The European Molecular Biology Laboratory Magazine

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EMBL etc.

Beneath the surface

Synapse Bending into shape

Nucleus Tara: An ocean odyssey

Cultures Celebrating 40 years of EMBL Grenoble

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PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Editorial

"Plankton porridge... magic gruel," wrote Norwegian adventurer Thor Heyerdahl, describing the multitudes of tiny creatures he saw shimmering on the surface of the ocean. This 'magic gruel', as Heyerdahl's colourful description implies, provides sustenance, directly or indirectly, for whales, jellyfish, turtles, sharks, salmon, and indeed practically all life in our seas. Yet we know very little about the miniscule organisms that make up the base of our oceans' food web, and our cover story focuses on a breathtaking scientific adventure that aims to change this forever (page 14). Our relationship with the microbes in and on us is also drawn into focus as we explore initiatives to map the molecular environment of our bodies in 3D (page 11), and follow an epic citizen science initiative aimed at learning more about our mouth microbiome (page 45). From stunning startups (page 22) to fond farewells (page 26), throughout this edition we dive deep into the lives and work of people in the EMBL community and beyond. Reflecting on the mass of mysterious creatures he also observed floating in the water, author John Steinbeck wrote: "It is advisable to look from the tide pool to the stars and then back to the tide pool again." It is with such a sense of pragmatism and adventure that we take you *beneath the surface*.

Adam Gristwood
Editor

Word to remember

Diatom

Noun, pronunciation: dī-ə-ˌtăm

Single-celled organisms that are a major group of algae, and amongst the most common types of phytoplankton (page 14).

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Editor-in-chief
Silke Schumacher
Director, International Relations

Editors
Adam Gristwood, magazine
Chloë Cross, digital
Sonia Furtado Neves, science
Isabelle Kling, science
Mehrnoosh Rayner, alumni
Mary Todd Bergman, EMBL-EBI

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Edenspiekermann, Amsterdam

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Contact
news@embl.de

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Bending into shape

Vesicles covered by clathrin proteins have been known for decades to be crucial for endocytosis, the mechanism by which cells engulf molecules. However, the process by which they form was still a topic for debate. Using new imaging techniques, the groups of John Briggs and Marko Kaksonen, both at EMBL Heidelberg, bring new data to settle the question.

BY ISABELLE KLING

Endocytosis involves making dimples in the cell membrane that deepen with time and eventually seal off to make a spherical vesicle inside the cell. Essential to the process is the formation of a lattice-like protein shell on the surface of the vesicle membrane. However, there was still no consensus as to the exact behaviour of this coat. Even for the best understood coat protein, clathrin, opinion was split between two different models.

In the first model, the clathrin lattice, or coat, first assembles as a flat structure, and then bends, essentially wrapping around the forming vesicle. In the second model, scientists suggest that clathrin assembles directly, assuming the shape of the membrane as it is drawn inwards.

Although the second model has been more generally accepted, the collaboration between John Briggs and Marko Kaksonen showed that, in fact, the first explanation is more accurate. They used human cell lines in which the sites where endocytosis was taking place had been tagged with a fluorescent marker. Then postdoc Ori Avinoam used 3D electron microscopy to take pictures of these sites and analysed them to understand how they changed shape over time.

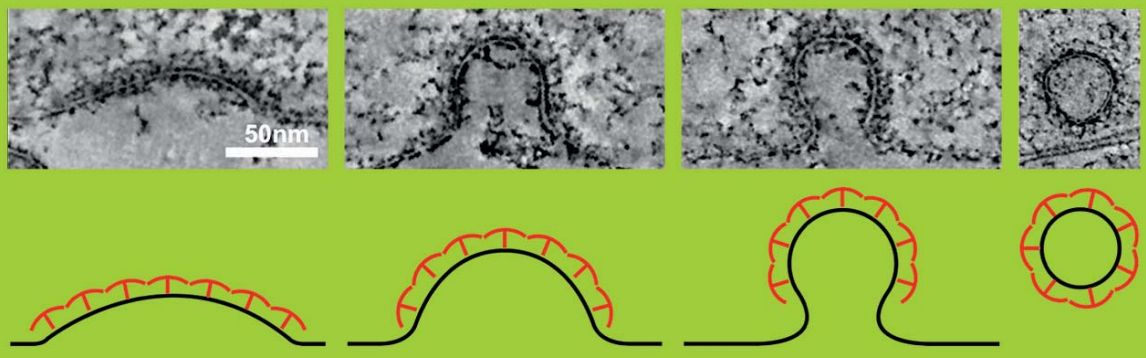
By analysing the images computationally, the team was able to demonstrate that the surface area of the clathrin coat does not change during endocytosis, and only its curvature changes as it draws the cell membrane inwards.

"Our results were surprising, because the proteins have to undergo some complicated geometric transformations to go from a flat to a curved shape, which is why the second model was favoured by scientists for such a long time," says John Briggs.

"The next stage of our research is to investigate more precisely how this rearrangement occurs," adds Marko Kaksonen. "We also want to look at other aspects of the process, such as how the molecules ingested by the cells might themselves influence the action of the clathrin proteins. Answering these fundamental questions of cell biology will help scientists better understand the whole process of endocytosis."

Avinoam, O., Schorb, M., Beese, C. J., *et al. Science*, 18 June 2015. DOI:10.1126/science.aaa9555

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=4301



Clathrin proteins involved in endocytosis form a lattice that can dramatically change its shape to form the vesicle

ORI AVINOAM/EMBL

The genome in the cloud

A *Nature* comment article co-signed by Jan Korbel and published on 8 July calls for the development of cloud-based solution to cancer genetic analysis, and urges funding agencies to take this responsibility.

BY DAN JONES

Today, genomics is well into the era of 'big data', with genomics datasets often containing hundreds of terabytes (10^{14} bytes) of information. Korbel's research focuses on genetic variation, especially genetic changes leading to cancer. While the majority of current cancer genetic studies assess the 1% of the genome comprising genes, the Korbel group is investigating genetic alterations within the 99% 'intergenic' regions that drive cancer. This approach logically generates and analyses much larger amounts of data.

So the problem is not a shortage of data but accessing and analysing it. Genome datasets from cancer patients are typically stored in 'controlled access' data archives. These repositories, however, need to be downloaded to a researcher's institution before they can be further studied. "With massive datasets, this can take many months and may be unfeasible altogether depending on the institution's network bandwidth and computational processing capacities," says Korbel. "It's a severe limitation for cancer research, blocking scientists from replicating and building on prior work."

An increasing number of scientists now use commercial cloud services or academic community clouds to store, share, and analyse vast datasets without first having to download them. Cloud computing also allows researchers to draw on the processing power of distributed computers to significantly speed up analysis without purchasing new equipment for computationally laborious tasks. Given the central role that such infrastructures are predicted to play in future research, the authors of this article urge funding agencies to actively support their implementation.

Safeguarding privacy

One concern about using cloud computing revolves around the privacy of people who have supplied genetic samples for studies. However, cloud services are now typically as secure as regular institutional data centres and earlier this year, the US National Institutes of Health lifted a 2007 ban on uploading their genomic data into cloud storage.

Another issue relates to the differing privacy, ethical and normative policies and regulations in Europe, the US, and elsewhere. Some European countries may prefer that patient data remain within their jurisdiction so that they fall under European privacy laws, and not US laws, which apply once a US-based cloud provider is used. Normative and bioethical aspects of patient genome analysis, including in the context of cloud computing, are another specific focus of Korbel's research, which is being pursued via an inter-disciplinary collaboration with the the University of Heidelberg's faculty of law.

Stein, L.D. *et al. Nature*, 8 July 2015. DOI: 10.1038/523149a

FULL STORY ONLINE: NEWS.EMBL.DE/?p=4514

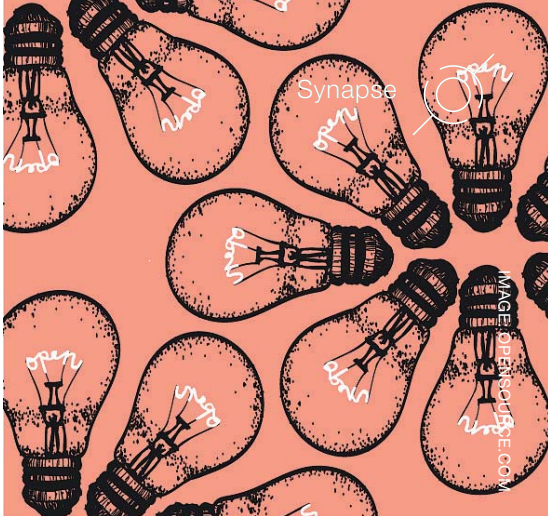
DNA protection, inch by inch

Scientists from the Pillai group in EMBL Grenoble have discovered how cells produce tiny pieces of RNA – called piRNA – that identify and silence 'jumping genes' or transposons. A piRNA and a PIWI protein bind to a transposon mRNA in the cytoplasm, cut its first section to silence it, and then work their way along, cutting off 30 letters of code at a time and converting these into new piRNAs. These can migrate to the nucleus and silence the gene: a process that had never been observed before.

Homolka, R., Pandey, G. *et al. Cell Reports*, 9 July 2015. DOI:10.1016/j.celrep.2015.06.030

FULL STORY ONLINE: NEWS.EMBL.DE/?p=4526

Open Access: the policy



EMBL's open access policy aims to make publicly funded research accessible and freely available to everyone to read.

BY MARY TODD-BERGMAN

The policy embraces the most comprehensive Creative Commons license, CC-BY, which requires attribution and lets people reuse information in innovative ways.

"Why should we remain stuck in this mindset, thinking that we'll all get around to reading every paper?" posits Jo McEntyre, Head of Literature Services at EMBL-EBI. "We all need to discover things from the literature – and that might be something big and obvious, but equally it could be just an aside in someone's paper. We need to make the whole process of exploring and consuming the scientific literature much more efficient, and text mining and analytics are a big part of that."

All of the articles in Europe PMC can be read by anyone, anywhere, any time. But open-access papers with a Creative Commons attribution license (CC-BY) or similar are much more useful, because they can be reused.

Enabling discovery

"We make full-text articles with the appropriate licence available for download, which means that text-analytics researchers can experiment with it," says McEntyre. "Having a CC-BY license makes it possible to do computation on swathes of articles, which is fundamentally important if we're going to scour the whole of the literature for relevance and serendipitous discovery."

The Protein Data Bank in Europe (PDBe) uses text mining with Europe PMC, including figures and captions from articles that provide much-needed context for structural data records. This gives researchers a rich, multi-dimensional view of complex information, saving time and improving understanding. "Open access is not only about articles being free to read, but also about making the outputs of science more discoverable by linking the article narrative to related information," explains McEntyre. "For example, data presented in figures can be linked to other core public data resources, or to other sources like spreadsheets and raw images. Things like this really add value and make the literature more useful over the longer term."

For the public good

EMBL's open access policy is a commitment to the public good. It makes science more open, scalable and sustainable, pooling an extremely diverse mix of results from thousands of journals covering every life science speciality.

"Many of the intellectual property laws around scientific publishing were established well before the web and certainly before bioinformatics came on the scene," explains Iain Mattaj, Director General of EMBL. "In many countries these laws create a barrier to analysis, although this has changed in the UK and is beginning to change across the EU as a whole. It really is a moral issue when a huge proportion of the world's scientists can simply not access new research at all. We have an obligation to address both of these barriers – not just EMBL, but the global scientific community."

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=4178

Decaying RNA molecules tell a story

Researchers from EMBL Heidelberg and Stanford University have shown that one end of the mRNA begins to decay while the other is still serving as a template for protein production. The protective 'cap' is removed while ribosomes are still associated with the mRNA, and the enzyme degrading mRNA follows the ribosome closely, pausing after each group of three nucleotides. Thus, studying the decaying mRNA also provides a snapshot of how proteins are produced.

Pelechano, V. *et al. Cell*, 4 June 2015.
DOI: 10.1016/j.cell.2015.05.008

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=4138

Union builds success

EMBL PHOTOLAB/MARIETTA SCHUPP

Matthias Hentze and Andreas Kulozik meeting at EMBL's Advanced Training Centre

With the goal of joining forces to further scientific and medical research, EMBL and the Medical Faculty of the University of Heidelberg have renewed the successful Molecular Medicine Partnership Unit (MMPU) agreement until 2025.

Together, they aim to achieve scientific and medical breakthroughs that each individually may not have been able to achieve.

The MMPU was founded in 2002 and today consists of eight research groups. "This kind of close collaboration really bridges the gap between basic and medical research and brings strong additional value to both institutions," explains Matthias Hentze, Director of EMBL. "But it is usually difficult to implement, so we are proud that the MMPU has been so fruitful for 13 years now."

One example is a research group focused on cystic fibrosis, led by an unusual but forward-thinking partnership between pediatrician Marcus Mall and chemist Carsten Schultz. Mall, Director of the Department of Translational Pulmonology at the University of Heidelberg, developed a mouse model for cystic fibrosis, while Schultz, Senior Scientist at EMBL, created chemical fluorophores that bind to the proteases causing lung inflammation, thus allowing the biologists to visually follow the evolution of the disease. Together they were able to pinpoint which proteases were driving the inflammation and would be efficient targets for future treatments in mice but also, further down the line, in humans. Other collaborations include groups studying HIV, leukemia, cancer, and chronic pain.

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=4662

EIPOD goes cubic

Flagship interdisciplinary postdoc programme opens its doors to academia and industry to foster cross-institutional academic research, industry collaborations and the development of commercial know-how and entrepreneurship.

Since its inception in 2007, the EMBL Interdisciplinary Postdocs (EIPOD) initiative has fostered interdisciplinary research projects each involving two or more research groups from across the Laboratory. As of July, EIPOD aptly becomes EI_3POD, with the addition of two new dimensions: 'inter-institutional' and 'inter-sectorial', enabling collaborations with other research institutes and with industry. With €12.8 million in support from a COFUND grant under the European Commission's Horizon 2020 Marie Skłodowska-Curie Actions, the EI_3POD scheme maintains the strong basic research path while encouraging interdisciplinary research that reaches beyond institutional and academic borders.

EIPOD fellows work on cutting-edge projects that make the most of the unique research environments at EMBL's five sites, and the new aspects look to connect fellows further with industry and academic

Oskar's structure revealed

Named after the main character from Günter Grass' novel *The Tin Drum*, who chose never to grow up, the Oskar protein is essential for development but its structure and mechanism remained poorly understood.

Scientists led by Anne Ephrussi determined the structure of two of its domains: OSK and LOTUS. They showed that only OSK binds to RNA, whereas LOTUS binds to an enzyme called Vasa helicase. This work was done on flies, but could have implications for understanding more about other animals.

Jeske, M., Bordi, M., Glatt, S. *et al.* *Cell Reports*, 16 July 2015.
DOI: 10.1016/j.celrep.2015.06.055

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=4606

partners from around the world. The evolved programme aims to diversify career pathways and international mobility of fellows. It provides new 'inter-institutional' opportunities to work between scientific groups at EMBL and another research partners, or 'inter-sectorial' prospects that involve industry collaboration or active participation in commercialising technologies.

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=4569

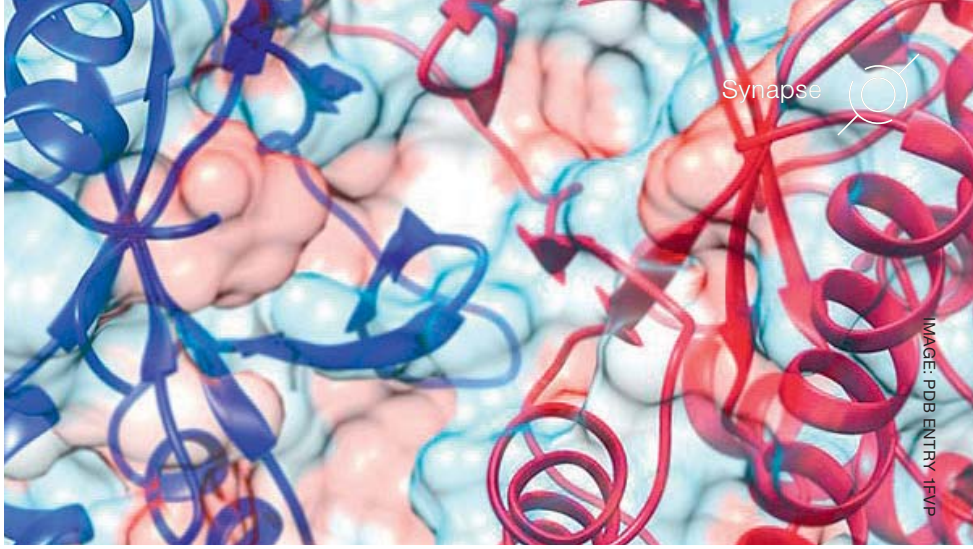


IMAGE: PDB ENTRY 1EVP

Are protein domains indivisible?

Proteins are everywhere, performing an endless variety of tasks to keep life moving along. They are made up of independent units called protein domains, which can be assembled in different combinations to build full proteins to order.

BY MARY TODD-BERGMAN

Protein domains are defined by core structural elements, much in the same way a gear on a bike, watch or car can be defined by the number, size and arrangement of its cogs.

But are protein domains really indivisible? The Bateman research group at EMBL-EBI set out to answer this question by searching and comparing millions of protein sequences and hundreds of protein structures in public databases. They identified some protein domains that have been retained throughout evolution, functioning just like their ancestors, despite having undergone large-scale structural deletions. "You can think of protein domains like cogs in an engine, with all these teeth that interlock and make each other move," explains Ananth Prakash, a PhD student in the group. "You can assume that a cog will need all its teeth to make a good enough connection to work properly. But we found that with some protein domains, the engine parts keep moving even if a large number of those 'teeth' are missing."

"Given that a mutation in a single residue can lead to a human disease, it is simply amazing that proteins can tolerate such extreme mutations," adds Alex Bateman.

Domain atrophy is extremely rare – for the most part, protein domains are indivisible, structural building blocks. But the findings reveal a fascinating phenomenon, and the group is looking forward to exploring the molecular mechanisms that cause parts of these protein domains to disappear in the first place.

Prakash, A. and Bateman, A. *Genome Biology*, 30 April 2015.
DOI: 10.1186/s13059-015-0655-8

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=4006

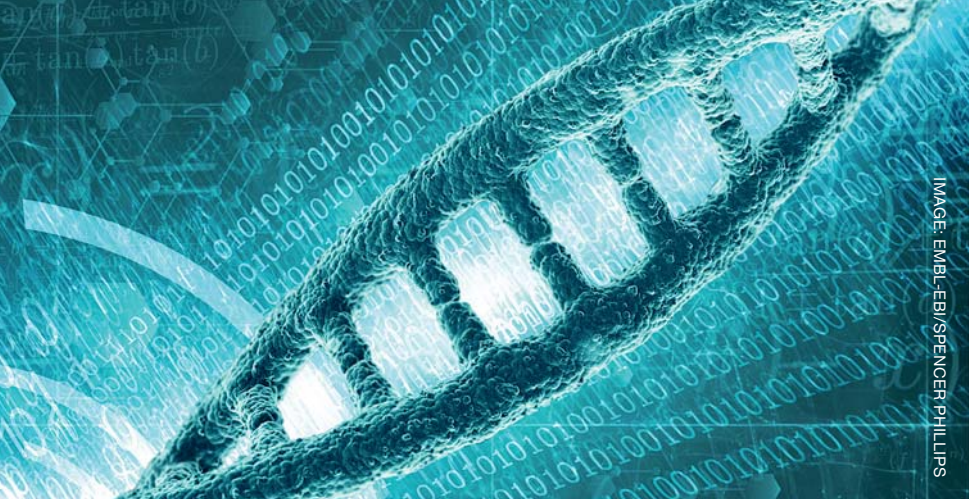


IMAGE: EMBL-EBI/SPENCER PHILLIPS

Comparing genomes: 500 000 at a time

The Stegle research group at EMBL-EBI developed a new algorithm that makes it possible to perform genetic analysis of up to 500 000 individuals – and many traits – at the same time.

BY MARY TODD-BERGMAN

The relationship between genes and specific traits is more complicated than simple one-to-one relationships between genes and diseases. Genome-wide association studies (GWAS) show that many genetic factors are at play for any given trait, but we are just beginning to explore how, specifically, genetic variations affect health and disease. Two major challenges to finding these connections are statistical: analysing associations between different genetic variants and multiple traits, and using data from hundreds of thousands of individuals.

"It is very challenging to identify genetic variants that underlie phenotypes, or traits, and usually we do this by analysing each phenotype and each variant one by one," explains Oliver Stegle. "But the simple models we normally use to do this are too simplistic to uncover the complex dependencies between sets of genetic variants and disease phenotypes."

mSet: A new method that makes complex, large-scale genetic analysis feasible.

Complex models that let you look at the combined action of many different variants have, until now, involved so much computation that it would take a year to run a single complex query. "The breakthrough here is that we've made it possible to perform an integrative analysis involving many variants and phenotypes at the same speed as current approaches," says Stegle. Using the new method, GWAS researchers can explore several variants of a gene at once while comparing them with several related phenotypes. This makes it much easier to pinpoint which genes – or locations on genes – are involved in a particular function, such as lipid regulation.

The new method, mSet, will help researchers in their quest to determine which specific aspects of our biology are inherited, and to uncover new insights into the genetics behind our countless biological processes.

Casale, F.P. *et al. Nature Methods,* 15 June 2015. DOI: 10.1038/nmeth.3439

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=4197

Dancing with the cells

The same kind of contraction that fires our muscles, thanks to myosin, also controls a key stage of mammalian embryo development called compaction. The research, conducted in the Hiiragi group at EMBL Heidelberg, measured and mapped how cells in very early stage embryos bond tightly together. The scientists also discovered a cellular behaviour that hadn't been observed before: cells in the embryo 'dance', each one making the same rhythmic movement.

Maître, J.L., Niwayama, R., Turlier, H. *et al. Nature Cell Biology,* 15 June 2015. DOI: 10.1038/ncb3185

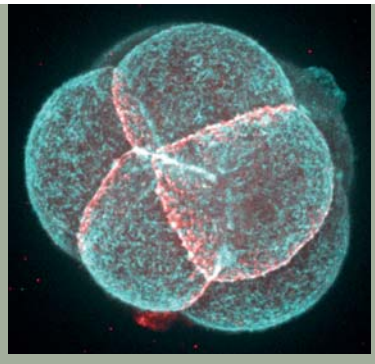


IMAGE: J.L. MAITRE/EMBL

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=4166

It's the economy, stupid

You might not think that your body's biology has much in common with the workings of your credit card or the global banking system. Neither, at first, did Theodore Alexandrov. But the EMBL team leader is now applying the mathematical algorithms used to delineate the workings of the economy to analysing information about the countless molecules produced by our cells.

BY CLAIRE AINSWORTH

Alexandrov and his team are developing a new technology that maps where these molecules are in relation to each other in three-dimensional (3D) space. The work is leading to a new, spatially-aware understanding of biological processes such as the metabolism of our cells or the interactions between microbes in the environment, as well as offering insights into how they can go wrong. "If we want to truly understand how all these processes work, then we need to see where all these molecules are," says Alexandrov. "This understanding is increasingly emerging in all fields."

Using mathematical algorithms and big data technologies, similar to those developed to explain how economic events such as banking transactions change over time, the team have identified further members of the bewildering array of molecules produced by biological processes and mapped them to specific locations. The field in which they work is known as metabolomics: the study of the biochemical fingerprints produced by the reactions occurring in the cells in our bodies. A person's metabolome is hugely complex and dynamic – doing something as innocuous as drinking a cup of coffee or eating a sandwich, for example, dramatically and in seconds alters the mix of substances produced by some of our cells and is thus detectable in our blood or urine. Different kinds of cells and tissues have different metabolomes, which can alter as a result of disease or a changing environment. Researchers are keen to understand these patterns in detail as they could give new insights into both normal and abnormal processes.

Molecular maps

But given that a metabolome contains thousands of ever-changing components, this is no easy task. To identify molecules in a sample, researchers usually turn to a method known as mass spectrometry, or mass spec for short. This involves ionising the molecules and passing them through a mass spectrometer, which uses electric and magnetic fields to 'weigh' each one. The machine detects the weights and produces barcode-like patterns known as 'spectra' that researchers can then interpret. However, some molecules come in a range of slightly differing forms, and so the spectra of samples containing many molecules can be extremely difficult to decipher.

"A new, spatially-aware understanding of biological processes"

New developments in the field are providing even more information for scientists to contend with. One of these is imaging mass spec, which not only identifies molecules but also determines their location in space and presents this information visually as a kind of molecular map. For example, scientists can place a thin section of a tumour or cell culture on a microscope slide and use a laser to systematically vaporise the molecules within it, point by point across the slide. They can then cross-reference the molecules they find to the points on the slide >>

>> from which they originate. Putting this location specific information together with the mass spec data requires powerful bioinformatics software – software that Alexandrov was in an ideal position to develop thanks to his background.

Maths to mass spec

Having completed a PhD in mathematics and statistics, Alexandrov embarked on a postdoc on a trans-European project in econometrics in Bremen, Germany, predicting bank transactions over time for a credit-card company. He was approached by a colleague who pointed out that Alexandrov's expertise in developing mathematical processes, or algorithms, that track how things change over time, could also be applied to similar problems in the rapidly growing field of mass spectrometry. "For me this is the perfect field," he says. "Now we're working with gigabytes, even terabytes of data, my background in mathematics really helps."

In 2012, together with Pieter Dorrestein from University of California San Diego, they came up with the idea of creating maps of metabolites on the human skin. This rapidly grew up into an ambitious project, also involving the labs of Rob Knight and Nuno Bandeira, aiming at mapping not only metabolites present on the skin, but also microbes. By combining mass spec and imaging information, the team was able to create a 3D map of the molecules clinging to the skin of two volunteers. What's more, they also correlated this map with information on the distribution of different microbial species.

They found that the molecules on our skin are surprisingly stable. "90% of the molecules we could attribute to their sources were from beauty products," explains Alexandrov. "This included shampoos, skin lotion and sun cream, even though the volunteers were asked not to apply them and not to take a shower for three days before the sampling." This rather surprising finding showed that such molecules persist on the skin for much longer than anyone expected. What's more, the spatial information in the map also allowed the team to uncover molecules that might act as communication avenues between human and microbial cells. "What's unique about our approach is that we always try to bring spatial information into the analysis," he says.

Molecules and microbes

Thanks to this spatial analysis, researchers now have a better picture of the molecular environment of our skin's surface. They also have a starting point to understand more about how this environment might affect our skin's ecological relationship with its resident microbes. This is particularly relevant as the interconnections between our cells and the trillions of microbes that inhabit our bodies are currently of intense scientific interest, as evidence mounts that these microbes have a profound influence on our health.

Moving mass spec into the third dimension promises to revolutionise many areas of research. "It's a very broad technology and its applications are unlimited," says Alexandrov. "It is now being used in clinics, biomedical research and pharmacy." One key example is cancer research. Individual tumours contain cells that differ from each other, a phenomenon known as tumour heterogeneity. These variations cause the cells to behave in different ways, perhaps making some more prone to spreading or invading local tissue than others. Understanding these differences is therefore very important if we are to learn more about how the disease develops and progresses. "One cell can change everything," says Alexandrov. Until recently, researchers studied such tumours by crushing them up and analysing them, thus losing sight of this heterogeneity. "Now, we can see molecular differences between the cells."

Researchers are developing a clearer picture of the molecular environment of our skin's surface

IMAGE: THEODORE ALEXANDROV

"Now we're working with terabytes of data, my background in mathematics really helps."

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Community conquests

Since joining EMBL in November 2014, Alexandrov and his team have been working on two flagship projects to push the technology forward. The first is a continuation of his collaboration with Dorrestein's group, and involves developing the bioinformatics tools to map the spatial distribution of molecules in any environment. The team has designed a Google Chrome-based browser that makes it easier to visualise the 3D data and this has already been used in collaboration with other researchers to map molecules on bee antennae and coral reefs. The tool is free and interactive and is already available for public use at https://github.com/ili-toolbox/ili.

The second project involves developing new algorithms and hardware infrastructure to allow users to identify more of the molecules in their samples. At the moment, the fact that one molecule can generate hundreds of different signals in a mass spec machine means that scientists can only interpret a small fraction of their spectra. "I'm pretty sure we're just scraping the surface: we're not getting the full molecular snapshots," says Alexandrov. This work forms the basis of a European Horizon 2020 project that Alexandrov is coordinating, which brings together eight partners from academia and industry. "They are all interested in really getting this working as a community effort," he explains.

But even as his team grapples with the challenges of moving mass spec into the third dimension, Alexandrov already has his sights set on the fourth. Being able to monitor metabolomes in time as well as space will let scientists track biological processes as they happen. "It's still very preliminary, and we would like to improve the resolution to really understand this complexity," he says. "But we can already see how metabolomes change over time."

ONLINE EXTRA: COMPETITION OR COLLABORATION? SCIENTISTS LED BY KIRAN PATIL AT EMBL HEIDELBERG HAVE DELIVERED INSIGHTS INTO THE SOCIAL NATURE OF SOME BACTERIAL COMMUNITIES. AND FIND OUT HOW ALEXANDROV GOT 'SUCKED INTO' BIOLOGICAL PROBLEMS. NEWS.EMBL.DE

An ocean odyssey

EMBL's Eric Karsenti (far left) joins UN Secretary General Ban Ki-Moon on Tara's bow.

PHOTO: J. GIRARDOT/TARA EXPEDITIONS

A journalist who spent six weeks chronicling life on board Tara, reflects on the extraordinary outcomes from the expedition.

BY ANDRES PEYROT

October 2011. I'm on night duty aboard the 36-metre schooner Tara as it glides across the Pacific Ocean, a black mirror that reflects the star-riddled sky above and hides everything that lies beneath its surface. For the next six weeks, I am here to observe the life and times of this unique research vessel as it explores some of the most mysterious parts of our planet. Tomorrow seems a long time away, but two things keep me awake: the smell of salt hanging in the air and a line from the song *A Horse With No Name* that keeps looping through my mind – *The ocean is a desert with its life underground and a perfect disguise above...*

Beneath the surface

At dawn, the deck is buzzing with scientists who comb through the upper ocean with thin nets, water pumps and a 'rosette', which traps water at different depths and measures its physical and chemical properties. I descend into the 'dry lab' cabin filled with microscopes and computer screens and find Jérémie Capoulade, an imaging expert then working as a postdoc at EMBL, who delicately places a drop of sampled water under a microscope. Suddenly, the boat is caught in waves that turn the entire lab into a swinging pendulum. I look for the edge of a table, anything, to keep my balance, while Capoulade, seemingly unaware of the complete havoc around us, sways in time with his microscope, captivated by what he sees beneath the lens. This single droplet is teeming with improbable forms of life: plankton, some so strange-looking that they were the inspiration for the creatures in the 1979 Hollywood film *Alien*. And as tiny and bizarre as they may seem, plankton represent nine-tenths of the living mass in the oceans and form the base of the food chain. Through photosynthesis, they generate half of the oxygen we breathe, draw carbon from the atmosphere to the deep sea, and play a crucial role in the global nitrogen cycle. Yet, despite their immense impact on the world's environment, we know very little about these microorganisms.

The Tara Oceans project (2009–2013), unprecedented both in scale and ambition, set out to change this forever. While navigating seven seas and oceans, evading pirates, weathering storms and hand-fixing complex equipment, the scientists on board sampled *all* types of plankton and have thus generated a bounty of data for comprehensive studies of these tiny creatures. I knew that what we were doing on Tara was important. It is only recently, though, that I have come to realise just *how* important. In May, researchers from EMBL and partner institutions reported the first findings from the analysis of these data in a package of five papers published in a special edition of *Science*, as well as publications in other journals cutting across many different fields. Their interdisciplinary work involved high-throughput sequencing, advanced imaging, big data storage management, bioinformatics and the very latest physical modelling technologies. "The data we collected enables researchers to look in unprecedented detail at the populations, environments and dynamics of the oceans' vital life support system," says EMBL's Eric Karsenti, Tara Oceans' Scientific Director and a senior author on the papers. "This is the first global description of the complete ecosystems."

Shotgun DNA sequencing on the samples has provided the scientific community with a staggering 7.2 trillion bases of genetic code from entire populations of plankton – from tiny viruses 0.02 micrometers in size to animals measuring up to two millimeters, roughly the ratio of a golf ball to ten Olympic-sized swimming pools. "These organisms aren't usually studied together and the techniques we've used aren't usually combined together – our approach allows us to bridge the molecular to the planetary scale," says Chris Bowler from the CNRS and another senior author on the papers. "This is the emergence of a new type of research in life sciences," Karsenti adds, smiling, with an excited glint in his eyes. "Five years ago, this was science fiction!"

"Five years ago, this was science fiction!"

From this massive census of the sea, researchers have begun to tackle questions that explorers of yesteryear would not have even dreamed of asking: What types of plankton populate our oceans? How do they interact with one another and their environment? How will they react to climate change? How will all this affect us?

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Charting millions of genes

At first glance, the labs at EMBL Heidelberg, a six-hour drive from the nearest coastline, might seem an unlikely place to take forward this endeavour. Yet it was here that Shinichi Sunagawa, a researcher in Peer Bork's group, led a project to develop an Ocean Microbial Gene Catalogue – more than 40 million genes from microbial plankton, 80% of which are new to science. Pointing towards a huge diversity

"It's like a treasure box"

of unknown plankton found in different parts of the ocean, this genetic catalogue led to an important observation: temperature is the main environmental factor shaping microbial communities. Scientists can now begin to consider wider issues connected to this striking finding, such as the potential impact rising temperatures could have on these sensitive ecosystems, how this will affect the planet's environment, and what might be done to better protect them.

Researchers are also aiming to assign functions to the genes in the catalogue. "It's like a treasure box in which you may find further variants of genes that produce bioactive substances or antibiotic effects," says Sunagawa. Some plankton have properties that exceed our own abilities. Diatoms, for example, are single-celled organisms that synthesise a protective layer of glass in the chilly temperatures of the deep, a material that humans are only capable of producing using extreme heat. It would be exciting to identify which genes are responsible for such an astonishing ability!

Learning from life

Diatoms belong to the most diverse kingdom of life, eukaryotes, which are organisms whose DNA is coiled within a nucleus. This complex and stable cell structure enabled the evolution of multicellular beings, like us, to form. It is perhaps this legacy that inspired Colomban de Vargas, a scientist at the Roscoff Marine Biological Station in Brittany, France, to focus his research on ocean eukaryotes. The incredible diversity he observed with his team – one hundred times more than previously known – challenges the classical division of plankton into phyto- and zooplankton. "Protists, which account for two-thirds of the eukaryotes discovered, don't belong to either plants or animals," explains de Vargas. Researchers have identified a total of 150 000 genetic types of protists from groups that had no match in a family tree of previously catalogued eukaryotes, a third of which could not even be classified. And one of the most fascinating discoveries for me is that underlying this hyper-diversification in marine plankton is their complex interactions.

Community dynamics

On Tara, scientists nicknamed the specimens they found under the microscope with titles such as Hubert the protist and Dana the diatom. Behind their humour, I did not suspect the full extent of 'social' interactions that occur in our oceans. Step forward the Oceanic Interactome, a sort of planktonic Facebook that tells us which plankton are 'friends' and are always found together and which are not. Developed by a team led by Gipsi Lima-Mendez, a postdoc in Jeroen Raes' group at the University of Leuven, researchers were able to reveal the remarkable impacts that some organisms have on community structures. One particularly astonishing interaction came from an unlikely partnership between a photosynthetic microalgae living inside a flatworm. Using computer-generated models and advanced microscopy, the team were able to predict and confirm that the microalgae, in order to hide from predators, takes up residence inside the flatworm – and in exchange synthesises nutrients to feed its host. "Ocean interaction is far from 'survival of the fittest'," explains Karsenti. "Eighty percent of interactions between organisms in the ocean are positive: most organisms help one another thrive. It can change the way we look at evolution."

Mapping new viruses

The most elusive plankton in the Interactome are also the most abundant – viruses, which are so small that we could not actually see them with the microscopes on board Tara. Ten million of them can squeeze into a single drop of seawater but their impact is enormous: they shape the populations they infect, drive evolution by transferring genes to different species, and influence the global cycling of nutrients, organic matter and atmospheric gases. Remarkably, a study led by Jennifer Brum, a postdoc in Matthew Sullivan's group at the University of Arizona, identified more than 5000 viral populations, of which only 1% could be found in existing databases. Put another way, it's as if 800 new planets were discovered in our Solar System, beyond the eight we already know. "The challenges ahead will be to determine which organisms

"It can change the way we look at evolution"

"The data represents 11.5 Terabytes, which is larger than the Wikipedia footprint"

each of these viruses infects," explains Patrick Wincker, Head of the Genoscope, the French National Sequencing Center that collaborated on the research. Importantly, the team also observed comparable local and global viral diversity, supporting the 'seed-bank' theory whereby viral communities are passively transported via oceanic currents and reshaped locally.

Such an understanding of oceanic currents is essential to the study of plankton distribution in our oceans. For some time, scientists hypothesised that plankton communities from the Indian Ocean were injected into the South Pacific by a peculiar current called the Aghulas rings – gigantic eddies that swirl around the tip of South Africa and transport plankton communities towards Brazil. Not so, found a team lead by Emilie Villar, a postdoc in Pascal Hingamp's group at the CNRS, after studying the fate of the microorganisms trapped inside these rings. "Plankton are subject to five degrees cooling and intense vertical mixing, thus limiting the species that manage to cross," explains Daniele Iudicone, from the Stazione Zoologica Anton Dohrn in Naples, Italy. This 'cold-wash cycle' constitutes a fascinating case study of how planktonic ecosystems evolve in response to variations in their environment.

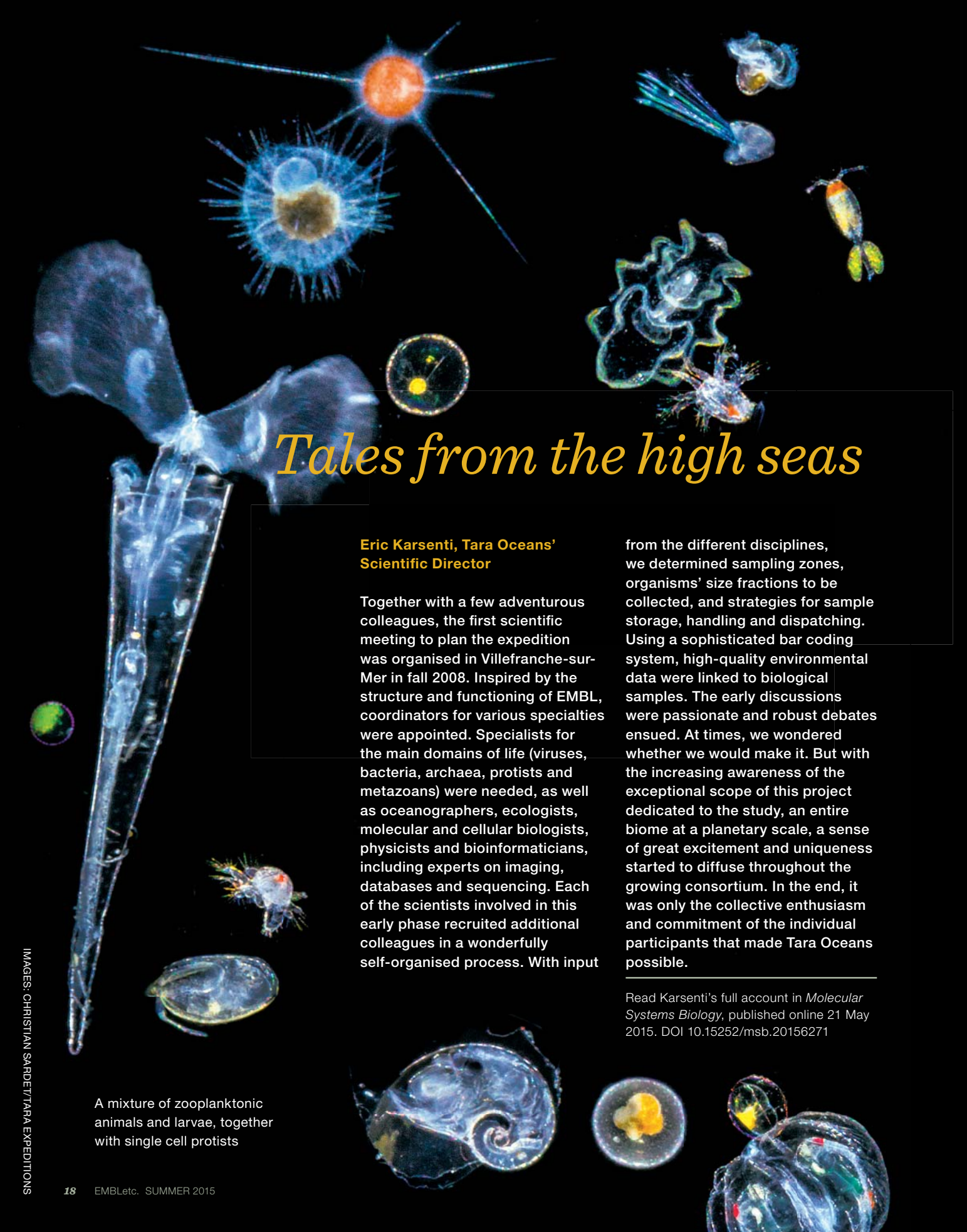
Navigating data

"Collectively, these studies give us a time zero reference point from which to monitor the health of our oceans in the future," Guy Cochrane, Head of the European Nucleotide Archive at EMBL-EBI explains. "The data we have available represents 11.5 Terabytes, which is larger than the Wikipedia footprint." The Tara Oceans consortium now invites the international scientific community to jump on board and tap into these huge reserves of data that will remain available as Cochrane notes, to "researchers working in different fields, for decades to come, when they think to ask questions that we didn't think to ask now." To some involved in the expedition this will come as little surprise: after all, scientists are still working with samples that Charles Darwin collected during his 1823 expedition on board the HMS Beagle!

With such a dizzying amount of samples, information and observations, one might think that grand scientific projects such as this are the product of a highly rationalised structure. But for Karsenti, "it usually starts with a hazy idea, a dream." Stefanie Kandels-Lewis, in charge of scientific operations and logistics for Tara Oceans, adds, "It's the dedication and the adrenaline that made it happen and kept us going." Tara's oceanic odyssey started with uncertainties and ended up revolutionising the way researchers think about plankton, allowing these tiny creatures to be studied on a planetary scale.

Read more in a special edition of *Science*, 22 May 2015. DOI: 10.1126/science.aac5605

Platynereis Dumereii, imaged during the expedition



Tales from the high seas

Eric Karsenti, Tara Oceans' Scientific Director

Together with a few adventurous colleagues, the first scientific meeting to plan the expedition was organised in Villefranche-sur-Mer in fall 2008. Inspired by the structure and functioning of EMBL, coordinators for various specialties were appointed. Specialists for the main domains of life (viruses, bacteria, archaea, protists and metazoans) were needed, as well as oceanographers, ecologists, molecular and cellular biologists, physicists and bioinformaticians, including experts on imaging, databases and sequencing. Each of the scientists involved in this early phase recruited additional colleagues in a wonderfully self-organised process. With input from the different disciplines, we determined sampling zones, organisms' size fractions to be collected, and strategies for sample storage, handling and dispatching. Using a sophisticated bar coding system, high-quality environmental data were linked to biological samples. The early discussions were passionate and robust debates ensued. At times, we wondered whether we would make it. But with the increasing awareness of the exceptional scope of this project dedicated to the study, an entire biome at a planetary scale, a sense of great excitement and uniqueness started to diffuse throughout the growing consortium. In the end, it was only the collective enthusiasm and commitment of the individual participants that made Tara Oceans possible.

Read Karsenti's full account in *Molecular Systems Biology*, published online 21 May 2015. DOI 10.15252/msb.20156271

A mixture of zooplanktonic animals and larvae, together with single cell protists

IMAGES: CHRISTIAN SARDET/TARA EXPEDITIONS

Steffi Kandels-Lewis, Scientific Operations Manager

Working on Tara Oceans required you to be very flexible and creative. At each stopover, there was a new hurdle and throughout the expedition there was just about as much planning to do, as it is possible to imagine! One of the best aspects for me was working directly with the unique group of people involved – there was a fantastic energy, people were highly motivated and we were all riding on a wave of adrenaline. Looking back, the biggest achievement of Tara Oceans is the integration of all the data collected: scientists from such a broad range of disciplines trying to make sense of the information and interpret the results. It brought together people from very different fields that often work in very different ways. They had to somehow find a common language to communicate, and that's the beauty of this – they did it! Researchers have seen their discipline from new angles, asking new questions they would not have thought about before. The team has spent a lot of time at sea together, as well as convening at many different meetings around the world – we are friends as well as colleagues, and a great community has built up around this dream. I'm incredibly proud of what we've achieved together.

Tara: a schooner for the

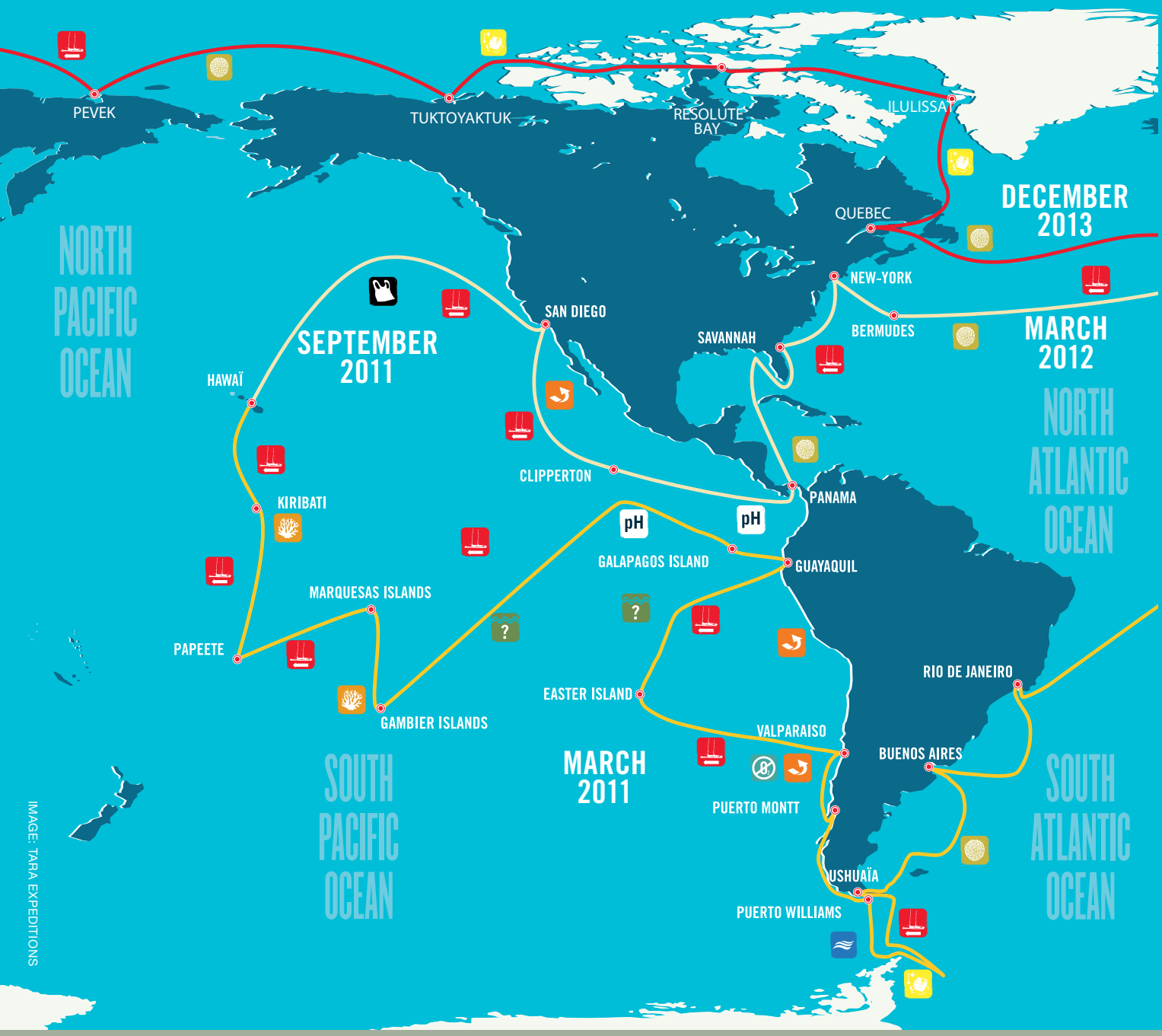


IMAGE: TARA EXPEDITIONS

Distance travelled:

14000 km

Samples collected:

35000

Scientific articles published in *Science* in May 2015:

5

planet

FIRST YEAR: Lorient - Cape Town
SECOND YEAR: Cape Town - Honolulu
THIRD YEAR: Honolulu - Lorient
FOURTH YEAR: Lorient - Lorient
PORT OF CALL

Crossing of oceanic province
Understudied coral reefs
Upwellings
Life in ocean deserts
Oxygen minimum zone

Overproduction of algae
Concentration of plastic waste
Ice melts
Life in acidic areas
Ocean exchange zone

Global media coverage, from *Le Monde*, to *The New York Times*, to the *BBC*, to *ZDF*, to *El País*, as well as

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1

*Watch the video at: youtu.be/baltHkJC0VE

Inspiration for future scientists:

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Decoding

Fay Christodoulou is now based in San Francisco

PHOTO: FAY CHRISTODOULOU

disease

We go behind the scenes of start-up company Miroculus to explore the roles of alumna Fay Christodoulou and EMBL's Genomics Core Facility in the development of a non-invasive test for early-stage disease.

BY ANNE KORN

"Everything started with a dream," says Alejandro Tocigl, an entrepreneur from Chile and CEO of Miroculus, a start-up company aiming to 'democratise' molecular diagnostics with a tool that could enable patients to be checked for diseases in a simple and affordable way, using just a millilitre of blood. His goal is clear: "To improve early diagnosis, to monitor diseases on a constant basis, and for this to be available to everyone, wherever they are in the world." Like Tocigl, most of the other founders of Miroculus are also from emerging economies and they are acutely aware of the lack of purchasing power of these countries, especially when it comes to what they call 'medicine for the masses'. "We want this tool to be available to all of them," says Tocigl. "We don't want to discriminate based on socio-economic status."

Miroculus' chief scientific officer is EMBL alumna Fay Christodoulou, an expert on microRNAs, which form the basis of the company's technology. She first met Tocigl and the rest of Miroculus' founding team in 2013 during a ten-week graduate studies programme at Singularity University, a California Benefit Corporation located at NASA Research Park in Silicon Valley, which offers programmes and activities that encourage the use of technology for change. Its graduate programme attracts individuals from a broad spectrum of disciplines and encourages them to pursue an ambitious goal: to develop an idea and a viable business plan that harnesses exponential technologies to positively impact one billion people within ten years. Christodoulou teamed up with Tocigl together with Pablo Olivares, a doctor also from Chile; Gilad Gome, a biotechnologist from Israel; Ferrán Galindo, an entrepreneur from Panama; and Jorge Soto, a Mexican electronic engineer. The six of them struck on the idea to develop a simple blood test that utilises the potential of microRNAs in the bloodstream as highly sensitive biomarkers for disease detection.

Bright biomarkers

MicroRNAs are small pieces of RNA that regulate gene expression, the building of proteins from the information encoded in DNA. First discovered in 1993, a relationship between microRNA dysregulation and cancer was reported in 2002. Six years later, researchers found that microRNAs circulate in biological fluids like blood, which makes them promising biomarkers for the early stages of cancer, heart disease and neurological diseases. The detection of specific microRNAs in a sample makes it possible to diagnose a disease, identify its type (each tumour, for example, has its own microRNA signature), and monitor its progression and treatment in minimally invasive ways. However, techniques involving microRNAs are challenging because these molecules are no more than 22 nucleotides long and cannot easily be detected with traditional DNA-based methods. Moreover, they are often very similar: two microRNAs may share all but one nucleotide. Hence, methods for their detection and classification need to be able to tell two microRNAs apart based on very small variances.

Christodoulou's expert knowledge of microRNAs stems from years of research in the field. She completed her doctoral thesis on ancient animal microRNAs at EMBL in 2010 and investigated the role of microRNAs in thyroid cancer during her postdoctoral research. "I have been following the field since 2005 and I am very familiar with the technologies that are available," she says. "When I think of what we are doing, something like this is definitely missing." What they are doing is building – and perfecting – a device that scans for diseases quickly, easily and affordably. Miroculus' method extracts the microRNAs from a standard blood sample and these are then pipetted into a 96-well plastic plate. Each well is filled with the company's patented biochemical assay that produces a fluorescent signal in the presence of a specific microRNA. To run the assay, the plate is placed inside the device – called mir.i.am – which can be connected to a smartphone. The phone takes photographs during the reaction and sends them to a cloud where the pattern of illuminated wells is matched against data on which disease is associated with which microRNA pattern. "It is the combination of specific microRNAs found in a sample which can reveal the source of a pathophysiological condition," explains Christodoulou. "By providing an affordable and easy to use platform that can 'read' which microRNAs circulate in a sample, Miroculus can potentially offer a disease agnostic screening test which simply interprets the microRNA signatures that are found." Thus, whereas other diagnostic tests look for a specific disease, Miroculus' method could be applied to multiple disease types.

"Bold innovation is about bringing forward the change you want to see in the world."

Design to development

Although, as Christodoulou points out, the clinical validity and utility of microRNAs as biomarkers has so far only been established for some cancers and cardiological conditions, Miroculus' team believe that their various advantages over other biomarkers mean that they have great potential for early disease detection. These advantages include the stability of microRNAs in plasma, which stops them from degrading easily even when stored at room temperature, and their high cell-type specificity. As certain microRNAs are only found in certain cells, the assay reveals which cells are present in a given sample. In tests, the team has been able to identify the microRNA patterns indicative of pancreatic cancer, breast cancer and hepatic cancer.

"We want to provide the enabling technology that can establish their use," says Christodoulou. Yet for Miroculus, simply providing that technology isn't enough. "After learning how important design thinking is in product development," Christodoulou recalls,

PHOTO: MIROCULUS

mir.i.am is a microRNA detection platform designed for molecular data gathering, analysis and interpretation.

"we follow a different approach to stereotypical spin-offs that have a very good assay or a very good biotechnological solution and then want to make it available as it is." Rather than simply providing a solution that can only be used under very specific conditions or by experts, the team wants to make the technology available as cheaply as possible to be used by minimally trained lab technicians in low-resource settings. The first two prototype versions of the mir.i.am, Christodoulou explains, were 3D-printed, using cheap, off-the-shelf components, which would make it possible for the device to be reproduced relatively easily.

GeneCore groundwork

As the development of the project began to take flight, Christodoulou conducted instrumental research at EMBL's Genomics Core Facility (GeneCore), which has been run by Vladimir Benes, a trained biochemist, since its inception in 2000. Christodoulou worked closely with Benes for many years, and since leaving EMBL she keeps returning as a regular tutor on a small-RNA analysis course he organises. Thus, when the Miroculus team realised that they needed to find a place where they could continue the experiments they had begun at Singularity University, Christodoulou's mind quickly settled on GeneCore, which she describes as "a paradise with all the toys a molecular biologist could dream of. The lab is fully equipped with everything and runs like a Swiss watch," she explains. "We literally turned up there with our suitcases and started pipetting."

EMBL had never hosted a start-up before but Benes explains that Christodoulou's tenacity, motivation and commitment convinced him that she would be able to sustain the project, even during its challenging phases. "So when she asked me if we could do this research together, my immediate thought was: 'Let's do it!'", he recalls. One such challenge occurred when Christodoulou had to significantly alter her scientific approach on realising that the original design of their isothermal assay had reached its limits: not all microRNAs would perform similarly at the same temperature. She praises the support of the team at GeneCore, with Miroculus staff scientist João Pereira de Lima based at the facility for six months to manage the project. "Working together we were able to deliver detailed analyses of individual parameters and components that provided robust data for Fay to present to investors," explains Benes.

Setting up shop

When Miroculus advanced from a part-time venture to a stage where the project needed the team's full attention and additional resources, the data produced at EMBL enabled the start-up to secure the funding for the first prototype, which was introduced at a TED

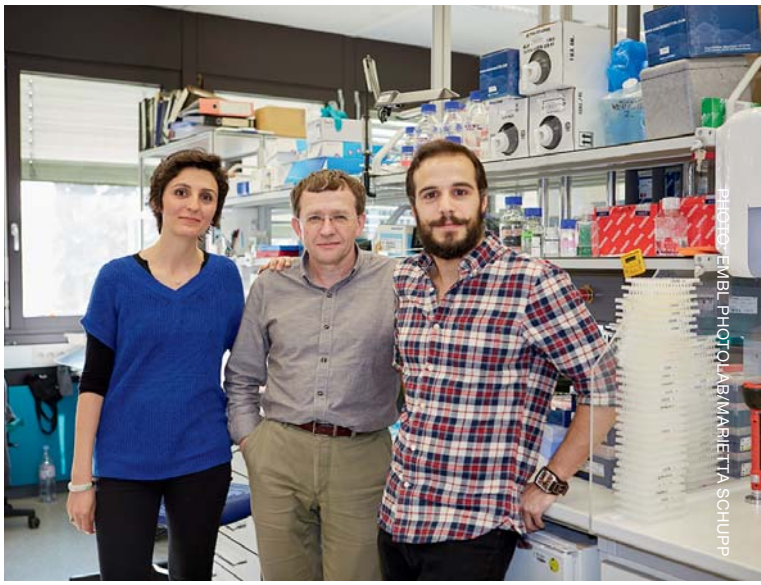

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Fay Christodoulou, together with EMBL's Vladimir Benes and Miroculus' João Pereira de Lima

global conference last year. This was followed by 25 days of touring the US, pitching it to almost 100 investors – a particular challenge for a company that did not yet have facilities in the country. Miroculus completed the first round of seed funding this year. The company is now based in San Francisco, focusing on optimising the product's workflow and user experience, while making the assay more robust so that it can tolerate inexpert handling and still produce accurate results. Silicon Valley, with its infinite, revolutionary ideas, excellence, and easy-access expertise has a lot to offer, says Christodoulou: "It is a very fertile environment for developing solutions that have the potential to make a real difference in the world... to where they could never be found before." EMBL, she insists, is its European equivalent in the life sciences.

Although the notion of leaving academia to pursue an entrepreneurial dream may seem daunting to some, Christodoulou and the others involved in Miroculus are an example of what interdisciplinary teamwork can achieve. To other researchers who 'flirt' with the idea of trying out their entrepreneurial skills, Christodoulou has a clear message: "Go for it and don't be afraid of failure. Bold innovation is about bringing forward the change you want to see in the world."

Janet Thornton stepped down as Director of EMBL-EBI on 30 June 2015 and continues to lead her research group. Here, she shares some reflections on her time as Director of one of Europe's fastest growing research institutes.

Transitions

There are few things harder than giving up something you love.

In 2001 I was offered a chance to be Director of EMBL's European Bioinformatics Institute, which had really just got off the ground – and I'm very happy to have taken it. But it meant leaving behind not only friends and colleagues at University College London, but also an environment where I was surrounded by experimental biologists, especially the structural biologists who produced much of the data which I so enjoy analysing. I deliberated for a long time on whether the risk would be worth it, but if I'd known then what I know now, honestly it would have taken me even longer to decide.

I came because I felt (and feel) that looking after data is so important

As I saw things then, here was an opportunity to lead an institute that is responsible for biomolecular data – collecting, curating and standardising it, to make it available to other scientists – and by doing so I could contribute to the progression of science in a very concrete way. Not just my own science, but the whole enterprise of life science research worldwide. From a personal research perspective, I understood that integrating many different types of data is critical for modern biology and EMBL-EBI seemed a good place to do this!

What I didn't realise was how demanding the job would be. In retrospect, I can see that the data explosion was only just beginning, but even at that time we had to run to stand still.

The compute infrastructure at EMBL-EBI was still limited, and the research had yet to coalesce. We had five databases and five research groups. The groups and teams worked very independently, making it difficult to integrate data and create common methods of working. The website was there, but a bit clunky. There was just one building, easily housing all the staff, who would meet regularly on the landing for tea! Although we dreamed of applications to medicine and agriculture, in reality they were very limited. All these things have changed.

What has not changed is that data is at the heart of our mission, whether it be in the service teams who work tirelessly to make it available for all, or in the research groups who have fun developing new methods and approaches to make sense of all the data.

"It's helped that I honestly enjoy talking to people about their work."

One of the challenges I had not really appreciated upfront was how challenging it can be to bring very different people to a common understanding of a problem, so you can work together efficiently. Individuals are so diverse, as are groups, organisations and governments, with different drivers, ways of thinking and motivation. Communication is critically important and difficult to do well.

It's helped that I honestly enjoy talking to people about their work, and working together towards a joint purpose; that's just part of who I am. What I had to learn as Director was that as an institute grows, it becomes more and more important to structure communication. Doubling the size of an organisation more than doubles the effort you have to put into communication, both internally and externally. Getting people to listen to one another and establishing two-way communication, whether it's between individuals, groups, EMBL sites, or government agencies, is very hard work.

PHOTO: ROBERT SLOWLEY

European collaboration: difficult, but worth it

ELIXIR has been a thread through most of my time here, and it's been fascinating to find my way through science policy and public affairs in different countries. The way each European nation has evolved has given us a very diverse economic, political and scientific landscape. It has been great seeing all the different scientific funding structures, how people interact in different countries, and learning how to find a win-win outcome. Whatever you're building together, it has to work for both sides. You have to keep at it – listening, communicating, and engaging – until you find that common ground.

This coordinated infrastructure has been a lot of hard work for everyone, and will continue to be so. It is only worthwhile because the data and science demand this organisation to allow scientific progress, by 'building on the data and tools of giants'.

Can you be a part-time research leader?

When I arrived at EMBL-EBI in 2001, there were about 150 people working here. Now, there are closer to 600. Directing a rapidly growing institute while leading a research group really brought home to me that there are many, many ways to run a group – and most senior scientists effectively do this part-time because of their many other commitments.

When you're time limited, your group needs a special modus operandi, and they need to be more independent. I was very nervous about this at first because I wanted to be on hand for everything – but I actually found that the need for my students and postdocs to work more independently helped them grow better. Some people

PHOTO: ROBERT SLOWLEY

EMBL-EBI staff got together at Hinxton Hall for an event to commemorate Janet Thornton stepping down as Director of EMBL-EBI in June

thrive in this kind of environment and some don't; it can be really hard to be a good mentor when someone needs you a lot and you simply do not have the time.

Being a good mentor is something that comes naturally when you're fundamentally interested in other peoples' work and it's a difficult thing to delegate. One thing I'm looking forward to is having more time to be more involved with my group members and their work. Another big plus will be having time to just think. Just, to think. Imagine.

Director Emeritus: science policy and support

But I'm not sure there will be as much time for that as I'd hoped! Two things I take very seriously are my role in promoting science, supporting young scientists and informing policy as a member of the Royal Society and the European Research Council. I have also agreed to serve on several Scientific Advisory Boards to help institutions and scientists face the Big Data challenge.

Family first

What have I enjoyed most about being Director of EMBL-EBI? I've enjoyed being part of the EMBL 'family': an intensely international collective built on scientific curiosity, love of learning and commitment to scientific excellence. I've enjoyed helping EMBL-EBI grow to serve so many areas of science so well, bringing communities together to speak a common language, and providing a solid foundation on which new discoveries can be built. It really has a unique role in the world, and I'm proud to have been a part of it. Finding that common understanding between many very, very different people – the best things we've done have been built on that.

EMBL is a brilliant organisation, and EMBL-EBI an ever-changing, outstanding part of it. Long may it continue, and go from strength to strength.

VIEW PHOTOS FROM THE CELEBRATION OF JANET THORNTON'S 14 YEARS AS EMBL-EBI DIRECTOR: NEWS.EMBL.DE/?p=4331

A bioinformatics timeline, captured in cake

PHOTO: ROBERT SLOWLEY

The curious case of the bi-specific enzyme

When Andrea Rentmeister from the University of Münster came across an enzyme with curious bi-specific properties, she was eager to find out more about its molecular 3D structure. As a chemist with no expertise in protein crystalisation, she turned to the Sample Preparation and Characterisation (SPC) facility at EMBL Hamburg for help. What started out as a shot in the dark, resulted in a crystal structure – shedding light onto this peculiar feature.

BY ROSEMARY WILSON

"When I first learnt about the possibility of sending my samples to EMBL Hamburg, I was curious to give it a try," Andrea Rentmeister says, recalling how she first heard about the services offered by the SPC facility. She wanted to learn more about the molecular structure of an enzyme found in cyanobacteria – a group of photosynthetic bacteria that can cause toxic blooms in lakes in the summer.

Specifically, Rentmeister was interested in one part of the multi-modular enzyme known as a nonribosomal peptide synthetase (NRPS). "NRPS enzymes are like assembly lines," she explains. "They are made up of multiple domains, all needed to assemble a peptide chain: the first domain picks up an amino acid, a second hands it to a third domain that binds the amino acid to the next to form a peptide chain." The first domain is usually specific to a single amino acid – only able to bind to one of the 20 common amino acids. "People have been bothered by this specificity for a long time," says Rentmeister, "There are already several crystal structures of similar enzymes that show the binding 'pocket' for the amino acid."

"We were puzzled: no one could explain how this was possible."

"Scientists have generated a specificity code based on the residues found on the inside surface of this pocket, enabling us to predict which amino acid might bind with the enzyme," continues Rentmeister. But this code is not 100% reliable and Rentmeister's co-author, Guntram Christiansen from the University of Innsbruck, claimed to have found a domain that recognises not one, but two amino acids. "It's intriguing that an enzyme can be specific to both Arginine and Tyrosine – structurally two very distinct amino acids," Rentmeister explains. "We were puzzled: no one could explain how this was possible – maybe there is a second separate binding pocket?" Hence, her expedition into the world of structural biology, and to Hamburg to try to crystallise the curious enzyme and study its molecular structure on the EMBL beamlines at PETRA III.

A re-think

Rentmeister's initial excitement was, however, short lived: "After a round of unsuccessful crystallisation experiments in 2011, I thought – ok, it was a nice experience, but no result." Fortunately, at this time, SPC facility manager Rob Meijers started to offer a follow-up service to users who had failed to crystalise their proteins – people like Rentmeister. Meijers got in contact to suggest another round of experiments focusing on quality control and optimisation.

"Crystallising a protein is not as easy as producing crystals from a solution of kitchen salt – that's why we decided to set up a service to help non-experts get the most out of their samples," explains Meijers. "Now when we receive a sample, like this enzyme, we set up hundreds of experiments each a few nano-milliliters in volume, with varying concentrations of buffers and salts to try to find the best conditions for crystallisation."

"Andrea is exactly the kind of person we want to support."

Soaking it in

"Based on Rob's feedback we re-designed the experiment and got nice crystals," says Rentmeister. But, once again, enthusiasm was fleeting: the data from the beamline experiments did not allow the researchers to completely observe the part of the enzyme of interest involved in amino acid specificity. Not to be beaten, Meijers' then-PhD student Heidi Kaljunen started a series of 'soaking' experiments, drenching the crystals in solutions containing amino acid molecules so that the enzymes would bind to their specific amino acids, Arginine and Tyrosine. At last, the team succeeded in crystalising and resolving structures of the enzyme in combination with the two amino acids. Moreover, the structures showed that, once the amino acid has taken its place, the pocket is sealed off so that the amino acid can be bound to the peptide chain.

Contrary to Rentmeister's initial theory – that the enzyme might have a second binding site – both amino acids are seen using the same pocket. "The most amazing thing is that if you superimpose the structures of the two amino acids bound to the enzyme, you see how the amino acid Arginine snuggles into the binding pocket pretending to be a Tyrosine," she says. The crystal structures show how one end of the Arginine molecule curls in on itself, mimicking the structure of Tyrosine. "It was both interesting and disappointing, because the answer was so simple and logical!"

PHOTO: ANDREA RENTMEISTER

Andrea Rentmeister, who is keen to return to EMBL Hamburg with more samples.

Pinpointed

Having solved the mystery of the bi-specificity, however, the story didn't end there. Rentmeister's team did a number of mutation studies, creating mutants of the enzyme to identify exactly which of the residues in the enzyme was responsible for the bi-specificity. "We pinpointed it to three residues," she explains. "By changing these residues, we could create mono-specificity for Arginine or Tyrosine, which as far as we know is not found in nature."

Looking at the structures of the two amino acids, Meijers wondered whether a so-called non-natural amino acid – 4-azidophenylalanine – could fit the pocket and be activated by the enzyme. "This man-made amino acid is a sort of chemical chimera of Arginine and Tyrosine," he says. And, indeed, one of the mutant enzymes took up this non-natural amino acid. The results, published in *Angewandte Chemie*, point to several promising future research directions. "That the NRPS enzyme could accept non-natural amino acids and potentially incorporate them into the poly-peptide chain, opens up a number of exciting possibilities," says Meijers. "For example, reprogrammed NRPS enzymes could be used to produce novel peptides with interesting properties." Rentmeister adds: "It is also not really understood why these cyanobacteria produce toxic blooms in summer – we can now design an amino acid to include a traceable tag and map cellular pathways and processes."

Worth it

Rentmeister explains that the experience with the SPC team at EMBL Hamburg proved indispensable. "Bi-specificity has not been observed in this group of enzymes before Guntram's work and now with the help of Rob's team we have shown how this is achieved and how we might use this for protein engineering and synthetic biology approaches. It took a while, but it was worth it!" she concludes.

"Andrea is exactly the kind of person we want to support," says Meijers. "As a non-expert, she came to us with an interesting structural biological question, which we helped to answer – this was a really exciting project to be part of." Rentmeister is now keen to come back to EMBL Hamburg with more enzymes and has signed up to access the SPC facility via the latest transnational access project, BioStruct-X. "I'll be back!" she says with a smile.

Kaljunen H *et al. Angewandte Chemie*, 11 June 2015. DOI: 10.1002/ange.201503275

Celebrating excellence

It's the one time of year when the EMBL community gets together in one place to celebrate scientific achievements, the Lab's unique spirit, and draw inspiration from friends and colleagues. And one of the highlights of Lab Day, which took place on 10 July, is where EMBL celebrates the very special work of alumni through the John Kendrew and Lennart Philipson awards. We caught up with this year's winners to find out more.

Science,

As a child, alumnus Jacques Dubochet was scared of the dark. One day, nervously watching the sun disappearing over the horizon, he headed to his local library determined to find out where it went.

BY ROSEMARY WILSON AND ADAM GRISTWOOD

"For me it was necessary to confront my fears with understanding," explains Dubochet, winner of the inaugural Lennart Philipson award. Taking comfort in knowledge instinctively led him to a career in science, where his defining work came not from studying disappearing light, but disappearing water, developing a technique that revolutionised structural biology.

Friend not foe

"Unfortunately water evaporates in an electron microscope, but when treated with suitable care, water is the electron microscopist's best friend," says Dubochet, who together with colleague Alasdair McDowall and Marc Adrian, invented cryo-electron microscopy (cryo-EM) sample preparation. The method enabled samples to be kept in their native state without the need for dyes or fixatives: its development over time has enabled researchers to zoom in on structures, viruses and protein complexes at unprecedented resolution. "Electrons are great: even a single molecule may leave a trace in their beam and electron microscopists have learned to make use of them with breathtaking effect," he explains. "But they are also rather destructive: the column of an electron microscope must be under a vacuum, while risks of structural damage lurk around every corner."

Scientists, including Dubochet had already tinkered with a variety of methods to try and fix biological

society & serendipity

samples for observations in the electron microscope, but working as a group leader at EMBL Heidelberg in the early 1980s, Dubochet recognised that in order to preserve the natural structure of biological samples for measurement under the electron microscope, they had to remain in their natural environment – water. But to avoid evaporation in the vacuum of the electron microscope column water needs to be frozen, with ice crystals causing further hazards to delicate samples. So Dubochet set out to find a way of freezing water without producing any ice crystals.

Visionary

"Jacques had a vision," explains Gareth Griffiths, incumbent Chair of EMBL's Alumni Association, as well as a friend and colleague. "He found a way of freezing thin films of water so fast that crystals had no time to form. At first the idea of "vitrification" of liquid ice was dismissed, but overtime the technique has become increasingly important to life science research, and it is clear today it is Nobel Prize-worthy." While other structural biology methods require extensive, complicated and potentially disruptive sample preparation techniques, cryo-electron microscopy enables the scientist to view the sample in its natural environment. It is central to the work of labs the world over, including several at EMBL, while cryoEM of vitreous sections (CEMOVIS), is widely regarded as having potential to become a powerful method in the future. "With a bit of chance it's going to be trivial to see the atomic structure of protein complexes!" Dubochet says excitedly.

After leaving EMBL, Dubochet took up a professorship at the University of Lausanne, fulfilling a passion for teaching, while also introducing courses on ethics and philosophy- an area he is still very active in. "With knowledge comes great responsibility," he says. Now retired, he looks back with a smile at all he has achieved and experienced. "I have been lucky," he adds. "Although 'serendipity' probably captures it better, being in the right place at the right time. EMBL was the best time of my life: my children were born, I had my best scientific moments and still have plenty of friends here. We often come back to visit, it's a great pleasure. Voila!"

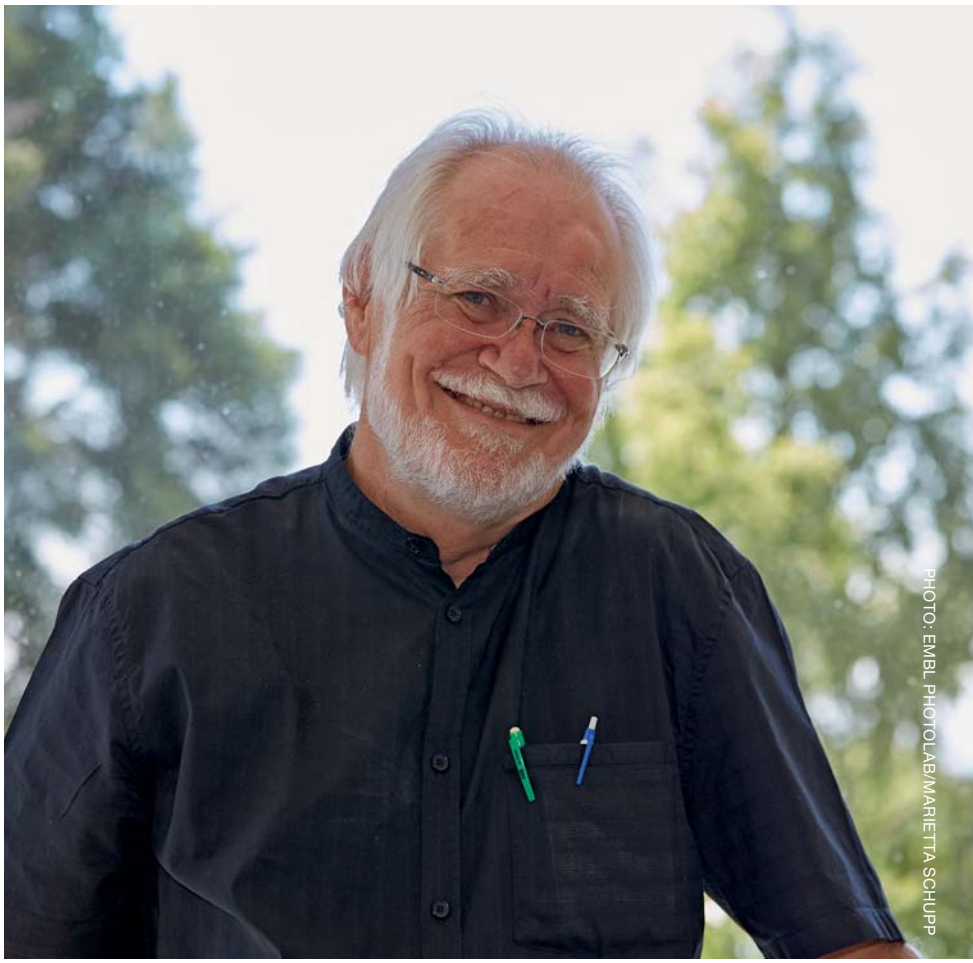

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Jacques Dubochet, who was a group leader at EMBL Heidelberg (1978–87), is the winner of this year's Lennart Philipson Award for outstanding contributions in translational research.

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Melina Schuh, who completed her PhD at EMBL Heidelberg in 2008, is the winner of this year's John Kendrew Award for excellence in science and science communication

High risk, high gain

Melina Schuh's approach to science has been described as "fearless". But dig beneath this steely description of this year's John Kendrew Award winner and you find a story of outstanding research, fast-track career progression, and innovative outreach.

BY JULIA FRANKE

"In both my diploma and PhD, I tried something high-risk, high-gain and it paid off," explains Schuh, an alumna whose group has made several important findings in the field of fertilisable eggs in mammals. "Understanding more about oocyte maturation could have important implications for human health, as errors during this process can lead to problems such as miscarriages, birth defects, and infertility."

While carrying out her PhD in the Ellenberg group at EMBL Heidelberg, Schuh immediately hit the ground running, and using confocal microscopy established new ways of directly imaging meiosis in mammalian cells. "This was an ambitious project because these cells are very sensitive and meiosis in oocytes is a very long process – but the collaborative working environment at EMBL was hugely motivating," she says.

After receiving her doctorate, Schuh achieved something rarely heard of in today's academic world: she was offered a group leader position at the Medical Research Council's Laboratory of Molecular Biology (LMB), despite having no formal postdoctoral training. "What distinguished Melina was her independence so early in her career," says Jan Ellenberg, proudly reflecting on the achievements of his mentee. "From the start, Melina showed courageous and strategic decision making, and in many respects her PhD was like a postdoctoral training."

Far beyond the bench

Her stunning images of polar body extrusion have graced the covers of several top journals, but Schuh has also been involved in projects that go far beyond the bench. One example is an acclaimed collaboration with artist Rob Kesseler as part of a travelling exhibition that aimed to explore mitosis, called *Lens on Life*. "There are many shades of research, and through this project we were able to devise creative and inspiring ways of explaining how this fundamental life process is applicable in everyone's lives," she says. "Artists and scientists have a lot to learn from one another."

At the beginning of next year, Schuh will move on to the next stage of an already remarkable career, as a director at the Max Planck Institute for Biophysical Chemistry in Göttingen, where ambitious projects in science and beyond will remain at the heart of her work. "It is important to go for projects you are enthusiastic about," she adds. "Recently, we led the first study of meiosis in live human oocytes, which has opened up a new and exciting field of research. By continuing to do fundamental biological research on the human system, we hope to contribute to the understanding of this fascinating field, and ultimately also to healthcare and society."

Cultures

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PHOTO: LUIS BEJARANO

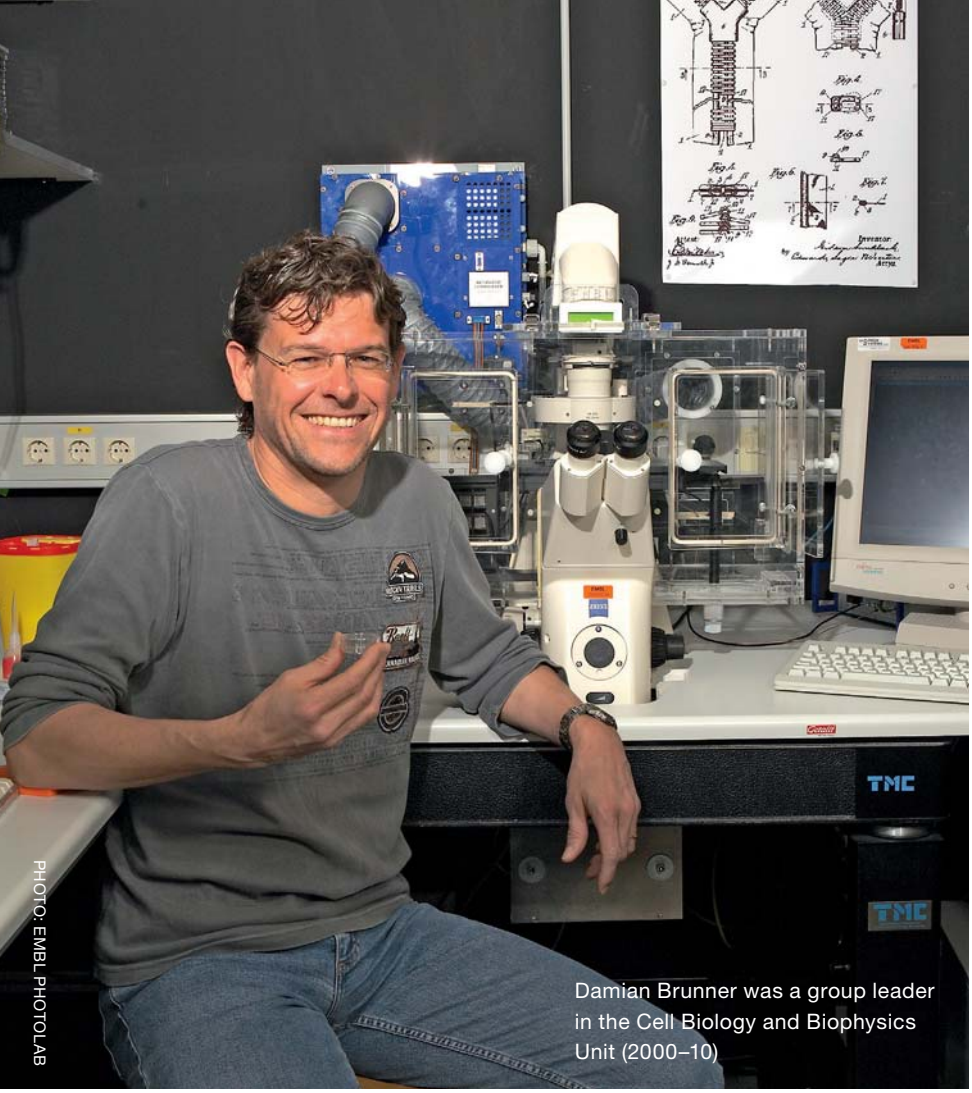


PHOTO: EMBL PHOTOLAB

Damian Brunner was a group leader in the Cell Biology and Biophysics Unit (2000–10)

Political science

Alumni often return to EMBL for collaborations, conferences or community building. But twice a year former EMBL Heidelberg group leader Damian Brunner visits the Lab in a very special capacity – as a Swiss delegate on EMBL's Council, discussing and voting on the Lab's policy in scientific, technical and administrative areas. We caught up with Brunner, who is now a professor at the University of Zürich, to find out more...

BY ADAM GRISTWOOD

How do you feel about your time serving as a delegate so far?

My first meeting was in Summer 2014 – it's a great feeling to stay connected to EMBL and to be able to give something back to an organisation that has supported my career significantly. Switzerland has two delegates on EMBL Council. As a "scientific" delegate, my main role is to advise our "political" delegate when scientific issues are discussed or voted on. However, one automatically takes part in political and financial discussions, too. Being an alumnus brings valuable experience, although delegates all differ from each other and bring with them a variety of skills.

What's been the best experience?

I have already had a lot of exciting new experiences; it is difficult to single any out! However, one example that immediately springs to mind is the friendly atmosphere amongst delegates, even when there are some tough debates taking place during the meetings. Last summer, for instance, Switzerland played Argentina during the football World Cup and us Swiss happened to be placed right next to the Argentinean delegation. There was a lot of friendly banter between us. But of course Argentina won...

Can you describe some of the more challenging times?

The biggest challenge is to deal with situations where we have to implement clear instructions given by our government that do not necessarily represent our own opinion. I then find myself in a situation where I have to defend a decision that I do not really believe in, in discussions with my former EMBL colleagues and friends. In such situations, being a master of diplomacy is a very useful skill.

Have you maintained a network of EMBLers since leaving the lab?

Yes of course! Manu, my wife, is an EMBLer too, and every year we go skiing for a week with several EMBLers. Many EMBLers have visited us in Zürich and I still closely collaborate with a number of present and former staff members, while another EMBLer, Christian von Mering, has his office just 10 meters away from mine. I am also very happy to still have regular contact with several of my former lab members.

Cellular synergy

Combining synergies, science and shared visions, experts from EMBL Monterotondo and the Institute for Molecular Oncology (IFOM) came together for their first joint symposium 29–30 June in Milan. Focussing on cell biology mechanisms in health and disease, the two-day conference included an extensive programme of presentations, networking and exchange. We caught up with alumnus Thomas Vaccari, now a principal investigator at IFOM, who was a speaker at the event.

BY JOSE VIOSCA

Thomas Vaccari completed his PhD at EMBL in 2003

PHOTO: IFOM

What are you working on?

Our lab is interested in understanding how vesicles going to and from the cell's 'digestive factories', lysosomes and endosomes, contribute to intracellular signalling, in both health and disease – for example in tissue and organ development or in cancer. In my talk, I discussed our recent findings on molecules that mediate these processes and how they could influence cell division and potentially cancer – an exciting observation that has inspired us to venture into a completely new field.

Which areas of research during the conference did you find particularly interesting?

There were some fantastic talks on a wide range of areas such as epigenetics, cell cycle control and cell plasticity. I really appreciated the work presented by Martin Jechlinger and Rocio Sotillo, which mirrored some of our interests in cancer studies. I also loved the talk by Cornelius Gross – his research has a distinctly different focus to ours, but he presented a wonderfully elegant approach to studying fear, which is such an intricate and elusive subject.

How did you first become interested in cell biology?

My interests originated at EMBL Heidelberg, where I did my PhD in Anne Ephrussi's group, studying how certain molecules within developing *Drosophila* oocytes migrate to specific regions, thus controlling the development of the fly's body. Anne was a great mentor, and I have fond memories working in her team. Not only did I have a terrific formal training and access to a global web of contacts, but working at EMBL instilled in me a deep love and wonder for science and discovery that still drives me today.

What do you think the future holds for the field?

We are on the way to understanding how amazingly adaptable the cell's endosomes and lysosomes are to the environment and the specific needs of the cell. Cells in the gut, kidneys, immune cells and skin cells are hugely creative in how they use their machinery, and crucially we will begin to understand how such processes are hijacked in several types of cancer.

Branches Sympathy for

Is it possible to pass cancer from one individual to another? For some animals, it is – and, sadly, a unique Tasmanian species is facing possible extinction as a result.

BY SUSAN WATT

You could say that sympathy for the devil is what led Elizabeth Murchison to her field of research – not for Satan himself, but for the fierce little marsupials known as Tasmanian devils.

This species, unique to Tasmania, is under threat from a form of cancer that, bizarrely, is spread by direct transmission from one individual to another: infectious cancer, in other words. Called devil facial tumour disease (DFTD), it causes large tumours on the face and inside the mouth of affected animals and has rapidly spread through the Tasmanian devil population. It appears to be both untreatable and invariably fatal.

Biting into evolution

Now based at the University of Cambridge in the UK, Murchison, who spoke at the joint EMBO|EMBL Science and Policy event last year, focuses her research on the genetic aspects of DFTD and other transmissible cancers. These strange diseases seem at first sight to completely contradict our understanding of the nature of cancer. Normally, cancers are caused by cells in the body that, due to mutations, have gained the ability to divide and grow uncontrollably. But in transmissible cancers, the tumours are not made up of cells from the individual with the disease but instead are derived from the individual in which the first case of the disease occurred: the original tumour, which has somehow gained the ability to jump from host to host. The disease is spread by cells descended from the original tumour, which attach themselves to a new host and then produce more tumour cells that can again transfer to another individual.

In DFTD, one particular aspect of the Tasmanian devil's lifestyle makes such transfer easier: their tendency to bite other animals, including their nearest and dearest – not just during fighting or when scrapping over food, but also during mating and social encounters. Because their biting habit is now exposing Tasmanian devils to a fatal illness, the disease may be providing a powerful evolutionary pressure against biting and favouring less aggressive individuals. However, even if the devils were to evolve to become more sweet-natured, this would not be certain to reduce the impact of the disease. In this case, says Murchison, the tumour would also change in ways that might help it to spread by other means. "The two things are co-evolving at the same time; if the devil were to change, then the tumour would also change," she says.

The ultimate cancers

"Cancers are the product of natural selection operating at the level of a single cell within an organism," she explains. "The only difference with transmissible cancers is that they have managed to escape from their hosts." Normal cancers are an evolutionary dead end, because they die with their hosts. "Transmissible

The Tasmanian devil has been listed as endangered by the Red List of the International Union for the Conservation of Nature (IUCN)

PHOTO: DARRAN LEAL

the Devil

cancers are the ultimate cancers, because they have evolved to survive beyond their hosts, and to continue the evolutionary process beyond the death of the host body in which they first evolved."

The ability of even normal cancers to evolve is shown, for example, in the way cancers develop resistance to chemotherapy. "If you throw something at a population of cells that kills 99 per cent of them but one per cent survives, then that one per cent is going to grow back," says Murchison. "By treating the patient, we are putting selective pressures on their cancer."

Even though cancers are evolving all the time, we know of only one other cancer in addition to DFTD that has evolved to become infectious. Canine transmissible venereal tumour (CTVT) is a disease that affects dogs in many countries of the world. However, CTVT is much more treatable than DFTD and is not usually fatal. The disease has been known for some 150 years but is thought to have evolved far earlier. "We think this cancer originated around 11 000 years ago, close to the time when dogs were first being domesticated by humans," says Murchison. So the tumours that are infecting dogs today are from the same cell lineage as this original ancient tumour – making them the oldest known living mammalian-derived cells on Earth.

Evading the immune system

Is it just luck that so few transmissible cancers seem to exist, or are there any fundamental reasons why this change to becoming infectious is so rare in cancers? After all, cancer cells can grow in a laboratory – so why do so few make the leap to being able to grow in a new body?

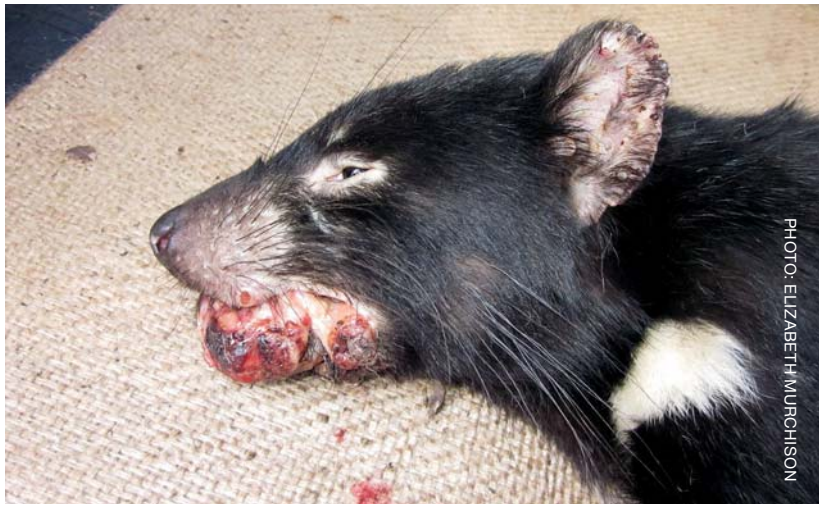


PHOTO: ELIZABETH MURCHISON

DFTD is a fatal condition in Tasmanian devils, characterised by cancers around the mouth and head

One obvious difference is that infectious cancer tumours have to find a way to avoid rejection by their new host's immune system, given that they are derived from a different individual. Recent research has revealed that in DFTD, the tumours stop producing a molecule that indicates to the immune system which cells are foreign invaders. Without this molecule, the DFTD cancer is able to get into an animal's body and escape detection by its immune system.

But, says Murchison, many researchers now believe that normal cancers are also able to hide from the immune system to some degree. "The immune system has mechanisms to detect cancer cells," she says. "Possibly the immune system is busy protecting us from thousands of incipient cancers that occur in our body all the time, so the tumours we do see have already acquired some immune evasion adaptation."

Chillingly, there are even a few cases in humans of cancers being transferred from one person to another. Most of these have occurred in transplant patients, where an undiagnosed tumour in a donated organ has led to cancer in the recipient. But there has also been a single case of a surgeon 'catching' cancer from a patient after he injured himself while operating.

So could we open our newspapers one day and read reports of newly discovered transmissible cancers in humans? Probably not, Murchison says. "Transmissible cancer is unlikely to happen in humans, because it's so rare in nature – we have only seen two examples." But if it ever were to happen, Murchison's work will have helped us to know what to expect, and perhaps to get started on developing useful therapies.

Article first published in the Summer 2015 edition of *Science in School*.

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Pathways Culture of care

As someone who has always held a great love for animals, it would be no surprise to those who knew Maria Kamper as a child that she went on to become a veterinarian. But inspired by medical science, her career led her not to a farm or an animal hospital, but to the lab bench, where she is now responsible for the health and wellbeing of animals turned into living models of human disease.

BY ADAM GRISTWOOD

"Without research using animals, breakthroughs such as antibiotics, organ transplants and vaccines would have been impossible, and this remains true in some important research projects today," says Kamper, who is head of the mouse facility at EMBL Monterotondo. "But laboratory animal veterinarians also understand that animal use in experiments is a privilege that must be carried out ethically. My role is to support scientific endeavour, while ensuring dignity, compassion and respect in the use of animals in science."

Veterinarians play a key role in driving animal care programmes and, with support from technicians and caretakers, develop practices that aim to meet the environmental, social and nutritional needs of animals. Kamper's role involves advising researchers on experimental design, training staff, policy development, facility inspections, interventions and treatment, post-procedural monitoring, daily care, and identifying alternatives to potentially painful procedures where possible.

"Most importantly, we are continuously striving to develop a culture of care at every level," explains Kamper. "This involves identifying non-animal models where appropriate, exploring ways to reduce numbers used in experimentation, refining procedures to improve wellbeing, and nurturing a compassionate approach to animal welfare. This is important not only ethically, but for the success of the science as well."

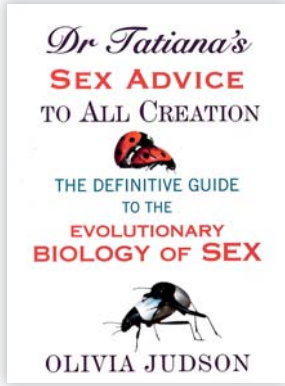
Empowering people

This ethos formed the cornerstone of a laboratory animal science course that Kamper organised at EMBL Monterotondo in April, one of just 16 centers in Europe approved by the Federation for European Laboratory Animal Science Associations (FELASA) to provide training for investigators to carry out animal research. The course brought more than 40 researchers, technicians, biologists, medical doctors and other professionals together with expert trainers to explore theoretical, practical, philosophical and ethical aspects of laboratory animal science, while also underscoring the importance of continual improvements in professional knowledge.

"New European legislation requires that people working with animals have proven high levels of competence," says Kamper, who has organised seven FELASA courses in total. "Through the course we wanted to emphasise the subtleties of animal care, raise awareness of the responsibilities involved in safeguarding animals and ensure that professionals do so in a way that minimises pain and maximises comfort. A key part of my job involves empowering people to meet their potential: I am proud to work in this inspiring environment, promoting animal research ethics, while also contributing to the advancement of scientific knowledge."

Reviews

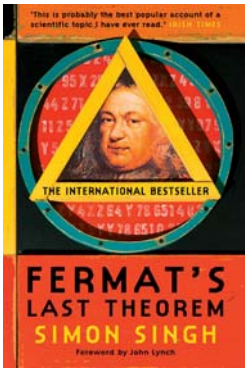
What's on your Summer reading list? If you're lost for inspiration, here are some of the favourites of staff in the Lab.



Dr Tatiana's Sex Advice to All Creation (2003) Olivia Judson

Written as a sex advice column for organisms great and small, this book explains evolutionary biology in a hilarious fashion. It begins with an age-old question between the genders – which is the most promiscuous? – followed by the reasoning behind immoral acts of rapes and cannibalism, and concluding with an open question: are men *really* necessary? In some instances, the author draws interesting parallels to humans, one of the reasons I find this book a must read. I was amazed by how nature has created an almost perfect gender balance in the various species, ranging from a slime mould that has more than 500 sexes, to the vicious praying mantis who slaughters her partner during copulation!

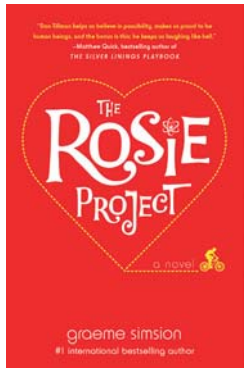
HEENA KHATTAR, POSTDOC, EMBL HEIDELBERG



Fermat's Last Theorem (2002) Simon Singh

Picture the scene: an amateur mathematician and a note next to an innocent looking equation: "I discovered a marvellous proof, which this margin is too narrow to contain..." It was 1637, and Pierre de Fermat unleashed a mathematical monster that would taunt the greatest minds for over three centuries. The Last Theorem was born, and author Simon Singh tells the amazing story of geniuses like Euler, Germain and Galois struggling to prove Fermat right or wrong. In 1963, a 10-year-old came across the riddle in his local library and set out to solve it. Three decades later that kid, Andrew Wiles, fulfilled his childhood dream after years of painstaking secret work. Full of thrill and emotion, *Fermat's Last Theorem* is impossible to put down until the last page.

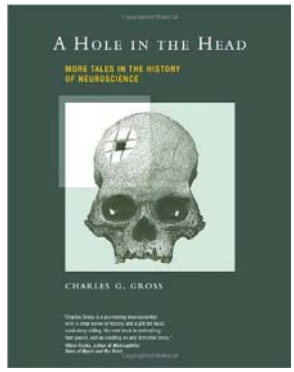
JULIA ROBERTI, POSTDOC, EMBL HEIDELBERG



The Rosie Project (2013) Graeme Simsion

As a stereotypical scientist with a slight touch of obsessive-compulsive disorder, genetics professor Don Tillman organises his entire life according to efficiency. His planned-to-the-minute daily routine and nutritionally balanced meals are long established aspects of his life when he begins 'The Wife Project'. Using a questionnaire to eliminate inadequate candidates, he attempts to find the most logically compatible life partner – a plan that fails when he meets barkeeper Rosie and develops these strange things called "feelings". Simsion has created a quirky, intelligent, and enjoyable character: I was hooked on the narrative voice from the first page. The novel, as well as its sequel *The Rosie Effect,* is set to be filmed in the coming years – certainly something to look forward to!

JULIA FRANKE, TRAINEE, EMBL HEIDELBERG



A Hole in the Head (2009) Charles C. Gross

Neuroscientists have historically learnt a lot from unfortunate accidents leading to brain damage – the inspiration behind this fascinating read. Charles Gross, a historian of neuroscience, explores the relationship between history and brain science from three fascinating angles. Beginning with a curious case study of a brain injury linking risk taking to a particular region of the brain, the book also explores how neuroscience has influenced art over the ages, before touring the reader through the work of several neuroscientists whose groundbreaking scientific ideas came before their time. Full of marvellous stories, *A Hole in the Head* will satisfy the curiosity of neuro experts and novices alike.

JOSE VIOSCA, EDITORAL INTERN, *SCIENCE IN SCHOOL* JOURNAL

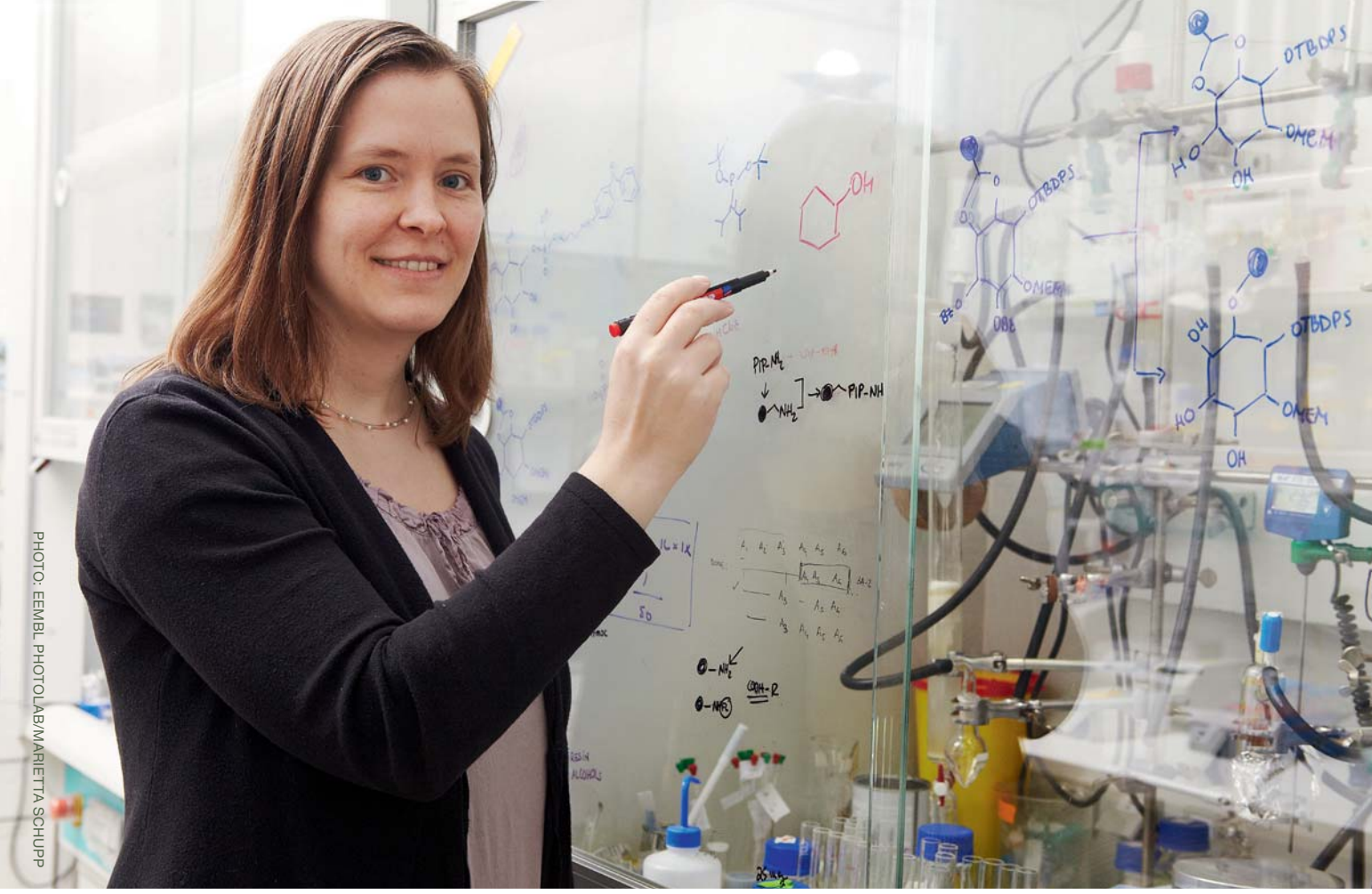


PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Chemical bonds

If you want to learn what life is like working on the interface of disciplines, a visit to Maja Köhn's lab at EMBL Heidelberg would be a great place to start.

BY ADAM GRISTWOOD

Awarded the 2015 Tetrahedron Young Investigator Award for "exceptional creativity and dedication" in the field of bioorganic and medicinal chemistry, Maja's work brings together chemists, molecular biologists, crystallographers, and bioinformaticians. Their common goal is to develop approaches that tease out the mysterious mechanisms of phosphatases – enzymes that have been linked to diseases such as cancer and Alzheimer's. As part of the prize, Maja gave an award lecture to more than 500 participants in Berlin, has another to come in Shanghai, and guest-edited a special edition of Elsevier's *Bioorganic and Medicinal Chemistry* journal.

What is your Lab working on?

We combine molecular biology, biochemistry and synthetic chemistry to investigate the functions and regulation of phosphatases. One of the main tasks for chemists at EMBL is to create tools for understanding difficult-to-study proteins: if there is no inhibitor or activator present, then we can create one using chemical methods. Increasingly our work is supported by advances in crystallography, bioinformatics and microscopy, enabling us to combine a large range of tools with the goal of simulating, imaging and ultimately understanding key biological questions.

What is the dynamic like?

Chemists tend to be very analytical (every milligram counts!), while biologists are sometimes geared more towards thinking about the bigger picture rather than the molecular detail – each has to learn how the other thinks. But the rewards of doing so are huge: ultimately it leads to a very creative atmosphere in the lab.

How was the experience of guest editing a journal?

It was a fascinating insight into the 'other side' of the publication process. There were many challenges such as soliciting papers and selecting peer reviewers. One of the most fascinating aspects was seeing the lively, detailed and oftentimes difficult scientific discussions that take place throughout the review process. The end product includes work from groups at Hamburg, Heidelberg and Hinxton, reflecting EMBL's broad involvement in phospho-signalling research, together with other works from colleagues and collaborators around the world. Overall, the experience was very positive, although not quite enough to lure me away from my lab in the long run!

Which philosophy do you live by?

Follow your interests, go as far into a new field or discipline as you feel comfortable with, and seek advice from other experts when reaching areas outside of your expertise or comfort zone.

Sarah Teichmann (pictured, bottom right) was amongst 17 female scientists elected to the Fellowship of the Academy of Medical Sciences. Teichmann is also the winner of an EMBO Gold Medal.

PHOTO: ACADEMY OF MEDICAL SCIENCES

Awards & Honours

Director of EMBL-EBI **Ewan Birney** and group leader **Sarah Teichmann** have been elected to the Fellowship of the Academy of Medical Sciences in recognition of their excellence in research and innovative application of scientific knowledge. The Academy of Medical Sciences is an independent organisation that campaigns to ensure advances in medical science are translated into benefits for patients, and its 1169 Fellows are the UK's leading medical scientists. The 48 new Fellows – 17 of whom are women – were formally admitted to the Academy at a ceremony on 1 July 2015.

Group leaders **Detlev Arendt** and **John Briggs** have both been named in EMBO's list of new members, among 58 "outstanding researchers" elected for their contributions to life science research. In total, EMBO membership now comprises more than 1700 life scientists in the international scientific community, whose input has helped to promote excellence in life sciences since 1964. EMBO Members serve on selection committees for EMBO programmes, mentor young scientists, and provide suggestions and feedback on the organisation's activities.

Stephen Cusack, head of EMBL Grenoble, has been elected to the Fellowship of the Royal Society. Founded in the 1660s, The Royal Society is the national academy of science in the UK, and is a fellowship of many of the world's most distinguished scientists drawn from all areas of science, engineering, and medicine. There are currently some 1600 fellows, including around 80 Nobel Laureates.

As winner of an EMBO Gold Medal, **Sarah Teichmann** will receive a hand-crafted medal and a bursary of 10 000 Euros. The award recognises her use of computational and experimental methods to better understand genomes, proteomes and evolution.

Alumni

Celebrating EMBL and our alumni

In this issue, we pay homage to the last of EMBL's anniversary events across our five sites at EMBL Grenoble – highlighting the event as well as individuals from Grenoble's past (pages 46–49). We also celebrate the Lab's science and culture with our annual Lab Day (now open to alumni worldwide) – by catching up with the winners of the John Kendrew and Lennart Philipson awards (page 32). We join alumni in Spain with their citizen science initiative that literally has tongues wagging (page 45). Finally, we reveal the results of the Alumni Association's online board elections, below – a huge thank you to all who participated!

Mehrnoosh Rayner
Head of Alumni Relations

PHOTO: EMBL PHOTOLAB

PHOTOS: ASTRID VON SOOSTEN

Iain Mattaj thanks the EMBL Alumni Association board, especially the six members stepping down at the end of 2015 (not all present at the meeting). Pictured, from left to right: Joep Muijrers, Giulio Superti-Furga (Chair), Gareth Griffiths, Iain Mattaj, Maria dM Vivanco (Vice-Chair), Jacqueline Mermoud, Matthias Hentze, Maj Britt Vorgrimmler, Mehrnoosh Rayner, Sarah Sherwood, Annabel Goulding.

Alumni board meeting

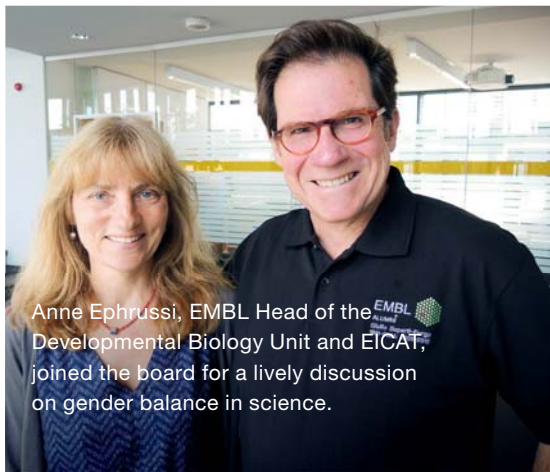
The EMBL Alumni Association board met for their last meeting in their current constellation at EMBL Heidelberg on Lab Day on 10 July. Agenda items included approval of the fast growing number of members, a review of the new board (which takes office in January 2016), the Lennart Philipson Award selection process, and recent and future alumni initiatives.

One highlight of the meeting was the update by EMBL Director Matthias Hentze on EMBL scientific breakthroughs as well as the Laboratory's strategy and plans for the next six years, together with news on EMBL infrastructure, training and integration in Europe. "This part alone, makes our visit to EMBL so valuable and inspiring", said outgoing Chair, Giulio Superti-Furga. Links to the EMBL update will be available online:

EMBL.ORG/ALUMNI/NEWS

New board from January 2016

Thank you to every one who participated in the online Alumni Association board elections. The new board will begin office in January 2016, and includes: Gareth Griffiths (Chair), Jacqueline Mermoud & Roberto di Lauro (Vice Chairs), Annabel Goulding (Treasurer), Des Higgins, Fatima Gebauer, Julius Brennecke, Alessia Buscaino, Joep Muijrers, Christian Engel, Mervi Lampinen, and Sarah Sherwood.



Anne Ephrussi, EMBL Head of the Developmental Biology Unit and EICAT, joined the board for a lively discussion on gender balance in science.

Stick out your tongue!

Luis Bejarano was a postdoc at EMBL Heidelberg 1996–99.

PHOTO: LUIS BEJARANO

It's not every day you see a molecular biologist jumping behind the wheel of a van in hot pursuit of data. Yet equipped with just a hand centrifuge and a battery-powered freezer, alumnus Luis Bejarano travelled the length and breadth of Spain to collect saliva samples from high school students, with the aim of learning more about the millions of tiny organisms that take up residence in our mouths. BY JOSE VIOSCA

Bejarano's epic two and a half month journey took him through 40 cities and villages to collect more than 2000 samples from 15-year-old students for the "Saca la Lengua" project – a citizen science initiative run by a team working at the Centre for Genomic Regulation (CRG) in Barcelona. "It's the longest business trip I've ever done," Bejarano smiles, now safely back in his lab after clocking up more than 7000km on route. "Our goal was to collect samples to study the relationship between people's behaviours, the environment, and the microorganisms that populate our mouths. But we also wanted students to get up close to research."

Using a mouthwash to flush some of the tiny inhabitants out of participants' mouths, researchers aim to study the genetic footprint of different microbial communities to better understand their role in health and disease. "Students had to fill out an anonymous questionnaire, with more than 50 questions about their lifestyle," Bejarano explains. "We want to know why certain individuals host certain microorganisms, and whether there are aspects related to their lifestyle that might have an effect."

The tiny guests in our mouths have been linked not only to dental diseases such as cavities and bad breath, but less obviously to conditions such as pancreatic cancer and heart disease. Yet scientists know relatively little about why this is so. "Up until now, the biggest mouth microbiome sample studied was from a few hundred individuals," Bejarano points out.

Cause or consequence?

By studying bacteria and fungi in the mouth, the team also aims to provide insights such as the impact of living in rural or urban areas and the influences of piercings or teeth brushing habits. "We are still some way off before we can begin to learn if certain microbes living in the mouth are the cause or consequence of certain environments or behaviours – but our study aims to identify correlations, which is a step towards this final goal," he explains.

In achieving this aim, he points out the importance of involving students directly in the project: "For example, in some villages students asked us what they should write in the questionnaire if they drink water from a well – we hadn't even thought about that!" Bejarano says. "Students and the wider public will also have the chance to analyse and interpret the data, while those who provide insights will appear as co-authors on research papers."

"Boot" and "lab coat" biology

Bejarano smiles recalling meetings with these students, who came from diverse communities and landscapes. "I was lucky not to end up with a flat tire!" he says. "It was a perfect combination of "boot" and "lab coat" biology, which often seem so remote from one another. We wanted to show that science can be fun, to raise awareness of the life sciences, and get people involved."

FIND OUT MORE AT:
SACALALENGUA.ORG

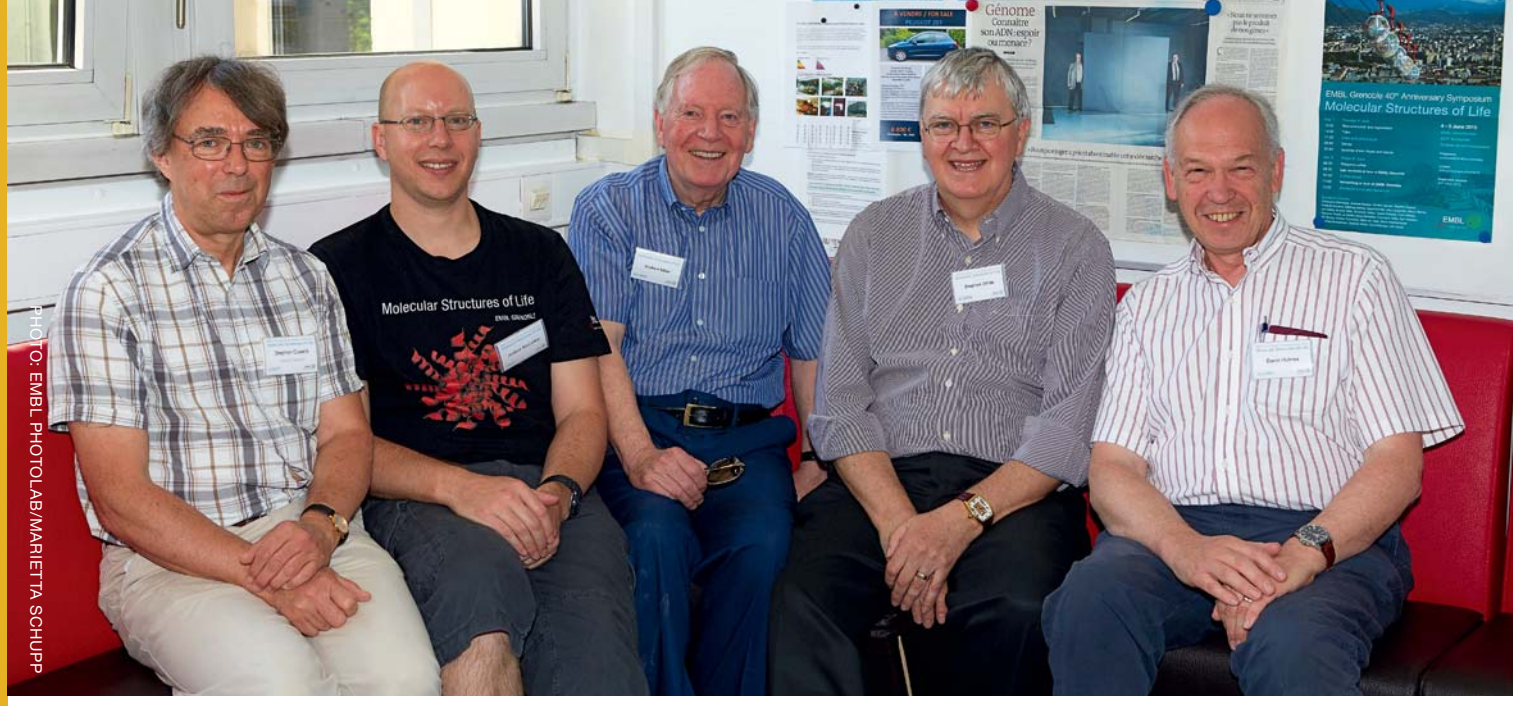


PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Molecular momentum

Speaking to staff past and present, Andrew Miller, the first head of EMBL Grenoble (1975–81) reflects on four decades of science, structures and spirit at the Outstation, while we catch up with other important players from its past over the following pages.

How did you end up at EMBL?

Two years before moving to Grenoble, I was talking science over coffee with neutron scattering pioneer John White who suggested my group use the technique to complement our X-ray studies on collagen – and we were delighted that it worked. John Kendrew, EMBL's newly appointed Director General, became aware of our work and wrote to me to ask if I would be interested in coming to lead an EMBL Outstation situated next to the Institut Laue-Langevin (ILL). There were not many biophysicists using neutrons at the time and I was very excited by the prospect of working within a few steps of a cutting-edge source of high-energy neutron beams.

Has the vision of the early days been fulfilled?

For EMBL Grenoble's pioneers there were major challenges, not least convincing the community of the potential of using neutrons to study biology. But the Outstation was productive from the outset and over the years has delivered astonishing technological advancements hand-in-hand with outstanding science. The opening of the new ESRF in the 1990s added to this momentum, bringing together highly complementary X-ray and neutron facilities in one place – and we are still reaping the benefits today. Close links between several institutes in Grenoble creates a model for other centres around the world and I think it is clear the early vision has been realised.

What are your most striking memories?

I remember our first visit to the building in which we were renting space for the Outstation. Our footsteps echoed as we entered the yawning, silent, empty laboratories in the Batiment Laboratoire de Moyen Activitie (LMA) and I thought to myself 'medium activity' must be an

Convening in the Carmen Cafe

The group, which reunited at EMBL Grenoble's 40th Anniversary celebrations, was pictured in the Outstation's Carmen Cafe, named after former staff scientist Carmen Berthet. "Carmen made a crucial contribution to the establishment of the Outstation and was a lively, happy and unforgettable personality," said Andrew Miller during a dialogue captured at EMBL Grenoble's 40th Anniversary celebrations. More excerpts from this interview will be made available online:

EMBL.ORG/ALUMNI

Grenoble alumni share their stories

Building up an EMBL Outstation

PHOTO: REUBEN LEBERMAN

Left to right: Stephen Cusack (Head of Outstation), Andrew McCarthy (group leader), Andrew Miller, Stephen White (PhD Student 1976–78), and David Hulmes (postdoc, 1976–78).

Reuben Leberman

Now: Retired, Palmerston North, New Zealand
At EMBL Heidelberg: 1976–1981 Group Leader.
At EMBL Grenoble: 1981–1998 Group Leader and Senior Scientist

What brought me to EMBL? Well, EMBL was brought to me since I was already in Heidelberg at the Max Planck Institute for Medical Research. The choice of EMBL building had just been made, and I was asked by Sir John Kendrew, EMBL's Director General, to design the layout of the labs based on my experience in redesigning the MPI labs. I also designed the P4 facility required for genetic manipulation.

When my contract was coming to an end, I applied to EMBL for a position that allowed me to continue with my group at the MPI and our studies on polypeptide elongation factor Tu (EF-Tu). This was going well and we had crystals. My application was successful, and I was appointed group leader in 1976, publishing the first study of protein crystals with synchrotron radiation at EMBL Hamburg with Arnold Hamsen and Georg Schulz.

To make neutron diffraction measurements for our studies, we visited EMBL Grenoble at the Institut Laue-Langevin (ILL). Here I met Bernard Jacrot, the future head of the Outstation, who offered me a post at Grenoble for my neutron diffraction studies and to organise the biochemical labs. I, and my assistant Bruno Antonsson moved to Grenoble in 1981. With my modifications for safety and the superb support of Jean-Marie Bois (electrics), Joe Sedita (workshop) and Annie Simon (stores and kitchen) the Grenoble building was eventually completed.

Subsequently, with Marie-Thérese Dauvergne a deuteration facility was established and Michael Härtlein introduced DNA manipulation. I led an extensive research programme into seryl- and asparaginyl-tRNA synthetases and organised the first international workshop on aminoacyl-tRNA synthetases in 1991. Our work led to breakthroughs such as understanding the relationship between the GTP-binding domain of EF-Tu and p21 and we collaborated with Outstation crystallographers to solve important crystal structures such as seryl-tRNA synthetase and the first G-protein-exchange factor complex (EF-Tu/EF-Ts).

Moving is not easy for family. My wife, Pat, established a social life with a small group of expat wives, organising meetings at the group's houses open to all; she called this "Open House". This became so popular that "Open House" still exists 30 years on with 150 members! I retired in 1998 with a certain amount of satisfaction in my role in building and establishing an EMBL Outstation in Grenoble.

exaggeration. But it quickly became a hive of activity and the staff in LMA and ILL were very helpful getting the Outstation moving. On another occasion, when travelling from Oxford to Grenoble, I was carrying specimens for the neutron work in the form of frozen rat tails in a thermos flask. The security guard at the French border inspected the contents of the flask then turned to me and asked what sauce I served them with – at that moment I knew I was really in gastronomic France!

What does the future hold?

Four decades ago, who could have predicted the impact that using neutrons and X-rays would have on our understanding of biology? Today, the growth of fields such as genomics and pharmacology present a limitless supply of molecular structures that need to be resolved in 3D. This is something that the next generation of synchrotrons is well equipped to tackle. Advancements in instrumentation, investigation and imaging at EMBL Grenoble will continue to be a major driving force for zooming in further on the molecular structures of life. While it's impossible to predict what's to come, it's very exciting to imagine what might lie in store.

Adventures in life and science

Jeremy Smith

Now: Governor's Chair at the University of Tennessee and founding Director of the Oak Ridge National Laboratory (ORNL) Center for Molecular Biophysics, USA.
At EMBL Grenoble: 1982–1985, PhD student, Cusack group


PHOTO: JEREMY SMITH

I arrived at EMBL Grenoble in August 1982 a day late, having dreamily got on the wrong ferry when travelling from London, thus arriving in France with only my passport and two pounds on me. After a night sleeping rough, some careful negotiations and a spot of hitchhiking, I somehow got back on track to be greeted by the then Head of Outstation Bernard Jacrot proclaiming: "Your reputation as an absent minded scientist is already firmly established!" It was the beginning of an adventure in life and science.

Led by my curiosity about neutrons and a desire to learn a foreign language, I set about performing calculations, simulations and scattering experiments as the first student in the lab of a young Stephen Cusack, who is now the Outstation Head. There were catastrophes, arguments about theory and much hard work, but a new field was established and we had a fantastic collaboration with protein dynamics pioneer and future Nobel Laureate Martin Karplus, who I went on to work with as a postdoc.

Stephen's interests shifted from physics to crystallography, and he moved briefly to Harvard to study while I remained in Grenoble playing rock music in a local bar and finishing my PhD! I remember being somewhat peeved that such a brilliant physicist as Stephen would be lost from the physical side of things, moving into what I then considered the relatively 'easy' field of crystallography. I know better now, of course, maybe.

After my postdoc I set up a group in Saclay, France, before becoming Germany's first Chair in Computational Biology, at the University of Heidelberg, and then moved to my current role at ORNL in 2006. There are some fantastic toys to play with here – including the world's most powerful neutron source and second most powerful supercomputer. Protein structures are beautiful, but to me unveiling the energies and conformational fluctuations needed to understand function will always remain more interesting than 'stamp-collecting' structures (I am evilly grinning right now!) – although many crystallographers, including Stephen, will disagree!

Space age science

Elena Seiradake

Now: Group leader, Department of Biochemistry, University of Oxford
At EMBL Grenoble: 2003–2006, PhD student, Cusack group


PHOTO: ELENA SEIRADAKE

When I arrived in Grenoble in Summer 2003, the town was engulfed in a massive heat wave, known as the 'canicule'. Neron, a big mountain close to the EMBL Outstation had been struck by lightning and was on fire, filling Grenoble with smoke and ash and most sensible people had fled to higher altitudes. Fortunately things quickly got better: the lab was air-conditioned, I had an exciting project, and everyone seemed to

Close connections


PHOTO: WINFRIED WEISSENHORN

Winfried Weissenhorn

Now: Director, Institut de Biologie Structurale (IBS), Grenoble
At EMBL Grenoble: 1998–2006, Group leader

After a postdoc at Harvard, I wanted to return to Europe and spotted a rare opportunity to become a group leader at EMBL Grenoble. Immediately, I was submersed in a fantastic environment for setting up a research group, and this atmosphere remains to this day. EMBL provides sufficient funding to establish teams, pursue projects, and publish independently, building and enhancing the international reputation of researchers in the process.

Using a range of molecular biology, protein chemistry, X-ray crystallography and electron microscopy approaches, our group at EMBL Grenoble made important contributions in the field of structural virology. One notable example is our work on Ebola virus assembly and the conformational flexibility of its matrix protein. We also carried out work revealing the molecular details of how RNA nucleoproteins polymerise with their genome into nucleocapsids and published the first crystal structure of an ESCRT–III budding factor.

Since leaving EMBL, our research focuses on HIV-1 entry and cellular budding factors that are recruited by enveloped viruses such as HIV-1 to complete budding. One of the most exciting aspects is just how much more there is still to learn – we ultimately want to understand how HIV-1 entry can be blocked by vaccine induced antibodies and how enveloped viruses get out of cells.

We maintain close connections with EMBL Grenoble through the Partnership for Structural Biology (PSB). EMBL is special due to our common mission of performing excellent basic science. Our vision for the future is closer links through the extension of existing bilateral infrastructure projects on electron microscopy and scientific projects by fostering scientific collaborations.

"One of the most exciting aspects is just how much there is still to learn."

love science – I immediately felt at home!

Some of my best scientific memories come from the ESRF synchrotron, where we collected diffraction data from crystals: the sophisticated electronic equipment gives the feel of being onboard a spaceship. Meanwhile, my supervisor Stephen Cusack was like the Captain Picard of crystallography, instinctively knowing how to get the best data from a crystal – sometimes even correctly guessing the 3D arrangement of molecules inside. Group leader Andrew McCarthy, who I still collaborate with, was another hero of my synchrotron time: he put together much of the beamline hardware, and his work in neural guidance factors inspired me to go into this field in my postdoc and beyond.

My projects also involved collaboration with teams outside EMBL – for example the lab of Eric Kremer in Montpellier, where I worked closely with a wonderful postdoc, Harald Wodrich. Looking back, I realise how incredibly lucky I am to have worked at EMBL Grenoble. Not only is Stephen a perfect supervisor, but working in his lab kindled my passion for science and led me to pursue a career in academic research.

Teachers were challenged to extract DNA from plant cells

Staff did a demonstration using photosynthesis to print the EMBL logo onto the leaf of a geranium plant

Learning to barcode life

A bubbling mix of 30 teachers from all over Greece seized the opportunity to meet research scientists, visit research facilities and get hands on in the laboratory themselves during a course organised by EMBL's European Learning Laboratory for the Life Sciences (ELLS).

The two-day event, which took place at the National Centre for Scientific Research's 'Demokritos' campus in Athens, involved a wet-lab practical and bioinformatics module on DNA barcoding, a technique that uses specific marker genes to identify living organisms at a species level. On the first day, course participants collected sample material from plants growing on the campus, extracted plant DNA, amplified a barcoding gene by polymerase chain reaction and prepared the samples for DNA sequencing. On the second day, teachers explored the use of freely available bioinformatics tools and databases, such as the European Nucleotide Archive, to determine the identity of the plants in question using the information provided by DNA sequencing. The course was organised with the strong support of environmental education officer Vasiliki Kioupi, who works for the Directorate of Secondary Education of Piraeus and who is the current ELLS visiting teacher, as well as researchers from NCSR.

FULL STORY ONLINE:
EMBLOG.EMBL.DE/ells/blog/archives/18146

The course was initiated as pilot to test the waters for potential future teacher training workshops in Greece using a similar format

PHOTOS: PHILIPP GEBHARDT

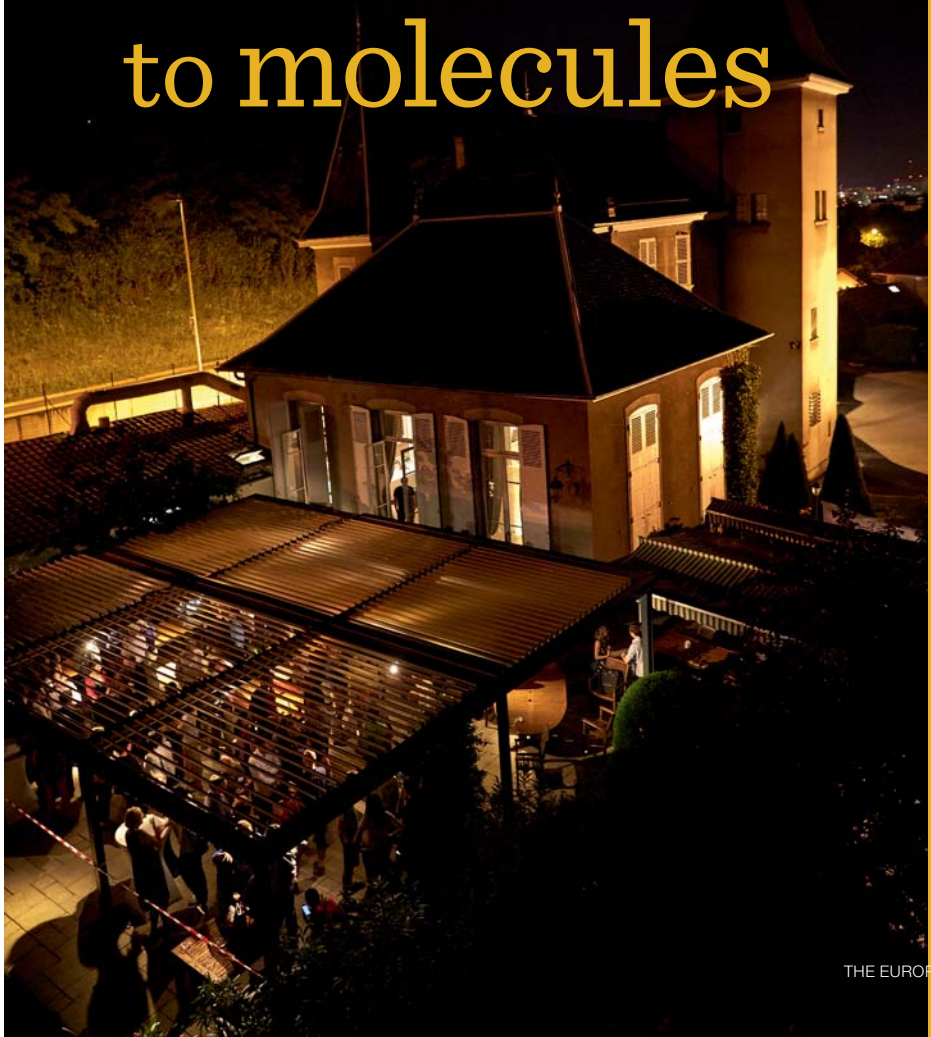
Top: Lab reunions brought together friends past and present

Bottom: Participants enjoyed good company, science, food, music and dance, as well as a surprise firework show

Stephen Cusack, Head of Outstation celebrates the milestone with Iain Mattaj, EMBL Director General

PHOTOS: EMBL PHOTOLAB/MARIETTA SCHUPP

From mountains to molecules



Countless crystals, stunning structures, tremendous technologies and neat narratives provided the focal points as more than 150 staff and alumni came together at EMBL Grenoble in June to celebrate the Outstation's 40th birthday. In the last in a series of events marking 40 years of EMBL, participants reflected on the scientific, political and personal stories underlying the growth of EMBL Grenoble – which is situated in the foothills of three mountain ranges – from an ambitious idea into one of the most important sites in Europe for structural biology.

For more on EMBL Grenoble's 40th Anniversary, see page 46

VIEW MORE PHOTOS FROM THE EVENT: NEWS.EMBL.DE/?p=4214

Events

September
5-8

ICC, Birmingham
The EMBO Meeting 2015 (EMBL staff-alumni reception on September 7)

IMAGE: SANDRA KRAHL

September
20

EMBL Heidelberg
EMBL Science and Society Symposium: What Makes us Human?

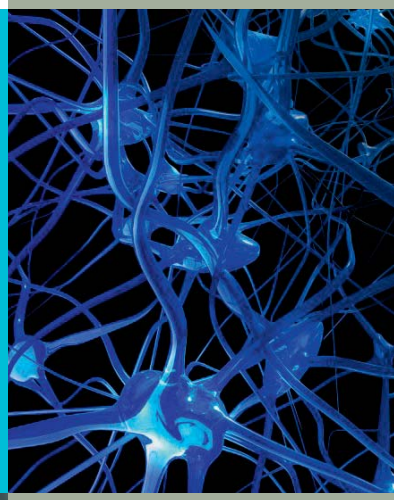
September October
28-1

EMBL-EBI
Course: Introduction to Next Generation Sequencing

IMAGE: EMBL-EBI/SPENCER PHILLIPS

October
2

EMBL Monterotondo
EMBL Distinguished Visitor Lecture: Neural Plasticity and Genomic Diversity – Fred Gage, The Salk Institute for Biological Studies



October
18-21

EMBL Heidelberg
EMBO | EMBL Symposium: The Non-Coding Genome

IMAGE: EMBL/PETRA RIEDINGER

October
22-24

EMBL Heidelberg
The 17th EMBL PhD Symposium: Just by Chance? Randomness & Variability Shaping Biology

November
5-6

EMBL Heidelberg
16th EMBO|EMBL Science and Society Conference: Emerging Biotechnologies: Hype, Hope and Hard Reality

IMAGE: SANDRA KRAHL

Upcoming meetings
Alumni

11 September: **EMBL Alumni Meeting, Copenhagen**
23 October: **EMBL-VIB Alumni Meeting, Leuven**
6 November: **EMBL Alumni Meeting, Zürich**

VIEW THE COMPLETE LIST OF EVENTS ONLINE
EMBL.ORG/EVENTS