The European Molecular Biology Laboratory Magazine

Issue 97 Summer 2021

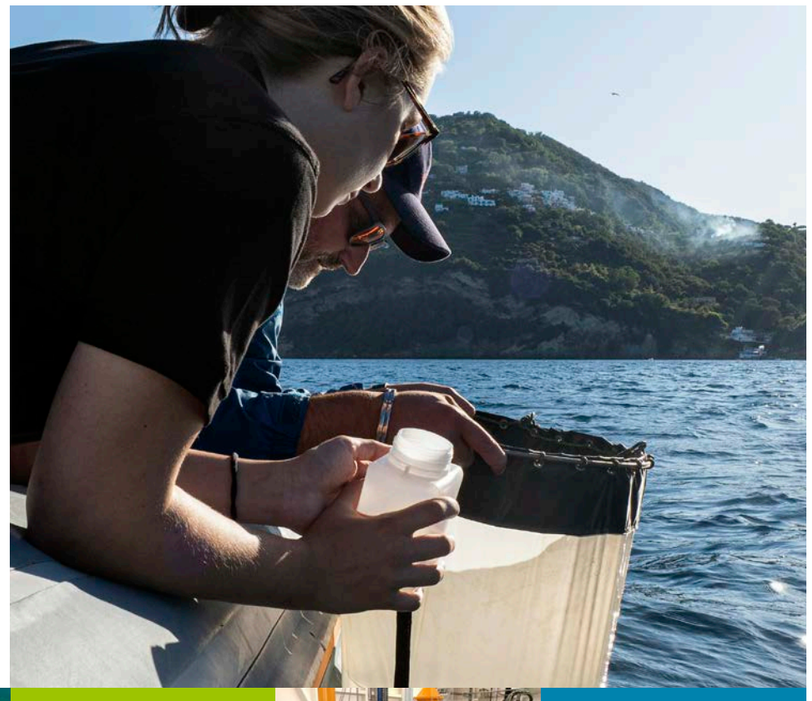
EMBL etc.

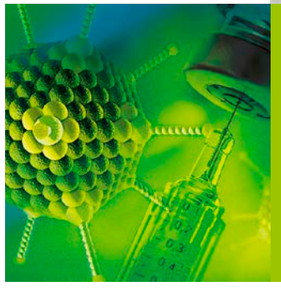
Communities

Contents

Nucleus

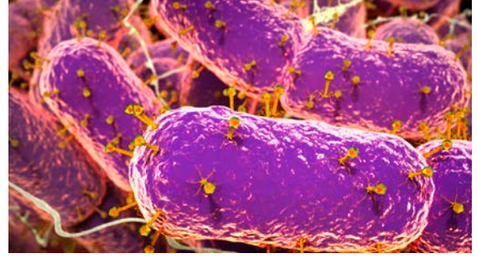
Feature stories





Synapse

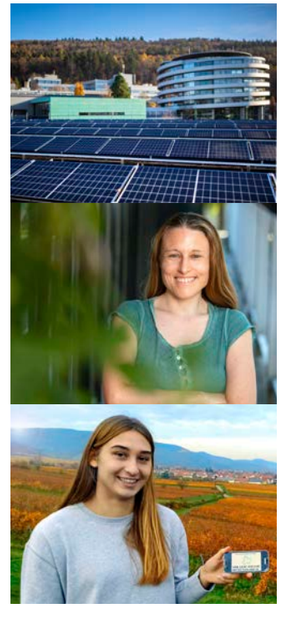
News stories



Cultures

EMBL community stories

Alumni



MASSIMO DEL PRETE/EMBL

Editorial

In all parts of our lives, communities can offer us support, provide a space for learning and sharing knowledge, and enable us to achieve things we could not do alone. Communities of scientists play a vital role in the research process, and this has been particularly evident in the global response to the COVID-19 pandemic, which has relied on rapid sharing of data and results between research groups and across borders. EMBL's coronavirus research projects, some of which we report on in this issue (pp. 5–7), exemplify this collaborative approach. We also report on work by EMBL alumni that shows how research communities build on each other's results over time, applying discoveries from previous decades to solve current challenges – in this case, the need to develop COVID-19 vaccines (p. 22).

Communities of scientists will be at the heart of EMBL's future research on the theme of Planetary Biology (p. 16), which will bring together experts in a wide range of disciplines, including molecular biology, ecology, epidemiology, chemistry, physics, engineering, and data science. The aim of this research is to understand at the molecular level how communities of organisms interact with one another and with their environment in the context of ecosystems. We also report on EMBL research that has provided insights into the microbial ecosystems at work in kefir and elsewhere (p. 8).

EMBL's research on Planetary Biology, like progress in so many areas of science, depends on technological advances that have expanded what scientists can do. Florent Cipriani, recently retired as Head of the Instrumentation Team at EMBL Grenoble, has developed innovative technologies in structural biology that have benefited the scientific community worldwide (p. 26). The close collaboration between communities of researchers and technology developers that Florent enjoyed at EMBL was crucial for the rapid development and validation of these technologies.

Support from the various communities in our lives has been more important than ever during the past year. In the coming months, I hope we can renew more of these connections – and make new ones – in person, as we continue to help and support each other, and build communities that enable us all to thrive.

Edward Dadswell
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Publisher
European Molecular Biology Laboratory

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ColorDruck Solutions

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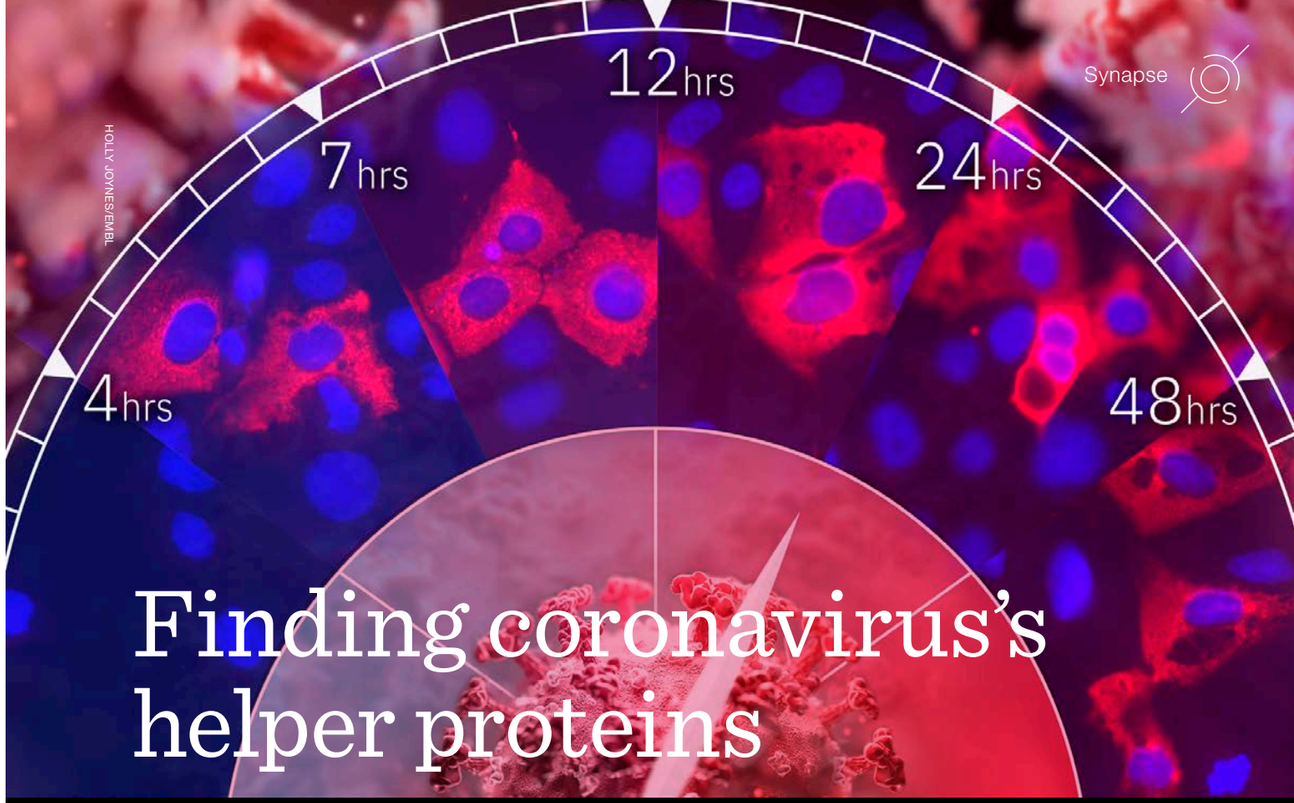
embl.org/news



HOLLY JOYNES/EMBL

Finding coronavirus's helper proteins

EMBL scientists identify human proteins hijacked by SARS-CoV-2, offering potential drug targets

BY MARIUS BRUER

A group of scientists led by EMBL's Mikhail Savitski, Nassos Typas, and Pedro Beltrao, and collaborator Steeve Boulant at Heidelberg University Hospital, have analysed how SARS-CoV-2 affects proteins in human cells. They identified several human proteins as potential drug targets to prevent viral replication.

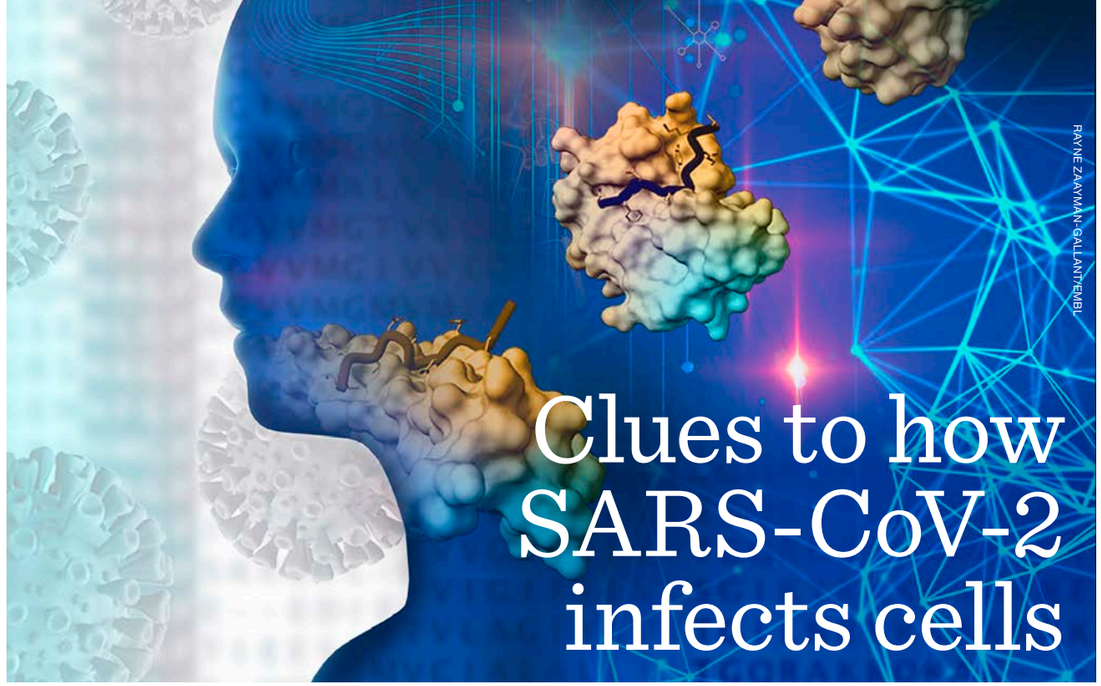
The researchers used a biophysical method called thermal proteome profiling (TPP) to gain a comprehensive overview of which human proteins are functionally altered during SARS-CoV-2 infection. TPP monitors protein amounts and denaturation temperatures – the points at which proteins heat up so much that they lose their 3D structure. A shift in denaturation temperature indicates that a particular protein has undergone a functional change upon infection, possibly due to the virus hijacking the protein for use in its own replication.

The scientists observed that infection with SARS-CoV-2 changed the abundance and thermal stability of hundreds of cellular proteins. This included thermal stability changes in proteins required to maintain the cytoskeleton – a protein network that maintains cell shape and stability – and a group of proteins called heat shock chaperones: proteins that take care of unfolded or misfolded proteins and help them to maintain their 3D structure.

Having identified candidate proteins and cellular processes that SARS-CoV-2 may hijack to promote its replication, the scientists used drugs to inhibit some of the host proteins that SARS-CoV-2 appeared to be exploiting. This resulted in a strong reduction in viral replication in the presence of two of the tested compounds, demonstrating their potential as antiviral therapeutics. The scientists believe that other proteins they identified could be targeted in a similar way to block SARS-CoV-2 proliferation.

As well as gaining new insights into SARS-CoV-2 biology, the researchers were able to expand the scope of the TPP methodology by adapting it to work with infectious samples under high biosafety conditions. This enables them to quickly analyse the effects of dangerous pathogens on the cell's proteins.

Selkrig J, Stanifer M, Mateus A, Mitosch K, Barrio-Hernandez I, Rettel M *et al. Molecular Systems Biology*, 16 February 2021. DOI: 10.15252/msb.202010188



Clues to how SARS-CoV-2 infects cells

EMBL researchers have identified sequences in human proteins that might be used by SARS-CoV-2 to infect cells

BY DOROTA BADOWSKA

In the early days of the COVID-19 pandemic, it was established that SARS-CoV-2 infects cells by binding to the human protein ACE2, which plays a role in regulating blood pressure. But ACE2 is almost absent in human lung cells, so how can the lungs be one of the most affected organs in COVID-19? This gave researchers a hint that ACE2 might be more than just a blood pressure regulator, and might not be the only player in the SARS-CoV-2 infection mechanism.

EMBL's Gibson Team and collaborators analysed sequences of ACE2 and other human proteins involved in SARS-CoV-2 infection, such as a class of proteins called integrins. They focused on short strings of amino acids called short linear motifs (SLiMs), which are involved in transmitting information between the inside and outside of cells. Quick identification and comparison of SLiMs was possible thanks to the Eukaryotic Linear Motif (ELM) resource, the largest curated SLiMs database, which the team and collaborators have been developing for 20 years.

They saw that ACE2 and several integrins contain SLiMs that are probably involved in endocytosis and autophagy – cellular processes of uptake and disposal of substances, respectively. This result suggests previously unknown roles of ACE2 and integrins in cell physiology.

Potential drugs for COVID-19

The findings might lead to new therapeutic approaches for treating COVID-19. The team gathered a list of existing drugs that interfere with endocytosis and autophagy. The list includes some surprising candidates, such as the antipsychotic chlorpromazine. "If clinical trials prove some of these drugs to work against COVID-19, this could be a game changer," says Manjeet Kumar, a bioinformatics scientist in the Gibson Team and a senior author in the study.

Working on SARS-CoV-2 research was an inspiring experience. "We wanted to contribute to combating COVID-19. This gave us a common aim," says Team Leader Toby Gibson. Bálint Mészáros, a postdoc in the Gibson Team and first author of the study, agrees. "It's strange, thrilling, and a bit unsettling breaking new ground in the COVID-19 field," he says. "As researchers we're enthusiastic about figuring out bits of the biology, but at the same time we're thoroughly excited to work on such an important topic."

Mészáros B et al. Science Signaling, 12 January 2021. DOI: 10.1126/scisignal.abd0334

Kliche J *et al. Science Signaling*, 12 January 2021. DOI: 10.1126/scisignal.abf1117

EMBL facilities support development of RNA vaccines

BioNTech and Johannes Gutenberg University Mainz conduct collaborative research with EMBL scientists at Hamburg beamline

BY DOROTA BADOWSKA

BioNTech, the biotechnology company that together with Pfizer presented the first positive results for a COVID-19 vaccine, used one of EMBL Hamburg's facilities at DESY's PETRA III X-ray source for their research on vaccine development.

The vaccine candidates from BioNTech and Pfizer belong to a new class of vaccines that use messenger RNA (mRNA). To safely deliver mRNA into cells, scientists must package it into tiny particles, known as nanoparticles. To analyse the molecular structure of nanoparticles carrying mRNA, BioNTech used EMBL Hamburg's beamline P12, dedicated to small-angle X-ray scattering. This enabled BioNTech to study the structure, efficiency, and behaviour of nanoparticles made of lipids, or a combination of lipids and biopolymers, under different conditions.

Although the mRNA-based technology is very new and its long-term efficacy still needs to be tested, it has great potential to enable rapid development of vaccines and treatments for various diseases in future. This work also shows the importance of collaboration between industry and research facilities such as those at EMBL, to drive progress and innovation in technology and medicine.

Siewert CD *et al. Cells*, 5 September 2020. DOI: 10.3390/cells9092034

Nogueira SS *et al. ACS Applied Nano Materials*, 25 September 2020. DOI: 10.1021/acsanm.0c01834

Uebbing L *et al. Langmuir*, 27 October 2020. DOI: 10.1021/acs.langmuir.0c02446

Replication cycle of SARS-CoV-2 in 3D

Learning how SARS-CoV-2 hijacks host cell machineries will help in developing therapeutic strategies

BY MATHIAS JÄGER

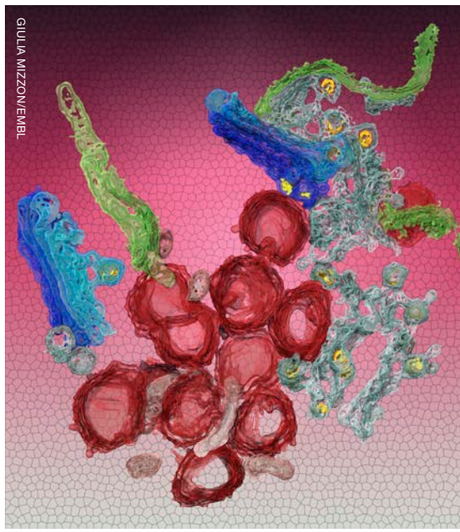
Researchers at Heidelberg University Hospital, assisted by EMBL's Schwab Team and Electron Microscopy Core Facility, have performed a detailed imaging analysis to identify the morphological changes that occur within a cell following SARS-CoV-2 infection.

Their images revealed an obvious and massive change in the endomembrane systems of the infected cells – a system that enables the cell to define different compartments and sites. The virus induces membrane changes in such a way that it can produce its own replication compartments where the viral genome is amplified enormously.

Understanding the mechanism by which SARS-CoV-2 infection leads to the death of infected cells will foster the development of therapies to reduce virus replication and disease severity.

The team has shared all the data they produced with the scientific community. This will support the global effort to study how SARS-CoV-2 interacts with its host, and will hopefully aid the development of antiviral drugs.

Cortese M *et al. Cell Host Microbe*, 17 November 2020. DOI: 10.1016/j.chom.2020.11.003



A 3D rendering of organelles visualised in a tomogram of SARS-CoV-2-infected cells.

In kefir, microbial teamwork makes the dream work

Cooperation among bacterial species allows them to thrive as a community

BY IVY KUPEC

The Patil Group at EMBL and the University of Cambridge have studied kefir, one of the world's oldest fermented food products. After studying 15 kefir samples, the researchers discovered that the dominant species of *Lactobacillus* bacteria found in kefir grains cannot survive on their own in milk: a key ingredient in kefir. However, when the species work together – feeding on each other's metabolites in the kefir culture – they each provide something the other needs. This shows how interspecies interactions can lead to stable coexistence.

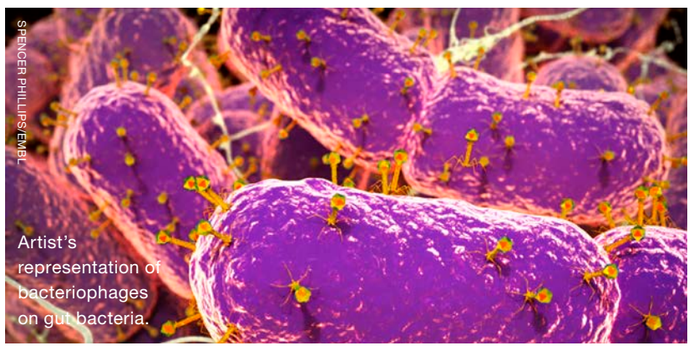
In another paper from the Patil Group, in collaboration with EMBL's Bork Group, scientists combined data from thousands of microbial communities across the globe – from soil to the human gut. They showed that groups of bacteria frequently found together are usually either highly competitive or highly cooperative. They also found that competitive communities can better resist the invasion of new species but not changes in nutrients; conversely, cooperative communities are susceptible to invaders but resilient to nutrient change. This polarisation in community types is a new finding, and sheds light on the evolutionary processes that shape microbial ecosystems.

Blasche S, Kim Y *et al. Nature Microbiology*, 4 January 2021. DOI: 10.1038/S41564-020-00816-5

Machado D *et al. Nature Ecology & Evolution*, 4 January 2021. DOI: 10.1038/s41559-020-01353-4

The thousands of viruses in your gut

Study opens up new avenues for understanding how viruses in the gut affect human health



SPENCER PHILLIPS/EMBL

Artist's representation of bacteriophages on gut bacteria.

BY OANA STROE

Using a DNA-sequencing method called metagenomics, researchers at the Wellcome Sanger Institute and EMBL's European Bioinformatics Institute (EMBL-EBI) have identified more than 140,000 viral species in the human gut. They analysed more than 28,000 gut microbiome samples collected in different parts of the world. The researchers were surprised by the number and diversity of the viruses they found.

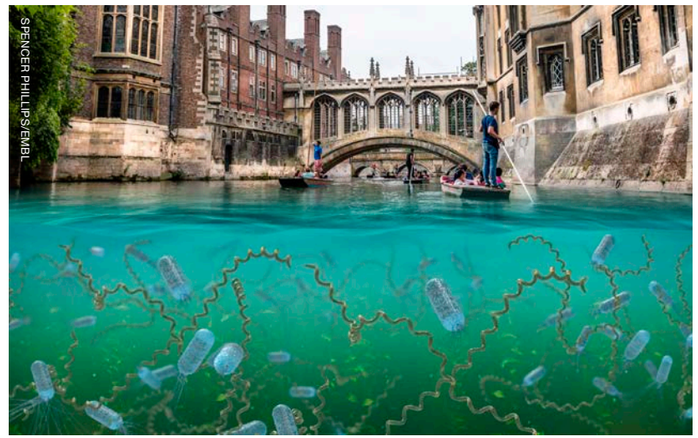
Among the tens of thousands of viruses discovered, a new highly prevalent clade – a group of viruses believed to have a common ancestor – was identified, which the authors refer to as the Gubaphage. This was found to be the second most prevalent virus clade in the human gut, after the crAssphage, which was discovered in 2014. Both of these viruses seem to infect similar types of human gut bacteria, but without further research it's very difficult to know the exact functions of the newly discovered Gubaphage.

The metagenomics analysis was carried out in the Finn Group at EMBL-EBI, and EMBL-EBI's Gut Phage Database hosts the study data.

Camarillo-Guerrero LF *et al. Cell*, 18 February 2021. DOI: 10.1016/j.cell.2021.01.029

Monitoring dangerous bacteria in freshwater

Researchers identify several potentially harmful species in Cambridge's River Cam



SPENCER PHILLIPS/EMBL

BY OANA STROE

Researchers from EMBL's European Bioinformatics Institute (EMBL-EBI) and the University of Cambridge have shown that portable DNA sequencing can easily be used to monitor bacterial species in a river ecosystem. They used a smartphone-sized DNA sequencing device to monitor water samples taken from nine locations on the river Cam.

The researchers found that potentially harmful and wastewater-related bacteria strongly increased downstream of the most urbanised river sections. One example is *Pseudomonas aeruginosa*, a bacterium that can cause disease in plants and animals, including humans, varying from pneumonia to sepsis syndromes. The study, called PuntSeq, also identified the well-known *Leptospira* bacterium, which can cause the life-threatening disease leptospirosis. However, the *Leptospira* species found on this occasion were probably not pathogenic.

The method used in this study – called environmental metagenomics – can identify the DNA of the many bacteria present in a sample of river water. In recent years, devices for mobile DNA analysis have made environmental metagenomics more accessible, allowing real-time sequencing.

Urban L, Holzer A *et al. eLife*, 19 January 2021. DOI: 10.7554/eLife.61504

Toadlet peptide transforms into a deadly weapon

Antimicrobial peptide from Australian toadlet could inspire new applications

BY DOROTA BADOWSKA

Researchers at the Technion – Israel Institute of Technology and EMBL Hamburg have solved the 3D molecular structure of a peptide named uperin 3.5, which is secreted on the skin of the Australian toadlet *Uperoleia mjobergii*. They found that the peptide self-assembles into a unique fibrous structure, which can change its form in the presence of bacteria to protect the toadlet from infection.

The antibacterial fibrils on the toadlet's skin have a structure that is reminiscent of amyloid fibrils, which are a hallmark of neurodegenerative diseases, such as Alzheimer's or Parkinson's. Although amyloid fibrils have been considered pathogenic for decades, it's recently been discovered that certain amyloid fibrils can benefit the organisms that produce them. For example, certain bacteria produce such fibrils to fight human immune cells.

The researchers hope that their discovery will lead to medical and technological applications, such as development of synthetic antimicrobial peptides that would be activated only in the presence of bacteria. Synthetic peptides of this kind could serve as a stable coating for medical devices or implants, or even in industrial equipment that requires sterile conditions.

Salinasa N, Tayeb-Fligelman E *et al. PNAS*, 11 January 2021. DOI: 10.1073/pnas.2014442118

EMBL becomes newest Instruct Centre

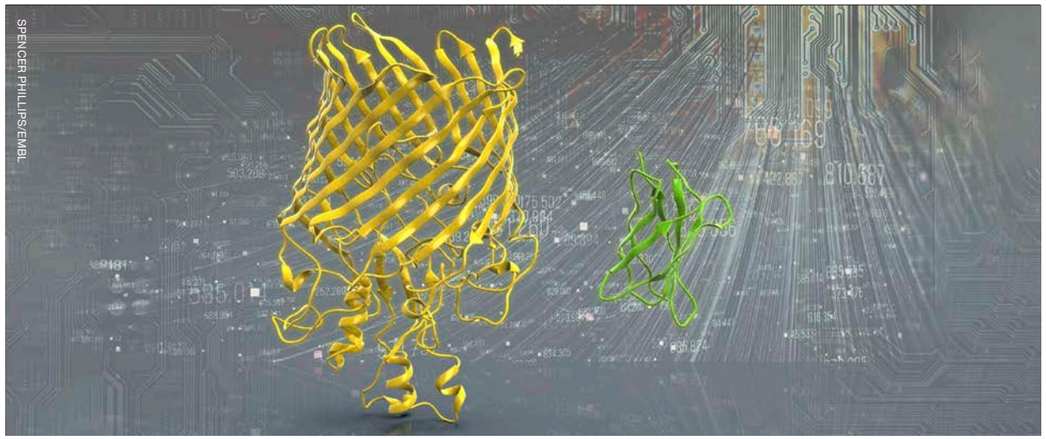
Instruct-ERIC and EMBL join forces to launch Instruct Centre EMBL

BY MATHIAS JÄGER

EMBL and Instruct-ERIC, a pan-European distributed research infrastructure for structural biology, have launched Instruct Centre EMBL, enabling Instruct users to benefit from EMBL's structural biology services, expertise, and training.

Instruct-ERIC operates Centres to provide high-end technologies and methods in structural biology to academic and industrial users. EMBL will be the 11th Centre in the programme. The new Centre, which includes EMBL's sites in Grenoble, Hamburg, and Heidelberg, offers access to a broad range of state-of-the-art facilities, along with some of Europe's most experienced infrastructure personnel.

"EMBL has always played a leading role in integrating European science and supporting national, regional, and European networks of excellence," says EMBL Director General Edith Heard. "The coronavirus crisis showed us that research works at its best when it's collaborative across institutes, borders, and disciplines. EMBL becoming part of the Instruct Centre programme is therefore not only a benefit for EMBL but for the whole life science community in Europe."


SPENCER PHILLIPS/EMBL

Pfam releases structures for every protein family

Thousands of new protein structures, predicted using machine learning, are now available in EMBL-EBI's Pfam database

BY OANA STROE

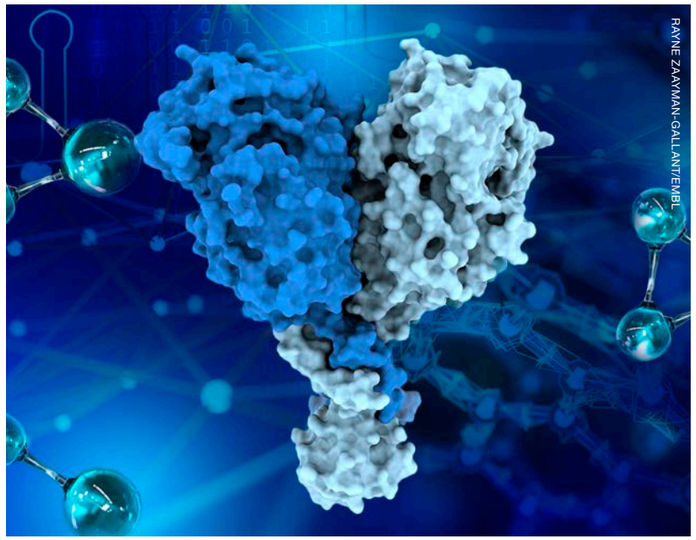
The field of protein structure prediction has greatly advanced in recent years, thanks to increasingly accurate deep learning methods. A new such method developed by the University of Washington, called trRosetta, has now enabled thousands of protein structures to be made available via EMBL-EBI's Pfam data resource. More than 6,300 protein structures have been predicted in this way and are now available in Pfam, with more to follow.

The Pfam database provides a complete and accurate classification of protein families and domains. Pfam is used by experimental biologists researching specific proteins, by structural biologists to identify new targets for structure determination, by computational biologists to organise sequences, and by evolutionary biologists tracing the origins of proteins.

"It's great to see so much progress in this field," says Alex Bateman, Senior Team Leader at EMBL-EBI. "Just 10 years ago, this kind of dataset was something we could only dream of, so to see it become a reality is amazing."

At the core of the Integrator complex

Scientists at EMBL Grenoble describe the structure of a protein complex that plays an important role in regulating gene expression


RAYNE ZAAYMAN-GALLANT/EMBL

Artist's representation of the three proteins forming Integrator's catalytic core.

BY MYLÈNE ANDRÉ

The Integrator complex, a protein complex consisting of multiple subunits, is involved in regulating the process of transcription, during which the cell's DNA is used as a template to make instructions in the form of RNA.

Discovered 15 years ago, Integrator has remained largely uncharacterised structurally, which triggered the interest of EMBL Grenoble's Galej Group. They combined biochemistry, cell biology, and cryo-electron microscopy (cryo-EM) imaging to determine its architecture. They used cryo-EM platforms at EMBL Heidelberg and the local CM01 beamline at the European Synchrotron Radiation Facility, which is run with the involvement of EMBL scientists.

Cryo-EM data allowed the scientists to determine the structure and the specific arrangement of the proteins comprising Integrator's catalytic core – a part of the complex responsible for cutting RNA during transcription.

Mutations in the Integrator complex can result in neurodevelopmental disorders. Ongoing studies in the Galej Group should help to unravel the molecular basis of some of these disorders, and could facilitate drug design to target these mutations in the future.

Pfleiderer MM, Galej WP. *Molecular Cell*, 5 February 2021. DOI: 10.1016/j.molcel.2021.01.005

Hamburg facility supports pan-European consortium

EMBL Hamburg's SPC Facility will offer services within the Molecular-Scale Biophysics Research Infrastructure

BY DOROTA BADOWSKA

From 1 July, the Sample Preparation and Characterisation (SPC) Facility, run at EMBL Hamburg and at Hamburg's Centre for Structural Systems Biology, will offer its services as part of the Molecular-Scale Biophysics Research Infrastructure (MOSBRI): a new integrated research infrastructure for molecular-scale biophysics.

MOSBRI will connect leading molecular biophysics facilities across 11 countries, including 13 academic centres of excellence and two industrial partners. Under the coordination of the Institut Pasteur in France, the consortium will make its services available across the continent to scientists from both academia and industry. Each facility will contribute cutting-edge instrumentation and unique expertise. MOSBRI's portfolio of services will span the entire field of molecular-scale biophysics – something that is currently not possible within any single European country.

As the only MOSBRI centre in Germany, the SPC Facility will share its expertise and provide access to important methods and tools, including some less widely available technologies that support time-resolved experiments and sample characterisation of protein complex assemblies.

Human genomes provide new reference for global genetic diversity

EMBL scientists co-initiate reconstruction of the most diverse set of reference human genomes ever assembled

BY MATHIAS JÄGER

In 2001, the International Human Genome Sequencing Consortium announced the first draft of the human genome reference sequence. The Human Genome Project had taken more than 11 years of work and involved more than 1,000 scientists from 40 countries. The reference sequence, however, does not represent a single individual but instead is a composite of genomes from several individuals, which cannot accurately capture the complexity of human genetic variation.

EMBL's Korbel Group and collaborators have now created a significantly more comprehensive reference dataset obtained using a combination of advanced sequencing and mapping technologies. The new reference dataset contains 64 assembled human genomes, representing 25 human populations from Africa, North America, East and South Asia, and Europe.

The new reference data provide an important basis for including the full spectrum of genetic variants in genome-wide association studies, which examine genetic variants across the whole genome to find out whether any variants are associated with specific traits or diseases. This might contribute to the development of novel approaches in personalised medicine, where the selection of therapies is tailored to a patient's individual genetic background.

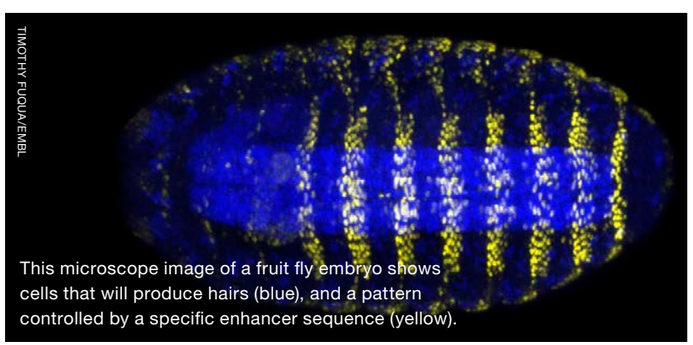
Ebert P, Audano PA, Zhu Q, Rodriguez-Martin B *et al. Science*, 25 February 2021. DOI: 10.1126/science.abf7117

Seeing evolution happening before your eyes

EMBL researchers find DNA enhancers more complex than previously thought

BY MATHIAS JÄGER

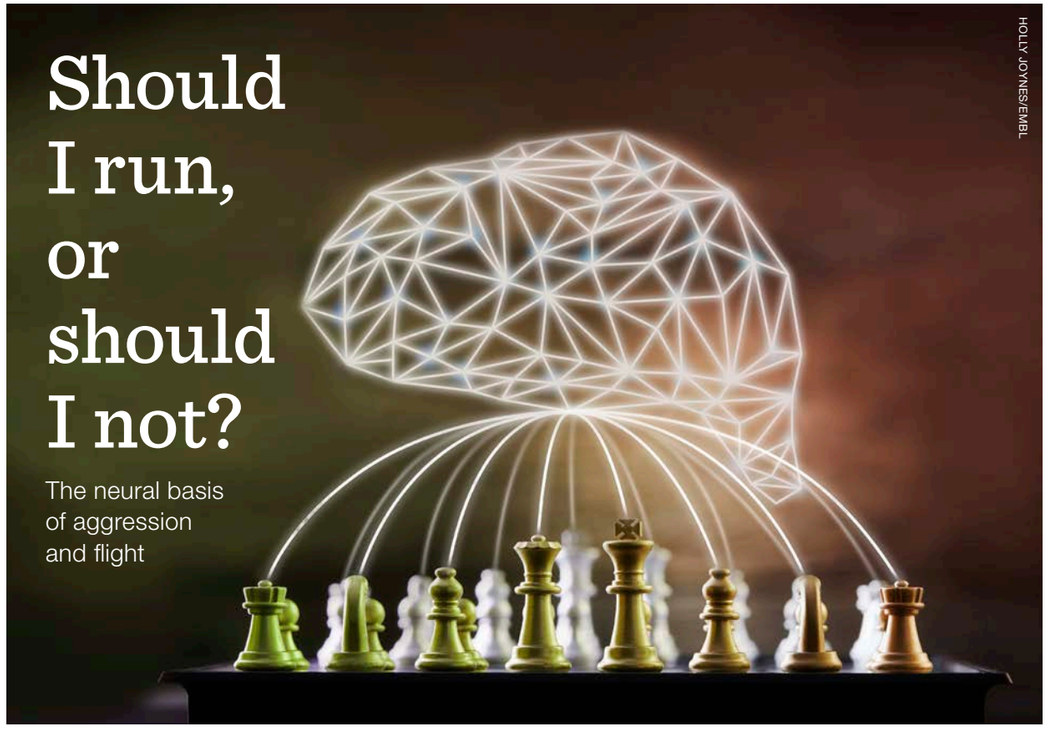
EMBL's Crocker Group and collaborators have performed an extensive study in fruit flies of a specific developmental enhancer – a region of DNA that controls where, when, and how strongly genes are expressed. They found that changing just a single letter of the enhancer DNA sequence could create a significant change in the pattern of gene expression it drove. They also found that almost all mutations to the enhancer altered the gene expression pattern in multiple ways. This showed that the enhancer encodes a lot more information than previously thought.



This microscope image of a fruit fly embryo shows cells that will produce hairs (blue), and a pattern controlled by a specific enhancer sequence (yellow).

These results were surprising and contradict what had previously been thought about enhancers. Importantly, the density of information encoded within the enhancer also constrains how animals can evolve. The study showed that each possible mutation has a certain possibility of occurring, giving scientists insights into where evolution could lead. In addition to driving the evolution of species, enhancers are also relevant to disease: mutations in enhancers are associated with more than 80% of human diseases.

Fuqua T *et al. Nature*, 14 October 2020. DOI: 10.1038/s41586-020-2816-5



Should I run, or should I not?

The neural basis of aggression and flight

BY ROSSANA DE LORENZI

Our brains are wired to protect us from threats. For social animals like humans, threats often come from other members of our own species when there is conflict over food, mates, or territory. Animals with a strong sense of territory will attack anyone who enters their territory, but will flee if caught in the territory of another individual. How is the decision between these two types of defensive responses made? How does our sense of territory drive our instinctive behaviour?

Previous studies from EMBL Rome's Gross Group have revealed the crucial function of a specific brain region, the ventromedial hypothalamus (VMH), in social fear. To investigate the possibility that the VMH is involved in the decision between attacking and escaping a social threat, scientists in the Gross Group measured the activation of neurons in mice while they were exposed to a more aggressive mouse. When the mice were in this situation, activity of a large class of neurons increased proportionally with the threat intensity, confirming that the VMH may encode an internal state of threat that is necessary to trigger defensive responses.

Unexpectedly, the scientists also observed activation of the same neurons when the animal returned to explore the place where it had been threatened previously, even though there was no longer any threat present. And, surprisingly, a second set of neurons now became active when the animal returned (via a corridor) to its home cage. This demonstrates that the VMH encodes spatial context – a function that has never before been attributed to the hypothalamus.

Finally, the researchers showed that exposure to a more aggressive mouse dramatically increased the ability of the VMH to promote flight. When the VMH was artificially activated after such a situation, the animal rapidly ran away from a threat, but not when the VMH was activated before this situation. This shows that social experience can change the VMH.

The results also suggest a novel role of the hypothalamus in behaviour, as a region that integrates sensory and contextual information, processing the level of threat and adapting survival behaviours to a changing environment.

Krzywkowski P *et al. eLife*, 21 September 2020. DOI: 10.7554/eLife.57148

EMBL prepares women postdocs for leadership

Members of EMBL's Equality, Diversity, and Inclusion Committee discuss the LEAP mentoring programme

BY ROSHNI MOONEERAM AND EILEEN FURLONG

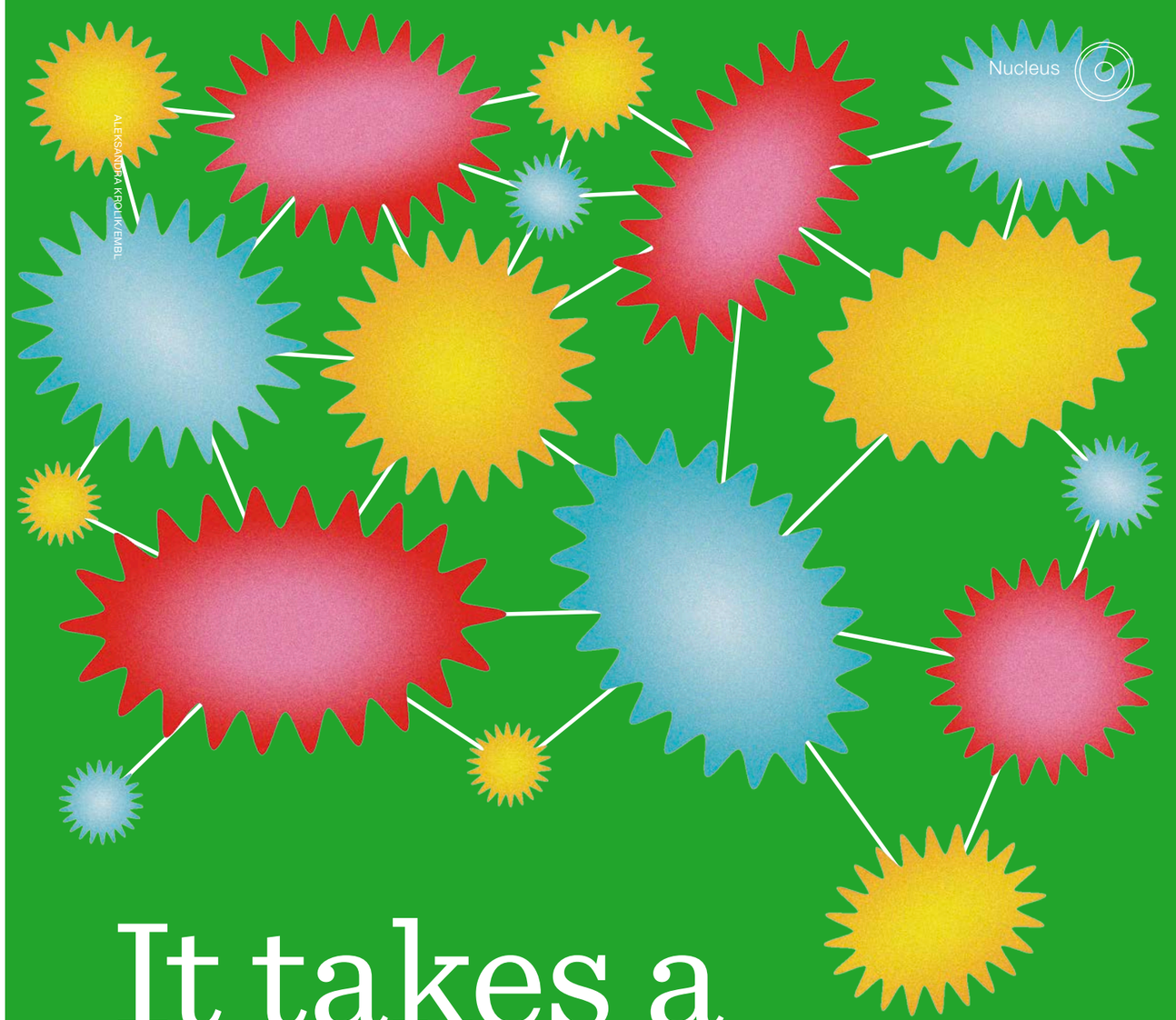
The Leadership and Excellence for Aspiring Postdocs (LEAP) programme at EMBL is an innovative mentoring and coaching programme with action learning designed to enable women postdocs to challenge themselves and their environment as they strive for their next career step as a group leader, principal investigator, or assistant professor in their field. LEAP is generously funded by the Friends of EMBL, and kindly supported by EMBL's alumni who are acting as external mentors, all of whom are group leaders or professors in universities or other institutes.

LEAP is learner led, using best practices in gender-inclusive leadership development. We also built in a strong sense of agency in both the design and the offering. The programme was built from scratch and tailor-made to the postdocs' exact leadership learning needs. The 23 current LEAP participants have selected their mentors and have established productive relationships that are helping them to develop their research vision and grow their networks. The workshops and one-to-one coaching sessions were co-developed with the LEAP postdocs at every step of the way. The professional training company that we have engaged has over 20 years of experience in coaching and development. Even with that background, our specific requirements for the LEAP programme have challenged them to think of new angles to gender and leadership training, enabling them to create a new pathway.

We will carry out a full evaluation of the LEAP programme this summer. Meanwhile, it is very encouraging to see that, in being bold, innovative, and rigorous, the LEAP programme is already having a positive impact. Based on the evaluation data gathered so far, LEAP is on track to achieve its goals and could have a knock-on benefit of attracting more women to pursue postdoctoral training at EMBL. As part of EMBL's equality, diversity, and inclusion strategy, we will explore the possibility of extending the programme to other under-represented groups of researchers, and will take into account intersectionality in our approach in future.

Roshni Mooneeram is LEAP Programme Manager and Head of Equality, Diversity, and Inclusion at EMBL.

Eileen Furlong is Chair of EMBL's Equality, Diversity, and Inclusion Committee; Group Leader; Head of the Genome Biology Unit; and a member of the EMBL Directorate.



ALEKSANDRA KROLIK/EMBL

It takes a community

Whether it's gaining a molecular understanding of ecosystems, developing vaccines to fight COVID-19, or driving technological innovation to accelerate discovery, it can only happen when many minds work together

DESIGN TEAM/EMBL

Living laboratories

EMBL scientists plan to study life in its natural context to help address global challenges

BY MARIUS BRUER

How does the environment affect animals, plants, and microbes? Organisms are perpetually interacting with each other and with the natural world around them, and have to adapt to changing environmental conditions. But how does this interplay work at the molecular level? Does the environment trigger changes to the structures inside cells, or does it affect the function of genes? And could we understand these changes to identify – and potentially mend – ecosystems threatened by pollution or climate change?

Planetary Biology

These are some of the questions EMBL scientists aim to answer as part of an innovative research theme named Planetary Biology, which combines molecular biology research with aspects of ecology, evolution, and geosciences. The overarching goal is to understand life in the context of its environment, and across scales. "Life on Earth doesn't exist in isolation. Species interact and react to changes in their environment within milliseconds, centuries, or geological ages. To fully understand life, we have to look at these interactions and study them at the level of molecules, cells, organisms, ecosystems, and the entire planet," explains Detlev Arendt, Senior Scientist and Group Leader at EMBL Heidelberg, who's one of three scientists leading this research theme.

Ecosystems around the world are changing at an unprecedented rate. Naturally occurring changes are accelerated by human activities, which means organisms must adapt faster to changing environments than they had to in the past. Many ecosystems are threatened by factors such as increasing temperatures, depletion of freshwater supplies, loss of biodiversity, and chemical contaminants.

These changes also favour the emergence of new pathogens, as well as the development and spread of antimicrobial resistance, which can reduce the effectiveness of our antibiotics. "Both processes can pose a serious threat to us. Human health is therefore closely linked to planetary health. If we want to tackle these environmental and societal challenges efficiently, we need a better understanding of how they arise," says Paola Bertucci, Research Scientist in Detlev's group, who is involved in coordinating the research theme's activities. >>

Platynereis dumerilii mate by swimming to the surface and releasing eggs and sperm into the water – and they do so only at night during a new moon. EMBL scientists collected sexually mature *Platynereis* and let them mate in plastic cups, obtaining thousands of fertilised eggs in each vessel. These were later analysed in the lab.

PATRICK MÜLLER/EMBL

EMBL scientists and their colleagues collected samples at various locations near Naples and around Ischia to study phytoplankton.

Collaboration is key

To gain this understanding, EMBL scientists want to study selected ecosystems and organisms, in close collaboration with researchers across Europe. The Planetary Biology theme builds on EMBL's existing research and brings together many scientific disciplines, from molecular biology to ecology and theoretical approaches. An important goal of the research theme is to create a pan-European network of scientists and research institutions to combine strengths, share expertise, and develop synergies to create the new field of Planetary Biology research.

"As part of the research theme, EMBL scientists will interact closely with colleagues from other research institutes. We aim to bring together molecular biologists, ecologists, and epidemiologists, and involve expertise from chemists, physicists, engineers, and data scientists," says Rainer Pepperkok, EMBL's Director of Scientific Core Facilities and Scientific Services, who co-leads the Planetary Biology research theme. Collaborations across EMBL's member states will be essential in making best use of existing research facilities and knowledge, and advancing the research of all partners.

From lab to field

Planetary Biology research involves studying animals, plants, fungi, and microbial communities in their natural environment. The approach involves detailed investigation, going down to the cellular and molecular level. Scientists can measure how genes are used in different cell types and different organisms. They can also study the shapes of cells and the proteins and structures within them. Ultimately, the scientists want to understand how all these building blocks of life function in relation to environmental conditions.

All of this is possible thanks to an impressive toolkit of experimental methods, including many developed at EMBL. What would have been technically impossible just a few years ago can now be achieved. "We have the technology to study molecules and genes in single cells. Imaging methods allow us to see where each of these cells is located in the body of multicellular organisms. We can also observe changes in cellular structures, molecules, and gene functions over time – and we have the computer power to combine and analyse all the data," says Peer Bork, Director of EMBL Heidelberg (Scientific Activities), who coordinates the research theme together with Rainer and Detlev.

One trip, three projects

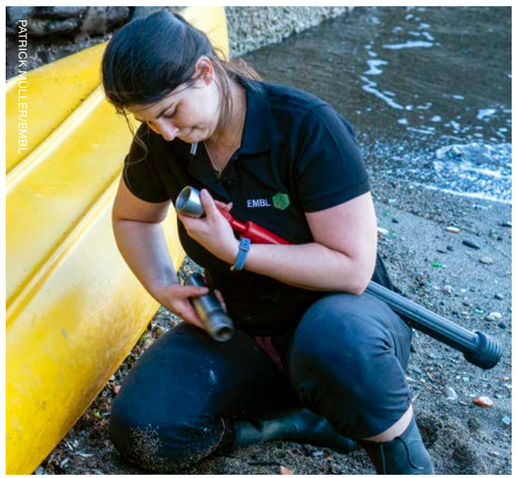
In 2019, a group of EMBL scientists travelled to the Italian city of Naples and the nearby island of Ischia. The region is a popular destination for tourists – but the purpose of their trip was not sightseeing. The scientists were there to collect samples of microbes and marine organisms at several spots along Ischia's coast, in collaboration with the Stazione Zoologica Anton Dohrn di Napoli (SZN), a marine research institute in Naples, which also runs a research station on Ischia.

The visit to Naples included discussions with local scientists and collaborative fieldwork in Naples and on Ischia. For Detlev Arendt and his group, it was the segmented marine worm *Platynereis dumerilii* that occupied their attention. A few centimetres in length, *Platynereis* thrives along European coasts in a variety of habitats. The broad distribution of *Platynereis* suggests a high level of adaptability, so the scientists are keen to find out how genetic variations allow these worms to survive under widely varying conditions, and how these variations are manifested at the cellular and organismal level. "*Platynereis* is even found in places where volcanic thermal springs acidify the seawater, and could therefore tell us how organisms might adapt to the acidification of seawater that occurs as a result of climate change," says Paola.

Meanwhile, scientists working in Yannick Schwab's team focused on phytoplankton – tiny aquatic organisms that obtain their energy from sunlight. The Schwab Team is developing advanced imaging techniques to study how the structures inside cells are linked to the expression of genes in phytoplankton. Their work requires the application of electron microscopy and single-cell sequencing techniques, which need to be adapted for fieldwork. "This expedition taught us how complex and diverse the samples we collect in the field can be," says Yannick.

Kiley Seitz from Peer Bork's group collected soil samples to study the microbes living on the coast. Peer's group is interested in the variation of microbial communities and the diversity of their genes, and in the effects of the environment on microbial communities. Samples of the marine microbes in the Naples area had already been collected by researchers from the SZN, and by members of the Tara Oceans expedition (2009–2013), which investigated marine biological diversity across the globe. By comparing terrestrial and marine microbial communities, the scientists hope to better understand whether and how these communities exchange genes or even entire species. The researchers also want to find out how microbes and microbial communities are influenced by environmental pollutants, such as pesticides or antibiotics.

The experiments performed in Naples and on Ischia served as pilot studies to >>



Kiley Seitz from Peer Bork's group collected soil samples to study the microbes living on the coast. The samples were dried and further analysed in the lab.

explore how molecular readouts can inform us about the interactions of organisms with their environment and with each other. For example, in this area the scientists found flourishing communities of previously unknown species that belong to a group of single-celled organisms called archaea. These species probably help the complex biological communities in the volcanic environment to utilise nutrients. The scientists tested standardised procedures, experimental methods, and logistics for sample collection and handling. This has set the stage for follow-up pilot studies and a scientific expedition that aims to study the interactions of marine and terrestrial species in ecosystems along Europe's coastlines.

Advanced research infrastructures to study ecosystems

Another experimental approach is to study organisms in a complex environment controlled by researchers. Small organisms can be housed in bioreactors – reaction vessels that hold cells, microbes, or other single-celled organisms under precisely controlled conditions. Bioreactors allow scientists to adjust environmental factors, such as temperature or nutrient availability, and observe how the organisms adapt.

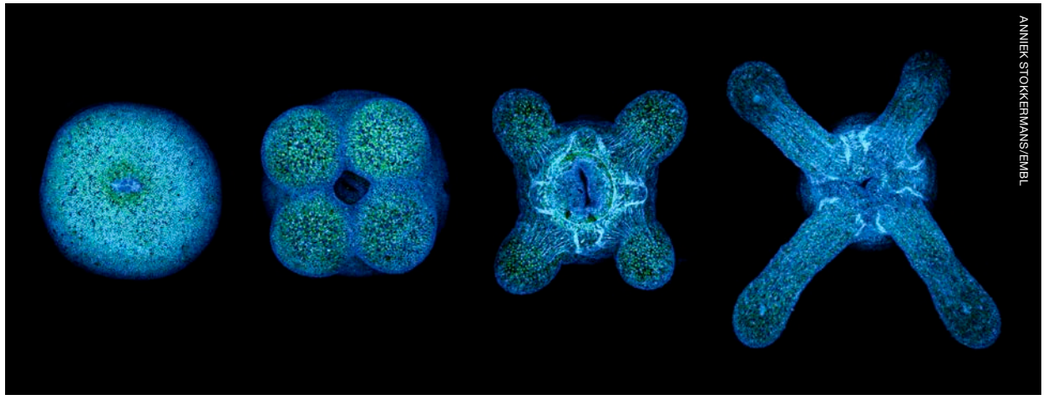
Larger systems are mesocosms and ecotrons, which can be used to reproduce natural ecosystems in a simplified form. Depending on the type of ecosystem studied, mesocosms and ecotrons can be containers of soil, tanks of water, greenhouses, or fenced-off areas of grassland, inhabited by organisms of at least two species. When they're closed off from their surroundings, these systems offer scientists control over many environmental factors, such as the amount of light, air temperature, humidity, and precipitation. But they can also be operated in a way that allows exchange with the physical world around them.

"Scientists have been exploring for a long time how the variation of individual environmental parameters influences organisms in the lab. But what we really want to know is how organisms react to a mix of changing parameters, and how they influence each other in their response to the environment," says Detlev.

Studying environmental influences on organisms in the lab

One of the organisms that can be studied in the lab under complex, controlled environmental conditions is *Platynereis dumerilii*; another is the starlet sea anemone, *Nematostella vectensis*, which is studied by Aissam Ikmi and members of his group at EMBL Heidelberg.

Sea anemones are special animals. Like corals, sea anemones are sessile, which means that they spend their entire life in the same spot. Unlike most other animals, which have fixed numbers of legs, wings, or fins, sea anemones can grow additional tentacles – the 'arms' they use to catch food from the seawater. Exactly how tentacle growth is regulated, and how it is triggered by environmental signals, was unknown until recently.

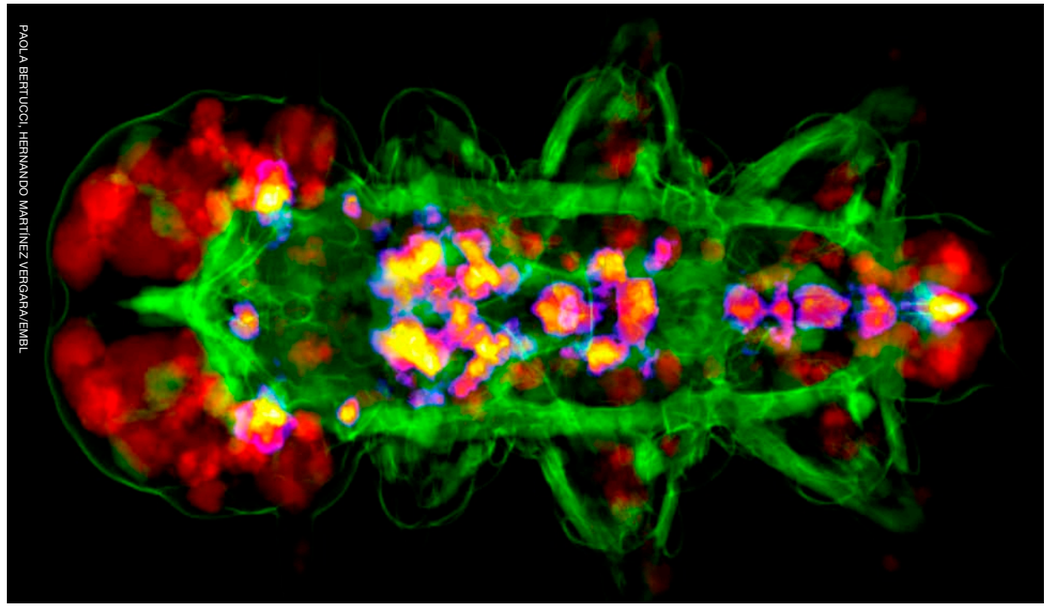


ANNIEK STOKKERMANS/EMBL

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

Members of the Ikmi Group and colleagues have now discovered that the growth of new tentacles in sea anemones is controlled by the amount of food the animals eat. The scientists also figured out some of the cellular and genetic switches that trigger tentacle growth. "As predominantly sessile animals, sea anemones must have evolved strategies to deal with unpredictable environmental changes," says Aissam.

Sea anemones can therefore help us to better understand how organisms react and adapt to changes in their environment. Knowing that the number of tentacles in sea anemones is determined by their food intake, the Ikmi Group next wants to define the key nutrients critical to this process. The scientists are also interested in how sea anemones can regrow new tentacles in response to environmental stresses, such as injuries.



PAOLA BERTUCCI, HERNANDO MARTÍNEZ VERGARA/EMBL

This image of a six-day-old *Platynereis* larva shows genes expressed in muscle cells (green) and in various neurons in the brain and ventral nerve cord (red, pink, and yellow).

Different approaches, one goal

Healthy ecosystems are the basis for our survival, and Planetary Biology research will enable us to develop diagnostic tools and therapies to maintain ecosystem health. For example, the identification of organisms as novel 'living biosensors' will allow us to detect a decline in ecosystem health as it occurs. Technological innovations and the provision of environmental data and analysis tools will benefit various scientific fields, as well as agriculture, forestry, and fisheries.

Importantly, Planetary Biology will link national initiatives and research across Europe. "It is only by exploring and understanding life that we can also help to preserve it. By joining forces with scientists across Europe and in different disciplines we can rise up to pressing environmental and societal challenges," says EMBL Director General Edith Heard. "Today, more than ever, we have the scientific tools and a responsibility to use them to tackle these challenges. The Planetary Biology research theme is a unique opportunity for us to make an impact together."

ADOBE STOCK. ADAPTED BY ALEKSANDRA KROLIK/EMBL

Community endeavour

EMBL alumni have developed key technologies behind some of the most prominent COVID-19 vaccines

BY ROSSANA DE LORENZI AND IVY KUPEC

The development of COVID-19 vaccines is a global effort, driving new scientific collaborations and building on the work of previous generations of scientists. Members of the EMBL community are playing their part in this endeavour, and the research of EMBL alumni in previous decades has helped to lay the groundwork for current advances.

Viral delivery systems

COVID-19 vaccines such as the Oxford–AstraZeneca vaccine deliver a genetic message to cells that is carried by a harmless type of virus called an adenovirus. To work efficiently, the trick is to use an adenovirus from primates, because a form that infects humans is more likely to be recognised and destroyed by our immune system.

The story that led to the first primate adenovirus-based vaccine began in 1979, when Riccardo Cortese – an Italian medical doctor convinced that fundamental research was the route to improved medicine – was recruited at EMBL Heidelberg. With his rare vision and talent, Riccardo was asked to set up and lead EMBL's Gene Expression Programme, to which he attracted a number of other Italian scientists. "We were all in the same corridor," he said in a 2015 interview, "which apparently had the permanent aroma of espresso." Among this group were two young scientists: Alfredo Nicosia and Alessandra Vitelli. The time the three of them spent together at EMBL sowed the seeds for a lifelong friendship and a professional partnership that gave rise to their work on chimpanzee adenovirus-based vaccines.

Bringing the EMBL spirit back to Italy

When the time came to leave EMBL, Riccardo was called back to Italy to found a new institute for molecular biology research, IRBM, near Rome, as the Italian site of Merck Research Laboratories. Alfredo and Alessandra joined him.

While working on a human adenovirus-based vaccine against the hepatitis C virus, Riccardo and his colleagues found that the vaccine's effect was weakened in people previously exposed to adenovirus. This prompted the idea of using a chimpanzee adenovirus as a carrier. This virus would be similar enough to human viruses that it could readily infect human cells, but different enough to avoid being rejected by the immune system. The approach worked, and was patented in 2004. Riccardo later negotiated the licence to further develop chimpanzee adenoviruses at Okairos, a new company he founded in 2007, along with Alfredo and two other colleagues.

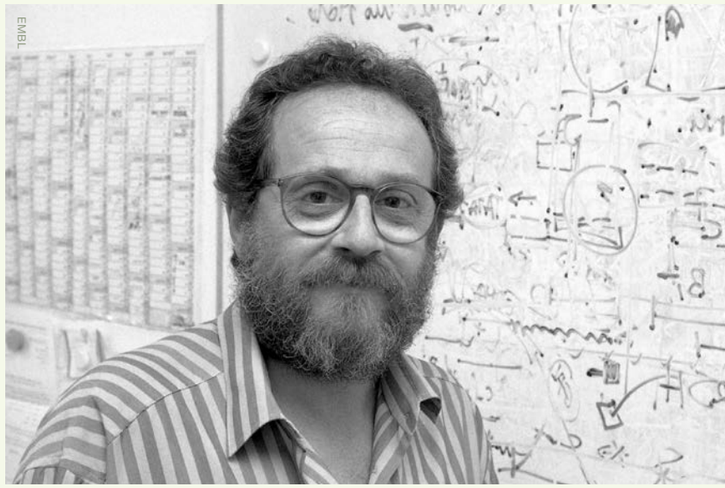
This pioneering work led to the development and manufacture of the first simian adenovirus vectors to enter clinical trials in humans. In 2013, Okairos was acquired by GSK under an agreement negotiated by Riccardo, in which the intellectual property was sold but the team of researchers was preserved and reborn as the company ReiThera.

Towards a COVID-19 vaccine

When the COVID-19 pandemic arrived in Italy in early March 2020, ReiThera moved rapidly to adapt their latest, improved adenovirus vector – based on a gorilla adenovirus – to produce a COVID-19 vaccine.

"After the experience at Okairos, we had acquired the know-how," says Alessandra Vitelli, now Chief Scientific Officer at ReiThera. "We had isolated a new adenovirus from gorillas, showing better delivery features and stronger immunogenicity in mice than the chimp adenovirus. We had just applied to receive a grant from CEPI – the Coalition for Epidemic Preparedness Innovations – to develop a vaccine platform ready for future epidemic outbreaks. When the current pandemic broke out, we decided to repurpose our new gorilla vector against SARS-CoV-2."

Riccardo Cortese passed away in 2017. Alfredo Nicosia headed ReiThera until 2019, when he took up a teaching post at the University of Naples Federico II. But a new generation of scientists are further developing and improving the original technology. Among them is another EMBL alumnus, Angelo Raggioli, who joined ReiThera in 2019 as Head of Vectorology.



EMBL

EMBL alumnus Riccardo Cortese (1944–2017).

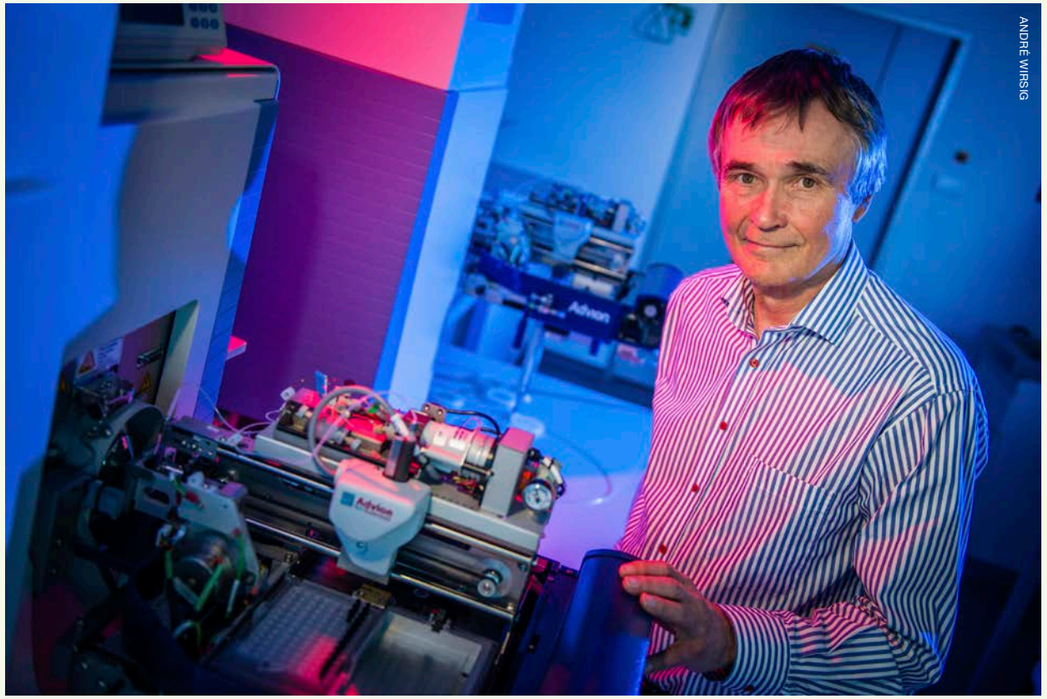
"My current job at ReiThera is very similar to what I did at EMBL Rome," says Angelo, who developed the vector that is currently being used in ReiThera's COVID-19 vaccine, called GRAd-COV2. "The only difference is that here we all work towards a single goal, while at EMBL we collaborated on many different projects. Working for a company, I am more limited in the kind of reagents that I can use, as many are covered by patents. On the other side, I enjoy the excitement that comes from the practical implications of my research."

Closing the circle

Riccardo and his colleagues contributed to EMBL's innovative and dynamic spirit and then brought this back with them to Italy, where they've applied it throughout their careers.

"EMBL gave me the opportunity to measure my skills, and to share my experiences," says Alfredo Nicosia. "It gave me access to tools and knowledge, and to an incredible range of expertise. It ingrained in me an open community culture, which I have used throughout my life to connect people and develop ideas. The challenge is to get things started, as Riccardo used to say." >>

Novavax vaccine uses EMBL's earliest virus research


ANDRÉ WIRSIG

EMBL alumnus Kai Simons uses a mass spectrometer to analyse lipids at Lipotype.

The early work of EMBL alumnus Kai Simons centred on Semliki Forest virus: an RNA virus enveloped by a membrane, which the virus acquires by budding out through the membrane of its host cell. Kai chose this virus to work on because its membrane was the simplest biological membrane in the world. It contains only one protein, the viral spike protein. Kai and his graduate student Ari Helenius became champions in taking the virus apart. Now, their research has played a crucial role in developing a COVID-19 vaccine currently under review by several regulatory authorities, including the US Food and Drug Administration and the European Medicines Agency.

Kai came to Heidelberg in 1975, just as EMBL was establishing itself. He brought with him two members of his group, Ari Helenius and Henrik Garoff, and together they continued their virus work. One line was to use detergents to break up the virus and produce subviral particles that could be used as vaccines. The result was protein micelles – essentially, small droplets made up of the viral spike proteins – that produced an immune response. The researchers vaccinated mice infected with Semliki Forest virus with this preparation, and found it was remarkably effective in small doses at fully protecting the mice from the virus.

This was a completely new way to make vaccines. In 1978, the group published their results in *Nature*, pointing out that the traditional strategy of using whole-virus vaccines – either killed or with diminished potency – was limited in both safety and effectiveness. By using only the spike proteins as a subunit vaccine, the approach of Kai and his group addressed those limitations and their research proved its effectiveness.

At the time, it attracted no interest in the vaccine field. It has taken until now for its full potential to be realised, with US biotechnology company Novavax building on Kai's research to produce protein nanoparticles for their COVID-19 vaccine, which they reported in a January news release had an 89% efficacy rate in a phase III clinical trial in the UK, involving 15,000 participants.

Membranes and cell biology

Kai's research subsequently took a new direction, focusing on the cell biology of Semliki Forest virus infection. Ari, Henrik, and Kai found out how the virus penetrates its host cell and how its progeny escapes the cell. This work described for the first time the complete life cycle of a membrane-bound virus.

Kai then turned his attention to other aspects of cell biology, still with cell membranes as the focus. He discovered how cell membranes can compartmentalise into specialised regions, which he called lipid rafts. These are dynamic collections of specific proteins and lipids, assembling into functional hotspots where cell signalling, immune defence, and many other cellular processes take place. Kai became the father of this important organisational principle.

"EMBL has been more successful than we could dream of in those early days"

Beyond EMBL

In 1998, Kai left EMBL, together with three other EMBL alumni – Wieland Huttner, Tony Hyman, and Marino Zerial – to start the Max Planck Institute of Molecular Cell Biology and Genetics. Today, he is CEO of Lipotype, a biotech company he founded to analyse lipids as a service to academia and industry. Lipotype is the only company worldwide that focuses on what is termed lipidomics.

"The slogan of Lipotype is 'lipidomics for a better life'," Kai says. "It reflects the central role that lipids play in health and disease, as well as the hope that Lipotype technology can guide our attempts to live a healthy life."

Kai is a steadfast supporter of increased vaccine development in all areas, not just for COVID-19, noting that vaccines are superior to drugs because they can prevent bacterial, viral, and parasitic diseases. "Why not start a European vaccine institute on a scale that is capable of developing a portfolio of vaccines that could change healthcare worldwide?" he asks.

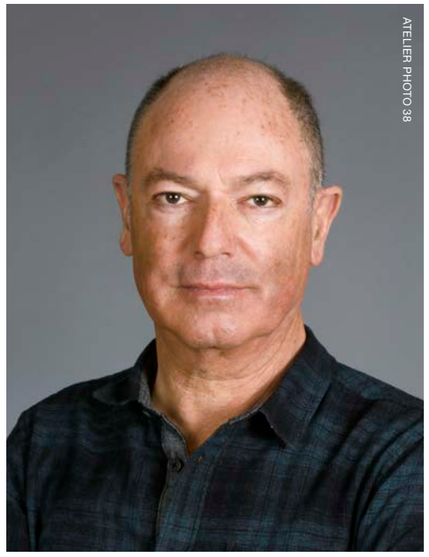
Kai believes his time at EMBL allowed him to get involved in shaping how research should be organised and also showed him the power of multidisciplinary research. "The most important phase at EMBL was the first phase when we learned to work together," Kai says. "It was really quite amazing how it all started – how humble it all was. You can do much more when you work together. Truly EMBL has been more successful than we could dream of in those early days."

Structural biology at EMBL:
Driving technology development

EMBL's Florent Cipriani has developed innovative technologies that benefit the scientific community worldwide

BY MYLÈNE ANDRÉ

Scientific breakthroughs are often only made possible by innovative technological developments. This is certainly true in structural biology, where researchers seek to gain insight into biological processes by determining the structure of macromolecules at the atomic level, for instance by X-ray crystallography or cryo-electron microscopy. Florent Cipriani, who recently retired as Head of the Instrumentation Team after a long career at EMBL Grenoble, is one of the pioneers of instrumentation development in this field, creating ingenious inventions with worldwide impact.

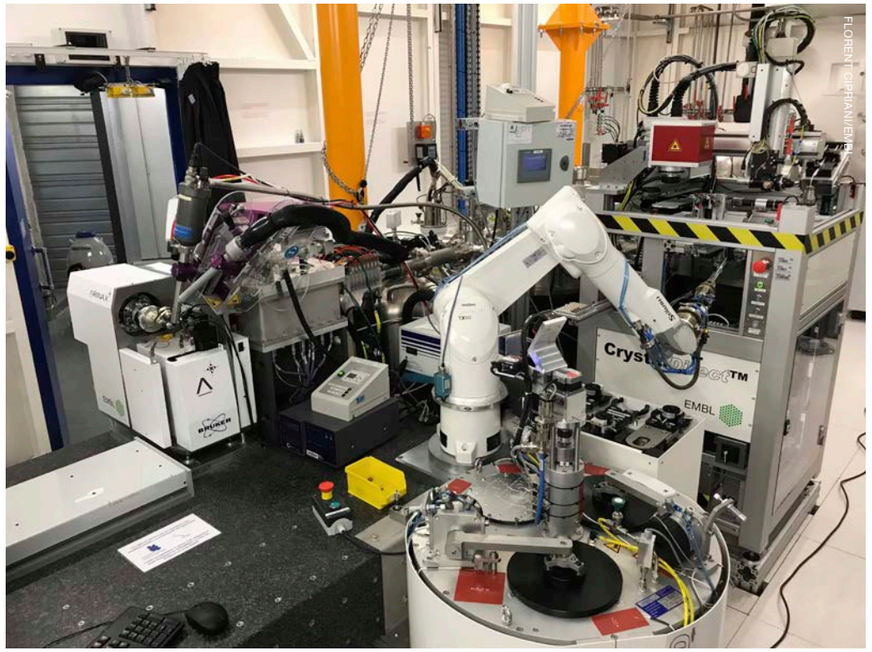

ATELIER PHOTO 38

Florent Cipriani recently retired as Head of the Instrumentation Team at EMBL Grenoble.

Florent, a French engineer, joined EMBL Grenoble in 1992. At that time, there was a small Instrumentation Team dedicated to supporting the development of structural biology methods for neutron sources, thanks to a collaboration with the Institut Laue–Langevin on Grenoble's European Photon and Neutron (EPN) Science Campus. With the opening of the first high-brilliance, third-generation synchrotron source at the European Synchrotron Radiation Facility (ESRF) on the campus in 1994, the intense X-ray beams opened up new opportunities for structure determination by X-ray crystallography. At the same time, they posed severe technological challenges in terms of how to exploit them.

From manual to automatic

X-ray crystallography involves shooting X-rays at regularly structured arrays of molecules, packed together in a protein crystal, to determine their structure. When the ESRF opened, the entire operation of sample handling on macromolecular crystallography beamlines was done manually. The starting point of one of Florent's innovations was a request from structural biologist Stephen Cusack, Head of EMBL Grenoble, who was trying to determine a protein structure from tiny microcrystals using the ESRF's ID13 microfocus beamline. The challenge: aligning a crystal 2 microns (two-thousandths of a millimetre) in size within an X-ray beam 10 microns wide, and maintaining this alignment as the crystal is rotated in the X-ray beam, all the while shooting it with X-rays.

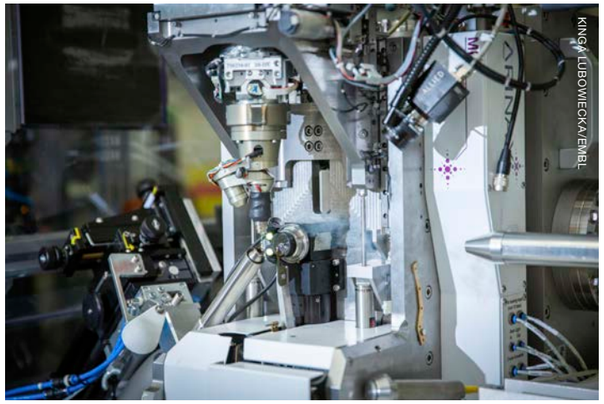


EMBL Grenoble instruments installed on one of the beamlines run jointly by EMBL Grenoble and the ESRF. Right of centre, the robot arm of the Flex sample changer can be seen.

Florent, together with Tassos Perrakis – then a staff scientist at EMBL Grenoble – and Stephen Cusack, led the development of a first-generation automated micro-diffractometer. "This device, very cleverly, included a digital camera that observed the crystal at high magnification along the same direction the X-ray beam is travelling, allowing the automated and precise positioning of the protein crystal in the beam. This was a revolution," says Stephen. The micro-diffractometer concept was patented, and improved versions (MD2 and MD3) are now in use at synchrotrons all over the world. Alongside this instrument, Florent created a first-generation automated sample changer (SC3) to accelerate the process of exchanging the crystals to be exposed to the beam. Instead of manually exchanging each crystal, this robot made it possible to load, one by one, up to 50 crystals into the beam without manual intervention. The latest version of the sample changer (FlexHCD) has a capacity of 368 crystals. Both iconic innovations, and their subsequent upgrades, have not only been incredibly time saving, improving the efficiency with which scarce X-ray beamtime can be used, but have also improved data quality and enabled structure determination on smaller and smaller crystals. "The process of obtaining enough X-ray data to determine a protein structure decreased from many hours to only a few minutes, and more recently takes only a fraction of a second. With the new fourth generation of synchrotrons like the ESRF-EBS, a complete dataset can be collected in a few milliseconds," explains Florent.

Working together

These innovations set the stage for a complete automation of the structure determination process. As Head of the Instrumentation Team, Florent worked closely with other technology-oriented teams at EMBL Grenoble and with the ESRF Structural Biology Group, merging technological innovation with software developments. One achievement was to >>


KINGA ULBOWIECKA/EMBL

The first member of the MD3 micro-diffractometer family installed at EMBL Hamburg.

completely automate data collection on one of the structural biology beamlines, MASSIF-1, eliminating user intervention completely. A second example is the joint development, with the Márquez Team, of the CrystalDirect robot. This is a unique instrument in the world, capable of automatically harvesting crystals from their growth medium and freezing them at liquid nitrogen temperatures. This led to the development of automated crystallography pipelines, which can be remotely controlled through the Crystallographic Information Management System software. A CrystalDirect robot will soon be incorporated directly into MASSIF-1, allowing the research community to put a crystallisation facility and a synchrotron remotely in every lab.

Over the years, Florent has played an active part in the close collaboration with EMBL's site in Hamburg, which also specialises in structural biology and operates synchrotron beamlines. Florent was a member of the executive committee in charge of constructing the Hamburg synchrotron's newest beamline, PETRA III. He also led the development of several new instruments, including the ultrahigh-precision MD3 micro-diffractometer and an automated sample changer for use in biological small-angle X-ray scattering (Bio-SAXS) – another method for analysing the structures of biological materials. Rapid cycles of design and testing of prototypes at EMBL made these innovations possible.

Innovations adopted worldwide

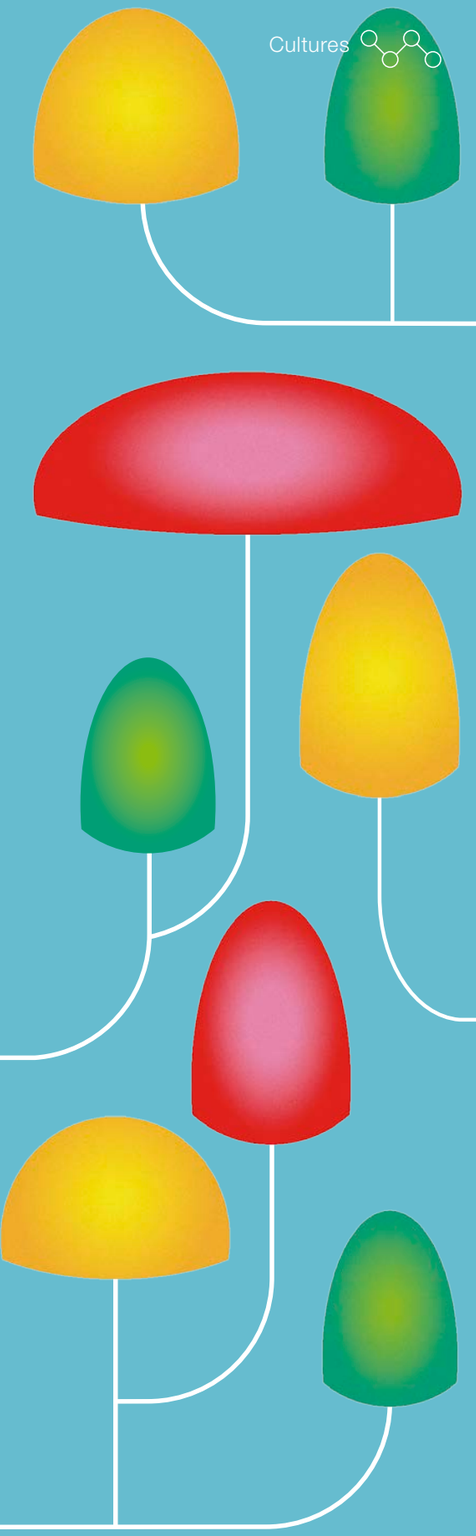
Ease of use by researchers is at the heart of the technology Florent developed. "Florent really understands what we need. He is tireless in looking for technological solutions and manages to put things together in a way that is easy to use. This is a service for the whole science community," says Thomas Schneider, a group leader at EMBL Hamburg, who worked closely with Florent. This adjustment to users' needs is one of the reasons why EMBL Grenoble's services and facilities are widely used by the scientific community and also by industry, such as pharmaceutical companies. It's also why instruments like MD2 – and later MD3 – have now been adopted by other synchrotrons all around the world.

With the support of EMBL's technology transfer partner, EMBLEM, the Cipriani Team has patented several innovations and developed collaborations with companies to industrialise their prototypes: principally with Maatel (now Arinax), a French company based in Grenoble with a unique specialisation in mechanics, electronics, and computer science, and also with MiTeGen and Molecular Dimensions. Ralf Siebrecht, CEO of Arinax, underlines the importance of the trust and shared values between EMBL Grenoble and Arinax, which Florent played an important role in building. "At Arinax, we are aware of this symbiosis that works very well with EMBL. Today, EMBL is very much aware of what to entrust to us, and we also know in return that we can have confidence in EMBL's projects," he says. Ralf also emphasises the special working environment at EMBL, which has enabled the Instrumentation Team to grow and support the needs of the technology development cycle: the emergence of a need from a scientist, the development of an innovation, and use by the research community, leading to validation of the new technology.

Florent is passionate about his profession. "It's exciting work from a technical point of view," he says, "but also in the relationship with the researchers. Innovations are often triggered by the needs of scientists, so making the instruments useful and ergonomic for the scientific community is very stimulating and gives a lot of satisfaction to the job. This is the common thread running through all these developments."

Cultures

Alumni


ALEKSANDRA KRYLUK/EMBL


JUSTYNA MASIEWICZ

(Opposite) Now Manager of mRNA Starting Materials at BioNTech, alumnus Pawel Masiewicz credits his experiences at EMBL with leading him to this unique opportunity.

From mRNA researcher to BioNTech manager

Alumnus Pawel Masiewicz has transferred skills and experience gained at EMBL to oversee starting materials for mRNA in vaccine manufacture

BY IVY KUPEC

When Pawel Masiewicz was expanding his scientific knowledge about RNA molecules at EMBL and honing his skills as a project manager, he may have hoped these experiences would land him a position at a company aspiring to individualise cancer medicine. It turned out that his hope became reality and then some, as he now works for the company that made the first approved COVID-19 vaccine.

BioNTech, which had just expanded vaccine production at a new facility in Marburg, Germany, had the perfect role for Pawel. His position had evolved to being a manager who played a crucial part in the logistics of RNA research. And this is exactly the role he has at BioNTech today – but on a much larger scale.

"My role had been at the interface between suppliers and researchers," Pawel says. "I worked with two research groups at EMBL, and it was all about RNA. This was around the time that mRNA was emerging as a way to develop new types of drugs."

The reason for this interest was that, over the past 10–20 years, researchers have worked on finding ways to stabilise messenger RNA (mRNA), which is essentially the DNA's personal mailman for delivering genetic material. In the case of the new mRNA vaccines for COVID-19, scientists use synthetic mRNA that carries instructions for building viral proteins. Our cells respond to the mRNA vaccine by building these proteins, but not in sufficient quantities to make us sick. Instead, they cause our body to mount a biological defence.

Making these vaccines starts with making the synthetic mRNA, and that's where Pawel is involved as Manager for mRNA Starting Materials.

BioNTech provided exactly the right opportunity for the Polish biochemist. A company known more for personalised medicine and cancer research, BioNTech had yet to be in the COVID-19 vaccine spotlight when Pawel signed on to work there. However, when he took up his post at BioNTech in May, he barely had time to get settled into his new position before the company's vaccine was approved and manufacturing began in earnest.

"It's an exciting place to be, and also one where you keep learning," Pawel says. "At every step of the process – from research and development, supply chain management, good manufacturing practices and quality management to the management board – you see remarkable dedication. My colleagues put a lot of heart into what they're doing."

Getting a head start at EMBL

Pawel credits his success at BioNTech to the opportunities he was given at EMBL – both scientifically and through EMBL's career development services. At EMBL, he was part of a team of 10 scientists studying the structure of RNA and RNA–protein complexes. EMBL expanded the experience he brought in this area from his home country, Poland. His job as a laboratory manager was to produce the RNA for structural studies, which placed him between suppliers and researchers. An evolution of work responsibilities, combined with opportunities available through EMBL's career development services, led Pawel away from doing scientific research to managing the practice of science. And he recognised this was his calling.

"I realised that I didn't want to pursue a scientific career *per se*, but rather to manage projects and collaborate with people from different expertise areas," he recalls, "so I took advantage of the many courses that EMBL offered to help me grow."

EMBL's interdisciplinary environment, too, felt like an important aspect, and something he welcomed to expand his scientific perspective. "I was very proud four years after joining EMBL to see a Polish flag flying there," Pawel says. "I've seen how being part of EMBL helps a country develop this kind of scientific expertise.

"I personally benefited a lot from the great community there, including a running club that helped me stay fit," he adds. "EMBL is a paradise if you're open-minded about taking your career path in new directions. From my perspective, what BioNTech has achieved in the past year is truly extraordinary, and now I'm really happy to be a part of that."

"I've seen how being part of EMBL helps a country develop this kind of scientific expertise"

The European Climate Pact: EMBL plays its part

EMBL's Environmental Officer, Brendan Rouse, explains his role as a European Climate Pact Ambassador

BY EDWARD PRIOR

As the European Climate Pact gets started with its ambitious plans, EMBL's Environmental Officer, Brendan Rouse, explains what it means for EMBL and the organisation's commitment to a sustainable future.

What is the European Climate Pact all about?

It's an initiative that aims to get people and organisations involved in building a greener Europe. It's about connecting people and sharing knowledge, so that solutions can be scaled up to match the size of the challenge we're all facing.

The pact is working to inspire citizen participation across the EU, through events and pledges. As one example, individuals and organisations are invited to submit pledges to the pact in the form of science-based, concrete actions. They can be based on broad actions, or simply small sustainable choices. The background to all of this is the EU's Green Deal. That includes a focus on climate change policies within the EU, including a carbon reduction target of 55% by 2030.

All parts of society and the economy will need to play a role, and that means finding solutions that can work at scale for everything from power generation to agriculture to the building industry. Organisations like EMBL have an important part to play in all of this.

You've been chosen as a Climate Pact Ambassador – what does that mean?

The Climate Pact Ambassadors are a group of 181 people who have been selected to promote the pact and climate protection in general. Ambassadors are there to engage people and organisations who are not yet involved in climate action, and to support climate action within communities. They also act as a bridge between the European Commission and those organisations and individuals who are keen to get more involved.

As well as helping to organise activities related to climate change and environmental action, Climate Pact Ambassadors are expected to advocate within their communities. Part of this involves the sharing of reliable information on climate change, by developing online channels and raising awareness through media coverage, public discussions, and events.

What will it mean for EMBL?

I see our network as the community of European life science research organisations, and there's a great deal of potential in reaching out to them and trying to collectively raise our ambition. We're currently working on some ideas that will act as a blueprint for life science organisations, and will help with our outreach work to those organisations. Beyond that, I'm also keen to reach new audiences. Where there are any suitable events, we'll be using the Climate Pledge initiative to forge connections with those whom we aren't currently reaching. It's vital that this work runs through all aspects of the life sciences.

It's easy to feel overwhelmed by the scale of the challenge that climate change presents. How do you see the balance between individual actions and top-level policy changes, and how can individuals best make an impact?

The first thing I would say is that we can allow ourselves to be cautiously optimistic with regard to climate change. At a global scale, we have all the technology and knowledge needed to tackle the problem, and – crucially – economies are starting to swing towards sustainable economics. That's being demonstrated by plans like the EU's Green Deal, for example. What's still missing, though, is the required level of political intervention, as well as people taking personal responsibility for the impact that they're having.

Within a scientific organisation like EMBL, the onus on the individual to take responsibility is actually greater than in other workplaces. Our staff have more freedom to work how they see fit, and with that great freedom comes great responsibility. For example, our labs use a lot of energy, so it's really important that our staff turn things off when not needed, and that they use equipment responsibly.

Another area where we have choices to make is on the amount of travel we do as individuals. The current pandemic restrictions have brought our flight emissions down to near zero. Once those restrictions are lifted, I really hope that society doesn't go back to flying as much as it used to. We also have individual control of the goods we purchase, and here I believe old habits die hard. Being a responsible consumer of goods is really important. Identifying greener products and generating less waste by reusing things goes a long way to reducing an individual's ecological footprint.

I will continue to work with our leadership team, administration, and facilities, to ensure that we do our best to become a more sustainable science organisation. As individuals we must also all play our part.

KINGA LUBOWIECKA/EMBL

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

MASSIMO DEL PRETE/EMBL

EMBL Director Matthias Hentze.

The power of community

EMBL Director Matthias Hentze describes the Environmental Research Initiative: a community effort to solve global environmental challenges

BY NIKI PHAM

EMBL Director Matthias Hentze has set a challenge for EMBL scientists – to find solutions to society's most pressing environmental issues through molecular life science research. Supported by philanthropy, this is the aim of the Environmental Research Initiative (ERI), which he launched in 2020.

What inspired you to start ERI? What are your hopes for the initiative?
My inspiration comes from three angles. First, it's clear that society needs solutions to environmental challenges. Second, EMBL's brilliant research culture, which empowers young scientists to make their scientific ideas and dreams a reality, is more than enough inspiration in itself, and is a goldmine of unexplored potential. The third is personal. I celebrated my 60th birthday last year and I feel a really strong commitment to making a healthier planet for my grandchildren and future generations. My hope is that ERI will contribute to research that helps pave the way for solutions for our planet.

How can research at EMBL help us find solutions to global environmental challenges?
Some environmental challenges, like loss of biodiversity and the spread of infectious diseases, are biological in nature and can also be solved biologically. On the other hand, some are not. Where biology is not a part of the problem, however, it can become part of the solution, for example with pollution and climate change. The next EMBL Programme, starting in 2022, will focus on understanding life at the molecular level in the context of its natural environment – not just in the laboratory. This is precisely why EMBL is an ideal place to help lay the groundwork for finding solutions to global challenges.

How did financial support from the community help to launch ERI?
Part of the initial support came from the Friends of EMBL: a community of individuals and businesses who support EMBL's work with annual donations. This enabled us to start three exciting ERI catalyst projects at EMBL, each of which reflects the ERI spirit. Our work wouldn't have been possible without the enthusiasm and drive of Niki Pham, our ERI Project Officer, who suggested the idea of launching a call for catalyst projects.

How can others get involved to support ERI?
The catalyst projects are a great example of what a team of scientists can do and what the community can achieve together – no contribution is too small to make a difference. We invite people to engage with us and learn about what we're doing, maybe give a small gift if that is possible, and help to spread the word and grow the community supporting environmental research at EMBL. With additional philanthropic engagement, we can fund more projects like the catalyst projects and expand even further to create new groups at EMBL delivering molecular environmental research.

What's next for ERI?
First, I'm curious to find out what these catalyst projects will deliver. Second, we're in conversations with major companies directly involved in research on climate change and carbon capture and storage. Hopefully, that will soon develop into meaningful collaborations between EMBL scientists and industry. Third, we will focus on reaching out to philanthropists, foundations, and corporations to fundraise for the grand ERI vision, which is to fully fund new EMBL research groups that contribute to EMBL's new scientific directions and pave the way to solving environmental challenges.

FOR INFORMATION ABOUT THE ENVIRONMENTAL RESEARCH INITIATIVE, CONTACT eri@embl.org OR VISIT: bit.ly/embletc-97-eri

FOR INFORMATION ABOUT THE FRIENDS OF EMBL, CONTACT solich@embl.de OR VISIT: bit.ly/embletc-97-friends

ERI catalyst projects

Fighting pesticide pollution with microbes
Zimmermann Group, EMBL Heidelberg
Pesticides used in agriculture are a major threat for soil and water ecosystems. It's still not well understood which microbes can break down pesticides and how. This project will develop novel approaches to answer these questions and will help to identify ways to better monitor the environment for pesticide contamination, to remove pesticides from the environment, and to design greener chemicals.

Tackling nanoplastic pollution
Svergun Group, EMBL Hamburg
Eight million tonnes of plastic waste end up in the oceans each year, eventually breaking down into tiny particles called microplastics and nanoplastics, which can cause serious problems for animals, humans, and ecosystems. However, the precise impacts of nanoplastics remain largely unexplored. EMBL scientists in Hamburg will combine advanced X-ray technology and biophysical techniques to better understand the links between nanoplastics and their impacts.

Cleaning wastewater polluted by artificial hormones
Zimmermann Group, EMBL Heidelberg
The daily use of pharmaceuticals introduces a high load of artificial hormones into wastewater and the environment, which is harmful to fish and local ecosystems. It's currently a major challenge to detect and identify these hormones. EMBL will develop a new approach, combining computer simulations and mass spectrometry, to improve detection and identification. This may help the search for efficient ways to remove artificial hormones from the environment.

Awards & honours

KINGA LUBOWIECKA/EMBL

EMBL Director General Edith Heard has been appointed to a new World Health Organization Science Council, and has been elected as a member of the US National Academy of Sciences.

Mariana R. P. Alves, a PhD student in the Crocker Group, has been selected as one of the Top 100 Women in Social Enterprise by Euclid Network. This recognises Mariana's science outreach activities with Native Scientist and co-founding Cartas com Ciência.

Peer Bork, Director of EMBL Heidelberg (Scientific Activities), has been awarded the 2021 Novozymes Prize for developing groundbreaking publicly available and integrative bioinformatics tools. The prize recognises outstanding research or technology contributions that help guide biotechnological science toward innovative solutions. **Peer Bork** has also received the ISCB Accomplishments by a Senior Scientist Award. This award, made by the International Society for Computational Biology, recognises individuals who have made major contributions to the field of computational biology.

Anne Ephrussi, Head of the Developmental Biology Unit and Director of the EMBL International Centre for Advanced Training, has been awarded the German Feldberg Prize 2022 in recognition of her outstanding research. The Feldberg Foundation promotes scientific contact between German and British scientists within the sphere of experimental medical research. Anne will give a prize lecture in the UK next year.

Edith Heard, EMBL Director General, has been appointed to a new World Health Organization Science Council. The council will advise WHO on science, research, and innovation priorities as part of an expanded role for scientific advice in its public health work. **Edith Heard** has also been elected as a member of the US National Academy of Sciences. This distinction recognises her significant and ongoing contributions to scientific research.

Matthias Hentze, EMBL Director, has been awarded the PRO-SCIENTIA-Förderpreis by the Eckhart-Buddecke-Stiftung zur Förderung der Medizinischen Grundlagenforschung. The prize is awarded for the advancement of fundamental medical research.

Wolfgang Huber, Group Leader and Senior Scientist, has been selected as a Fellow of the International Society for Computational Biology. The society's Fellows programme seeks to highlight outstanding contributions in the fields of computational biology and bioinformatics.

Julia Mahamid, Group Leader, has received an Early Excellence in Science Award from the Bayer Foundation. The foundation presents this international award annually to outstanding young scientists and physicians in the early stages of their academic and clinical research careers.

Nassos Typas, Group Leader and Senior Scientist, has received the German VAAM (Vereinigung für Allgemeine und Angewandte Mikrobiologie) Research Award. The award recognises his creative and original research and its impact on society.

Cristina Viéitez, a postdoc in the Typas Group, has received an award from the Christiane Nüsslein-Volhard Stiftung. The awards are made to support talented young women scientists with children.

Alumni

A community with global impact

EMBL

The impact of EMBL can be seen all over the world through the outstanding work of our alumni in research, industry, government, and other sectors. Highlighting and celebrating how fundamental EMBL research has helped to solve global challenges is a priority for us, and we're keen to identify even more of your success stories.

In this issue, we highlight how fundamental research has enabled several members of EMBL's alumni community to make valuable contributions to COVID-19 vaccine development (p. 22), and explores how the skills and training that alumnus Pawel Masiewicz gained at EMBL prepared him for his current role at German biotech company BioNTech, which developed one of the first approved COVID-19 vaccines (p. 38).

Alumnus Angus Lamond shares advice on translating fundamental research into applications with impact, and explains why effective cooperation between academia and industry is so crucial (p. 38). We celebrate the winners of this year's EMBL Alumni Awards, who have been recognised for their research (p. 42). And you can learn how a community of scientists is overcoming challenges to develop new ways of treating heart disease, as alumna Mariëlle van Kooten explains (p. 40).

EMBL alumni also make an impact through the support and mentoring they offer to members of their communities. EMBL's LEAP programme (p. 14) is supported by 70 alumni who will mentor women postdocs at EMBL. And we report how alumna Malvika Sharan helped to mentor a member of the EMBL Teen community who went on to develop a prize-winning smartphone app (p. 43).

We hope to see many of you online at our monthly 'Coffee with EMBL' events and our celebrations for EMBL World Alumni Day on 16 July.

Mehrnoosh Rayner
Head of Alumni Relations

Supporting EMBL and fundamental research

EMBL alumnus Angus Lamond explains the value of fundamental research and how it can be translated into wider impact

INTERVIEW BY MARIUS BRUER, ADDITIONAL TEXT BY TOM FURNIVAL-ADAMS

Angus Lamond, a former Group Leader and Senior Scientist at EMBL Heidelberg, is an example of how EMBL alumni help to galvanise the community through their passion for EMBL and the life sciences. Angus, now a Professor at the University of Dundee, has been involved in the EMBL Alumni Association from the beginning. He was its first Chair, from 2002–2008, and he has supported various initiatives and events through the years.

Following the first lockdowns of the COVID-19 pandemic in March 2020, Angus and EMBL's Alumni Relations team identified the need for a virtual alumni forum to help the community stay connected. As a result, they launched 'Coffee with EMBL': a series of events that bring the community together with special guest speakers and scientists for open, topical debate, with Angus moderating the discussions. In April, 'Coffee with EMBL' celebrated its first anniversary, highlighting its longevity and success. The Alumni Relations team would like to thank Angus for his tireless efforts in supporting the events as an instigator, contributor, and host.

In early 2020, Angus was co-organising an 'EMBL in the UK' event in Dundee, which would focus on how research discoveries can be effectively translated into impact. Following a postponement due to the COVID-19 pandemic, the event is now due to take place in 2022. Here, Angus reflects on the process of translating research discoveries, and discusses the importance of fundamental research – to EMBL and wider society.

EMBL alumnus Angus Lamond.

I will always be a passionate defender of the need for fundamental research. Companies, technologies, wealth, new healthcare products, and so forth came from people doing high-quality fundamental research. I think we must continue to make the argument that this kind of research, with excellence as its main motivation, must be supported. The idea of only funding what is perceived as applied research is a massive mistake, because our understanding about what types of knowledge and research can most usefully be applied is changing and evolving over time as new discoveries are made.

We need to have an intelligent, broad-based dialogue between leaders of academic research and those funding research, because we should all be on the same side. This dialogue would allow us to come up with a more productive strategy, with a continued focus on excellence. This would involve not only funding basic research, but broadening its impact – breaking barriers and strengthening opportunities for new start-up companies to form. It's only by stimulating a culture that makes it relatively easy to start new companies that the success stories of the future will come through.

In my experience of starting spin-out companies and seeking venture investment, the funding process is very different from academic grant writing. It's common for academic researchers to focus almost exclusively on issues around technology, problem solving, and product development, because that's what they know best and are most interested in. However, you need to understand what the people on the other side of the table are thinking if you're asking them for investment, because they're usually approaching the proposition from a different perspective. The more mutual understanding there is, and the less suspicion, the more productive the discussions will be, and the higher the chances of a successful outcome.

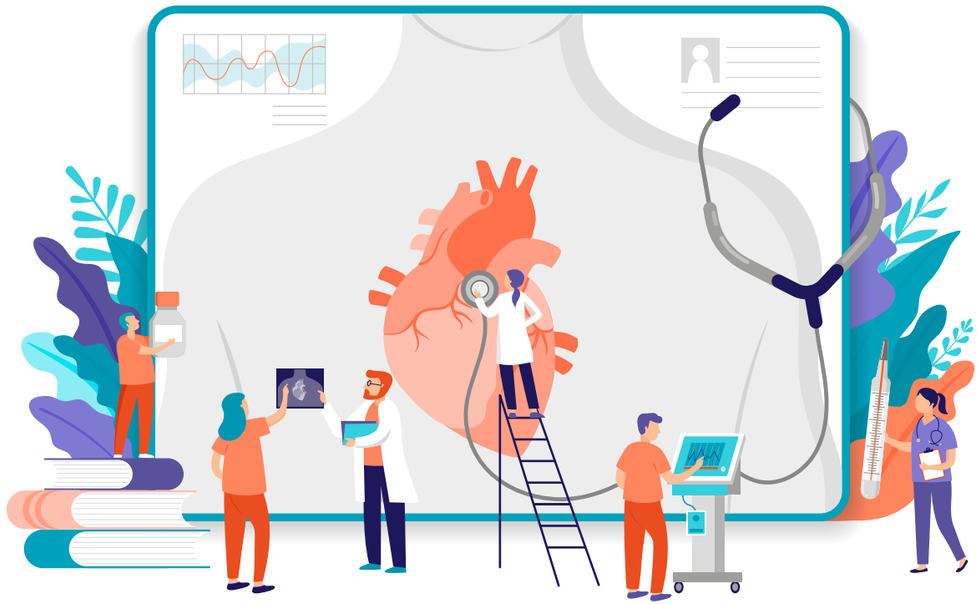
There are a lot of lessons from my own experience that may be useful to other academics considering launching a new spin-out. For example, it's important to move from thinking only about your research and new technology to also understanding the needs of your future customers. How do you deal with customer experience and marketing your product? You also need to understand accounting and cashflow. Most start-ups fail because of cashflow, not because of fundamental problems with the technology or even the potential market value of new products. I think we need to build an environment in the community where there's more connection between people with these complementary skills, so that when new start-up companies are launched, they include the combination of talents and expertise that's really needed to be successful.

Don't strangle a small seed before it can grow into a large fruit-producing tree. We need to keep explaining to the funders the potential benefits of the investments we're asking them to make in fundamental research. At the same time, we as researchers also need to listen to society and reflect on what's needed from us in return. I think society can benefit greatly from a flourishing fundamental research environment, especially one that encourages researchers to innovate, tackle difficult problems, and take risks. Fear of failure and losing funding encourage researchers to play safe, leading to only incremental advances. EMBL can showcase the value of a thriving, ambitious research culture that addresses the major challenges of our age and inspires and enables the research leaders of the future.

Capturing the impact of your fundamental research

Members of the EMBL community bring many benefits to society, through work carried out at EMBL and afterwards. Case studies showing the impact of EMBL's alumni can be found in the EMBL Annual Report.

What did your research lead to?
Let us know at alumni@embl.org.



All heart

EMBL alumna Mariëlle van Kooten is part of a research community working to beat heart disease

BY MARIËLLE VAN KOOTEN, MARKUS GROSCH, AND JULIA KORNIENKO

With scientific cliffhanger endings to each Zoom catch-up, a massive community of scientists edges closer to therapeutic strategies for heart disease. Centre of operations: Heidelberg, Germany.

Our object of study, the human heart, contains an estimated three billion cardiomyocytes, or heart muscle cells, which undergo relentless mechanical contractions throughout life. Cardiomyocytes have to adapt their metabolism to ensure continuous mechanical activity, but it's a trade-off: these changes in the cell's chemistry also lead to age-related decline in cardiac performance. More importantly, mammalian cardiomyocytes have a limited ability to regenerate. In a literal sense, the heart does not heal.

Heart disease is the leading cause of death worldwide, and donor replacement of the heart is the sole option available in life-threatening conditions. We don't yet understand the cellular mechanisms behind the healthy, the maturing, and the diseased heart well enough to prevent, repair, or regenerate heart tissue.

The development of heart disease is a complex process that involves many factors, requiring unprecedented research breadth and detail. Take, for example, dilated cardiomyopathy (DCM) – a disease in which the heart muscle becomes larger and weaker, and is less able to pump blood. DCM may be caused by environmental factors, but familial DCM has a genetic origin. Together, DCM and familial DCM have an estimated prevalence of 1 in 250 people worldwide. A subset of familial DCM patients carry mutations in the gene coding for a protein called RBM20. The mutations may cause RBM20 to form granules. Because this process has similarities to the neurodegenerative disease amyotrophic lateral sclerosis, the granules are expected to play a much wider role in heart disease. "The mechanistic parallels with neurodegenerative disease are compelling and fascinating, opening a new avenue of research that cuts across both fields," says Jay Schneider, a cardiologist at the Mayo Clinic.

This is just one example that demonstrates the need for in-depth, comprehensive study of heart disease. It's a process that requires broad expertise – and many minds. "We're collaborating with biologists, engineers, data scientists, and clinicians across the globe to get to the bottom of RBM20 DCM," says EMBL Senior Scientist Lars Steinmetz. "Our genome is not our destiny. Understanding how RBM20 mutations cause degeneration of the heart will help us identify biomarkers to monitor disease progression and even design new therapies so these patients can live longer, healthier lives, and ideally never develop DCM in the first place."

It's not easy to get donor material, so one way to study heart tissue is by using cells with the elaborate name of human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs). These are created by taking cells from another part of the body and genetically reprogramming them to become heart cells. After reprogramming, the cells undergo a transition in which they assemble the central structures responsible for creating mechanical force in the heart, known as sarcomeres. These are interconnected molecular structures that are responsible for – and help to synchronise – the contractions of each cell. They create your heartbeat. Observing how gene activity is translated into functional molecular machines is absolutely stunning: hiPSC-CMs beat in a Petri dish.

In addition to the wide-ranging causes of heart disease and the limited availability of sample material, researchers meet with a number of confounding hurdles in experimental studies of the heart. For one, cardiomyocytes form a highly diverse cell population. Although each cell carries the same genome, gene expression depends, among other factors, on a cell's location. For example, the gene *TTN* gives rise to two distinct gene products, and the ratio between these products differs in the cells of the heart's upper and lower chambers, known as the atria and ventricles. During the process of converting information from DNA into proteins, instructions from genes like *TTN* can be cut and spliced together in different ways, giving rise to different gene products, called isoforms. In the case of *TTN*, the expression ratio between the isoforms allows the ventricles to contract and recoil rapidly.

The diversity of cell types means that any study should be set up in a way that distinguishes individual cells. However, cardiomyocytes can reach immense sizes – too large for typical single-cell measurement platforms. In addition, cardiomyocyte cell biology involves several long isoforms like those arising from *TTN*, and making quantitative measurements of these is a painstaking and difficult process. Indeed, another gene that plays an important role in heart cells, *DMD*, is one of the largest genes found in humans, containing around 2.3 million letters of the DNA code.

A further hurdle appears after making the transition from the Petri dish to studies in living organisms, because there are significant differences in heart disease processes between humans and organisms that are used to study these processes in the lab, such as zebrafish and mice. This hinders the translation of experimental results, and means that findings from different model organisms have to be pieced together to form a logical storyline, in which not all puzzle pieces will fit. To overcome these hurdles, we need novel experimental and analytical tools.

The interdisciplinary expertise of our consortium's members and their willingness to work together help to drive our research, leading to faster problem solving and accelerating the process of identifying and testing drug candidates for treating heart disease. Dr. Benjamin Meder, a physician scientist at Heidelberg University Hospital, likens it to a symphony orchestra: "Heart disease is a complex composition. But, by working in harmony, combining insights from genomics, molecular biology, artificial intelligence, and medicine, our research can be life changing."

EMBL Alumni Awards 2021

Committee recognises outstanding contributions of EMBL alumni

BY TOM FURNIVAL-ADAMS


DAVID AUSSERHOFER

Ilaria Piazza is the winner of the John Kendrew Award, in recognition of the excellence of her research. Ilaria performed groundbreaking work as a postdoc at ETH Zürich, including the development of a method to analyse protein–metabolite interactions in their native environment at a global level. This is a widely enabling technology in both fundamental and translational research.

Ilaria is now a group leader at the Max Delbrück Center for Molecular Medicine in Berlin. She is supported by grants from the European Research Council and Germany's Helmholtz Association, and is a member of the Early Career Research Committee at the international Human Proteome Organization. She was a PhD student at EMBL Heidelberg from 2009–2014.

Ken Holmes is the winner of the Lennart Philipson Award, in recognition of his pioneering work in the use of synchrotron radiation for X-ray diffraction. In 1971, Ken published work that served as a starting point for the construction and use of beamlines, and for entire synchrotrons dedicated to X-ray diffraction studies. Access to synchrotron facilities is now an essential part of structural biology research for scientists around the world.

Together with EMBL's first Director General, Sir John Kendrew, Ken helped to establish EMBL's site in Hamburg, which he headed from 1974–1976. Beyond his contributions to our understanding of muscle structure and function, people who worked with Ken have gone on to become leaders in the world of beamline design, carrying forward the transformative work that he began.

The **John Kendrew Award** recognises excellence in science or science communication. It is open to all former EMBL PhD students and postdocs, between two and seven years after leaving EMBL.

The **Lennart Philipson Award** recognises outstanding and validated contributions in translational research in human health or technology innovation in the life sciences. It is open to all EMBL alumni, irrespective of leaving date.

Each award consists of a gold-plated medal and a prize of €10,000.

WATCH THE AWARDS CEREMONY AS PART OF EMBL WORLD ALUMNI DAY ON 16 JULY: bit.ly/embletc-97-wad

Coding between the vines

An EMBL Teen discusses the value of allyship in STEM as she develops an app to identify grapevine diseases

BY IVY KUPEC


IVO LICKA

EMBL Teen Maria-Theresa Licka has created an app that helps winemakers to identify early stages of disease on their vines.

A member of the EMBL Teen community, which is part of the Friends of EMBL programme, has made identifying leaf diseases on grapevines as easy as taking a picture with a smartphone.

Maria-Theresa Licka and teen collaborator Mario Schweikert won the jury prize in Germany's national artificial intelligence competition for pupils last November. For their entry, they harnessed artificial intelligence (AI), using smartphone pictures to detect and differentiate between vine leaf diseases. They started with more than 5,000 pictures of leaves infested with algae and fungi during different seasons, classifying the photos with help from the Dienstleistungszentrum Ländlicher Raum: a centre for rural services. This enabled them to create a dataset to teach the AI system that they use in their app.

Maria-Theresa joined the EMBL Teens community in 2018, which gave her the opportunity to interact with scientists in various ways. The following year she met Malvika Sharan, then a computational biologist at EMBL Heidelberg; now a research associate and community manager at the Alan Turing Institute: the UK's national institute for data science and AI. Malvika invited Maria-Theresa to her lab, providing mentorship in a variety of ways. It was a relationship that gave Maria-Theresa both know-how and self-confidence.

"During these visits I got a good feel for her work as a Bio-IT community coordinator and computational biologist," Maria-Theresa recalls. "She introduced me to her EMBL team and community. She also taught me some coding and how to use GitHub [a software development tool that also facilitates collaboration] – both things that were very helpful to my follow-on projects in AI."

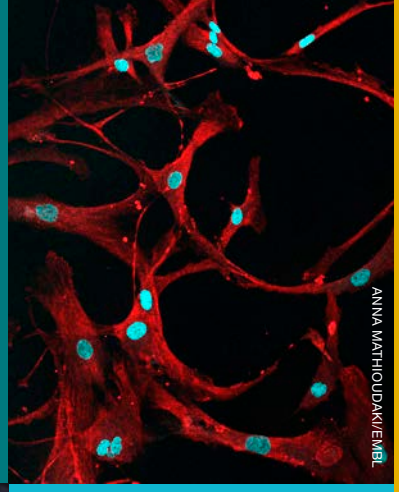
Malvika also encouraged Maria-Theresa to create her own YouTube Channel, INFOrmAtIc Teens. Maria-Theresa's concept is to continue publishing small tutorials for other students who want to start coding.

"As a child I was always interested in informatics and robotics – courses not 'typically' for girls, so I was often the only female. Even at a student trip in 2018 to Silicon Valley, there were only two girls and 17 boys," Maria-Theresa says. "The numbers continue to grow – even just within the past two years. Women are capable of doing informatics, data science, and AI, but society has a way of discouraging them. Thankfully, we have successful female researchers to show us the way, like my role models Marie Curie, Jennifer Doudna, and Emmanuelle Charpentier, who I personally look up to and who have enriched science so much. These women inspire and encourage me about the future of women in science."

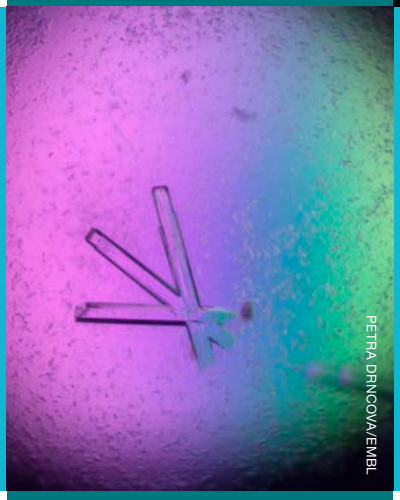
FRIENDS OF EMBL: bit.ly/embletc-97-friends

Events

September
6–10
Virtual
EMBO Practical Course: In-situ CLEM at Room Temperature and in cryo


ANNA MATHIOUDAKI/EMBL

September
7–10
Virtual
EMBL Conference: Protein Synthesis and Translational Control


PETRA DRNCOVA/EMBL

September
15–17
Virtual
EMBO | EMBL Symposium: Multiomics to Mechanisms – Challenges in Data Integration

Upcoming meetings
Alumni

16 July
EMBL World Alumni Day, virtual and EMBL Heidelberg

16 September, 15 October, 11 November, 10 December
Virtual: Coffee with EMBL

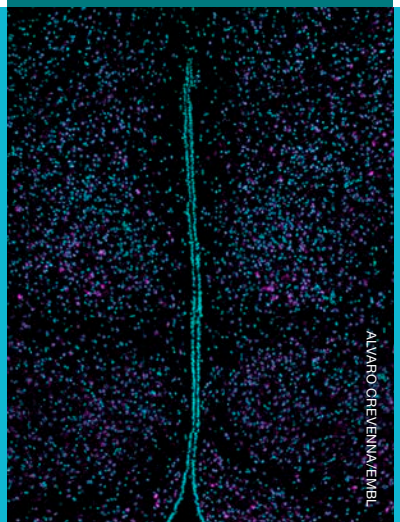
bit.ly/embletc-cwe

3–4 December
EMBL in Denmark, Technical University of Denmark

October
20–22
Virtual
EMBL Conference: Bringing Molecular Structure to Life: 50 Years of the PDB

November
8–12
Virtual
EMBL Course: Metagenomics Bioinformatics

November
22–24
Virtual
EMBL Conference: Cancer Genomics


ALVARO CREVENNA/EMBL

December
3
Virtual
EMBL Science and Society Conference: One Health: Integrating Human, Animal and Environmental Health

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