.1038/s42003-020-01283-8

(Above) A model of the *Plasmodium* essential light chain protein.

Upgraded beamlines at EMBL Grenoble unveiled

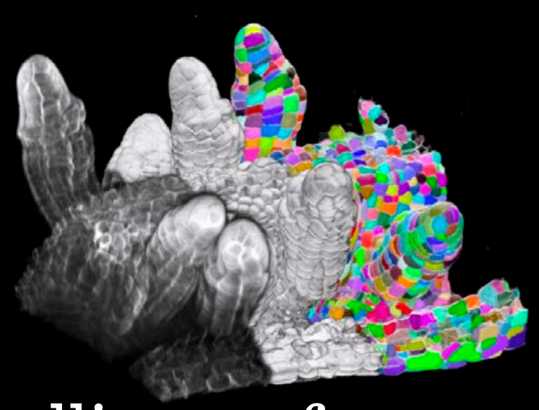
The beamlines run jointly by EMBL Grenoble and the ESRF have reopened, with significant upgrades that exploit the brand new fourth-generation ESRF synchrotron source

BY MYLÈNE ANDRÉ

Almost two years ago, the European Synchrotron Radiation Facility (ESRF) was shut down for 20 months, during which time the synchrotron ring was completely rebuilt and upgraded into the world's first Extremely Brilliant Source (EBS) – a €150 million project that runs from 2017 to 2022.

The innovations brought about by the EBS project have now been unveiled to the scientific community. Apart from the construction of a new storage ring, they include an advanced instrumentation upgrade programme and improvement of all the JSBG's structural biology beamlines, notably a significant upgrade of MASSIF-1. This is one of the seven beamlines run jointly by the ESRF and EMBL Grenoble, and was the world's first automated beamline.

In its new form, MASSIF-1 will be operated in coordination with the EMBL HTX Lab, which will bring a new level of efficiency, particularly in intensive fragment screening campaigns for drug discovery. The new developments will maintain EMBL and ESRF at the forefront of innovations in macromolecular crystallography beamline technology for the benefit of structural biology.



KRESHUK GROUP/EMBL; HAMPRECHT LAB/HCI HEIDELBERG UNIVERSITY

Intelligent software tackles plant cell jigsaw

PlantSeg complements microscopy methods to reveal how plant tissues develop

BY IVY KUPEC

An EMBL research group led by Anna Kreshuk has joined a consortium of plant biologists and computer scientists to develop a tool that enables them to sort through cells to study morphogenesis: the origins of the structures in an organism and the way it develops.

To study morphogenesis of tissues at the cellular level, researchers need to image individual cells. They have to separate or 'segment' them to see each cell individually and analyse the changes over time. The team designed a tool called PlantSeg to carry out this segmentation process, providing the most accurate and versatile analysis of plant tissue development to date.

Microscopy provides imagery to the algorithm, which then delineates the cellular structures, making the segmentation clearer.

Machine learning-based algorithms, like the ones at the core of PlantSeg, are trained from correct segmentation examples. The group has trained PlantSeg on many plant tissue volumes, so that now it generalises quite well to unseen plant data. The underlying method is, however, applicable to any tissue and could easily be retrained for animal tissue.

PlantSeg is an independent tool, but one that Kreshuk's team will eventually merge into another tool her lab is working on, ilastik Multicut workflow.

Wolny, A, Cerrone, L *et al. eLife*, 29 July 2020. DOI: 10.7554/eLife.57613

PLANTSEG:
bit.ly/embletc-96-plantseg

ILASTIK MULTICUT WORKFLOW:
bit.ly/embletc-96-ilastik

Achieving personalised therapeutics

EMBL is part of a growing movement to achieve cell-based medicine in Europe

BY IVY KUPEC

The LifeTime Initiative, which includes EMBL Heidelberg and EMBL's European Bioinformatics Institute (EMBL-EBI), has developed the LifeTime Strategic Research Agenda to integrate breakthrough technologies to further develop personalised treatments for five major classes of disease: cancer, cardiovascular and metabolic disorders, chronic inflammation, infectious diseases, and neurological disorders. LifeTime is a consortium of more than 90 leading European research institutions, together with international advisers and over 80 supporting companies.

Scientists – and ultimately healthcare providers – can now understand molecular details and changes responsible for driving the onset and progression of diseases or the emergence of therapy resistance in each patient. Single-cell and imaging technologies allow scientists to observe and analyse cells individually and understand how cells 'make decisions'.

This roadmap explains how technology can be rapidly co-developed and transitioned into clinical settings to address key medical challenges. This requires close interactions between research institutions, hospitals, industry, and European infrastructures to deploy and analyse medical big data across European borders.

Rajewsky, N, Almouzni, G, Gorski, SA *et al. Nature*, 7 September 2020. DOI: 10.1038/s41586-020-2715-9

Launch of ELLIS Heidelberg

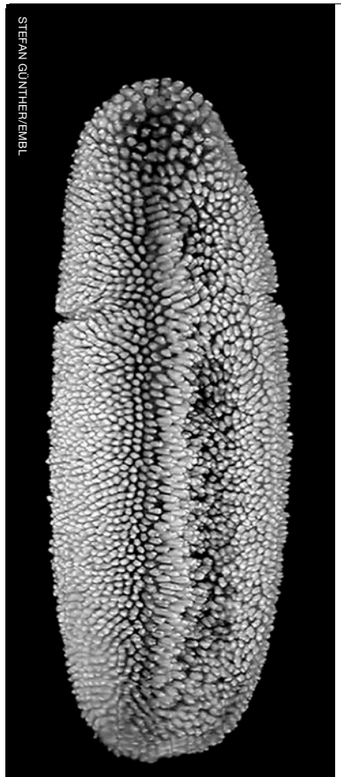
A newly established research unit will support artificial intelligence and machine learning in the life sciences

BY MATHIAS JÄGER

A newly founded research unit of the European Laboratory for Learning and Intelligent Systems (ELLIS) will bring together the best artificial intelligence (AI) researchers in Heidelberg to increase the level of cooperation between participating institutes, ensuring that AI research in Heidelberg can have international impact.

ELLIS is a pan-European network of leading researchers in the field of artificial intelligence, currently comprising 28 units in 14 countries. The new ELLIS unit brings together scientists from three leading Heidelberg research institutes: EMBL Heidelberg, Heidelberg University, and the German Cancer Research Center (DKFZ).

The newly established unit will increase the international visibility of AI research groups in Heidelberg, and will make it easier to hire talented people in this very competitive field. The unit has already planned not only its research activities but also an interdisciplinary training programme for young scientists. This new initiative is open for joint projects with industry and is supported by an existing network of industry partners.



STEFAN GÜNTHER/EMBL

An embryo of the fruit fly *Drosophila*. EMBL scientists studied 75 such embryos to understand how gene expression varies between individuals.

Predicting how gene expression varies

Discoveries at EMBL will help researchers to interpret one of the most common types of experiments in genomics and medical studies

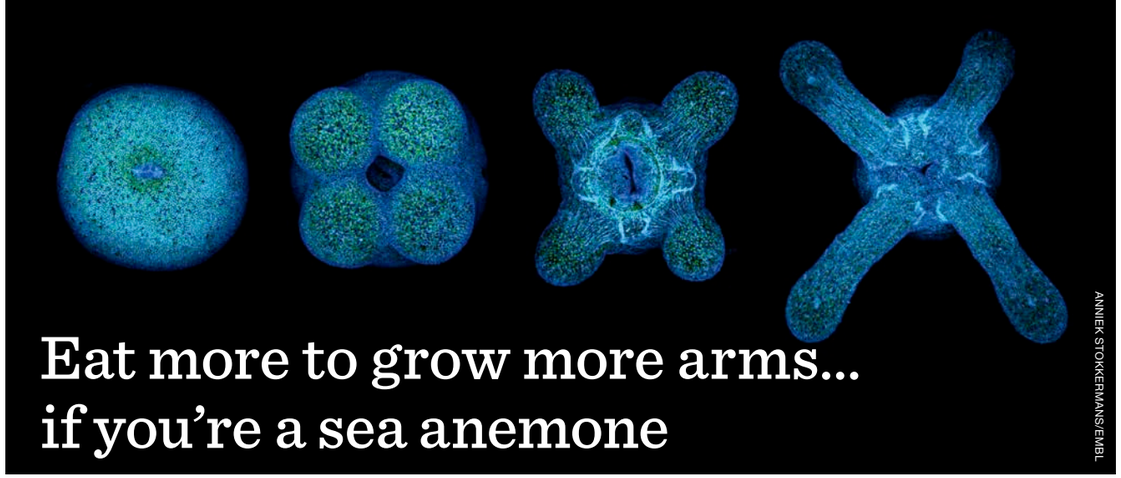
BY FABIAN OSWALD

By studying the genomes of fruit flies, scientists from the Zaugg and Furlong groups at EMBL Heidelberg have identified a set of genomic features that can predict how much the expression of a gene varies between individuals in a species.

The scientists examined 75 embryos of the fruit fly *Drosophila*, using a machine learning approach to identify the features that are fundamental to gene expression variation. They found a set of around 100 genetic features that made the expression of some genes especially robust, allowing them to maintain their normal function while the organism reacts to environmental change. Knowing these features now makes it possible to predict whether a gene will show high or low expression variation.

These findings will help scientists to interpret one of the most common types of experiments in the genomics and medical community, known as differential expression experiments. These experiments are used to compare gene expression levels between two groups, for example patients receiving treatment and a control group. Scientists can now identify which genes are variable by nature and which variations are specific to the experimental conditions, such as a particular medical treatment.

Sigalova, OM *et al. Molecular Systems Biology*, 7 August 2020. DOI: 10.15252/msb.20209539



Eat more to grow more arms... if you're a sea anemone

ANNIEK STOKKERMANS/EMBL

A group led by scientists from EMBL has discovered that the number of tentacles a sea anemone grows depends on the amount of food it eats

BY MATHIAS JÄGER

Your genetic code determines that you will grow two arms and two legs. Sea anemones, however, defy this rule and have a variable number of tentacle arms. Until now, it's been unclear what regulates the number of tentacles a sea anemone can grow. Scientists from the Ikmi group at EMBL Heidelberg and collaborators have shown that the number of tentacles is defined by the amount of food consumed.

The scientists found that muscle cells pre-mark the sites of new tentacles. These muscle cells change their gene expression signature in response to food. While this finding is novel on its own, it also shows that sea anemones, which are traditionally used for evolutionary developmental studies, are well suited to study morphogenesis in the context of organism–environment interactions.

This sequence shows the development process of a sea anemone's tentacles.

Knowing that the number of tentacles in sea anemones is determined by their food intake, the group plans to define the key nutrients critical to this process. They also want to further investigate the unconventional role of muscles in defining the sites where new tentacles form.

Ikmi, A *et al. Nature Communications*, 2 September 2020. DOI: 10.1038/s41467-020-18133-0

Human and mouse cells run at different speeds

EMBL scientists uncover the biochemical mechanisms that govern the tempo of embryo development

BY LUCA TANCREDI BARONE

In the early phase of vertebrate development, the embryo develops into a series of segments. This process is governed by an oscillating biochemical process, known as the segmentation clock. In mice, each oscillation of this clock takes about two hours, while in human cells it takes five hours. Why the length of this cycle varies between species has remained a mystery.

A team including scientists from EMBL Barcelona suspected that the difference might be due to a master gene called *HES7*. They performed a number of experiments in which they swapped the *HES7* genes between human cells and mouse cells, but to their surprise this did not affect the cycle.

The team then looked at the degradation rate of the HES7 protein, observing that both the human and the mouse version of HES7 were degraded more slowly in human cells than in mouse cells. They also discovered that the time it took cells to transcribe the *HES7* gene into messenger RNA (mRNA), to process the mRNA molecule, and to translate it into proteins was significantly different. This showed that it's the cellular environment in human and mouse cells that makes the difference in the timescales involved.

Matsuda, M *et al. Science*, 18 September 2020. DOI: 10.1126/science.aba7668

New partnership in Lithuania

New agreement establishes the VU LSC–EMBL Partnership for Genome Editing Technologies

BY ROSSANA DE LORENZI

Soon after Lithuania became an EMBL prospect member state in September 2015, a memorandum of understanding was signed between EMBL and the Life Sciences Center at Vilnius University (VU LSC), to foster collaboration as Lithuania progressed towards full membership. In June 2019, Lithuania became EMBL's 27th member state. To intensify institutional synergies, a framework agreement for the establishment of the VU LSC–EMBL Partnership for Genome Editing Technologies was signed in September 2020.

The partnership builds on complementary scientific and technological strengths in the field of targeted genome modification. It will include the establishment within the LSC of a partner unit based on the EMBL model, which will employ six high-level groups of international researchers and will pursue a collaborative programme in genome editing.

The scientific focus will be the development and application of novel genome editing tools and technologies to improve our understanding of fundamental biological processes and disease mechanisms. The partnership will also promote cooperation between VU LSC and other EMBL partnership institutes, enabling the sharing of knowledge, scientific services, and scientific training.

The Nordic EMBL Partnership: supporting national research

EMBL and four Nordic research institutions stimulate scientific exchange and inspire scientific collaborations

BY DOROTA BADOWSKA

The Nordic EMBL Partnership was initiated in 2007 to connect EMBL and Nordic research institutions focusing on diverse approaches to molecular medicine, including infection biology, genomics, and translational neuroscience. Besides EMBL, the Partnership involves four Nordic nodes: the Institute for Molecular Medicine Finland (FIMM), the Laboratory for Molecular Infection Medicine Sweden (MIMS), Centre for Molecular Medicine Norway (NCMM), and the Danish Research Institute of Translational Neuroscience (DANDRITE).

NORA LEHOTAI/MIMS

Oliver Billker, Director of MIMS, at the opening of the conference of the Nordic EMBL Partnership for Molecular Medicine.

The annual conference of the Nordic EMBL Partnership is an opportunity for members to get together, exchange information across nodes, and inspire collaborations. At this year's conference (22–25 September 2020), EMBL Director General Edith Heard welcomed participants and presented updates on EMBL's future plans. The conference's scientific programme comprised many talks, including several by scientists from three of EMBL's sites. This was possible thanks to the virtual format of this year's meeting, and reflected the interest on both sides in strengthening scientific interactions.

READ MORE ABOUT THE CONFERENCE: bit.ly/embletc-96-nordic

New fellowships to boost infrastructure

ARISE fellowships to offer first-ever comprehensive training for bioscience infrastructure operations


KINGA LUBOWIECKA/EMBL

BY IVY KUPEC

EMBL will soon be accepting applications for its newest fellowship programme, ARISE, which will train future research infrastructure scientists. ARISE will be the first long-term preparatory programme of its kind. A diverse group of engineers, computer scientists, mathematicians, and others will be trained 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 the next five years, EMBL will train 62 fellows to become future leaders in technology development and to take senior positions in life science research infrastructure, either in 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's 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 comprehensive experience offers exposure to different approaches to infrastructure as well as experiences to prepare fellows 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.

THE ARISE PROGRAMME:
bit.ly/embletc-96-arise


ALEKSANDRA KROLIK/EMBL

Challenge accepted

Members of the EMBL community are sparking debate on extinction and biodiversity, unravelling the biology behind tropical diseases, and breaking technological barriers to expand what scientists can see and do

Understanding the impact of mass extinction

EMBL invites experts and activists to discuss the effects of biodiversity loss and how scientists and wider society can respond

BY EDWARD PRIOR

EMBL's 21st annual Science and Society Conference took place from 4–5 November, near the end of a year that has seen widespread media coverage of threats to the natural world, including climate change and loss of biodiversity. Entitled 'Our House Is Burning: Scientific and Societal Responses to Mass Extinction', the conference drew high-profile speakers from the worlds of academia, activism, and conservation, and generated engaging discussion from a large online audience worldwide. Topics ranged from microbial diversity to the protection of the Amazon and indigenous rights, and covered issues as diverse as the sustainability of the built environment and the use of microbes on a global scale to help reverse the effects of pollution. While travel restrictions prevented a physical gathering, participants made full use of opportunities to meet with speakers virtually, posing questions and offering perspectives from a range of disciplinary backgrounds.

From speculation to testable science

The key question posed at the start of the conference was whether the Earth is currently in the midst of a mass extinction. Speakers gave a scientific overview of the loss of biodiversity during the current human-dominated age – the Anthropocene – as well as exploring key drivers of biodiversity change.

The keynote speaker on the first day of the conference was Mike Benton, a professor of palaeontology at the University of Bristol, UK. His fascinating and wide-ranging talk drew connections between palaeontological evidence and the situation on Earth today. He gave details of his work featuring climate models and fluctuations in biodiversity, showing how the study of deep time can inform our predictions about the future.

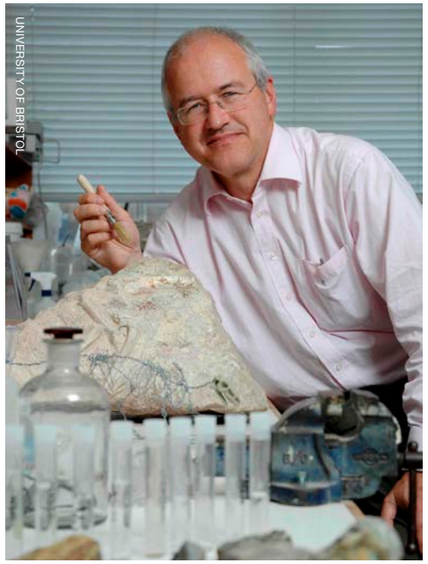
Mike's work has been at the heart of transforming palaeobiology from a speculative subject into testable science. Palaeontologists have studied mass extinctions for over 50 years, developing knowledge about the way global environments have changed and the impact that this has had on life. As the scale of global climate change emerges, along with its impact on life on Earth, palaeontologists' understanding of past extinction events has come to the fore.

In part, Mike's work builds on the climate models that have been developed for use in the present. "Now that we have functioning climate models for the present day that capture at least some of the complexity of the way the world works, we can use them to look at the effects of small-scale historical changes in climate," he explains. "Take the aridification of North Africa since Roman times as one example. We can look at what that meant for movements of wildlife. We know that there were hippos and ostriches in Egypt a thousand years ago, and that they aren't there any more. That's the kind of thing we can track."

Looking back to understand the future

Mike's work is able to harness a similar approach to delve much further into the past. "We can go deeper in time. We use the same approaches that we know work in the present day. We're careful to constantly road-test the models against the present day, and ensure they're making reasonable predictions. Then we apply them to the past."

Mike's talk made clear just how relevant such models and measurements are, as researchers grapple with the impact of climate change today. Gaps in knowledge and understanding are being bridged, and a clearer picture is emerging. "Many people are familiar with the extinction of the moas, and of course the dodo.



Mike Benton's research has helped to transform palaeobiology from a speculative subject into testable science.

But what we're looking at is potential events over the next few centuries that are much bigger and more serious than anything like that. It's something quite different from the extinction of the dodo, or a few species here and there. What we're looking at is losses of tens of per cent. Perhaps thirty, forty, fifty per cent of biodiversity. It's by looking back at the deep time mass extinctions that we can find sources of data that allow us to project into the future."

Extinction as part of life

Some voices in the public debate on climate change highlight that extinction is a natural part of life on Earth, bringing little cause for concern, especially given that biodiversity on Earth today may be at record levels. But Mike is clear that there is a marked difference between what we might expect in the normal course of events, and the rate of extinction being recorded now. "It's completely true to say: 'extinction is normal'. Most species last for one or two million years. That means that, in the long history of life, more species will have died out than are currently in existence on Earth, even though biodiversity on Earth now may be at its highest ever level. Sometimes people quote those two points and then say, 'so, why worry?' Well, there is a big difference. The rate of extinction at the moment is between a hundred and a thousand times higher than it ought to be. The rate and volume of extinction at the moment is right up there with a mass extinction." >>

Spotlight on global youth activism

EMBL's Science and Society Conference also involved talks from climate change activists and those seeking to radically shift the terms of the current discourse. Among the speakers was Ugandan campaigner Vanessa Nakate.

Untold stories and ignored communities

Vanessa is the founder of the Africa-based Rise Up Movement, which aims to boost awareness of environmental and climate challenges from an African perspective. In recent years she has become a well-known figure in the campaign to highlight the impact of climate change on communities that receive little media attention. But she didn't set out to be a climate activist. "I remember wanting to do something to help the lives of the people in my community, so I started trying to understand the struggles they face in their daily lives," she says. "It was clear that there were quite a number of challenges, things like poverty and unemployment. As my knowledge grew, I found that climate change was not just a major issue for people: it was the greatest challenge they faced."

"I found that climate change was not just a major issue for people: it was the greatest challenge they faced"

As Vanessa's understanding increased, suddenly she could see the effects of climate change all around her. "It dawned on me that I had actually seen the impacts of climate change when I was growing up, without understanding their cause. The landslides, the flooding, the droughts. That was the point when I accepted that I had to become a voice in the climate movement." Soon after committing herself to activism, she began her work to bring attention to the cause. This included going on strike every Friday, along with other young climate campaigners from around the world.

The road to activism

The Science and Society Conference explored how the personal experiences, environment, and cultural backgrounds of activists influence their chosen paths. Vanessa faced significant challenges from those around her. "People found me very weird! They said I was embarrassing myself, wasting my time," she explains. "Some of the reactions were really quite unpleasant. I remember my school put a lot of weight on values like respect and dignity, and I was viewed as going totally against those kinds of values when I took to the streets with a placard."

But even in those early, uncertain times, she found glimmers of hope. "I remember a man talking to me in the street. He was an older farmer, and he said that he agreed with what I was doing. He explained that he had witnessed change in the weather patterns, how his crops had been affected because of the increasingly uneven distribution of rainfall. He believed we had to demand change from our leaders." Understanding the struggles that were affecting the daily lives of so many, but receiving so little attention from those in power, gave Vanessa the resolve to keep going despite the disapproval she faced from many in the early days.

COURTESY OF VANESSA NAKATE

Vanessa Nakate is the founder of the Africa-based Rise Up Movement.

Discrimination and climate justice

Getting people on board with her work has become easier as her profile has grown. But Vanessa's experience has made her deeply aware of the intersectional nature of activism. Back in January 2020, she was cropped out of a global news photo of young climate activists taken at the World Economic Forum in Davos, Switzerland. The experience reinforced the exclusion that she had sensed even before the incident. "It was already quite disturbing that I was the only activist from my country, actually the only one from Africa as a whole. When I was cropped out of that photo it was a clear form of discrimination: my presence was not being valued in any way."

A large part of Vanessa's work deals with the intersection between climate justice and racial justice. She sees effective action as something that can only come about if we move beyond the traditional boundaries and discussions around environmentalism. "When you look at the communities that are most affected by climate change and pollution, they are communities of colour, communities of black people, communities of indigenous people in the Global South. It's these people who are facing most of the wrath of climate change. You can even see this when you look at wealthy countries. Take the United States, for example: the communities most affected by pollution are communities of colour and communities of black people. Racial injustice is an important fight in the climate movement: we cannot achieve climate justice without racial justice."

Vanessa's participation in the EMBL conference is part of her work aimed at sounding the alarm. "I really feel like too many people think that climate change is a minor issue, simply because they haven't personally seen its effects or felt its force. It is here. This is happening right now. It is destroying livelihoods and lives. We've got to get people to understand, so that there can be more pressure on leaders to really take action."

EMBL'S SCIENCE AND SOCIETY PROGRAMME:
bit.ly/embletc-96-science-and-society

Tackling tropical diseases

Members of the EMBL community are working to improve our understanding of the parasites that cause malaria and sleeping sickness

BY MYLÈNE ANDRÉ AND LUCA TANCREDI BARONE

The World Health Organization (WHO) reports that more than one-sixth of all infectious diseases are vector-borne diseases – in other words, diseases in which a pathogen is transmitted from one host to another by an intermediate organism, known as a vector. Many of these vectors are insects that feed on blood, such as mosquitoes or ticks. Vector-borne diseases result in hundreds of millions of cases and around 700,000 deaths each year. These diseases tend to be concentrated in tropical and subtropical areas, and they have a disproportionate impact on the poorest communities, which may suffer from factors such as a lack of shelter, poor sanitation, or limited access to healthcare.

Given the serious impact of these diseases on human health, and the severe economic burdens they cause, there is a pressing need for research to better understand the processes of infection and the biology of the pathogens involved, to enable the development of new and more effective methods of prevention or treatment.

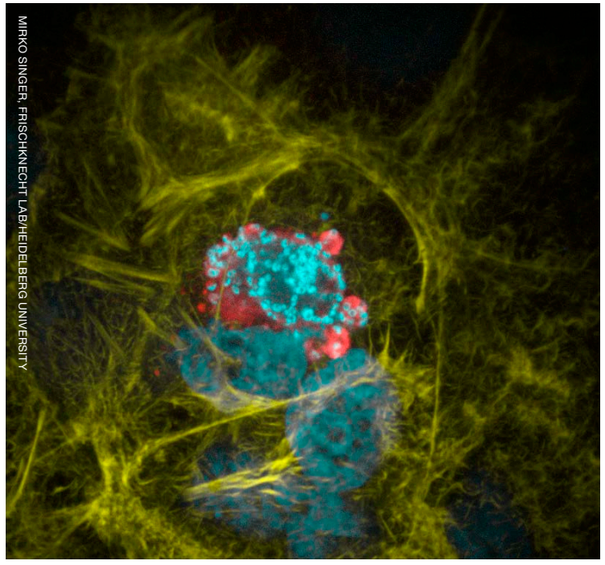
A complex foe

The deadliest vector-borne disease is malaria, which claims 400,000 lives each year, most of them in Africa. Malaria depends on two organisms, both of which are necessary for the disease to attack: a female *Anopheles* mosquito and a tiny but very sophisticated single-celled parasite called *Plasmodium*. The cycle begins when a mosquito bites a human to feed on their blood. If the insect hosts the parasite, it carries an infective form called a sporozoite, which can be passed on to its human victim. Once the sporozoite reaches the bloodstream, it moves towards the liver. Here it can reproduce and create thousands of offspring of another form, called merozoites. These attack red blood cells, where they reproduce. The red blood cells eventually burst, liberating yet more merozoites, and this is when patients experience fever and the other symptoms of malaria.

EMBL alumnus Freddy Frischknecht, a professor at Heidelberg University, carries out research on *Plasmodium*. He focuses especially on the extraordinary method the parasite uses to move around inside its host. “Everybody assumed that the sporozoite was injected by the mosquito directly into the blood, but instead they’re injected into the skin,” he explains. “From there, *Plasmodium* looks for a blood vessel.”

Gliding through the blood

Research in Freddy’s group has revealed how the parasites move ten times faster than any other migrating cell in the body. “The fastest moving cell in our body is the neutrophil cell, part of the immune system. It’s as if the fastest police car runs at a tenth of the speed of the villain,” he says.



Malaria parasites, shown in red, replicate in liver cells (pictured) before infecting red blood cells and causing disease. Host and parasite DNA is shown in cyan and host cell actin filaments in yellow.

EMBL alumnus Freddy Frischknecht.

Freddy and his group have made important steps in understanding how *Plasmodium* manages to be that fast. They found that the parasite tries to avoid sticking to a substrate. Instead it glides, which it can do thanks to an interplay between filaments of a protein called actin, which determine the shape and movement of the cell’s surface. Recent work led by group leader Christian Löw at EMBL Hamburg has provided further insights into the structure of the proteins that enable this gliding motion (p. 11).

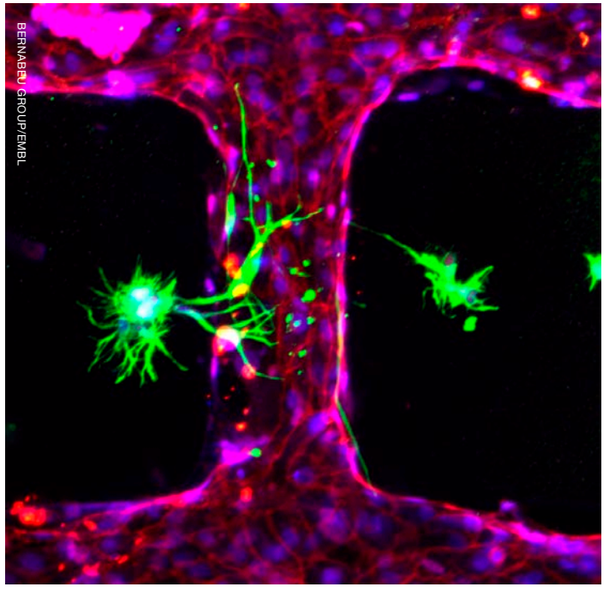
Freddy is working on a type of *Plasmodium* that attacks mice: his group discovered that if you modify the gene sequence coding for some proteins involved in the migration mechanism, the parasite could still infect mice, but the mice would survive. “We think this is because the parasite then multiplies more slowly in the blood, and the immune system is better at controlling fewer parasites,” he says. His goal now is to generate a human-infecting parasite that grows more slowly than the normal one, but can still be transmitted by a mosquito. Just as in mice, the hope is that the human immune system would be capable of fighting off this form of the parasite, enabling the host to gain immunity to other strains of *Plasmodium* that infect humans. This is the kind of novel approach that’s needed to tackle malaria, since designing a conventional vaccine – using proteins on the parasite’s surface – is extremely difficult, as there are many such proteins and they undergo significant changes during the parasite’s life cycle. There is currently only one approved malaria vaccine, which offers protection in only about 30% of cases and for a limited time.

Monitoring malaria progression

At EMBL Barcelona, group leader Maria Bernabeu is tackling malaria from a different perspective. Her research – for which she was recently awarded a €1.5 million ERC Starting Grant – focuses on cerebral malaria, a deadly complication of the disease that involves severe neurological symptoms, and is responsible for approximately three-quarters of malaria deaths worldwide.

“One of the things that prevents us from understanding how this disease evolves is that we don’t have direct access to the brain until after a patient has died, so we do not understand its progression,” Maria explains. A collaboration between her group and clinicians at Ispat General Hospital (IGH) in Rourkela, India, will help overcome this problem. IGH is one of the few places in the world using MRI scanning to study the brains of patients with malaria, offering a way to closely monitor the development of the disease in living patients. >>

A 3D artificial blood vessel, used to study the mechanism of cerebral malaria. Endothelial cells are shown in red, astrocytes in green, and cell nuclei in blue.



EMBL group leader Maria Bernabeu.

Breaking the blood–brain barrier

The brain is usually protected from infection by the blood–brain barrier (BBB). Maria's group is studying how cerebral malaria breaks down this barrier. They are growing cells on collagen scaffolds to recreate living human blood microvessels of the same size and shape as the real ones in the BBB. "Through this blood vessel tree, we can flow blood cells – both healthy ones, and those infected with malaria," Maria says. "This allows us to recreate aspects of the human pathology in a dish – using human cells and the human-specific version of the parasite – to better understand the mechanism of cerebral malaria."

This is the first time anyone has used artificial blood vessels to study malaria, and the methods being developed in Maria's group could bring us an important step closer to tackling this disease. "If you find a strategy to prevent the complications of cerebral malaria," says Maria, "you can save many lives."

Unravelling RNA processing

At EMBL Grenoble, group leader Eva Kowalinski and members of her lab are carrying out research on *Trypanosoma*: a genus of single-celled insect-transmissible parasites that can cause human and animal diseases. The Kowalinski group studies RNA – a molecule that plays an important role in carrying genetic information to be converted into a gene product such as a protein. The group uses structural biology, biochemistry, and cell biology methods to study the mechanisms of protein–RNA interactions and RNA metabolism: the ways in which RNA molecules are produced, modified, processed, and broken down.

Members of the group study RNA molecules in *Trypanosoma* parasites to understand how the genetic information is processed, modified, or even rewritten. These pathways differ significantly between *Trypanosoma* and humans. "We study in particular how the protein complexes involved differ from those in human cells. Trypanosomes have very special forms of RNA processing. From a fundamental research aspect, it's really interesting to understand how it works," says Eva, whose group recently received a grant from the French National Research Agency (ANR) for this research.

Parasites of the species *Trypanosoma brucei* are transmitted between humans or animals by the bite of an insect vector, the tsetse fly, when taking a blood meal. Infection with the parasite causes so-called sleeping sickness in humans and a disease called nagana in animals. Sleeping sickness produces a range of symptoms such as fever, swelling of the lymph nodes, and subsequently neurological symptoms including sleep disturbances. It is fatal if left untreated, and is a severe health threat in sub-Saharan Africa, a region which is also widely affected by other diseases and economic hardship. According to WHO, the number of infected people has dropped significantly over the past 50 years, thanks to a sustained effort to tackle this disease. However, its diagnosis and treatment are still very complex, and there is no vaccine.

Micrograph of *Trypanosoma brucei.*

EMBL group leader Eva Kowalinski.

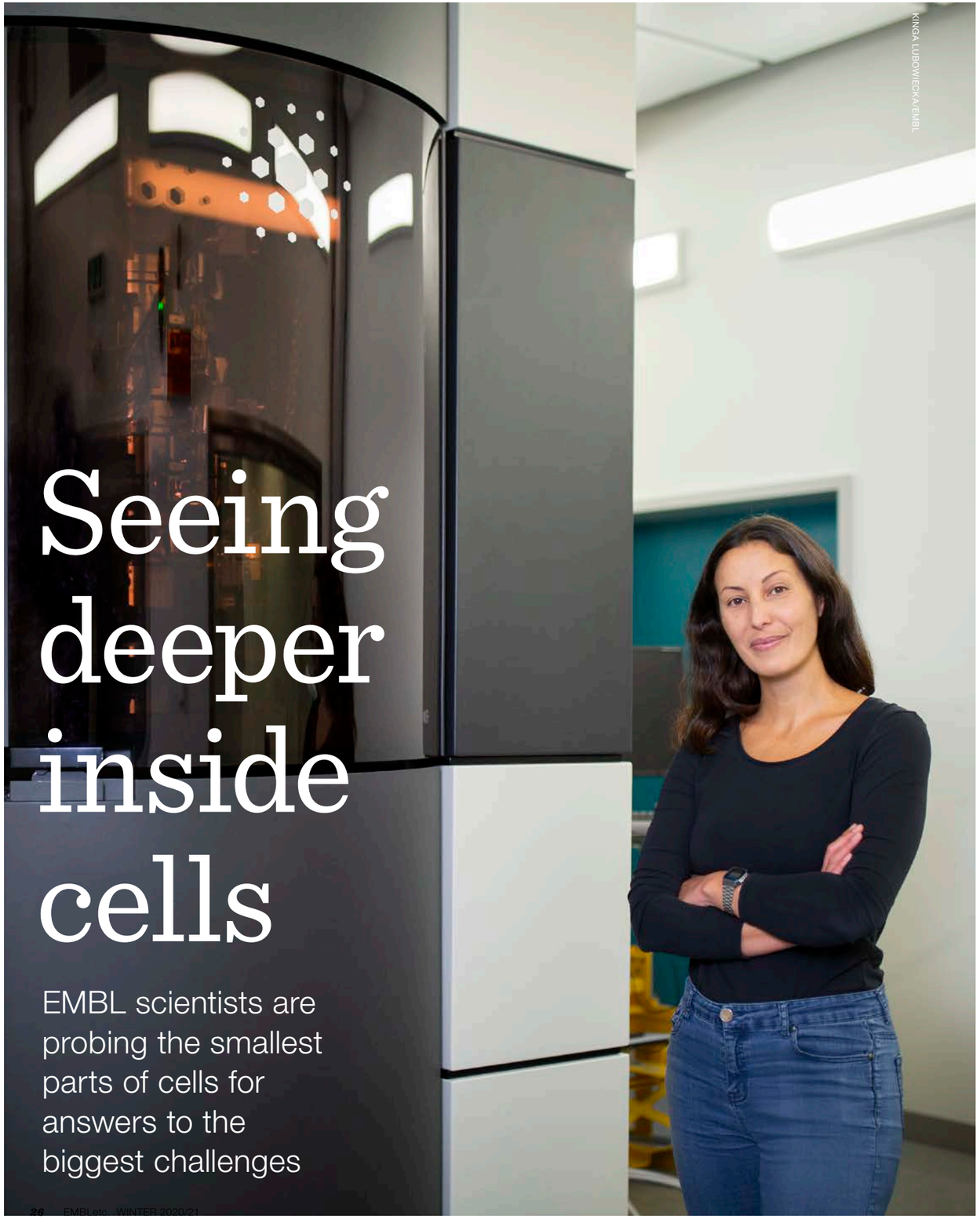
Finding a target

There is a growing quantity of cell biology data demonstrating the importance of the RNA processing pathways for proliferation of trypanosomes. Targeting these pathways with drugs could prevent the parasite from reproducing or – in the best case – could kill the parasite. By determining the structures of the proteins involved in trypanosomal RNA processing, scientists can begin to design drugs that specifically target only the proteins of the parasite and not the corresponding proteins – if they exist – in humans. The more a target differs from the human one, the more likely it is that a drug can work effectively without causing the kind of strong side-effects that are seen in current *Trypanosoma* treatments. "Understanding why the metabolism of this organism is different from ours will then be very useful for applied research to develop efficient drugs and find straightforward therapies," says Eva.

The Kowalinski group use a lab-safe strain of *Trypanosoma brucei* for their research. Fortunately, any results from studies on *Trypanosoma brucei* can be more widely applied to other *Trypanosoma* species and to another genus of parasites called *Leishmania*, which also cause an infectious tropical disease and process their RNAs in a similar way.

Thinking ahead

The impact of climate change on tropical and infectious diseases is hard to predict, but it seems certain that global warming will reshape the regions in which insects transmit infectious diseases. Due to the narrow temperature window that favours the proliferation of insect vectors, zones with a certain disease prevalence will probably move, and the insects might invade new regions that have been previously untouched. "If this happens, it will cause huge problems because the health systems and vector control infrastructure are not prepared for it," says Eva. "The current COVID-19 crisis shows us the importance of fundamental research on infectious diseases. We already need to be thinking ahead to what could be the next global challenges. Rigorous research needs time. Investing in research on diseases that we predict could become more widespread in the coming years is really important, to avoid human catastrophes."



KINGA LUBOWIECKA/EMBL

Seeing deeper inside cells

EMBL scientists are probing the smallest parts of cells for answers to the biggest challenges

EMBL group leader Julia Mahamid uses cryo-electron microscopes like the one pictured here to study molecules in their natural context within the cell.

BY IVY KUPEC

The lab looks like many others. PhD students and postdocs alternate between staring deeply at computer screens and gliding office chairs across the floor to consult with a colleague. There's the concentrated hush of scientists at work. But the quiet belies the energy and excitement that members of the Mahamid group convey as they talk about their work and the technology they're helping to shape.

"Complex biology can be explained by multifaceted but simple interactions, and what this technology provides seems like magic," says Xiaojie Zhang, a postdoc who uses the technology the group is quickly developing and mastering to study stress granules – a type of structure involved in the cell's stress response – in HeLa cells. She laughs. "The reason I get excited is that seeing is believing, and we can potentially see at near atomic resolution how molecules interact, directly in their biological context."

While cryo-electron tomography (cryo-ET) was first envisioned in 1968, the advances the Mahamid group are bringing to this 3D method for studying molecules directly inside cells are new, and are likely to greatly expand its use. A tour through their projects hints at solutions to molecular puzzles and promises a future with innovative automated technology that will change the way biologists think about cells.

"These past few years have been transformative for those of us engaged in cryo-ET," says group leader Julia Mahamid. "We're at the point of pushing what was once thought to be a dream to become a high-throughput method. Two years ago, we didn't think this kind of capability was possible. Now, here we are."

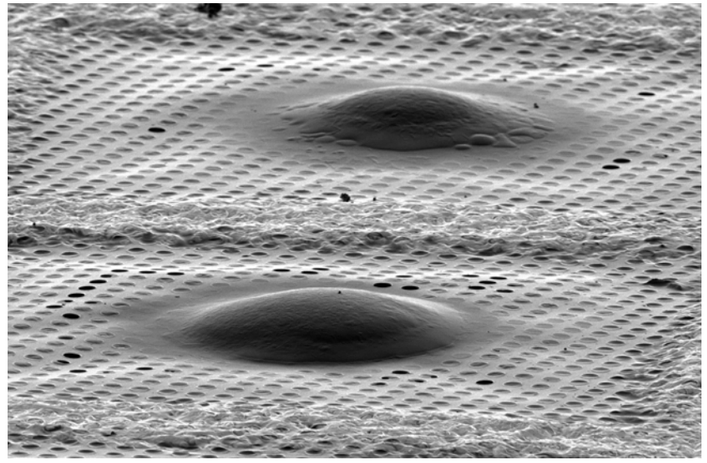
Julia first began working with cryo-ET as a postdoc at the Max Planck Institute of Biochemistry in Martinsried, near Munich. Her mentor was Wolfgang Baumeister, who pioneered key aspects of cellular cryo-ET. Since 2017, Julia has led her own group at EMBL, working with them to further develop and refine this technique.

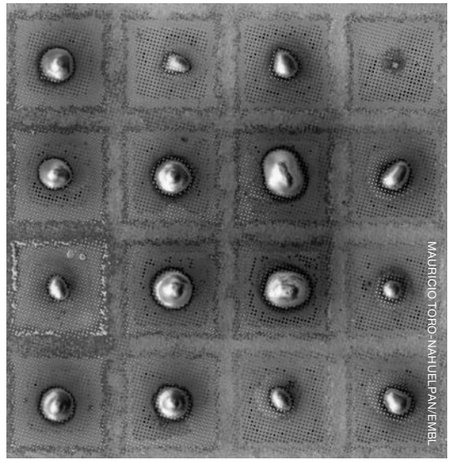
Cryo-ET evolving

Cryo-ET piggybacks onto another state-of-the-art technique, cryo-electron microscopy (cryo-EM), which emerged from the pioneering work of Nobel laureate Jacques Dubochet at EMBL in the 1980s. Cryo-EM involves rapidly freezing samples at very low temperature and imaging them using a beam of electrons. By freezing samples, it's possible to reduce the damage caused by the electron beam, and the rapid freezing process prevents the formation of ice crystals, which would damage and distort the fine structure of molecules.

Scientists can use cryo-EM to study biological structures at the atomic level. It's possible to glimpse structures in high resolution, but this requires scientists to create highly purified samples taken out of their natural context of the cell. The age of cryo-ET seized on technical advances in electron microscopes, detectors, and computational analysis to create something akin to a CT scan for cells. It uses some of the same instruments as cryo-EM, but expands what scientists can see and do.

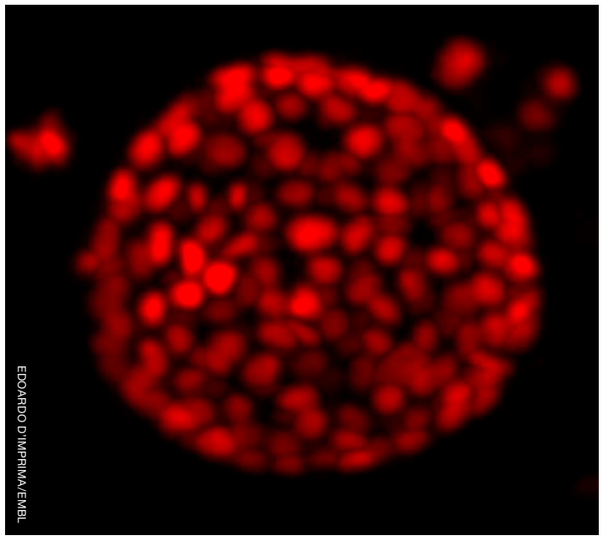
With cryo-ET, scientists can produce 3D snapshots of a cell to observe the activity and interactions of the molecules inside it at the highest resolution. Researchers prepare specimens by growing cells on a thin gold or titanium grid overlaid with a thin film that supports electron microscopy samples. They rapidly freeze the grid and then use a focused ion beam to shave away surplus material bit by bit, producing a thin layer, or lamella, around 200 nanometres (one five-thousandth of a millimetre) thick. A critical factor is that the cells are unperturbed, frozen in time, and the molecules within them are visualised *in situ* – in their natural habitat – having experienced a minimum of interference. >>





MAURICIO TORO-NAHUELPAN/EMBL

Group member Edoardo D'Imprima studies 3D tissue cultures, or organoids. This image is of a primary mammary gland organoid. A fluorescent marker (red) highlights the cells' nuclei.



EDOARDO D'IMPRIMA/EMBL

"At the moment, the skill set required to do cellular cryo-ET is fairly unique, but efforts towards automation will streamline the processes and make it a far more routine, push-button technique," Julia says. "Scientists will be able to spend far more time thinking about experimental design than how to get their samples imaged."

Mauricio Toro-Nahuelpan, a postdoc in the Mahamid group, recalls his work of only three or four years ago when automation was still just a dream and he'd need to be in the lab for 72 hours straight, babysitting his samples so he could manually reposition them to capture the high-resolution imagery.

While samples ultimately need to be about 200 nanometres thick, they might begin around 5,000 nanometres (one two-hundredth of a millimetre) in the case of yeast cells, or even bigger in other samples. Scientists can shave away or 'mill' the sample to achieve the thin lamella. Its thinness allows them to capture high-resolution images inside the cell.

Sara Goetz, a third-year PhD student in the group who uses cryo-ET to study how stressors impact yeast cellular structures and behaviour, helped to automate this process, along with Herman Fung – a shared postdoc with EMBL's Müller group – and Sven Klumpe, a PhD student from the Max Planck Institute of Biochemistry. They created software with a graphical interface that enables scientists to pre-program the thinning process that they'd previously had to do manually. In addition, they worked with Wim Hagen, a senior engineer for EMBL's Cryo-EM Service Platform, to make the imaging highly automated. Now, instead of taking only 12–14 tomograms over a weekend, with the automated system they can get at least 24 tomograms overnight. Additionally, group members can periodically check on the process remotely, and the microscope will email them if it encounters a problem. The scientists have also worked with Irene de Teresa – a shared postdoc with EMBL's Zaugg group – to adapt deep learning techniques, enabling them to further automate data mining to locate molecules in tomograms and therefore in their native environments.

"There are so many technological limitations to this work, but this is no longer one of them," Sara says. "This automation and high throughput mean we can tackle even more complex biological questions."

When cells are placed on the grid used for creating cryo-ET images, they grow randomly across it. For the milling step, however, cells must be positioned at specific locations to be accessible for milling. To help with this issue, Mauricio has led the way in developing a micropatterned grid so cells can selectively grow at specific locations that have a suitable biosubstrate. Micropatterning not only provides a good substrate for culturing cells, but also ensures a surplus of cells available for the milling step, increasing the throughput. Micropatterning, together with the automation of the milling step by Sara and colleagues, is significantly helping to streamline the cryo-EM pipeline for cells.

"Micropatterning also allows us to create complex shapes, such as stars and crosses, on the grid where cells can grow," Mauricio says. "In this way, cells adopt the shape of these patterns, rearranging their internal architecture. We can use these patterns to study cellular mechanical behaviour, expanding the scope of questions that can be addressed by cryo-ET."

Layering techniques for better outcomes

Another group member, Edoardo D'Imprima, is tweaking the cryo-ET process to better pinpoint how, where, and when tumours first arise within a healthy tissue. His work involves organoids: 3D tissue cultures often described as mini organs because, even though they may not look like the organ they represent – mammary glands in the case of Edo's work – they're capable of the same functions.

Organoids are much larger and more complex than yeast cells, HeLa cells, or any other samples studied in the Mahamid group. To have a comprehensive structural understanding of organoids, one single imaging technique is not sufficient. Edo's aim is therefore to develop an integrated pipeline that encompasses four other imaging techniques across different spatial scales – from millimetre-sized to near-atomic details.

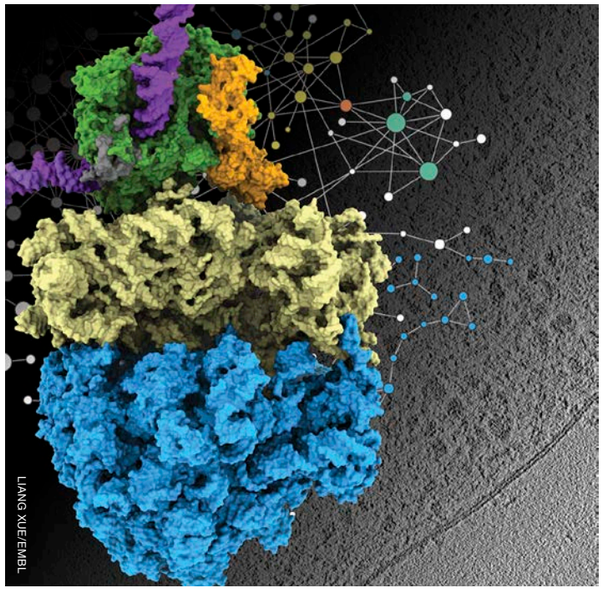
Maintaining a frozen state without sample-distorting formation of ice crystals is a major challenge for Edo in using cryo-ET for his research. To solve this problem, he applies high-pressure freezing, in which a specimen is exposed to liquid nitrogen but at very high pressure (2,000 bar) to slow down ice formation.

"We have to 'trick' physics and use the high-pressure freezing approach," Edo says. "That's the beauty of water – it always gives you a chance to trick physics."

Like Edo, other group members incorporate various observational tools to expand what they can see and learn from cryo-ET. Xiaojie, for example, combines live-cell imaging, cryo-confocal light microscopy, and cryo-ET in her research involving HeLa cells. To observe dynamic cellular structures, she uses genetically modified cell lines that produce fluorescent labels on the key component of the stress granules she is studying. By overlaying images produced by other methods, showing cells under stress at various time points, Xiaojie can more precisely navigate her cryo-ET images. Eventually, high-resolution structural information will help to provide a full perspective on how these dynamic structures assemble and disassemble, when cells respond to and are released from stress.

Earlier this year, Liang Xue, a PhD student in the group, and collaborators published results from a study involving *Mycoplasma pneumoniae* – a bacterium that causes a mild form of pneumonia. The research team combined cryo-electron tomography with cross-linking mass spectrometry and computer modelling to refine their findings, producing the highest-resolution images of cells ever obtained. The scientists were able to confirm that, in bacterial cells, which have no nucleus, the processes of transcription >>

Researchers prepare specimens by growing cells on micropatterned grids overlaid with a thin film that supports electron microscopy samples, such as these HeLa cells, seen here in side view (above left) and from above.



This visual representation shows the newly identified architecture (left) of the molecular machines responsible for transcription (green; DNA in magenta) and translation (blue and yellow), accompanied by the protein interaction network from mass spectrometry (centre) and the cryo-electron tomography data (right) that were used to model the structure.

and translation – which cells use to convert information from DNA to proteins – can be coupled together, with the molecular machinery for these processes in physical contact. This had been a hypothesis for decades, but had never been confirmed. They also learned that the observed molecular activity in its natural context inside cells is different from what had been observed in previous studies outside the cell, further validating the importance of the *in situ* perspective.

"Image processing is a significant challenge. More than large datasets and heavy computation, we need new concepts and new algorithms," Liang says. "It's never easy and perfect, but that's why we do it. With the new methodologies, we hope to lead structural biology into a new era: cellular, physiological, integrative, and systematic."

Tomorrow's cryo-ET

The innovative spirit isn't lost on others outside the group, who look at the methods being refined and see how cryo-ET could expand their own research. In an interview earlier this year about his research on influenza, head of EMBL Grenoble Stephen Cusack explained how the work of the Mahamid group could help him to look directly at one of the flu virus's key enzymes – influenza polymerase – and see it at work inside the nucleus of its host cell.

Many other scientists are excited by the potential of cryo-ET. Universities around the world, Julia explains, are investing in the technology so they too can make new leaps forward in understanding cellular structure and function. Cryo-ET has emerged as the most powerful technique for the structural understanding of biological molecules in their natural context.

"The big advantage of cryo-ET is how it opens up possibilities to discover new things," Julia says. "You aren't labelling one specific thing and only looking at what that thing is doing. Instead, you're looking at everything at once, over a very wide range of spatial resolutions. The discovery potential is enormous."

Julia acknowledges that this can be both a blessing and a curse, as it adds dimensions that bring a new complexity to the research. A scientist may begin with the intention of investigating one area but then encounter unanticipated new questions that challenge their assumptions. "Our current bottleneck is mining our data to get information from the images. Right now, we have 3D images, but we need to somehow convert them into a scientific understanding. This is where the field still needs to develop," she acknowledges.

In the next 10 years, microscopes and detectors will continue to improve, but the computational side is where Julia sees the greatest likelihood for growth. In an era when artificial intelligence is rapidly developing, finding a way to incorporate AI, deep learning, and computer vision into cryo-ET image processing will be important.

"There's a state of mind that develops in working with cryo-ET," Julia says. "Scientists working in this field – like those in my group – are excited about science and don't see limitations. That's true for all method developers: we can't be restricted by what's available. We are problem solvers. If a tool that we need doesn't exist, we have to create it."

Cultures

Alumni

CLARIFICATION: EMBL Archivist Anne-Flore Laloë was credited as an author of the article 'Fallingwater filled with mice', which appeared in Issue 94 of *EMBLetc.* (p. 36), in recognition of the fact that she had carried out the oral history interview on which the text was based. However, we would like to emphasise that Anne-Flore was not involved in editing this text for publication. We apologise for any confusion this may have caused.

EMBL Fellows' Career Service celebrates first birthday

Early-career scientists benefit from growing professional development programme

BY IVY KUPEC

Tobias Wenzel is a biophysicist who knew early on in his EMBL postdoc where he wanted to go and what he wanted to do next. His eyes were on a tenure-track position at a university in Chile where he could expand the research he began at EMBL, leading a group of his own. While he had clear goals, he still needed guidance on the best way to achieve them.

And after Nadezda Volkova, a mathematician, completed her PhD in cancer genomics at EMBL's European Bioinformatics Institute (EMBL-EBI), she decided to move outside academia. In many ways, this job market was uncharted territory. Finding the way to best present herself and identifying appropriate jobs to apply for would be critical to her success.

Tobias and Nadezda ended up finding exactly the help they needed in the same place: the EMBL Fellows' Career Service – now celebrating its first year of supporting both PhD students and postdocs. Led by career advisors Rachel Coulthard-Graf and Patricia Cabezas, this service supports fledgling scientists in identifying the best career fit for them and provides the tools to make that road an easier one.

Providing support to EMBL fellows

As part of the EMBL International Centre for Advanced Training, the programme offers services that range from personalised individual career guidance sessions and job application materials checks to a variety of career workshops and events. Together with the Postdoc Office, Rachel and Patricia also co-organise the EMBL Complementary Scientific Skills Programme, which offers training on non-technical skills required for a scientific career, such as scientific presentation skills and project management.

"We learned that the needs of PhD students are slightly different from those of postdocs," Rachel says. "The postdocs tend to focus specifically on continuing their research and whether to do it within academia or industry. PhD students, on the other hand, seem open to a lot more possibilities for what they might do with their science education."

The COVID effect

Starting a new programme like the EMBL Fellows' Career Service is challenging at any time, but starting one and then recalibrating it for a pandemic presents new, unexpected considerations. For the EMBL Fellows' Career Service, it shifted the focus from in-person encounters to maximising the service's online space. The challenge was to keep the service feeling personalised.

"In some ways COVID had a positive impact," Patricia says. "Beforehand, we had the challenge of how to equally serve all six EMBL sites. Then COVID forced us online, where we could offer regular workshops to serve fellows from all six sites at once, suiting their schedules rather than waiting until the service offered one at their site."

KINGA LUBOWIECKA/EMBL

Career advisors Rachel Coulthard-Graf (left) and Patricia Cabezas run the EMBL Fellows' Career Service.

This year, EMBL's annual Career Day turned into an online webinar series. Despite the change in format, the event attracted at least 300 participants to the webinars, including PhD students and postdocs from outside EMBL.

Looking back, Patricia and Rachel view their first year as one that accelerated their approach for the Career Service. "We had plans to expand our reach in the coming years through virtual outreach," Patricia says. "COVID has forced us to do that now, and our plan is to get even better."

The proof is in the testimonials

This year has been an important one, as a result of COVID and an unusual job market, so use of the service and survey results have provided important insights. Approximately 20% of fellows have attended individual career guidance sessions, with more than 30% returning for follow-up appointments. A survey of participants showed that 100% would recommend the service to a colleague.

"The consultation I had was super helpful because it taught me what language and forms to use to describe my experiences and achievements, and what key phrases a recruiter would look for," Nadezda says. "We initially thought that a position I brought as an example was too high for my experience level, but after two rounds of tailoring my CV I got the courage to apply, and then successfully interviewed and received an offer – a Senior Cancer Analyst position at Genomics England – the position I'm in now."

Tobias, despite heading in a different career direction, shares similar satisfaction. "I was very clear about where I wanted to go and what I wanted to do," he says of his assistant professor position, in which he heads his own lab at Pontificia Universidad Católica de Chile. "A grant-writing workshop from the EMBL Complementary Scientific Skills courses, and several others, plus one-on-one guidance were invaluable, and helped me get familiar with non-technical skills that are all required for the application, as well as to fill out the role I'm now stepping into."

As Patricia and Rachel look to the future, they're also looking back at participant feedback. "We're further ahead in some ways than we expected," Patricia says. "At this point, we assess what is working, what participants are still seeking, and where we can help provide further information and support."

"We had plans to expand our reach...COVID has forced us to do that now"


HORST HAMANN

Phil Avner in his office at EMBL Rome.

Arrivederci Phil!

As he enters retirement, Head of EMBL Rome Phil Avner reflects on his scientific career and memories from his time as Head of EMBL's site in Italy

BY ROSSANA DE LORENZI

The farewell party had been planned for months. It was meant to be in June, when the mild weather and the scent of the flowers would provide the perfect setting for enjoying some good Italian food and homemade beer in the beautiful courtyard at EMBL Rome.

It was being arranged in honour of Phil Avner, retiring after a long career in science and eight years as Head of EMBL Rome. Amid the coronavirus pandemic, however, everything had to be rethought. It took some creativity to organise a proper farewell party via Zoom, but the fancy background set up by Phil's personal assistant Helen Barker – and the affection of the people who attended, including EMBL staff and alumni – succeeded in making it a memorable and emotional event.

Here, Phil reflects on a career at the forefront of developmental biology and epigenetics, marked by changes both in the places he has worked and the scientific questions he has explored.

What have been your main challenges and achievements at EMBL Rome?
When I arrived, my initial preoccupation was to make sure that we more clearly focused our scientific interests, and raised our profile to be considered a fully worthy partner first of all by the rest of EMBL. Over time, as we made recruitments, we have exclusively focused on epigenetics and neurobiology. We then moved towards defining a core of potential partner laboratories interested in what we were doing. This work is very much ongoing, supported by the 'EMBL in Italy' alumni events, with the aim of building confidence with other partners and a platform for interactions over the long term. A major thrust of the 'EMBL in Italy' events has been to move the meetings out of purely academic settings to other settings including biotech companies. Some of our people subsequently have received job offers at these companies because their qualities were recognised, they met people and started to build networks, and that's exactly what we need to encourage, so that our students have the opportunity to continue their careers in varied settings in Italy if they wish to.

"There's so much willingness at EMBL Rome to make things work"

What will you miss most?
The people. There's no doubt. An amazingly warm community. There's so much willingness at EMBL Rome to make things work, and you don't get that everywhere. At EMBL Rome, with 99% of the recruitment we've done, we've managed to recruit people who are competent, willing, and good community members, and that's amazing. I feel blessed by the people I've worked with over the last few years.

Overall I think this is a super interesting and stimulating time for everyone working at EMBL, with the new lines of research that EMBL is developing and promoting, and a new Director General. I know her very well: she was my first postdoctoral student at the Institut Pasteur, and a fantastic scientist.

Tell us more about your career.
In my career, I've always moved and tried to stretch myself with new ideas. I was also very keen on living in Europe. In 1972 I moved to the French National Centre for Scientific Research (CNRS) in Gif-sur-Yvette as a postdoc in the lab of geneticist Piotr Słonimski, a Polish expatriate and a super scientist. It was an amazing time, just after 1968 – I was moving from an English laboratory where we talked about football, football, football, to a French laboratory where almost all they were talking about was politics. This cultural ferment and stimulating environment didn't just remain linked to politics, but spread across the work we were doing.

The lab and I had good publications and Słonimski was an extraordinary person and yeast geneticist, but I had the impression that things were going so well that I could well spend my entire life in front of Petri dishes and yeast, and I wanted to change. I followed the advice of another distinguished scientist – Boris Ephrussi – and I ended up working with François Jacob at the Institut Pasteur, who, at the time, was part of a generation of scientists all working on bacterial systems, who were moving into the field of developmental biology.

My work on X-chromosome inactivation started at the Institut Pasteur and was carried on a little bit in Rome. However, we tried not to stay completely wedded to a single system and started working on human genetics using mouse models. We made some big contributions to the mapping of mouse genes at a time when sequencing was not around. We were interested in applying such data to diseases, and got involved with excellent clinicians to work on type 1 diabetes in the mouse.

I've based my career on a degree of change and flexibility. Each time you change, it's very stimulating. You lose expertise, and you lose some of your contacts – you have to be prepared for that. But it keeps you awake and you meet a lot of very interesting people.

Awards & honours

CAMILLE GOEMANS BY AXEL DEBRY/EMBL; AGNESE LODA BY MASSIMO DEL PRETE/EMBL; JOANNA WANDZIK BY JEAN-CHARLES CASLOT FOR FONDATION L'ORÉAL

Alexander Aulehla, Group Leader and Senior Scientist, and **Paul Flicek**, Associate Director of EMBL-EBI Services, have been elected EMBO Members, in recognition of their research excellence and outstanding achievements in the life sciences.

Alex Bateman, Senior Team Leader – Protein Sequence Resources at EMBL-EBI, has been elected as a Vice-President of the International Society for Computational Biology (ISCB). The ISCB is a scholarly society for advancing understanding of living systems through computation and for communicating scientific advances worldwide.

Camille Goemans, a postdoc in the Typas group, and **Agnese Loda**, a postdoc in the Heard group, have received L'Oréal–UNESCO For Women in Science Fellowships. Their awards, made as part of the German national programme, support doctoral and postdoctoral researchers in the natural sciences who are also mothers. **Camille Goemans** has also received the Eugène Yourassowsky Prize from the Fonds de la Recherche Scientifique, awarded for a doctoral thesis in medical microbiology and infectious diseases.

Edith Heard, EMBL Director General, has been elected a senator of the Max Planck Society, one of Germany's leading scientific research organisations. The Senate is the central decision-making and supervisory body of the Max Planck Society, and aims to bring together experts in a diverse range of fields, including science, business, politics, and the media. **Edith Heard** has also received the German Stem Cell Network (GSCN) 2020 Female Scientist Award for her outstanding achievements in epigenetic and developmental biology research on X-chromosome inactivation.

Andrea Imle, a postdoc in the Diz-Muñoz group, has received an award from the Young Investigator Fund for Innovative Research Ideas, run by the Schering Stiftung and the Fritz Thyssen Foundation, Germany.

Christopher Reinkemeier, a PhD student in the Lemke group, has received the International Birnstiel Award for Doctoral Research in Molecular Life Sciences. The award acknowledges outstanding talent in molecular life sciences and celebrates research successes of young scientists.

Camille Goemans (left), Agnese Loda (centre), and Joanna Wandzik have each received fellowships from the L'Oréal–UNESCO For Women in Science programme.

Yannick Schwab, Team Leader and Head of the Electron Microscopy Core Facility, has received a Mid-Career Scientific Achievement Award from the Royal Microscopical Society, UK, recognising his outstanding scientific achievements in the field of electron microscopy.

Joanna Wandzik, a PhD student in the Cusack group, has been awarded a L'Oréal–UNESCO For Women in Science French Young Talents Fellowship. These awards are made annually to women in science who have shown excellence in their research. **Joanna Wandzik** has also been distinguished with an honourable mention from the International Birnstiel Award committee.

Alumni

Building communities in challenging times

EMBL

We may not have been able to meet in person this year, but the situation we find ourselves in led to a uniquely inclusive online World Alumni Day in July – thank you to everyone who contributed and got involved, from the USA to the UAE!

The occasion enabled former staff to gain an insight into plans for EMBL's new scientific Programme from Director General Edith Heard, and to learn of a new initiative launched in support of EMBL's future directions by EMBL Director Matthias Hentze. Find out what they said on p. 38.
We also shared stories of alumni tackling important environmental challenges (p. 42). More recently, we co-hosted the first ever Advancement Summit for Life Sciences, bringing life science institutes from around Europe together to discuss the power of harnessing alumni communities (p. 40).

We recently launched a new brochure, *How EMBL supports you*, which showcases the range of benefits and resources available to EMBL alumni and the wider life science community. Please do read, download, and share it with colleagues (bit.ly/how-embl-supports-you).

Finally, our alumni event programme continues online, so please do keep checking and registering (bit.ly/embl-alumni-events). It's been lovely to see so many new faces this year, and we hope to meet many more of you in the coming months.

Mehrnoosh Rayner
Head of Alumni Relations

In memory...

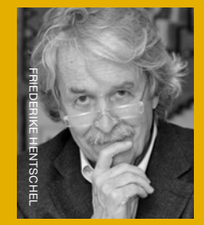
...of colleagues and good friends we have lost in 2020.
Our thoughts are with them and their loved ones.

STEFAN FIEDLER

Viktor Renkwitz
d. 15 February, aged 83
Was: Retired
EMBL: Mechanical Engineer, EMBL Hamburg, 1975–2002

ELIZABETH SZTUL

Kathryn Howell
d. 10 April, aged 80
Was: Professor, University of Colorado School of Medicine, USA
EMBL: Group Leader, Cell Biology and Biophysics Unit, 1981–1988



FRIEDERIKE HENTSCHEL

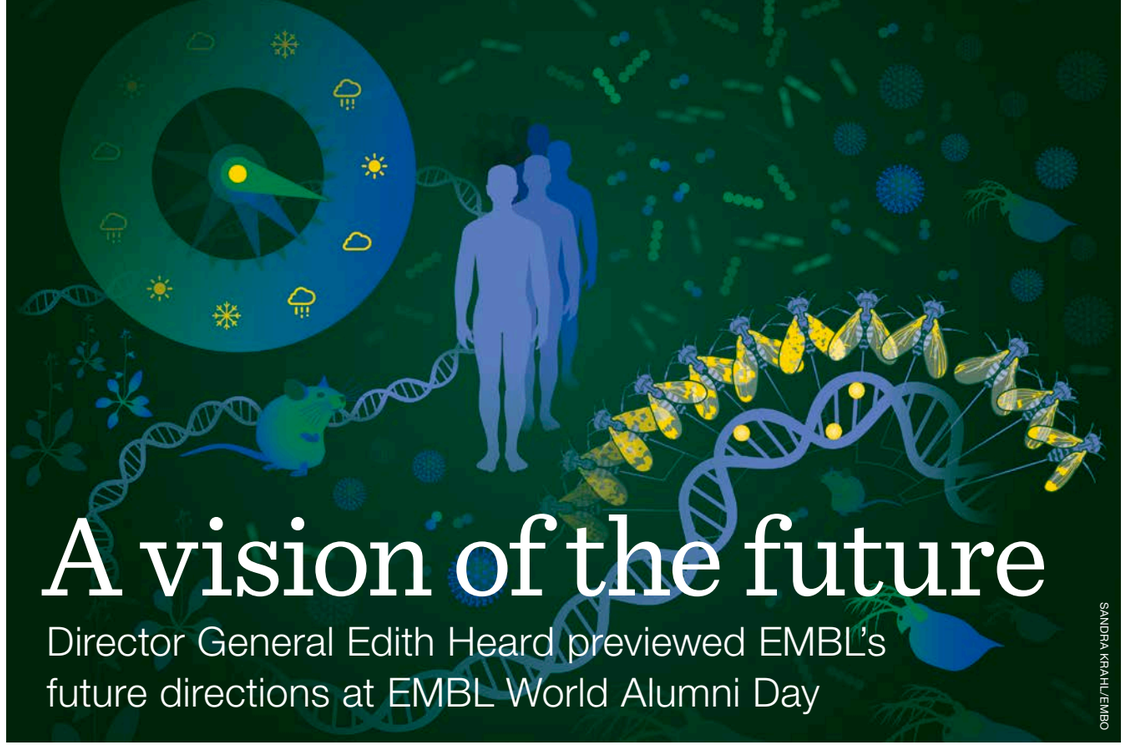
Hermann Bujard
d. 31 July, aged 86
Was: Professor, Heidelberg University, Germany; co-founder of the Center for Molecular Biology of Heidelberg University (ZMBH)
EMBL: EMBO Director, 2007–2009

HANS LEHRACH

Annemarie Frischauf
d. 9 October, aged 73
Was: Professor, University of Salzburg, Austria
EMBL: Group Leader, Cell Biology and Biophysics Unit, 1978–1987

BJARKI JOHANNESSON

Guillem Casanovas
d. 25 October, aged 37
Was: Postdoc, Columbia University, USA
EMBL: PhD student, MMPU and Directors' Research Unit, 2006–2011



SANDRA KRAHL/EMBO

A vision of the future

Director General Edith Heard previewed EMBL's future directions at EMBL World Alumni Day

BY TOM FURNIVAL-ADAMS

EMBL Director General Edith Heard gave alumni around the world an insight into EMBL's future directions as they celebrated EMBL World Alumni Day 2020 in July. Approximately 150 former and current staff members joined the annual event, which this year took place fully online.

During World Alumni Hour, participants also heard from EMBL Director Matthias Hentze as he introduced EMBL's Environmental Research Initiative to the alumni community.

Exploring the molecular basis of life in context

Offering a preview of EMBL's forthcoming five-year Programme, *Molecules to Ecosystems,* which will begin in 2022, Edith explained that EMBL will remain true to its scientific ambition of understanding the molecular basis of life, and will build on this to understand life in the context of its environment. This means proudly maintaining EMBL's tradition of excellence in fundamental research and applying cutting-edge technology and scientific expertise to explore new research questions. Some of these fascinating questions relate to major societal challenges. "EMBL can really rise up to the challenge of understanding at a molecular level how organisms exist in the context of environmental parameters, be that microbes in the human gut or marine organisms in oceans that are constantly adapting and responding to environmental changes," she said.

Edith explained how EMBL's unique technologies, dynamic staff turnover, and interdisciplinary approach make it ideally placed to harness molecular biology to tackle big scientific questions that will advance our knowledge of the molecular basis of life and inform solutions to societal challenges. EMBL will continue to build collaborations across Europe and drive forward impactful life science research.

Molecules to ecosystems

Building on EMBL's existing strengths, the new Programme includes several exciting scientific areas within which life can be explored in a variety of contexts. "This Programme comes at a time when there is a pressing need to understand living systems in the context of environmental change," said Peer Bork, Director of EMBL's Heidelberg Scientific Activities, speaking after the event. "By using EMBL's longstanding expertise in molecular biology and applying powerful experimental, computational, and theoretical approaches, we will gain valuable knowledge about the impact of the environment on living systems, and the impact of organisms on their environment; both will help to inform the response to global challenges like climate change, pollution, or loss of biodiversity."

Key areas to build on will include the study of how molecules, cells, tissues, whole organisms, and populations respond to environmental changes. Researchers will also seek to elucidate some of the molecular mechanisms that underlie the way microbes, algae, plants, and animals on Earth respond to such changes. EMBL will advance current research to understand microbes, their functions, and their interactions in various communities. Infection biology, from both the host and pathogen perspective, will also feature prominently. The effect of the environment on humans, both at the individual and population level, will be another important area of focus.

Edith praised EMBL's existing and growing expertise in data science, which will be key to the organisation's future success. EMBL's experimental and data services, training and innovation will also be core components of the new Programme.

Building bridges from molecular biology

Collaboration was central to the development of the Programme, and will continue to be important in the future. "It's about building bridges from molecular biology and bringing together people from different areas to work with us," said Edith, "from epidemiologists and ecologists to mathematicians and theoreticians."

To support this, EMBL hopes to further its engagement activities, create new sabbatical programmes, and launch new initiatives with young scientists, including a visitor programme, summer schools, and other training opportunities. Training activities at EMBL will support a new generation of researchers looking to apply molecular technologies and approaches to explore life in the context of the environment.

Edith also highlighted the key role that former staff will play as ambassadors. "Alumni are an important part of EMBL because you represent where we came from and where we'll be going to," she said.

The Environmental Research Initiative

Following Edith's talk, EMBL Director Matthias Hentze introduced the Environmental Research Initiative (ERI) to the alumni community. The ERI aims to support EMBL's future directions and enable creative new research across all EMBL sites to tackle some of the biggest environmental challenges.

By harnessing the power of EMBL's cutting-edge technologies and world-class infrastructure, interdisciplinary collaborative scientific culture, proven research mentorship capabilities, and global strategic partnerships, ERI will empower top research scientists to deepen our understanding of the fundamental principles of the environmental challenges we face, paving the way for innovative, impactful, and sustainable solutions.

If fundraising efforts are successful, ERI will complement five-year funding from EMBL's member states. "ERI, drawing on everything that EMBL has and will develop, is a synergistic opportunity for the EMBL community to contribute to something that is urgently needed," said Matthias. ERI is currently undergoing strategic planning and its roadmap includes three phases: a catalyst project (which will be supported by seed funding from donations this year), a pilot phase, and – if proven successful – a third phase, during which new groups funded by donations to ERI will become part of EMBL's research activities, provided that ERI's fundraising efforts succeed.

Highlighting the important role that alumni will play in making ERI a success, Matthias said: "We are looking for a network that identifies with the idea and that wants to contribute its own ideas and connections."

The next EMBL World Alumni Day will take place on 16 July 2021 – please mark your diary.

WATCH THE TALKS BY EDITH AND MATTHIAS AND THE EMBL ALUMNI AWARDS CEREMONY:
bit.ly/embletc-96-wad2020

FORTHCOMING ALUMNI EVENTS, INCLUDING MONTHLY COFFEE WITH EMBL:
bit.ly/embl-alumni-events

Boosting the life sciences through alumni networks

EMBL is supporting other life science institutes in establishing alumni relations and nurturing their own networks

BY EDWARD PRIOR

Although many life science institutes have begun to engage their alumni in recent years, many more are not yet aware of the potential of investing in their alumni communities. The common goal that unites current and former staff puts life science institutes in a stronger position than many universities or large organisations when it comes to building mutually beneficial networks to aid scientific progress. Alumni also play a crucial role as ambassadors for their former institutions, raising their profiles through highlighting impact and fostering collaboration.

To share its experience and explore new opportunities, EMBL has partnered with CASE, the Council for Advancement and Support of Education. CASE are global leaders in the field of advancement (alumni relations, communications, and fundraising). From 8–9 October, EMBL and CASE organised the first summit specifically supporting advancement professionals working in life science institutes.

The summit marked the beginning of a dialogue between colleagues working for various organisations, who were enthusiastic about learning from each other and working together as they build their advancement programmes. In a question-and-answer session the evening before the summit, topics of particular interest to participants included gaining support from senior leadership, starting an alumni engagement programme and establishing a roadmap for its development, effectively building alumni relations online during the coronavirus pandemic, and exploring some of the unique aspects of working in advancement at a life science institute rather than a university.

The summit was chaired by EMBL Director Matthias Hentze and by Bruce Bernstein, Executive Director, Global Engagement at CASE Europe. Sessions were moderated by EMBL staff or other experts and explored ways to deal with the challenges of coordinating alumni networks from a leader's perspective, as well as how alumni relations, communications, and fundraising can best help to support institutional goals.

Based on feedback from partners and participants, the summit will become an annual event and will be supplemented by additional workshops. While this inaugural summit had a focus on alumni relations, future summits will focus on all advancement fields in support of life science institutes.

New perspectives

EMBL alumna Erin Tranfield discusses her new role on the Alumni Association Board, and the personal challenge of recovering from a life-changing event

IVO TELLEY

Erin Tranfield recently joined the EMBL Alumni Association Board as one of 15 newly elected members.

BY MARIUS BRUER

Members of the EMBL Alumni Association Board serve as ambassadors for EMBL across its six sites. They develop the Alumni Association's initiatives, helping EMBL to fulfil its missions and maintain lifelong connections with its alumni community. Erin Tranfield recently joined the board as one of 15 newly elected members.

In 2017, you had a serious accident – how did this change your outlook on life and work?

I think it's been a humanising process. I fell from a horse and crushed three vertebrae in my spine, spent 40 days in hospital and four months in rehab, and then it took me another year to get back to full-time work. I basically had to learn how to walk again, and I still suffer some paralysis. An experience like this reminds you of what's important in life. I also have to approach work in a different way now. Some days are inexplicably bad, while others are almost normal, and I'm trying to navigate my way through with as much patience and compassion as possible towards myself and towards others.

How do you approach your new role on the board?

Most of the board members are new – we're still dating, getting to know each other and everyone's background and experience. As we go ahead, we'll learn how EMBL can benefit from our input, how we can support what already exists, and I think there will be opportunities for new initiatives as well. But I'm a fan of doing only a few things at a time. I'm hoping we can pick a few excellent projects first, and once we get those running, we can pick a few more.

What impact do you hope your work for the board will have?

I think the board faces the challenge of making sure that people realise the opportunities that being an active member of the community brings. I think we can support this by advocating for the value of the Alumni Association, encouraging participation, and fostering collaboration. If, at the end of my four years on the board, the alumni community is a little bit more tight-knit and a little more connected, that would be a success.

Working for a healthier world

We're proud to showcase EMBL alumni whose work is helping to solve current environmental challenges such as pollution, malnutrition, the energy crisis, climate change, and loss of biodiversity. If you're an EMBL alumna or alumnus carrying out environmental research, please let us know by contacting alumni@embl.org.

FURTHER STORIES ONLINE:
bit.ly/embletc-96-challenges


UNIVERSITY OF CAMBRIDGE

Paul Dupree

Professor in Biochemistry, University of Cambridge, UK; Postdoc, EMBL Heidelberg, 1991–1993

"I am a plant biochemist and cell biologist, and work on the enzyme machines that make polysaccharides, and how these polysaccharide structures provide remarkable properties to plant cell walls and materials made from them. This has impact in four areas. First, pollution: we work on replacing plastics with biocompostible materials. Second, malnutrition: we work on improving dietary fibre and reducing sugar in food. Third, the energy crisis: the sugars in the polysaccharides can be fermented to transport fuels or biogas. And fourth, climate change: we work on understanding and improving wood and timber for building construction, to reduce steel and concrete use and to lock up CO_2 in buildings."


TOMASZ JOSCHY/ VCU UNIVERSITY MARKETING

Peter Uetz

Associate Professor, Virginia Commonwealth University, USA; PhD student, EMBL Heidelberg, 1993–1997

"I started the EMBL Reptile Database, alongside Thure Etzold and Ramu Chenna, when I was at EMBL. At the time it was a small side project, but after nearly 25 years of continuous operation it's taking much of my time now. The Reptile Database provides data for more than 11,000 reptile species (more species than birds) and the reptile taxonomy for projects such as the IUCN Red List of Endangered Species and the Catalogue of Life, but also data for the National Center for Biotechnology Information (NCBI) taxonomy and many others."


BASF

Andrea Herold

Head of Microbiology – White Biotechnology Research, BASF, Germany; PhD student, EMBL Heidelberg, 1999–2003

"Our research department is developing sustainable innovations for the chemical industry. Examples are chemicals based on renewables and produced by microbial fermentation (instead of petroleum-based chemistry) or biologicals (microorganisms) and natural-compound-based actives for agricultural use."


OANA STROE/EMBL

Lara Urban

Alexander von Humboldt Research Fellow, University of Otago, New Zealand; PhD student, EMBL-EBI, 2015–2019

"During my PhD at EMBL-EBI and the University of Cambridge, I applied and developed methodology in the fields of statistical cancer genomics and single-cell genetics. I now combine this expertise in genomics with my background in applied and theoretical ecology to investigate how these approaches can be leveraged together with established population and evolutionary genomics approaches to inform the fledgling field of conservation genomics. My research concentrates on two critically endangered avian species endemic to New Zealand, the takahē and the kākāpō, which were considered extinct. Some exciting initial results are currently allowing us to adjust their management according to individual infectious disease susceptibility. I am also co-founder and -organiser of the UK-based organisation PuntSeq, which employs real-time nanopore sequencing for freshwater monitoring."

Facing challenges together

With the generous support of its donors, EMBL can face societal challenges and seize new opportunities in the life sciences

BY JOANA WITKOWSKI,
EMBL HEAD OF RESOURCE DEVELOPMENT

These are challenging times – and EMBL is keen to contribute to finding solutions. We know that partnering can often lead to greater impact, and we work together with numerous other research institutions and business partners.

We're also proud that we can count on many individuals, foundations, and companies that give their time, as well as generous support in the form of donations and as members of the EMBL Advanced Training Centre Corporate Partnership Programme. Working together in this way helps to turn opportunities into potential solutions for pressing societal challenges.

These efforts include giving researchers access to the most advanced microscopy technologies, developing young talent, fostering transatlantic scientific exchange, kindling interest in and deepening understanding of life science research, and bridging the gap between current research and science taught in schools.


MASSIMO DEL PRETE/EMBL

Attendees of the Business Friends of EMBL Brunch in March 2019.

In addition to the recent supporters listed below, we would like to thank those who wish to remain anonymous, and the many more who have partnered with us through the years.

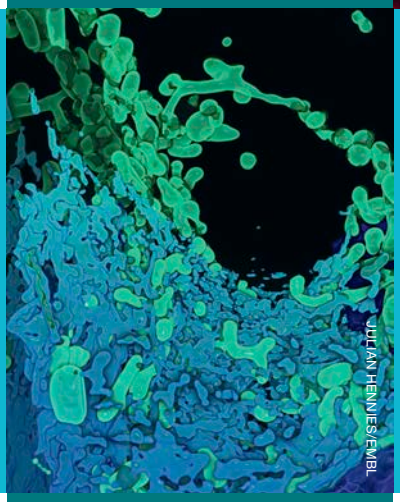
- 10x Genomics
- abcdruck GmbH
- Becton Dickinson GmbH
- Bio-Rad Laboratories
- Boehringer Ingelheim
- Boehringer Ingelheim Stiftung
- Dr. Alexandra Budde & Dr. Florian Budde
- Cellzome, a GSK company
- Dieter Schwarz Stiftung
- Dr. Helga Drews & Dr. Jürgen Drews
- Eppendorf AG
- Dr. John Feldmann
- Dr. Manfred Fuchs
- Sabine Gora & Alexander Gora
- HeidelbergCement Group
- Dr. Sabine Hentze & Prof. Dr. Matthias Hentze
- Intermedex GmbH
- Bank Julius Bär Deutschland AG
- Renate Junge & Michael Junge
- Monika Marlene Kley & Max Dietrich Kley
- Dr. Martina Kulozik & Prof. Dr. Andreas Kulozik
- Dr. h.c. Manfred Lautenschläger & Angelika Lautenschläger
- Leica Microsystems
- Barbara Mancini & Dr. Benedikt Mancini
- Manfred Lautenschläger-Stiftung
- Merck
- Miltenyi Biotec
- NetApp
- New England BioLabs GmbH
- Nikon Instruments Europe BV
- Olympus
- Promega Corporation
- ProMinent GmbH
- Roche Diagnostics Deutschland GmbH
- Dr. Hedwig Runnebaum & Prof. Dr. Dr. Benno Runnebaum
- Sanofi-Aventis Deutschland GmbH
- Sartorius
- Dr. Kornelie Schütz-Scheifele & Dr. Bernd Scheifele
- Dr. Manfred Schüßler
- SNP Schneider-Neureither & Partner AG
- Sparkasse Heidelberg
- Stilla Technologies
- Thermo Fisher Scientific
- Wolf Liegenschaften GbR
- Zukunft Metropolregion Rhein-Neckar e.V.

Events

January
11–15
Virtual
EMBO Practical Course:
Drosophila Genetics and
Genomics


MALTE PAULSEN/EMBL

February
8–12
Virtual
EMBL Course:
Deep Learning
for Image Analysis


JULIAN HENNES/EMBL

February
15–19
Virtual
EMBL Course:
Next Generation Sequencing
Bioinformatics

February
22–26
Virtual
EMBL Course:
Introduction to Multiomics
Data Integration and
Visualisation

March
2–3
Virtual
EMBO | EMBL Symposium:
Life at the Periphery:
Mechanobiology
of the Cell Surface

March
17–19
Virtual
EMBO | EMBL Symposium:
Synthetic Morphogenesis:
From Gene Circuits
to Tissue Architecture


ANNEK STOKKERMANS/EMBL

March
24–26
Virtual
EMBL Conference:
Visualizing Biological Data
(VIZBI 2021)

Upcoming meetings
Alumni

19 March
Virtual: EMBL Retirees' Afternoon

3 May
EMBL in the UK, University of Dundee

20–21 May
EMBL in Italy, IIT, Genoa

16 July
EMBL World Alumni Day, virtual and EMBL Heidelberg

Virtual: Coffee with EMBL
11 December

bit.ly/embletc-96-cwe

VIEW THE COMPLETE LIST OF EVENTS ONLINE:
embl.org/events