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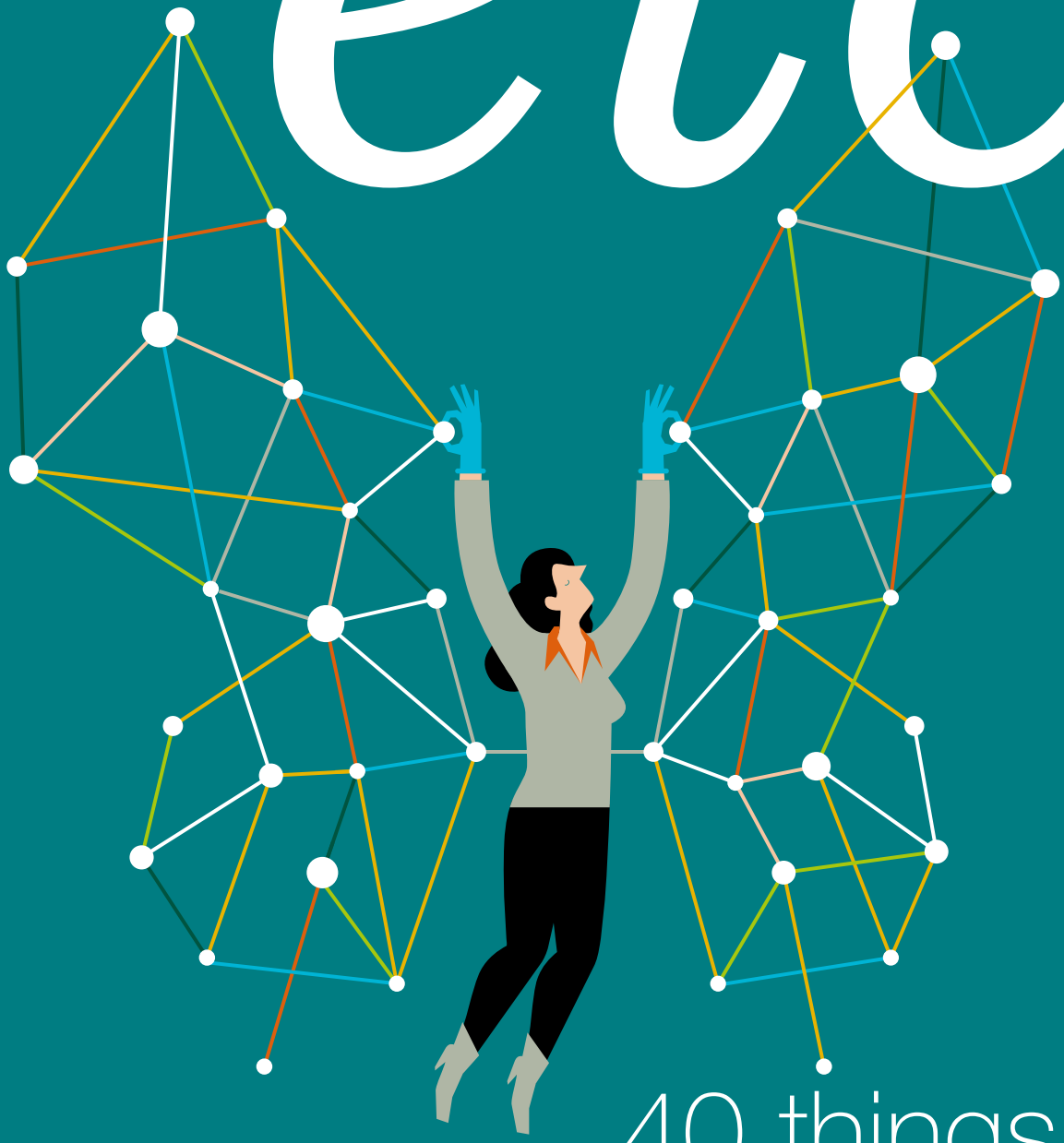
Issue 80 Summer 2014

EMBL etc.



40 things that make EMBL

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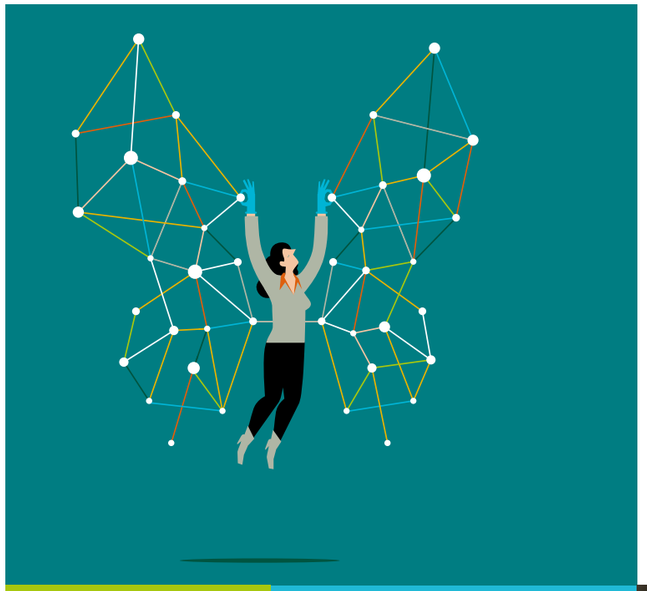

Synapse

Cultures

Regulars

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Editorial

When we were researching our cover story, choosing between the hundreds of thoughtful ideas collected was no easy task. While it is clear that EMBL is an academic powerhouse, for the people who know us best, the Lab also reflects diversity, intelligence, collaboration, internationality, quirkiness, fun, and much more besides. Such attributes have also inspired this redesign of *EMBLetc.* The bold and modern print publication that you hold in your hands combines with a dynamic online platform – both of which allow us to further support the Lab's leading role in discovery and discussion of the molecular life sciences. This is the first major overhaul of *EMBLetc.* in more than five years, and while you will still find familiar aspects that our readers love, there is also much more of what you told us you wanted: more science coverage, deeply reported feature articles, and more stories about the Lab and the world around it. In this magazine we have created three aptly named sections: Synapse – an overview of the hottest research coming out of the Lab; Nucleus – in-depth stories that address big ideas, successes, or challenges; and Cultures – articles that reflect on life in and around EMBL. Our aim is to deliver content that is engaging, thought-provoking and inspiring, and we hope you enjoy these platforms as much as we have enjoyed creating them. As always, we welcome ideas for future editions and we would love to know your thoughts at news@embl.de.

Adam Gristwood

Editor

Word to remember

Enhancer

Noun, Pronunciation: /ɪnˈhɑːnsə(r)

***Genetics* – Stretch of DNA that acts as a remote control to turn genes on. Enhancers can act across surprisingly long distances, e.g. as an embryo's face develops (page 7).**

Rearrangements that bring specific genes unexpectedly close to enhancers may drive particular tumours (page 31).

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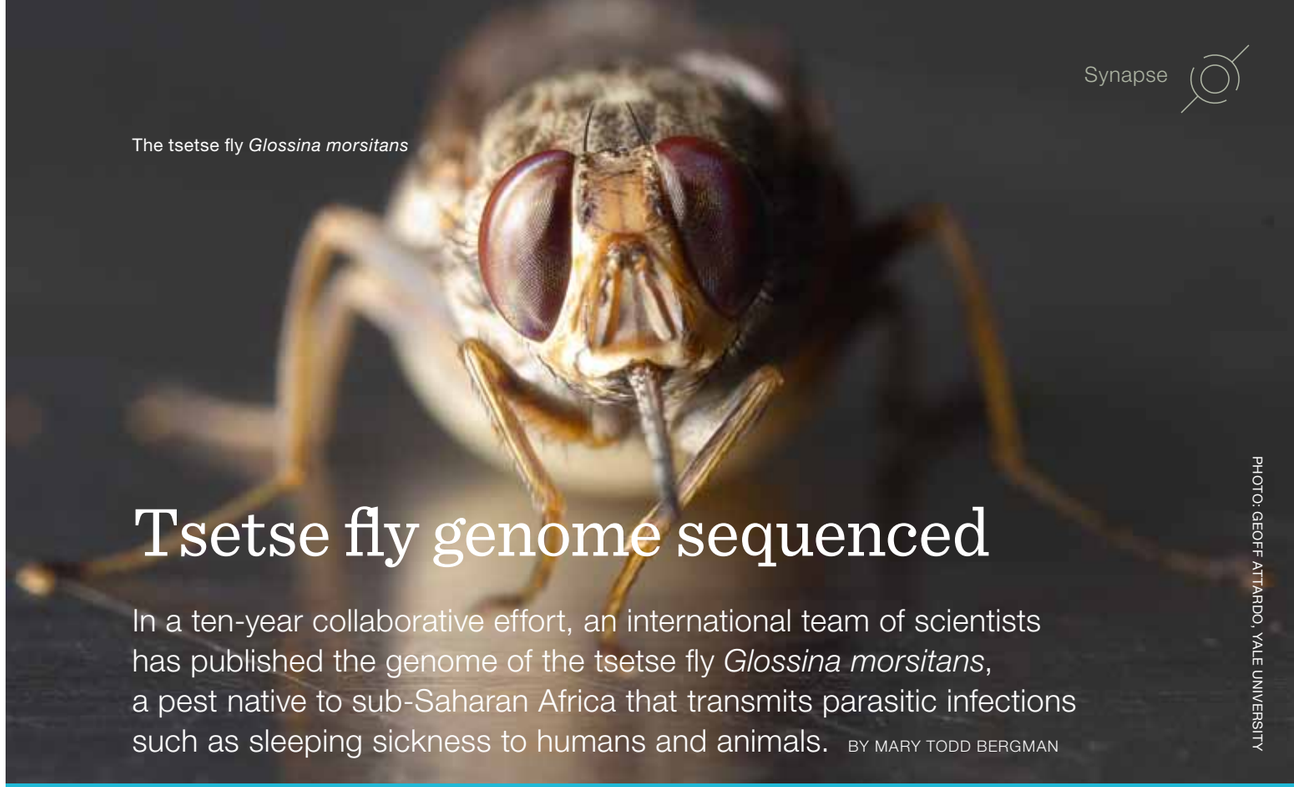


The tsetse fly *Glossina morsitans*

PHOTO: GEOFF ATTARDO, YALE UNIVERSITY

Tsetse fly genome sequenced

In a ten-year collaborative effort, an international team of scientists has published the genome of the tsetse fly *Glossina morsitans*, a pest native to sub-Saharan Africa that transmits parasitic infections such as sleeping sickness to humans and animals. BY MARY TODD BERGMAN

Unlike most insects, tsetse flies produce one offspring at a time, which they feed by lactation before the larva is born. They feed exclusively on the blood of animals, and live comfortably with three different symbiotic bacteria including *Wolbachia*, which modulates insect reproduction. Comparing the genome of this fascinating species to other organisms can provide insights into evolutionary biology, for example the development of lactation in mammals. Most importantly, an in-depth understanding of the genetic makeup of the tsetse fly will help research into new ways of controlling the spread of sleeping sickness.

Beyond sequencing

Sequencing a genome is the first step in a long and complex process. Using computational methods, the scientists identified the genes that give instructions for making different proteins in the tsetse fly and compared them to other organisms. This comparison gives some indication of the function of the genes.

Over 140 insect disease vector biology scientists – half of whom work in African research institutes – examined and manually curated the annotations, bringing to bear their specialist knowledge in all aspects of tsetse fly biology, from sense of smell to reproduction and immunity. The result is a foundational resource for research into new ways of controlling the spread of sleeping sickness.

A community-driven resource

"This is a major milestone for the tsetse research community," said Geoffrey Attardo, research scientist at the Yale School of Public Health and lead author on the paper. "Our hope is that this resource will facilitate functional research and be an on-going contribution to the vector biology community."

"The contribution of so many scientists, especially those from African countries where *Glossina* is a pest species, was key to unlocking the value of the genome annotations," says Dan Lawson from the Kersey team at EMBL-EBI. "Getting the community involved with genome projects early greatly improves the likelihood of long term utility of the resource."

"I've loved being involved in this project from the very beginning," says Karyn Megy from the Brazma team at EMBL-EBI. "I've met great people who specialise in all aspects of vector disease, taken part in workshops with interesting people who are eager to learn, travelled several times to Africa and even went on a field trip in Kenya, to see how they capture the tsetse flies."

Attardo *et al.* Science, 25 April 2014.
DOI: 10.1126/science.1249656

THE DATA ARE FREELY AVAILABLE IN VECTORBASE: WWW.VECTORBASE.ORG.

Remodelling the cell

Cells, like people, come in all shapes and sizes. To get to their final shape they have to make important changes in the membranes that form their borders. BY DAN JONES

As cells get bigger, they obviously need to create more membrane, but sculpting the cell into a defined shape also requires tightening and contracting parts of the membrane. Coordinating these processes is essential for cells to acquire their correct form. New research from Stefano De Renzis' group at EMBL Heidelberg has begun to show how this is achieved.

De Renzis's group studies the way cells change shape as embryos grow and develop, and the signals cells rely on to make sure they change shape appropriately. In recent experiments, De Renzis and colleagues looked at how the embryo of the fruit fly *Drosophila* goes from being a 'syncitium' — a giant cell with many nuclei — to a collection of 6000 individual cells, each with one nucleus.

"During this process, the surface area of the embryo's cell membranes increases 30-fold, as membranes grow around each nucleus to define a new cell," says De Renzis.

Balancing act

Using tools developed by Carsten Schultz's lab, Alessandra Reversi, postdoc in the De Renzis group, found that this is achieved by altering the ratios of the different building blocks of cell membranes, in particular two kinds of molecules: phosphatidylinositol 4,5-bisphosphate (PIP2) and phosphatidylinositol (3,4,5)-triphosphate (PIP3). High levels of PIP2 relative to PIP3 lead to contraction of the membrane; by contrast, high levels of PIP3 prevent this contraction and allow the membrane to expand.

PIP molecules do not themselves cause contraction of the membrane, however. Instead, networks of actomoysin, which are made up of actin and myosin proteins and are attached to the cell membrane, do this hard work. "We found that PIP3, along with another protein called bottleneck, inhibits the assembly of actomyosin, which prevents contraction of the membrane," says De Renzis.

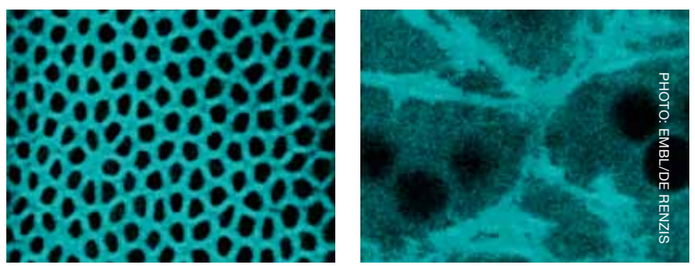
The next step for De Renzis and colleagues is to identify the upstream signals affecting PIP levels. It's already known that proteins called PIP kinases and PIP phosphatases are crucial in determining the ratios of PIP2 and PIP3. "So the regulators of these proteins are the key molecules to focus on," says De Renzis.

Reversi *et al. Journal of Cell Biology*, 5 May 2014. DOI:10.1083/jcb.201309079

Tools of the Trade

If the requisite tools are not available in a researcher's own lab, collaboration becomes essential. Stefano De Renzis' lab is focused on unravelling the cellular dynamics and signalling processes involved in morphogenesis, during the development of *Drosophila* embryos. Carsten Schultz's lab frequently develops tools for studying signalling pathways, especially those involving lipids.

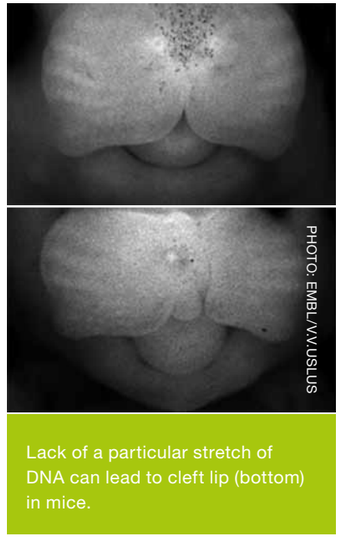
After hearing a talk by De Renzis at EMBL, Schultz realised that his tools would be ideal for tackling the processes De Renzis studies, and the collaboration was born. And once the group leaders had decided to work together, their energetic postdocs – Alessandra Reversi and Devaraj Subramanian – took over, says Schultz. "They really grabbed the ball and ran with it."



Network collapse: If the ratios of two PIP molecules in the cell membrane are skewed (right), the actomyosin network (bright blue) breaks down.

Insights into genetics of cleft lip

Scientists at EMBL Heidelberg have identified how a specific stretch of DNA controls far-off genes to influence the formation of the face. The study helps clarify the genetic causes of cleft lip and cleft palate, which are among the most common congenital malformations in humans. BY SONIA FURTADO NEVES



Lack of a particular stretch of DNA can lead to cleft lip (bottom) in mice.

"This genomic region ultimately controls genes which determine how to build a face and genes which produce the basic materials needed to execute this plan", says François Spitz, who led the work. "We think that this dual action explains why this region is linked to susceptibility to cleft lip or palate in humans." Previous studies had shown that variations in a large stretch of DNA are more frequent in people with cleft lip or cleft palate. But there are no genes in or around this DNA stretch, so it was unclear what its role might be. To answer this question, Spitz and colleagues genetically engineered mice to lack that stretch of DNA, as the mouse and human versions are very similar, and are therefore likely to have the same role in both species. They found that these genetically engineered mice had slight changes to the face – such as a shorter snout – and a few had cleft lips. The scientists also used this mouse model to look at what happened during embryonic development to lead to those changes. "We found that this stretch of DNA contains regulatory elements that control the activity of a gene called Myc, which sits far away on the same chromosome," Spitz explains, "and it exerts that control specifically in the cells that will form the upper lip."

In the face of mouse embryos that lack this stretch of DNA, Myc becomes largely inactive. This affects two groups of genes: genes directly involved in building the face, and genes that make ribosomes, the cell's protein-producing factories. The latter effect could make the developing upper lip more sensitive to other genetic conditions and to environmental factors – like smoking or drinking during pregnancy – that can influence cell growth. Making the face, and the upper lip in particular, are very complex processes, requiring different groups of cells in the embryo to grow and fuse with each other at the right time. If the cells involved have their protein production impaired, any additional burden could disrupt that growth, increasing the likelihood of a malformation like cleft palate.

The EMBL scientists would now like to use their genetically engineered mice to untangle the interplay between genetic and environmental factors, investigate how the enhancers in this stretch of DNA can control Myc across such a long distance, and determine the exact role of the genetic variants found in humans.

The study was performed in collaboration with John Marioni's group at EMBL-EBI, who conducted the RNAseq analysis that yielded the list of genes affected.

Uslu *et al. Nature Genetics*, 25 May 2014. DOI: 10.1038/ng.2971

HIV maturation

SFN When HIV particles burst from a cell, and before they can infect other cells, they have to mature. John Briggs' group in Heidelberg have pinpointed interactions between parts of a viral protein called Gag which are crucial for this maturation. The group used a combination of cryo-electron microscopy and tomography to look at viral structures assembled in the test tube. The similarities and differences they have found between HIV and Mason-Pfizer monkey virus – often used to study the human pathogen – could help distinguish key viral building blocks from pieces fine-tuned by each virus depending on the cells it infects.

Bharat *et al. PNAS*, 19 May 2014. DOI: 10.1073/pnas.1401455111

FULL REPORT AT NEWS.EMBL.DE

How immune cells use steroids

MTB Sarah Teichmann's group at EMBL-EBI and the Wellcome Trust Sanger Institute have discovered that some immune cells turn themselves off by producing a steroid. The findings have implications for the study of cancers, autoimmune diseases and parasitic infections.

Mahata *et al. Cell Reports*, 8 May 2014. DOI: 10.1016/j.celrep.2014.04.011

FULL REPORT ONLINE
NEWS.EMBL.DE

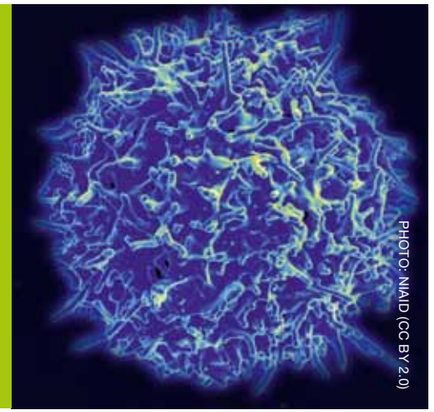


PHOTO: NIAID (CC BY 2.0)

Healthy human T cell

Chain reactions

Auxins are small molecules with big effects, which they achieve via intermediaries. At EMBL Grenoble, the mode of action of those middlemen is coming to light. BY DAN JONES

They were among the first plant hormones to be identified, and play important roles in guiding the growth of plants from the earliest stages of development. The reason auxins have such powerful effects is that they're able to turn on the expression of genes within cells, with profound consequences for the way cells function. Auxins do not directly interact with DNA to activate genes; this is the job of auxin response factors (ARFs), a kind of transcription factor that binds to auxin response elements in DNA and initiates reading (or transcription) of auxin-responsive genes.

At low auxin concentrations, ARFs become associated with specialised transcriptional repressors called AUX/IAA proteins, which block their ability to turn genes on. When auxin levels rise, these repressors are broken down and the ARFs again become able to switch auxin-responsive genes on.

Face Value

Knowing how ARFs and their repressors interact is crucial to a full understanding of how auxins regulate gene expression. So Max Nanao, a staff scientist at EMBL Grenoble, teamed up with an international group of researchers to work out the atomic structure of the parts of ARF that interact with the repressors. "There were hypotheses about what these might look like, but there were no structural data", says Nanao. Now there is, as Nanao and colleagues report in a recent paper in *Nature Communications*, and another published in *PNAS*. They found that the parts of ARF that bind to the repressors have two faces, one positively charged, the other negatively. These allow ARFs to form chains linked head-to-tail.

Breaking the Chain

Notably, AUX/IAA proteins can also bind to both the positive and negative faces of ARF proteins, thereby competing with ARFs for binding to these faces — and this competition is likely to be involved in the regulation of gene activation. Although it's common for gene activating proteins to need to form pairs, Nanao and colleagues believe that the capacity of ARFs to form larger complexes involving many ARF subunits may be important for carrying out their biological functions. "This is a question for future research," says Nanao.

Nanao *et al. Nature Communications*, 7 April 2014. DOI: 10.1038/ncomms4617.

First, catch your DNA

SFN Christian Haering's group in Heidelberg have discovered how chromosomes get into rings formed by a group of proteins called condensin – rings which the group had previously showed keep chromosomes coiled up.

The secret, the scientists found, lies in a part of condensin that they describe as "a rather unconventional DNA binding domain." It seems that when this part of condensin binds to DNA, another section of the ring opens up, allowing chromosomes to enter.

Piazza *et al*. NSMB, 18 May 2014. DOI: 10.1038/nsmb.2831

FULL REPORT ONLINE
NEWS.EMBL.DE

40 things that make EMBL

What comes to mind when you think of EMBL? As the Lab turns 40, and with the help of staff and alumni, here is an unofficial and by no means complete list of what it is about our institution that gets people excited, energised or enthralled. In no particular order, here are 40 things that make EMBL, EMBL.

BY ADAM GRISTWOOD

ILLUSTRATION: AAD GOUDAPPEL

1

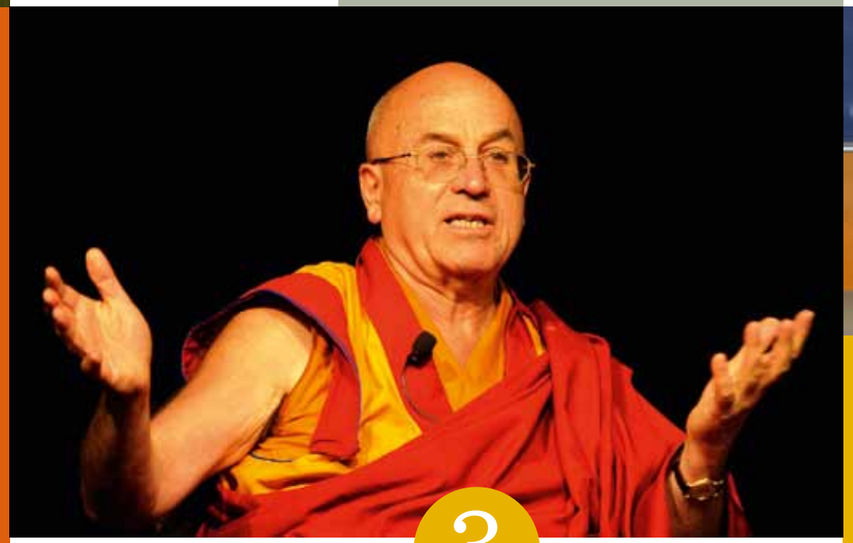
Our member states

EMBL owes its existence to funding from public research money from 21 full members and two associate members… and counting. The Lab was established in 1974 as an intergovernmental organisation – initially by 10 member states – with a long-term strategic perspective and relatively stable funding that is agreed upon every five years together with the EMBL Programme. This stability has allowed EMBL to hire generations of young, brilliant researchers that are provided with the resources needed to carry out audacious research projects without the pressure to publish as fast as possible or the need to raise external funding (page 28).

2

Scientific freedom

Our scientists are given the freedom and the means to follow their instincts, inspiration and interests.



3

Guest speakers

As a leading research institution, it is no surprise to find Nobel Laureates or other big name speakers gracing EMBL's seminar programmes. But one could be forgiven for doing a double-take when Buddhist monk Mathieu Ricard came to EMBL Heidelberg to deliver a Science and Society Forum lecture – a long-running series of seminars that seeks to raise awareness of the impact that research is having on society. During his talk in 2009, Ricard, who has acted as a French interpreter for the Dalai Lama, discussed how he has brought meditation and neuroscience together. "The main thing is about the mind, about changing the mind and the science of mind," he said. "We're looking for truth – we're not trying to prove that a particular truth is the truth. That's why Buddhists feel very comfortable with scientists."

Graduation ceremony

An army of more than 600 young scientists has graduated from the EMBL International PhD Programme since its launch in 1983. For many, the graduation ceremony is a time when blood, sweat and tears are finally replaced with relief, happiness and pride. The ceremony is followed by an intimate reception that allows the new doctors to celebrate in the company of peers, friends and family. "It was a celebration of becoming part of a family with such friendly and talented people from all over the world," says EMBL Heidelberg's Veli Vural Uslu, who graduated last December.

5

4

Outstanding research

10th best institution in the world for molecular biology research

613 scientific publications in 2013

18 European Research Council grantees

75% of staff dedicated to science (research and services)

6

Beer sessions

"Informal meet-ups in the Lab provide a place to network, take time out, and discuss surprising results," says Dermot Harnett, a PhD student at EMBL Heidelberg. Indeed, whether it is over beer, tea, coffee or pizza, these gatherings have become institutions in their own right.

7

Core facilities

Quality services, diverse expertise, and high user satisfaction characterise our shared research facilities for advanced light microscopy, chemical biology, electron microscopy, flow cytometry, genomics, protein expression and purification, and proteomics. The facilities are heavily used by scientists throughout EMBL, as well as researchers from our member states and beyond. Staff in all our core facilities are also involved in research; method and technology development; training; industry relations and international projects, as well as providing advice to similar facilities in our member states.

8 Corridor conversations

Whether you are waiting for your experiment to finish, simulation to run, or code to complete, there is always a friend around to discuss your ideas with. “When you wander around the Lab you are certain to get chatting to people – this was how the PhD Symposium idea was born... and there is always someone around to sing Monty Python songs with at midnight!” explains alumnus Freddy Frischknecht, who is now a professor at the University of Heidelberg.

9 We reach out

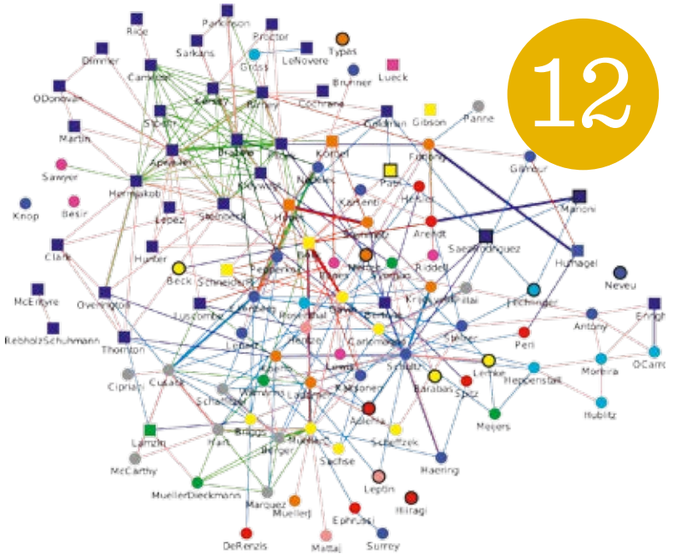
Tours, visits, open days, nights of science, and matinées bring hundreds of researchers, students, and members of the public to EMBL sites every year. Our European Learning Laboratory for the Life Sciences (ELLS) delivers an inspiring educational programme that supports secondary school biology teachers (page 39). Our presence at career fairs and scientific conferences raises awareness of the Lab. And we work with other major European organisations on initiatives such as the EIROforum journal *Science in School*, as well as contributing to the CommHERE project – an initiative to improve communication on the outcome of EU-funded health research projects.

10 Big thinking

Realising the huge potential of life science research in key areas such as medicine, agriculture and the environment is dependent on the development of infrastructures that enable scientists to store, manage and analyse massive and diverse datasets – and EMBL is at the heart of these efforts. One initiative that aims to address this issue is the ELIXIR project, which will unite the European bioinformatics community under a sustainable, coherent infrastructure system that supports both services and training. £75 million in funding from the UK government enabled the construction of ELIXIR’s central hub at EMBL-EBI and it is set to become the nerve centre for bioinformatics in Europe.

11 Location, location, location, location…

Rome has ruins, romance and really sunny weather. Grenoble has gastronomy, great skiing and the Grande Chartreuse. Heidelberg has history, hills and the Hauptstrasse. Hamburg has harbour life, H2O and hundreds of bridges. Cambridge has culture, canoes and colleges. OK, so that’s not all there is to the cities in our necks of the woods, and that is exactly why they have such a special place in people’s hearts.



12 Interdisciplinarity

Interdisciplinarity is not just part of our culture, it defines it. Shared faculty appointments, inter-Unit and international collaborations, as well as a host of other initiatives enable those with similar interests and complementary skills to work closely together and achieve research goals. Since its launch in 2008, the EMBL Interdisciplinary Postdocs (EIPOD) initiative, for example, has recruited more than 130 postdocs and has provided them with at least three years of secure funding to work on cross-disciplinary projects that push boundaries in overlapping fields. A prime example is Wanda Kukulski who, while working in Marko Kaksonen’s and John Briggs’ groups at EMBL Heidelberg, developed a new method that couples fluorescence microscopy’s ability to follow events in the cell as they unfold, with the high resolution of electron microscopy to locate individual HIV virus particles inside cells, amongst other applications.

PHOTOS: 8. EMBL PHOTOLAB/MARIETTA SCHUPP, 9. EMBL PHOTOLAB/HUGO NEVES, 10. ROBERT SLOWLEY

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Clubs

There are clubs for climbing, wakeboarding, cooking, culture, diving, football, golf, juggling, percussion, magic, choir, photography, volleyball, theatre, tennis, swing dance and more. And if you're still bored after all that, employees can found new clubs by contacting the Staff Association.

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Nightcaps

Whether it's the Bauhaus-style ISG Hotel, the Tudor-era Red Lion pub or the cosy Albergo Dei Leone, our lodgings of choice make a visit to EMBL that bit more memorable.

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People

1800 talented researchers, computer scientists, technical staff, software engineers, interface developers, administrators, support staff, communicators, IT professionals, technicians and more form the living, breathing heart of the Lab.

The Advanced Training Centre

When the ribbon was officially cut at the EMBL Advanced Training Centre in 2010, Annette Schavan, then German Minister of Research and Education, declared that it would "form a central European platform where scientists from different countries, disciplines and generations can meet to exchange ideas and best practices." We have never looked back, and today the Centre builds on EMBL's long history of delivering first-rate courses and conferences, attracting more than 5000 course and conference participants a year from all over the world, making it one of the leading scientific meeting hubs in Europe. The building, conceived by benefactor Klaus Tschira and brought into fruition by architects Bernhardt + Partner, is inspired by the double-helix structure of DNA and boasts a 450-seat auditorium, foyer, stunning poster display areas, teaching laboratories, computer training rooms, and staff offices – all in 'just' 17 000 square metres of space. Phew!

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17

International

We have more than 60 nationalities of people working at EMBL from six different continents. Watch out Antarctica, you're next!

18

Innovation

EMBL's technology transfer company EMBLEM lists an impressive 503 inventors with nearly 700 invention disclosures, more than 150 patents granted, 16 start-up companies and more than €50 million revenue since inception in 1999. And from imaging techniques, to data storage, to technology development, bright ideas continue to flow out of the Lab, like a recent invention that is creating a stir amongst crystallographers – an automated crystal harvesting technology called Crystal Direct. Chalking ideas out on a blackboard, EMBL Grenoble group leaders Josan Márquez and Florent Cipriani were searching for ways to automate a process that has become a frustrating problem for scientists – the painstaking removal of crystals from solution using nylon loops. They struck upon an idea: why not grow the crystals within the loops? They put a thin layer of film on the crystallisation plate that could be cut using a laser, and used a pin controlled by a robot to collect the film complete with the crystal – and it worked! Three years of tenacious development work followed, leading to the first prototype now in operation at the outstation to the benefit of many research projects.

PHOTOS: 13. EMBL PHOTOLAB/MARIETTA SCHUPP, 14. EMBL/DOROS PANAYI, 15. AND 16. EMBL PHOTOLAB/MARIETTA SCHUPP, 17. EMBL/CHRISTINE PANAGIOTIDIS

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EMBLISH

For Raffaele Totaro, who greets hundreds of staff and visitors at EMBL's main reception every day, speaking one, two, three, four… languages can go a long way: "EMBL is a unique place where in a single day you can hear a German speaking French, a French woman speaking Spanish, a Romanian speaking Hungarian or a Japanese child speaking perfect German – and of course everyone speaks EMBLish to each other!" he says. Capisce?

Lab Day and Career Day

If you want the real EMBL experience, come to Lab Day: our annual extravaganza of science that brings staff from all sites to EMBL Heidelberg to learn, network and get creative. Scientific talks and fun posters showcase the work going on in the Lab, while musical performances and more keep innovative ideas flowing into the early hours. Career Day, on the other hand, provides a chance to explore alternative, non-academic career opportunities. "It's a great way to bring staff together, learn about the work colleagues are doing, and even form new collaborations – and literally every part of the Lab gets involved," says Annelie Wünsche, an alumna who now works at Maiwald Patentanwalts GmbH.

GET A VIDEO SNAPSHOT OF LAB DAY AT NEWS.EMBL.DE

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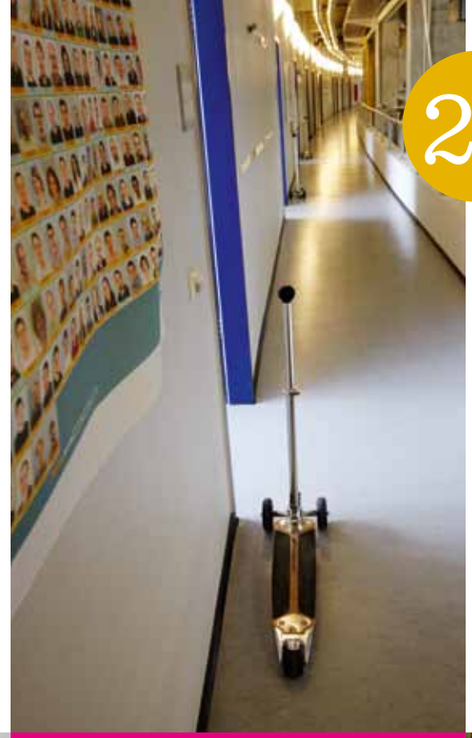

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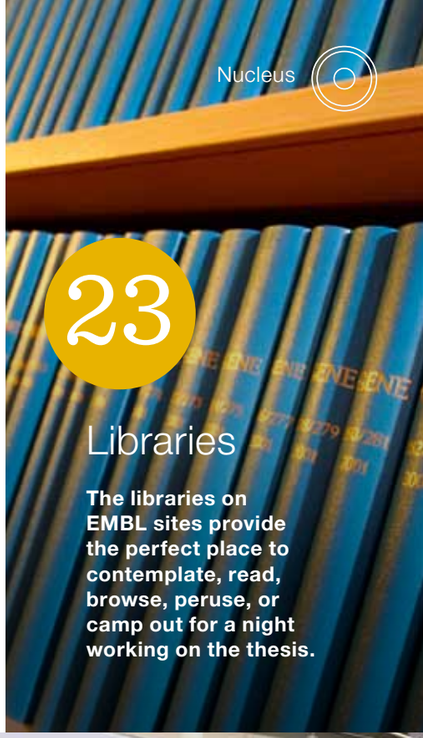
How we move

Packed buses, gruelling cycle rides, or long treks through the forest – there are plenty of memorable ways to get to and around the EMBL sites. But it is the structural biologists at EMBL Hamburg who really know how to pull out the moves – using two wheels to navigate synchrotron rings on scooters. "It is by far the most effective and efficient way of getting from one side of the PETRA III hall to the other – and it keeps you fit as well!" explains Daniel Passon, a postdoc at EMBL Hamburg.



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Libraries

The libraries on EMBL sites provide the perfect place to contemplate, read, browse, peruse, or camp out for a night working on the thesis.

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Think pink

Group leader seminars (coded pink in the calendar) feed us the latest research hot out of the lab, just as we like it.

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PhD Symposium

Organised by first-year PhD students, the EMBL PhD Symposium has attracted big name speakers for the past 15 years to discuss forward-looking subjects such as science fact to fiction, cycles in biology and overcoming chaos. "It was an invaluable and unforgettable experience – an opportunity to develop new skills, contacts and friendships," says Simone Li, who was among the organising committee of last year's conference.

PHOTOS: 23, EMBL/MAJ BRITT HANSEN, 24, EMBL PHOTOLAB/HUGO NEVES

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Creative young thinkers

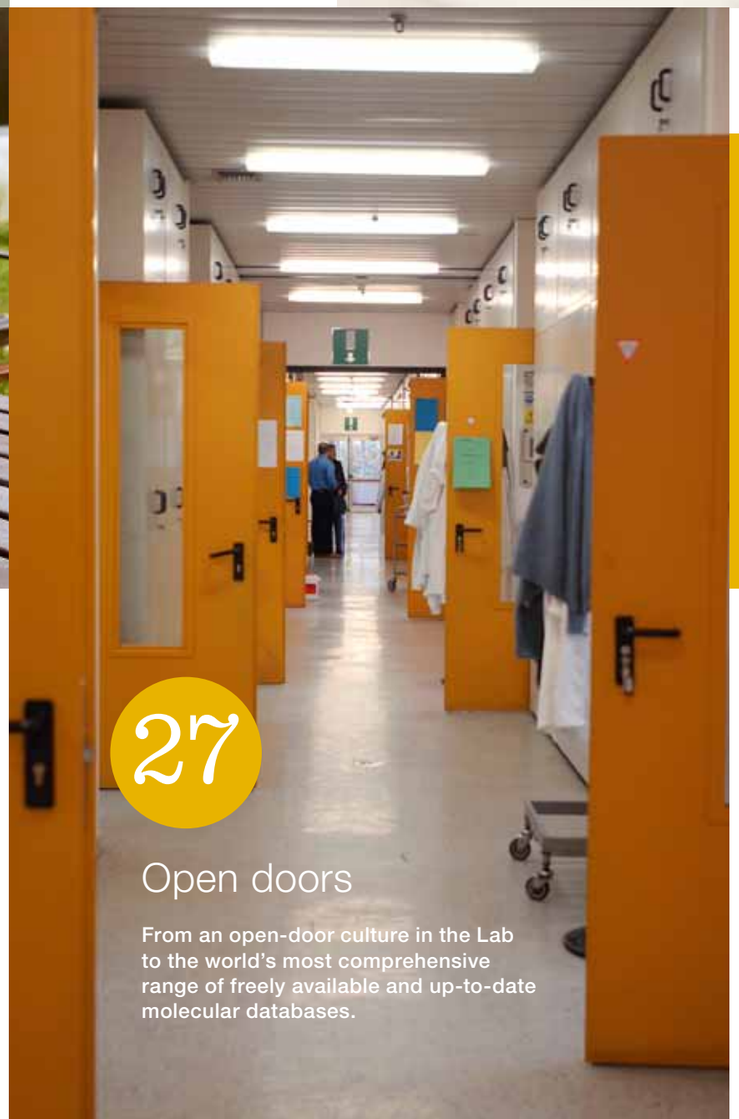
Average age of an EMBL employee:

39.6 years young

26

Our ‘wildlife’

There are life-forms just outside EMBL labs, too: ducks paddle in the East Wing water feature at EMBL-EBI, friendly cats slink around the courtyard area in EMBL Monterotondo, and some very hungry sheep ‘mow’ the lawn at EMBL Heidelberg.



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Open doors

From an open-door culture in the Lab to the world’s most comprehensive range of freely available and up-to-date molecular databases.

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Food for thought

Whether it’s the scones at EMBL-EBI, the pretzels at EMBL Hamburg, or the kaiserschmarrn at EMBL Heidelberg, there are mouth-watering offerings to be had. In Heidelberg, for example, amidst the chopping, sizzling, steaming and pureeing is a team of more than 20 led by head chef Michael Hansen, who prepare food in the canteen and cafeteria for armies of hungry scientists and sell-out conferences.

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Family friendly

They work hard, play hard, and can even bake a mean cake… no, not EMBL’s workforce, but their children! Family-friendly activities take place across EMBL sites throughout the year, from barbeques, to excursions, to summer parties. And EMBL Heidelberg and EMBL-EBI even host on-site kindergartens.

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Away days

A change is as good as a rest – so they say – and retreats and meetings away from the Lab are an important way to renew, reflect and rediscover.

31

Friends in the right places

If you need spare parts for your microscope, an old style of centrifuge, or even a Mongolian wine to impress guests, it’s easy to find someone to help out. “Our friendly mailing list community is capable of advising on virtually any aspect of life – from car repairs to finding a person to bring something back from Moscow,” explains Vladimir Volynkin, a software engineer at EMBL-EBI. Now that is what international research is all about!

32

Celebrations

Should auld acquaintance be forgot… get down to an EMBL party! Burns’ Night – a supper in celebration of the Scottish poet Robert Burns – is just one of the many themes chosen for parties across EMBL sites, providing staff with a chance to share cultures, connect, unwind and dance the night away.

PHOTOS: 26. EMBL/CHRISTINE PANAGIOTIDIS, 27 AND 28. EMBL PHOTOLAB/ MARIETTA SCHUPP, 29. MAJ BRITT HANSEN

33

Support staff

Whether it is clearing snow at four o'clock in the morning, designing and constructing custom-made animal facilities or sample changers, working out why your beamline is not firing, or printing the poster you're presenting at that important conference, EMBL's many support teams are always on hand to help.

34

Partnerships

Close collaborations with institutes in EMBL member states who would like to adopt aspects of our culture such as time-limited contracts for young group leaders, international recruitment, and external scientific reviews. This provides opportunities to share expertise, resources and projects. These can be in research areas that are complementary to EMBL's own, such as molecular medicine or marine biology, or synergistic, such as structural biology or systems biology.

35

Our neighbours

Amongst the prestigious institutions with whom we share a campus are EMBO, the Wellcome Trust Sanger Institute, the Deutsches Elektronen-Synchrotron (DESY), European Synchrotron Radiation Facility (ESRF), the Institut Laue-Langevin and the Consiglio Nazionale delle Richerche's Institute of Cell Biology. "It enhances the intellectual working environment and presents tremendous opportunities to combine expertise and resources in achieving mutually beneficial research goals," says Matthias Wilmanns, Head of EMBL Hamburg.

36

Courses and conferences

60 courses and conferences a year

5 000 delegates a year

82 000 users of the Train Online e-learning resource last year

800 young scientists awarded fellowships from our Corporate Partners since 2010

20 years of the longest-running conference, Transcription and Chromatin

70 000 coffees served at EMBL Advanced Training Centre last year

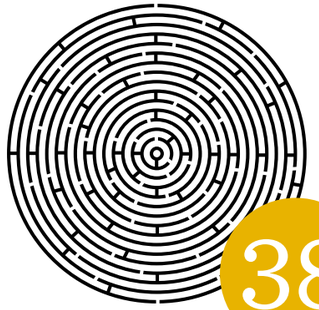
300 posters at largest ever conference

250 EMBL-EBI training events taken to 28 countries in 2013

37

Stunning imagery

Science or art? Seen under an electron microscope, one of a yeast cell's energy factories – mitochondria – appears to be perfectly heart-shaped. This image by Charlotta Funaya and Pedro Machado, both technical officers in the Electron Microscopy Core Facility at EMBL Heidelberg, was one of a flood of entries submitted for a competition organised by EMBL's communications department last year. The winning images were featured in a calendar commemorating the Lab's 40th anniversary year, which highlights the huge depth, diversity and creativity of research happening across the EMBL sites.



38

The LAByrinth

"After more than ten years at EMBL Heidelberg, I explored parts of the Lab I had never seen before – and trying to tell people who are not familiar with the building where to go is a major challenge, if not impossible!" says alumna Gerlind Wallon, now Deputy Director of EMBO.

PHOTOS: 32. EMBL PHOTOLAB/MARIETTA SCHUPP, 35. ESRF, 37. EMBL/CHARLOTTA FUNAYA AND PEDRO MACHADO

Alumni

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EMBL's 6000 international alumni are a body of highly trained scientists, communicators and administrators based predominantly in Europe, and are connected to the Lab and one another through a lifelong network of friends and collaborators. More than one-third hold senior positions as professors, directors, group leaders and managers.

"We are ambassadors for the Lab and play a major role in its reputation, growth and continued success," says alumnus Giulio Superti-Furga, who combines his commitments as Scientific Director and CEO of CeMM in Vienna, with chairmanship of the EMBL Alumni Association board. "And as ambassadors we carry out critical objectives for EMBL in passing on our knowledge and expertise, and exporting concepts of the EMBL model and culture to our institutes."

EMBL and its Alumni Association work together to highlight the impact alumni are having worldwide via EMBL news channels, online resources, events and prizes. Two examples are the John Kendrew Award, which recognises outstanding science communication and research, and the new Lennart Philipson award, which recognises translational research and technology innovation.

"Both return alumni to the Lab to share their success with EMBL Fellows," explains Superti-Furga. "Our most ambitious project to date – the EMBL Archive – is being launched this year on EMBL's 40th birthday following five years of planning. It will organise, preserve and make accessible EMBL's extraordinary history and will be a valuable resource for the Lab, the community, and the public."

PHOTO: 39. CEMM

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Services to scientists

EMBL-EBI services averaged almost

9 000 000 web hits per day in 2013

And at EMBL Grenoble and EMBL Hamburg, services for structural biology users range from sample preparation to data analysis, including almost

3 000 beamline user visits last year

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Did we miss one?
Let us know!
news@embl.de

Five for the future

Scientists from EMBL's five sites reflect on the hot opportunities and tricky challenges that might lie ahead in the coming years in their fields of research.

Anniversaries inevitably turn our thoughts to the past. But as these five visions make clear, the life sciences continue to hold enormous potential for future discovery. One of the most important objectives lies in unravelling the complexity inherent in all living beings. We have come a long way in understanding the components of biological systems, but there is still a lot to learn about how these components interact and create higher-level phenomena. This requires us to bring together increasing amounts of knowledge from diverse fields, and to develop ways of using technologies and statistical methods to analyse and present huge volumes of data such that they can be intuitively understood. Doing so could enhance a wide range of fundamental and clinical areas and, crucially, bridge the gaps in our knowledge between levels of organisation – from molecules, through cells, to organisms. Forecasts are inherently difficult to make, but we can be fairly sure that, if harnessed properly, molecular life science will contribute as much to our understanding of the human condition in the next 40 years as it has in the previous four decades.

Iain Mattaj
Director General, EMBL

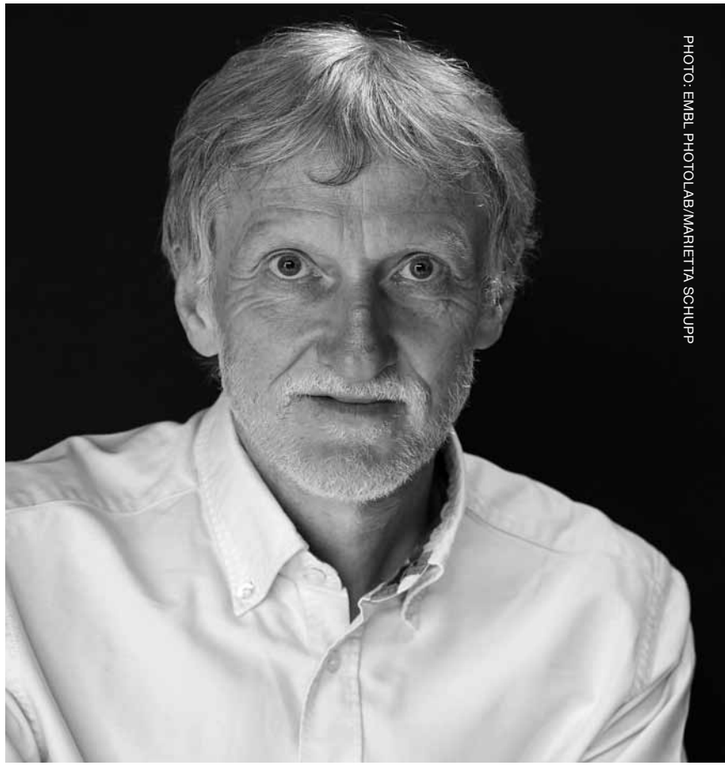


PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Faster, higher, stronger

How do drugs bind to a target? Why do enzymes only work with certain substrates? How can gene mutations cause fatal diseases? Innovations in structural biology continue to advance, allowing us to extract detailed information on the atomic structure of target molecules, unravel their function and properties, and enable scientists to shed light on fundamental questions in molecular biology. And the targets we work with are now larger, more complex and more fragile than ever.

At EMBL Hamburg, we have had the first taste of our brand new beamlines at PETRA III, one of the most brilliant storage ring-based X-ray radiation sources in the world. It's very exciting to be part of the crystallography team as we move towards faster data collection, higher precision and stronger integration of interdisciplinary approaches. During the past year, we have demonstrated our excellent beam quality at a very broad energy range and proven we can determine structures of extreme samples: the tiniest crystals composed of the largest repeating units. Our armoury enables researchers to tackle this type of challenging project in a truly integrated way, as PETRA III brings together sample characterisation, high-throughput crystallisation, crystallography and small-angle scattering beamlines, computational services and, most importantly, inspirational scientists.

In Hamburg we are also on the brink of a new era with serial femtosecond crystallography and single particle imaging – techniques that will be made possible by the European Free Electron Laser (XFEL) facility, which is currently under construction. We are curious and excited to have a complementary source on site that will enable us to capture 'diffraction before destruction' and deliver structural information not amenable to other means. EMBL is coordinating the XFEL-based biology infrastructure at the European Free Electron Laser and, together with the launch of the new Centre for Structural Systems Biology, the emerging facilities will reinforce our position at the forefront of molecular biology.

JOHANNA KALLIO, STAFF SCIENTIST, EMBL HAMBURG

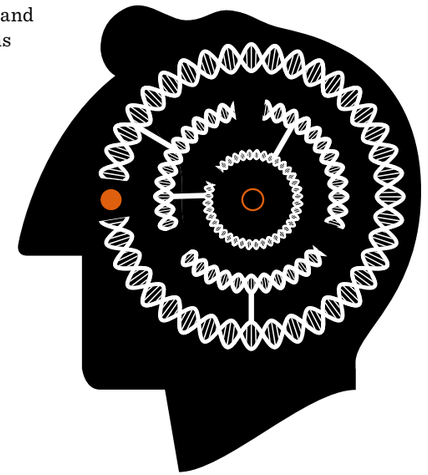
Of genes and behaviour

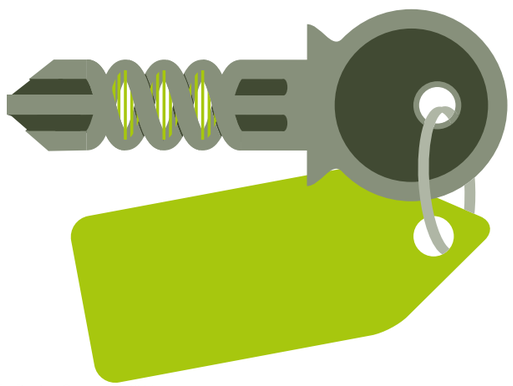
In the past few years, pharmaceutical companies all over the world have closed their neuroscience research facilities. Why? Because the drugs developed in cell culture and animal models don't work in the clinic. This is particularly true in the area of psychiatric disorders for which no novel drugs have entered the market since the 1980s.

The reason for this is the poor understanding we have of what makes us tick – and how this goes wrong in mental illness. At the moment, there is no blood test for anxiety or scan for bipolar disorder – their fundamental causes are dependent on complex interactions between molecular players – and we just don't know what these are nor in what cells in the brain they occur. What's more, we still know next to nothing about the push-and-pull between these molecular aspects and environmental factors such as stress, diet, and lifestyle.

But things could soon change. New tools in genetics and circuit manipulation have seen a boost in the past few years. Large multisite research programmes are starting to reliably find genes that underlie mental conditions – we are not sure yet how they control behaviour, but there is hope that they will give us an entry point for at least some disorders. We don't know how they act because we don't know the cells involved. That's because until recently, it was impossible to block or selectively mimic neural activity in defined cell types in the brain in the living animal. Optogenetics has radically changed that and now we can re-engineer neurons essentially at will. This will help us understand the missing link between genes and behaviour. Initial breakthroughs will come from simple organisms such as flies and worms. But mice and monkeys are not far behind and the time will come quickly when we can turn emotions on and off and reshape cognitive capacities. The next challenge will be how to make novel drugs that interact with these circuits to improve resilience, turn plasticity up or down, help us reshape our responses to the world around us, and curb our pathological impulses. Keep tuned for the new you!

CORNELIUS GROSS, DEPUTY HEAD, EMBL MONTEROTONDO





The next generation

The dramatic advancement of DNA sequencing technology over the past five years has transformed the DNA sequencer into the microscope of modern biology.

Just as the invention of the microscope changed the world by making it possible for scientists to study essentially everything around them, DNA sequencing has opened up an entirely new way of understanding nearly all aspects of biology. Sequencing is radically changing the way we track disease or infection outbreaks, as it can be used to clearly identify life forms on surfaces in hospitals.

Similarly, it is allowing us to discover and explore whole new worlds of life: in the seawater, in the soil and in the communities of microorganisms with whom we share our bodies. In the not-too-distant future, sequencing will detect and monitor the growth of cancer and help suggest treatments.

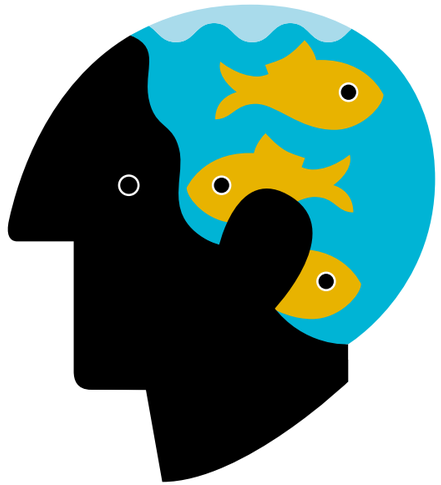
Today's newest sequencing machines are smaller than a chocolate bar, but future tools for DNA sequencing will be smaller and faster still, making them ever more useful and flexible. Of course these tools will be crucial in the age of genomic medicine, which is arriving in healthcare systems throughout ››

ILLUSTRATIONS: AAD GOUDAPPEL

›› the world, but their impact will also be felt far beyond the hospital. In everyday life, DNA sequencing will certify the food we eat and help solve crimes. Together with the science of genomics, DNA sequencing has brought about the most important and far-reaching shift in the practice of biology since the rise of molecular biology in the first half of the 20th century.

But what's next? These technologies are advancing so quickly that we are bound to start equating today's sequencing with the sound of a dial-up modem, or typing an email as green text on a bowed black screen. It will be fascinating to see how future hand-held devices might read sequences and combine them with expression and many other types of molecular data – from many different sources – and change the way we ask questions about the world, again.

PAUL FLICEK, GROUP LEADER, EMBL-EBI



Wonders of the deep

Imagine a person living in the late 1970s – a time when the Walkman cassette player hit the streets, the videogame Space Invaders crackled onto our screens, and rollerblades began to spin off the production line. Now try to imagine how he or she would have predicted today's world based on their knowledge and experiences then – I dare say the forecast would have been quite different to what we find now. Because the great thing about the future is that it is much more than just an extrapolation from the current reality.

Even so, I find it incredibly exciting to imagine the potential for new discoveries – particularly in studying the world's oceans. Modern satellites, remotely operated vehicles, and computer simulations allow researchers to explore the deep in increasingly scientific and systematic ways. Yet 95% of the ocean remains unexplored. What is down there? Can we match our knowledge of sea creatures with what we know about terrestrial life? What secrets might we reveal?

One exciting prospect is that, by studying the ocean's inhabitants, we can learn a great deal about how life works – and in surprising ways. Life began in the ocean, and learning more about it presents a great chance to put our understanding of the basic building blocks of life and the organisation of processes and organisms into perspective. We can start to understand, for instance, how parasitic and symbiotic relationships have shaped evolution; we can shed light on the different stages of evolution; and even learn more about possible forms of life. Using genomic and molecular techniques, we can begin to fill in gaps in our knowledge – and learn more about our transition from primitive sea creatures into complex mammals that can speak, hear, feel, learn, and think. By doing so, we can enrich our view of life and learn much more about ourselves, perhaps in ways one cannot even dream of today.

SILVIA ROHR, PHD STUDENT, EMBL HEIDELBERG

Instrumental to success

The field of X-ray crystallography is celebrating 100 years of incredible discoveries – from helping to make medicine, to enhancing the efficiency of batteries, to improving the taste and texture of chocolate.

Today, surprises seemingly lie in wait around every corner, with fields such as genomics, proteomics, and pharmacology benefiting from significant increases in analytical speed, throughput and accessibility. Their continual evolution provides an endless supply of tiny molecular players to be determined in 3D so that fundamental questions about their role in biology, health and disease can be identified. The next generation of synchrotrons and X-ray free electron lasers add to this sense of anticipation – presenting an opportunity to overcome many of our current limitations, particularly in the study of larger and more complex biological systems.

Crystallography, however, remains a very difficult science – and the quantities, size differences and unique nature of crystals demanded by modern research projects increasingly require us to quickly think on our feet. One current challenge is the routine growth of diffraction-quality crystals – particularly difficult in studies involving complex membrane proteins or biological assemblies.

Another is the efficient measurement of diffraction data from these crystals. With ingenious approaches to automation, robotics, computation, software and more, we will enhance our efforts to interpret the wealth of information produced by modern science. I am confident we can meet these challenges, and go far beyond: recent innovations in sample handling, instrumentation, computational methods, and data collection here at EMBL and elsewhere show what can be achieved by smart thinking, persistence and teamwork. Such developments can be a driving force for science, and our combined efforts will accelerate the pace of discovery, aid drug design and allow us to better understand the folds, functions and fabrics of life.

ANDREW MCCARTHY, TEAM LEADER, EMBL GRENOBLE

New Dehli, Brno, Warsaw, Buenos Aires, Copenhagen, Cape Town… looking at **Silke Schumacher**'s agenda, you could be forgiven for thinking she is an air hostess, global celebrity, or diplomat. As EMBL's Director of International Relations, the last probably comes closest. But when *EMBLetc.* caught up with her during a 'layover' in Heidelberg, Silke revealed that the institute's true ambassadors are its scientists.

BY SONIA FURTADO NEVES

Still growing at 40

Who are the most recent additions to the EMBL family?

So we have three new countries joining this year, at different levels. At the beginning of the year, the Slovak Republic became the first prospect member state of EMBL, in April Argentina joined as our second associate member state, and the Czech Republic has officially become a member state. Plus, Malta has applied to become an EMBL member state, which I hope will happen early next year.

You say 'finally' – it sounds like it has taken some time?

Yes, this was a very long process that started in 2005, when both the Czech government and the scientific community expressed a strong interest in joining EMBL. And then they were hit by the financial crisis and just couldn't afford it for some time… so now they have come back and completed all the necessary steps to become a full member, which they will be from the beginning of this year on.

But in the meantime we have already had a lot of interactions with scientific institutions in the Czech Republic. We have established very close links to CEITEC, the new institute being set up near Brno, and also to BIOCEV, which is just outside Prague. And there have been a lot of visits, both of EMBL people to these institutes and to the universities in Brno and Prague, and the other way around, to exchange know-how, to learn about how to set up facilities… Particularly in the two institutions that are being newly established, we have already transferred a lot of know-how: the organisational model, how to set up core facilities, organise technology transfer… That has been a really very nice interaction and has also resulted in some scientific collaborations.

Although EMBL's current growth spurt was influenced by international events like the financial crisis, it's not all down to external factors, is it?

No, there has also been a strategic change. Sometime around 2010, we actually had a Council working group which also included representatives from the European Molecular Biology Conference [EMBO's governing body], from ››

›› countries that had joined EMBC but not EMBL, to try to come up with ideas about what we could do for these countries, to facilitate them joining EMBL. Out of those, the idea that in the end was approved by EMBL Council was the prospect membership scheme – which the Slovak Republic was the first to join. This allows countries to basically sign an expression of interest, and for three years have observer status at EMBL Council and participate in all EMBL activities as if they were a full member, and then by the end of the three-year period they have to join as a full member state. I can see when visiting countries that the interest in this scheme is much greater than in previous approaches.

One other thing that we offer in the context of this prospect member scheme are promotional activities in the country. So we offer to go, to send a group of EMBL group leaders, heads of the Core Facilities and people that organise the PhD and Postdoctoral Programmes to the country, and to meet the young scientists and present what opportunities EMBL offers. We also invite scientists from these countries to come and visit EMBL, to collaborate, to use the Core Facilities… We see that the countries really appreciate being visited; the scientists like to discuss what the possibilities are.

The *European* Molecular Biology Laboratory is also expanding beyond Europe. What's the reasoning behind that move?

Science is global; if we look at the collaborations EMBL faculty have, many are outside Europe. So the thinking is that a European institution like EMBL will always have the majority of its activity in Europe, but we can make use of existing links and collaborations further afield. We can do this through the associate membership scheme, which establishes formal links to countries where our scientists, but also our member states, already have very, very good interactions. This really was made clear to me when Argentina applied for associate membership. In the EMBL Council there were several delegations that said 'This is wonderful, we already have very well-established links bilaterally.' So bringing the country into the EMBL community extends those relationships and brings added value to European member states, too.

And of course, Argentina has excellent biomedical researchers, who I'm sure will benefit from establishing more collaborations with scientists in Europe, in EMBL and EMBL member states. Both EMBL and the Argentinian government are keen to foster those collaborations. We even took the opportunity of the signing ceremony itself, and combined it with a two-day workshop where EMBL scientists went to Buenos Aires to talk to their Argentinian colleagues.

So it's about exploring existing synergies, not a drive to become the World Molecular Biology Laboratory?

No, nothing like that. The associate membership scheme is a scheme that's not going to grow too much – it's a small set of countries that we already have well-established relationships with. Countries like India, with whom we've been jointly operating a beamline with ESRF, in Grenoble; or South Africa, where we have already very good scientific links in bioinformatics and structural biology; or Chile, where there have been a number of visits, and EMBO courses organised by EMBL group leaders.

What's in it for the countries, what do they gain from EMBL membership?

I think there's a lot we can offer that makes membership attractive to the countries. For their investment into the EMBL operation, they get well-trained scientists, access to world-class facilities and services, fellowships for the EMBL PhD and Postdoctoral Programmes and – thanks to funding from our corporate partners – for attending EMBL courses and conferences… and one other thing that countries have found very valuable is that they can join the EMBL partnership programme.

And finally, where next – for you and for EMBL?

This year I'm visiting Hungary, Poland and Lithuania… We have to see if this will result in anything. Sometimes things move fast, sometimes they are slow – and there are always factors outside our control, like elections, which always slow everything down. Overall, my goal is to get all the EU member states to join EMBL, plus Turkey and Russia, and to slowly also increase the number of associate member states.

WANT TO KNOW MORE?
READ THE FULL INTERVIEW
ONLINE: NEWS.EMBL.DE

Taken out of context

In 1631, the printers tasked with reprinting the King James' Bible made a disastrous typographical error. They failed to spot a missing 'not' in one of the Ten Commandments, leading to a Bible that pronounced: "Thou shalt commit adultery." Hauled in front of a furious King and Archbishop, they were deprived of their printing licence and fined. The offending copies of this bible, known today as the Wicked Bible, were hunted down and destroyed.

BY CLAIRE AINSWORTH

This story is a classic example of how a small change to the construction of a sentence, such as losing or changing a word, moving words to different places, or altering punctuation, can dramatically change our interpretation of the information contained within it. When it comes to meaning, context is everything.

The same is true of the genetic 'words' in our DNA that are our genes. The way a cell uses the information contained in genes is heavily influenced by their context, such as their location on a chromosome. The biological equivalent of punctuation, the physical and chemical changes to chromosomes that tell the cell how genetic information should be read, is also key.

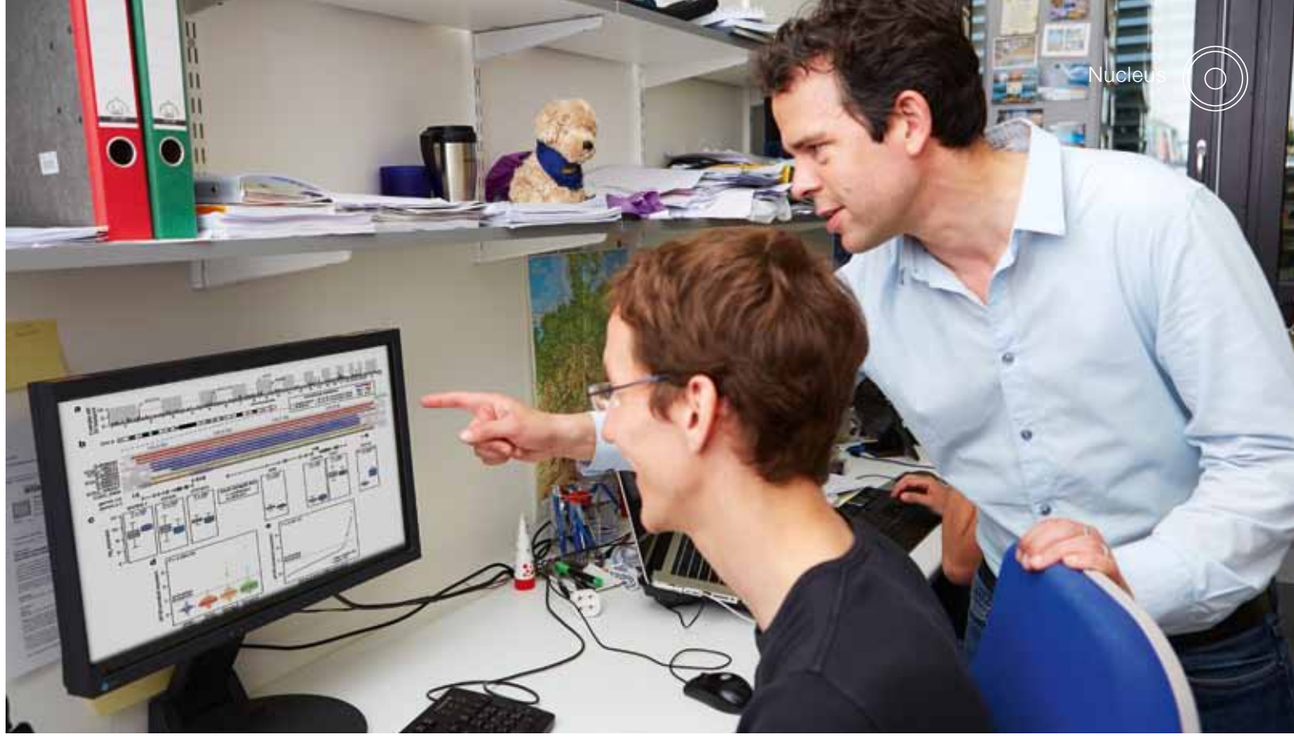
Like written sentences, our DNA can also suffer from typographical errors that disrupt chromosome structure and 'punctuation'. The consequences can be severe. If genes are lost, altered, relocated or misread, this can lead to serious illnesses such as cancer. Now, Jan Korbel's team at EMBL Heidelberg, in close collaboration with colleagues at the German Cancer Research Centre (DKFZ), have discovered how changes in a gene's location and context help to drive the development of medulloblastoma, a deadly kind of brain cancer that affects children.

Genes can shuffle their position within the genetic code, or DNA, through changes to the structure of the chromosome to which they belong. These can happen by accident when chromosomes copy themselves, and can result in sections of DNA moving to new places (translocations), being turned upside-down (inversions), copied (duplications) or simply disappearing (deletions). This switching around can dramatically alter the instructions coded in that section of DNA. A duplication, for example, would look *something like this something like this*; inversion would look *siht ekil gnihtemos*. Other variants include translocations, where *the wrong place* pieces of DNA break off and get moved to in the chromosome. ››

PHOTOS: EMBL PHOTOLAB/HUGO NEVES

"The pocess we uncovered here may be much more prevalent in solid tumours"

Left: Jan Korbel
Right: Thomas Zichner (left), Jan Korbel and colleagues uncovered a gene-activation process not typically looked-for in solid tumours



›› These changes to the DNA are known as structural variants and have, until recently, been difficult to detect with the DNA sequencing methods used to analyse the human genome. While working as a postdoc at Yale University, Korbel developed a new technique called 'paired-end mapping' that allows researchers to spot structural variants much more easily. When he joined EMBL five-and-a-half years ago, his group soon began applying, and further refining, this technique to study how structural variants cause genetic differences between individuals. But Korbel's group soon also developed an interest in cancer cells and the changes to their chromosomes, which are notorious hotbeds of structural variation. Cancerous cells often end up with the wrong number of chromosomes, or chromosomes that appear grossly abnormal when inspected under the microscope. Korbel and his group wanted to find out whether smaller structural variants – that are much more abundant but which cannot be seen with a microscope – are also implicated in the disease, how they arise and what effect they have on cells.

They decided to focus on medulloblastoma, a rare but deadly form of brain tumour that affects children. "There are no suitable treatments to combat the disease, at least for the majority of patients," says Korbel. One of the key barriers to the development of treatments is that medulloblastoma tumour cells seem to arise very differently to those from many other cancers. Tumour cells often contain combinations of changes, or mutations, to their DNA sequence that are characteristic of a specific cancer, and can therefore be used to aid diagnosis and treatment. These mutations can make a gene – or the protein it encodes – hyperactive, causing the cell to behave abnormally. Many modern anti-cancer drugs target these pathways, such as the leukaemia drug Gleevec.

But few such mutations have been found in medulloblastomas. Based on their biology and clinical symptoms, doctors have grouped the tumours into four different types, and for two of these – group 1 (also known as the WNT-group) and 2 (also known as the SHH-group), some mutations have been identified. But the underlying genetic causes of groups 3 and 4 were mysterious.

Researchers already knew that structural variations are present in group 3 and 4 medulloblastomas, but had little idea of what these variations might be doing. This, together with the fact that Korbel's group had a long-standing collaboration with Stefan Pfister at the German Cancer Research Centre (DKFZ) in Heidelberg, led them to investigate further. "It made a very nice case for a strong collaboration, as we could join our group's expertise on understanding variation in the genome with Stefan Pfister's strong clinical research expertise," says Korbel.

The team sequenced the genomes of medulloblastomas from patients and found a region on chromosome 9 that harboured structural variations. The variations took different forms in different patients: some had inversions, some had deletions, others had duplications, and still others had more complex changes. But they all had one thing in common: the variations all resulted in a gene called *GFI1B* becoming abnormally active. But unlike overactive genes in other cancers, the DNA of the *GFI1B* gene in the medulloblastoma cells was normal. Its sequence had not altered; all that had changed was the gene's location, similar to a word being in the wrong position in a sentence. Further investigation revealed that GFI1B's new location contained chemical and physical 'punctuation' that encourages the cell to use the information contained in the nearby genes.

This punctuation relates to the way genomic information is packaged into chromosomes. DNA is wound around proteins called histones, which both offer protection and help control gene activity. Genes that are supposed to be inactive are wound tightly around histones to stop the cell's gene-reading machinery from accessing the DNA sequence of that gene. By contrast, the DNA that contains active genes is much more loosely wound, allowing the cell to read the information contained within. Because these changes affect gene behaviour rather than its sequence, they are known as 'epigenetic' effects.

In brain cells, the *GFI1B* gene is usually switched off, its DNA packed away tightly. But in the medulloblastoma cells, Korbel's group found that regions of DNA containing *GFI1B* had been moved to another part of the chromosome, next to regions known as 'enhancers' that can promote gene activity. Enhancers encourage the DNA and histones with which they come into contact to become more relaxed and open and the genes within them more active. "For us, they are the most plausible culprits for the overactivation of the gene," says Korbel. To prove this beyond doubt, the team will need to conduct further experiments, he adds.

Although similar processes have been seen in various leukaemias, this is the first time such a mechanism has been described in solid cancers. "The process we uncovered here may be much more prevalent in tumours," says Korbel. This could give researchers new insights into how hyperactive genes drive cancer. It could also give them a new approach to study tumours in which the genetic drivers are unknown, and highlights how the interaction between a gene and its epigenetic environment can make all the difference it its behaviour.

Northcott, Lee, Zichner *et al. Nature* (in press)

LISTEN TO KORBEL DISCUSS WHY CANCER RESEARCHERS DON'T USUALLY LOOK FOR THIS KIND OF GENE ACTIVATION AT NEWS.EMBL.DE

Earlier this year, structural biologists at the European Synchrotron Radiation Facility (ESRF) in Grenoble, France celebrated a remarkable milestone: the number of protein structures determined at the facility reached an impressive 10 000.

BY CLAIRE AINSWORTH

The future's bright

The milestone itself was the structure of a protein from a flu-like virus, determined by Stephen Cusack and his team at the neighbouring EMBL outstation.

When it began in 1996, the ESRF's next-generation synchroton transformed structural biology by expanding the number of proteins biologists were able to study. Until then, scientists had studied proteins by getting them to form crystals, shining powerful X-rays on them, and deducing the structure of the protein from the way it scattered the rays. But many proteins crystallise poorly, if at all, with some producing crystals that were far too small to use with conventional X-ray sources.

The new, higher-strength X-rays on the ESRF beamlines allowed researchers to study these "micro-crystals", which are less than one-fifth of the width of a human hair in diameter. But handling these tiny crystals, which are prone to radiation damage from the high-intensity beams, was not easy. "The technology wasn't there at that time to do this in a routine way," says Cusack.

Precision and automation

Two key innovations helped the number of structures determined at the ESRF to take off. In the late 1990s, Florent Cipriani's team at EMBL Grenoble, together with colleagues at the ESRF, developed an instrument known as a micro-diffractometer, which allows the precise measurement of tiny crystals in very fine focused X-ray beams. Then, at the turn of the millennium, the EMBL and ESRF teams introduced automated systems, such as robotic sample changers, which increased the speed, accuracy and reproducibility of the experiments performed there. Since then, the number of structures solved has increased exponentially, with two of them resulting in the award of Nobel prizes.

The ESRF's 10 000th structure is a classic example of the intrinsic awkwardness of some proteins. Stephen and his team have long been interested in the protein used by the influenza virus to read and copy its genetic material inside infected cells. This protein, the polymerase, is a very attractive target for much-needed new drugs to treat flu. The team had previously succeeded in determining the structures of fragments of the enzyme, but wanted to solve the structure of the whole protein. They struggled, however, to produce enough enzyme to form crystals.

Unexpected outcome

Cusack and his team turned to the polymerase from a similar member of the family of viruses to which influenza belongs, the Orthomyxoviruses. Working with colleagues from the FLUPHARM project, they chose a virus called Thogotovirus, which normally infects insects but can also infect mammals. The Thogotovirus polymerase proved easier to produce in large amounts, and the team began by looking at the fragments equivalent to those they had already determined the structures of in influenza. These fragments form part of sections, or subunits, of the polymerase called PA and PB2, which fool the cell's machinery into making the proteins encoded by the virus' genes, a trick known as cap-snatching.

The structures of the Thogotovirus polymerase fragments, however, were a big surprise. Although their overall structures were similar to their influenza counterparts, they were not able to interact with the cell's protein-making machinery, suggesting that Thogotovirus' cap-snatching mechanism differs dramatically from that of the flu virus. "This is still a bit of a mystery," says Cusack. It may reflect the way the virus has evolved to adapt to its host, he adds.

Forging ahead

Continuing technological developments at EMBL Grenoble and the ESRF beamlines will hopefully crack influenza's intransigent polymerase, as well as opening up new avenues of research into other proteins. Work is currently under way, for example, to increase automation on the ESRF beamlines, and the end of the decade should bring an upgrade of the synchrotron ring and even more intense, brighter X-rays.

Guilligay *et al. PLOS ONE,* 15 January 2014. DOI: 10.1371/journal.pone.0084973

LISTEN IN AS VELANKAR AND BATTLE FROM PDBE LOOK FORWARD TO THE GOOGLE MAPS OF PROTEIN DATABASES: NEWS.EMBL.DE. VISIT THE PDBE AT WWW.EBI.AC.UK/PDBE.

The shape of things to come

As structural biologists tackle ever larger and more complex proteins, the databanks that store the information they uncover have to find new ways of handling and distributing data. The Protein Data Bank in Europe (PDBe), run by EMBL-EBI, is in the process of launching a new website and data-handling innovations to enhance the amount of information researchers can glean from protein structure data. A timely step, as the number of protein structures in the database reached 100 000 in May this year.

One new feature is the rollout of a common data deposition system that allows researchers to upload information about very large proteins in one go, using a file format called mmCIF. Previous systems could only handle smaller datasets, meaning that information about large, complex proteins was fractured into several sections. The new system will also allow researchers to integrate structural information from a range of methods, such as X-ray crystallography and electron microscopy. "Structural biologists are basically using whatever is at their disposal to solve a structure," says Gary Battle, Outreach Coordinator for the PDBe. "The challenge for us is to cope with all of these hybrid methods."

Another key aim is to integrate structural data with other information about a protein, such as its amino-acid sequence, says Sameer Velankar, a team leader at the PDBe. "The main aim is to bring structure into its biological context so that you can understand more about the biological relevance and function of that structure in that system," he says.

The team has also developed a system that allows users to assess, or validate, the accuracy of the information about a protein. This system will form part of the new website, which will be launched in beta version by the end of 2014.

Obituary
Christian Boulin

BY IAIN MATTAJ

PHOTO: EMBL PHOTOLAB

Christian Boulin, EMBL's Director of Core Facilities and Services, died on April 27, 2014, of complications resulting from treatment he was receiving for lung cancer. From his first diagnosis, barely a month had passed. Christian was one of the longest-serving EMBL staff members. He was a close friend, an esteemed colleague and a valued advisor to many of us. Christian was deeply committed to the success of EMBL, to which he made countless contributions over his many years of service.

Christian joined EMBL Heidelberg in 1976 as a member of the computer group, part of the Instrumentation Division. Born in Thann, a wine-producing village in Alsace, he studied Mathematics and Physics in Strasbourg. Afterwards he went on to do advanced training in computer science, electronics and automation before returning to Strasbourg for a PhD in high-energy physics.

Looking back at his early EMBL research reports, describing fledgling attempts to develop software for Electron Microscopic image capture and analysis, one cannot but turn to his native language "... plus ça change, plus c'est la même chose..." (The more things change the more they stay the same). Even if the scientific and technical challenges were similar to the ones we are facing today, their dimension was slightly different. In those days the very large files Christian handled ranged from 138 Kbytes to an almost unimaginable 16 Mbytes. The medium-term goal was to be able to have computer graphic protein structure representations for as many as 200-300 atoms.

Under EMBL's second Director General, Lennart Philipson, Christian joined the Detector Group. He worked over a number of years with André Gabriel, Jules Hendrix and many other colleagues in Heidelberg, Grenoble and Hamburg and outside EMBL on X-ray detector developments, specialising in electronics and software. As EMBL evolved over time, Christian took on more responsibility and activities: Cryo-EM data acquisition, control software for laboratory robotics, light microscopy (Nomarski and Confocal) image acquisition and analysis software, 3D image analysis software and a combination of hardware and electronics support for Matthias Mann's development work in mass spectrometry.

Towards the end of Lennart's period at EMBL, by which time I was a Unit Coordinator in Gene Expression, I had one of my first non-scientific encounters with Christian. Lennart had organised a senior faculty weekend retreat in a small castle along the Neckar. I drove there with John Tooze through a worsening snowstorm, arriving to find that only we two and Christian had made it. As our wait dragged into its third hour, Christian's admiration for a magnum of Bordeaux decorating the room became more and more evident, until John asked a waiter to open it for us. By the time others started to arrive two hours later, we had solved most of EMBL's problems – and virtually emptied the magnum. Lennart was incensed at the cost and our condition, and blamed John and me. He refused to believe Christian had anything to do with it.

Under Fotis Kafatos, who became EMBL Director General in 1993, Christian took over as joint Head of the Cell Biophysics Unit with Eric Karsenti. There, he played an important role in the creation of the Advanced Light Microscopy Facility (ALMF), EMBL's first 'modern' core facility, in 1996. In 1997 Fotis made Christian Head of EMBL's Technical Services. At the time, this included IT Services, the ALMF, a fledgling core facility in Genomics, the Library, the Photolab, the Workshops and the Instrument Maintenance Team. Christian also acted as the interface between EMBL researchers and Building Maintenance, ensuring scientific requirements were taken into account in spatial planning. Making sure all these services ran smoothly, Christian provided crucial support to EMBL's scientists and allowed them to focus entirely on their research.

"He symbolised the collaborative, good-humoured spirit that distinguishes the Laboratory."

Christian's particular strength was revealed in the development of the Core Facilities. He was adept in choosing excellent core facility heads who combined research motivation with a service mindset. Together with this group he formed a highly efficient set of cutting-edge technical support structures that enlarged the scope of EMBL's research groups enormously and that have served as models that have been copied (often with Christian's help) by many other research organisations throughout Europe and beyond. The Core Facilities and IT Services Unit was reviewed at the end of March. Christian could not be present as he was undergoing diagnostic tests. But his performance, as well as that of the Unit as a whole, was regarded as outstanding by the review panel. He was justifiably proud when I visited to tell him the news and he immediately outlined new plans for the next four years that he had developed in his 'spare time' in hospital.

A final, very important aspect of Christian's activities was his involvement in interaction with industry. Over many years, he had built a trusting, collaborative relationship with many companies. He played a critical role in developing technology transfer at EMBL and took on major responsibility for interactions with EMBLEM.

In the words of one of my colleagues, Christian was sensible, kind, insightful and determined. He demonstrated an unselfish commitment to EMBL and its many activities and symbolised the collaborative, good-humoured spirit that distinguishes the Laboratory. Christian leaves behind his wife, Marie-Claire, three children, Anne-Sophie, Caroline and Thomas, and two grandchildren on whom he doted. He also leaves behind a host of saddened friends and colleagues at EMBL and elsewhere. Their numerous expressions of grief, sympathy and condolence reflect the respect with which he was regarded. He leaves a big hole in EMBL that will only be filled by time and a combination of different people who together will be needed to cover his unique mix of scientific and human experience and his embodiment of the EMBL spirit.

Cultures

PHOTO: ESO/L. CALÇADA

What does it mean to be a researcher? Practising scientists know very well that research is not an off-the-rack career: it is multifaceted, exciting, challenging and rewarding. Helping the next generation recognise that a scientist is more 'role model' than 'mad professor' is the task of a growing team of EMBL School Ambassadors.

Led by the European Learning Laboratory for the Life Sciences (ELLS), the ambassador scheme is a platform for EMBL scientists to share their experience of living and loving research, and rekindle school students' enthusiasm for enquiry and discovery. Going into classrooms – real and virtual – across Europe and beyond, the ambassadors' diaries show how much fun they are having in the process.

BY PHILIPP GEBHARDT

Back to school

PHOTO: VASILY SYSOEV

Verena Tischler, PhD student
October 2013, ELLS Design Thinking Workshop, Heidelberg, Germany
I'd never heard of 'design thinking' – a creative, team-based process to solve given challenges by developing and testing new ideas. Beforehand, I undertook training to learn more and go through the process myself. I was soon standing before a crowd of kids talking about 'big data challenges in the life sciences'. Instructed by an expert from software giant SAP, I assisted the teams as they addressed related issues. It was amazing how enthusiastically they engaged in the process, and how well they presented their own solutions!

Vasily Sysoev, PhD student
December 2013, Moscow, Russia
Home for Christmas, I used the opportunity to talk to high school students about my work: DNA sequencing and the discoveries it has made possible. My first audience – an extracurricular biology club at my former school – easily grasped the presentation and together we delved into more advanced details. The following talks were to younger, broader audiences, who were no less interested in the topic. I learnt that these talks had sparked interest in biosciences: the teacher answered many more related questions in subsequent lessons.

Jose Viosca, Postdoc
March 2014, Rome, Italy
A friend, a teacher in Rome, showed great interest in bringing his students into contact with EMBL. Connecting with the school via the ELLS Science Chat web platform, Federico Rossi in Heidelberg and me in Monterotondo gave live talks about ourselves and our work. Without doubt, the best part was the students' questions: so many current scientific challenges were broached, unprompted, by the class. The experience was as stimulating for me as it was for them.

READ MORE ABOUT THE SCHEME AND HOW YOU CAN GET INVOLVED AT EMBLOG.EMBL.DE/ELLS

Nothing but blue skies

"There does not exist a category of science to which one can give the name 'applied science'. There are sciences and the applications of science, bound together as the fruit of the tree which bears it." – Louis Pasteur.

BY CLAIRE AINSWORTH

At first sight, Emmanuelle Charpentier's favourite quote might seem rather incongruous. Only two years ago, she and her colleagues published a paper whose contents are already revolutionising the world of genetic engineering. In it, the team described a mechanism that allows scientists to cut and paste genetic material into DNA with much greater ease and precision than ever before. The finding was listed as one of the top 10 research discoveries of 2012 by the journal *Science*, and opens the possibility of new treatments into genetic disease.

But for all the exciting possible applications of the mechanism, its initial discovery owes a great deal to basic, blue-skies research, says Charpentier. She credits the academic freedom afforded to her by the Nordic EMBL Partnership for Molecular Medicine for helping her make the discovery. "It was giving the time and the means to take some risky roads," she says. "And I think this is very important in research."

Targeted defence

After some years researching microbiology as a postdoc in the US, Charpentier moved to the University of Vienna in 2002 to build up her own research group. There, she researched virulence, or the ability to cause disease, in *Streptococcus* bacteria. This led her to develop an interest in small fragments of a molecule called RNA that were known to help bacteria defend themselves against attack by viruses. This defence system, called CRISPR, lets bacteria recognise and cut the DNA sequences of re-invading viruses, thereby destroying them specifically.

Molecular attraction

While at Vienna, Charpentier heard about a call by the Swedish node of the EMBL Partnership for new group leaders at Umeå University. Attracted by the focus on molecular medicine and by the EMBL model of funding and supporting researchers, she applied. While joining the Laboratory for Molecular Infection Medicine Sweden (MIMS), she discovered a new RNA called tracrRNA, which revealed a new arm of the CRISPR mechanism, called CRISPR-Cas9. Unlike the other CRISPR mechanisms known until then, CRISPR-Cas9 was simple enough to use as a tool for genetic engineering.

Scientists around the world are now using CRISPR-Cas9 as a tool for tailoring DNA. But while she has high hopes for the transformative potential of the technology, Charpentier still has her eye on the basics. "If you don't focus on fundamental research," she says, "no translation is possible."

PHOTO: HZI/HALLBAUER + FIORETTI

Emmanuelle Charpentier

Jinek, Chylinski *et al. Science*, 28 June 2012. DOI: 10.1126/science.1225829

LISTEN TO CHARPENTIER DISCUSS HER WORK AT NEWS.EMBL.DE

On target

The Centre for Therapeutic Target Validation (CTTV), a new public-private initiative for biomedical science on the Genome Campus, is now up and running. Using data from genome-scale experiments, the centre's scientists are working to find which molecules are the most promising targets for medical intervention.

BY MARY TODD-BERGMAN

The CTTV offices in EMBL-EBI's new South Building are home to disease biologists from GSK, data integration and analysis experts from EMBL-EBI and genomics experts from the Wellcome Trust Sanger Institute. Ewan Birney, Interim Head of the CTTV, answers a few questions about the initiative.

What is target validation? Is it about designing new drugs?

Target validation is about understanding which gene products, if you change them, would change the course of a disease. That is not the same as finding which gene products are involved in a disease. A protein might be involved in a disease, but that doesn't necessarily mean that changing it will make a person better or worse. So we want to know, if I change this protein, would it change somebody who has a disease – would it make them better?

Don't pharmaceutical companies work on target validation already?

Pharmaceutical companies are very good at finding or designing the molecule that can change the activity of a protein; but it's much harder to figure out which proteins are the right ones to target. This is too big a puzzle to solve inside of one company, so GSK has brought their expertise to the Genome Campus so we can make some real progress in this area. Drugs take many years to develop, and that costs a lot in terms of effort and resources. At the moment, companies often choose the wrong target from the beginning, and the failure rate is really high. We want to help turn that around. The time is right because the technology has matured, and because we have the critical mass of expertise you need to make something like this work.

What's been happening in the CTTV's first month of operations?

Our scientific programme has been given the stamp of approval by all the institutes involved, so we can start getting the right people in place to work on the projects.

What do you find most interesting about the CTTV?

This is a transformative collaboration that's tackling a problem that really affects healthcare. What I'm particularly excited about is that it is being done in a pre-competitive way. All the data we generate and the systems we make will be open to everyone. So the benefit will be for all biomedical researchers and, most importantly, for the people who have a real need for new and effective therapies.

READ THE FULL INTERVIEW ONLINE: NEWS.EMBL.DE

PHOTO: JON MOLD


PHOTO: HORST HAMANN

In our DNA

Photographer Horst Hamann looks out towards Mannheim from atop the EMBL Advanced Training Centre with a sparkle in his eyes. Whilst growing up in the Quadratestadt, he used to break into his school dark room, work all night developing photos, before sneaking back to bed before he was noticed. "I was always the black sheep," he smiles.

BY ADAM GRISTWOOD

Horst Hamann initially came to the Lab to take photographs of the EMBL Advanced Training Centre

Hamann, whose work has taken him to more than 70 countries around the world, is producing an exhibition and book to mark EMBL's 40th anniversary. His original concept – to image the Lab's architecture – soon swerved to the people in and around it. "What became clear is that EMBL is a very cosmopolitan and intellectual environment," he explains. "It feels like its own universe with people from all walks of life who all have a story to tell."

Instinctive images

A chat with EMBL Director Matthias Hentze spawned an idea: *DNA | Portraits by Horst Hamann* will feature eyes-shut, black and white photographs of nearly 200 staff and alumni, chosen instinctively by Hamann during visits to EMBL sites. "I asked people to close their eyes because this ties them together, regardless of age, gender or nationality," he explains. "They relax more, and their body language becomes more prominent, especially as there is no dress code here."

For a black sheep, Hamann has come a long way: turning the world of panoramic photography on its head with compelling vertical images of New York's skyscrapers and boasting an impressive portfolio of cityscapes, desertscapes, intimate portraits, and more. His career took off in the Big Apple – where he lived for 15 years – first assisting a commercial photographer, but soon his images were hanging in the subway and occupying spreads in the *New York Times*. A medal of honour from Rudolph Giuliani, then city mayor, followed.

PHOTO: HORST HAMANN

Horst Hamann with his hero, German footballer Gerd Müller

People person

He fondly recalls shoots with the likes of Bill Clinton, Claudia Schiffer and Jon Bon Jovi – but most unnerving was meeting his hero, footballer Gerd Müller. "My whole legs were shaking, but he turned out to be a very nice guy!" Hamann says. "My heart lies in photographing people, and this is one of the most exciting things about this project here at EMBL."

And as for the exhibition itself? "You will have to wait and see," he smiles coyly. "The photography will create an interactive dialogue with the architecture – one needs to be creative as there are no straight walls here, but I will follow my instincts and then let the pictures speak for themselves."

A public preview of *DNA | Portraits by Horst Hamann* takes place at 11:00 on 13 September at the EMBL Advanced Training Centre, Heidelberg

"This award is recognition of the work we do in Hamburg and of the successes we have seen here in the field of structural biology."

Matthias Wilmanns

Head of EMBL Hamburg, on his inauguration as a member of the German Academy of Sciences Leopoldina on 22 May.

Awards & honours

EMBO announced more than 100 new members in May, among them group leader **Anne-Claude Gavin**. "I truly feel honoured and proud," she says, "this represents a great opportunity to more actively participate in the dissemination and promotion of biochemistry and systems biology." She joins more than 1600 EMBO members recognised for their outstanding contributions to the life sciences, including numerous alumni and 18 current EMBL scientists.

Group leader **Maja Köhn** has been awarded the Friedmund Neumann prize 2014. Established by Berlin's Ernst Schering Foundation in 2012, the 10 000 Euro prize goes to young scientists undertaking outstanding basic research in biology, chemistry or medicine. The prize rewards her interdisciplinary approach, combining molecular biology, biochemistry and synthetic chemistry to study phosphatases.

Ewan Birney, Joint Associate Director of EMBL-EBI, has been elected to the Fellowship of the Royal Society. Founded in the 1660s, the Royal Society includes the most eminent scientists, technologists and engineers in the UK and Commonwealth. "This fellowship represents both recognition of the prominence of bioinformatics in the life sciences and an opportunity to discuss infrastructures for contemporary life science research at the highest levels," says Ewan.

Janet Thornton, Director of EMBL-EBI, has been elected to the Fellowship of the Academy of Medical Sciences, alongside alumna and Scientific Head of EMBL Australia, Nadia Rosenthal. The Academy of Medical Sciences is an independent organisation that campaigns to ensure advances in medical science are translated into benefits for patients – its Fellows are the UK's leading medical scientists.

Pathways Science writing

To uncover a good science story, journalist and blogger Lucas Brouwers suggests a simple formula: "Follow your instincts," he says, smiling.

BY ADAM GRISTWOOD

An evolution enthusiast, he finds the subject a rich hunting ground: recent stories include the origins of the sabre tooth tiger's tooth, the intellectual capacity of Neanderthals, the evolution of extreme longevity in some animals and why hermit crabs only smell their favourite peanut snacks when it's wet. "Scientists are creative people and it is not a surprise to find engaging stories – we are surrounded by them," he explains. "Of course discussions over theories and ideas can get heated, but this is part of what makes these stories so absorbing."

When studying for his master's degree in the Bork group at EMBL Heidelberg, Brouwers kept a blog in his spare time as well as taking on other writing projects. When it came to reflecting on his future – and deciding to go for it – he had a portfolio of diverse articles to showcase. "I started an internship with *NRC Handelsblad* – I thought I had a good grip on science, but then I came here and discovered I had been working on just a slither of highly specialised knowledge," he says. "It was necessary to take a step back and see the bigger picture. But I got some stories published – they liked them and eventually took me on as a full time biology and medicine editor."

A typical week involves juggling article writing with planning, interviewing or time out in the field. On one assignment Brouwers scrambled over icy rocks, with Adelie penguins looking on curiously, at a research station in the Antarctic. In another he interviewed his own grandmother after she had taken a direct-to-consumer genetic test as a means of exploring what can and cannot be deduced from them. "One of the best things about this job is that you get a flavour of what life is like for scientists in many different areas of life and often in extraordinary situations," he explains.

He urges those wanting to break into science writing to follow his curiosity-driven philosophy. "If you get excited every time you read an embryology paper, that will be a great subject to write about," he points out. "It is also important to practice: at first it might come out horribly, but persist and you will improve – and even if you decide it is not for you, writing can also help you as a researcher – it encourages you to organise thoughts and to reason."

READ BROUWERS' BLOG AT BLOGS.SCIENTIFICAMERICAN.COM/THOUGHTOMICS/

Lucas Brouwers during a recent visit to Antarctica

PHOTO: LUCAS BROUWERS

Branches The search for our neighbours

Either we're alone in the universe or we are not: both answers are equally terrifying, wrote science fiction author Arthur C. Clarke. Astrobiologist Lewis Dartnell disagrees: "Finding life on other planets might be the most profound discovery in the history of science," he says.

BY ADAM GRISTWOOD

Lewis Dartnell is a research fellow at the University of Leicester. He gave a Science and Society seminar at EMBL Heidelberg on 11 June 2013, and was one of the keynote speakers at EMBL-EBI's Science and Society symposium What is Life? at the Cambridge Union on 4 June.

Astronomers are developing the capability to scan the atmospheres of alien worlds for oxygen and water, while robotic space missions look for signs of life on Mars. But for Dartnell the search begins closer to home. "We want to learn more about how life was formed on Earth, to understand how it might develop elsewhere and how we can detect it," he explains.

To do this, astrobiologists study extremophiles – creatures that wallow in sulphurous lakes, burrow in high-altitude deserts, or snuggle up to hydrothermal vents. Dartnell is particularly interested in one that sets up camp in the Mars-like dry valleys of Antarctica: "*Deinococcus radiodurans* is the most radiation-resistant organism on the planet," he explains. "It can survive being blasted with ultraviolet radiation and zapped with gamma rays – it is a superhero of survival."

Mars is a freeze-dried desert that is continually bombarded by sterilizing radiation – but about four billion years ago, it was warmer and wetter and likely had a protective atmosphere. "We are trying to understand what any biosignatures might look like," Dartnell explains. "The European Space Agency is due to launch the ExoMars probe in 2018 to search for signs of life and our work is helping to inform the best places to look."

Further afield, Europa, a moon of Jupiter, and Enceladus and Titan, two moons of Saturn have also sparked interest. "While Europa and Enceladus are covered in thick ice, there is evidence of liquid oceans below, that – if enough oxidising material is transported from the surface ice – could sustain rich ecosystems," Dartnell explains. "Titan, on the other hand, has seas and rivers flowing across its surface – not water, but liquid ethane and methane, which may be able to sustain exotic life."

He suspects, however, that the first convincing evidence of extraterrestrial life will come not in our own solar system, but by locating another pale blue dot orbiting a different star in our galaxy. "Astronomy is in the midst of an exciting exoplanet boom," says Dartnell. "Scientists have the ability to identify atmospheric signatures that could be telltale signs of life. We might see a day where we can look up to a twinkle in the night sky and know a world circles there which harbours alien life: our neighbours. But as we could not physically get there, astrobiology will play an important role in identifying what that life might be like."

PHOTO: ESO

Q&A Which scientific breakthrough would you most like to see in the next 40 years?

Addressing climate change

One of the most pressing issues we need to solve is climate change. Addressing this massive, global challenge will require significant changes in the way we live as well as innovations in our approaches to energy and our environment. This includes the development of technology, buildings and transport that are much more energy efficient, as well as 'clean' energy production. Also important will be sustainable mechanisms for carbon capture and storage to be able to keep the projected rate of climate change in check. Such developments would also support progress in many other areas including food production, health, and overall quality of life.

Stephanie Suhr, BioMedBridges project manager, EMBL-EBI

Understanding ageing

Arguably the most interesting thing about biology is the fact that people are made of it. Our thoughts, our happiness, our lives and deaths are all biological events. The last one, in particular, raises an interesting question: do human beings have to die, and when? Death is everywhere in biology, and it may be that disposability is built into us on such a fundamental level that the human body will always age and decay. Yet the lifespans of organisms vary widely, and as we uncover the causes of ageing, the human lifespan, for some at least, may dramatically increase. This will raise a new set of problems.

PHOTO: EMBL PHOTOLAB

Dermot Harnett, PhD student, EMBL Heidelberg

Developing commercial fusion

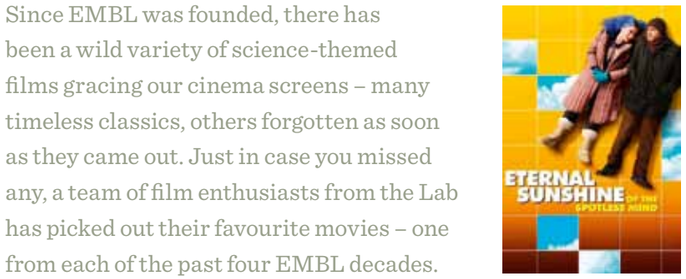
About 300 000 years ago, the Neanderthals figured out how to control fire. Burning sticks, straw and dried dung, they had discovered the first source of energy. Much later (probably about 1000 BC, China), coal started emerging as the main source. Soon after, water (about 280 BC) and then wind (first century AD), are used as renewable sources and have been perfected ever since. Petrol, natural gas, solar and nuclear fission are rather recent developments which have profoundly changed the way we live, but have yet to quench our needs for energy. It is time for the next big thing: the first commercial fusion reactor.

PHOTO: EMBL PHOTOLAB

Paul Costea, PhD student, EMBL Heidelberg

Reviews

Since EMBL was founded, there has been a wild variety of science-themed films gracing our cinema screens – many timeless classics, others forgotten as soon as they came out. Just in case you missed any, a team of film enthusiasts from the Lab has picked out their favourite movies – one from each of the past four EMBL decades.



FOCUS FEATURES

1995–2004
The Eternal Sunshine of the Spotless Mind (2004)

What would you do if technology and science had reached the level of giving you the opportunity to remove selected memories from your brain? After breaking up with his girlfriend, Joel decides to go through with that and erase her from his memory. But as he experiences the loss of every bitter moment they had, he realises he is also giving up on all the loving and happy ones. A deeply touching and meaningful story, that makes one think you cannot manipulate the human mind like a computer hard disk: select, delete, overwrite. After all, what's left of us if you take away our memories?

VASILIKI KARYOTI, DESKTOP SUPPORT ENGINEER, EMBL HEIDELBERG

20TH CENTURY FOX

1974–1984
Alien (1979)

In space no one can hear you scream. And yet Ripley Scott's masterpiece managed to echo through time, appraised as few science fiction movies ever were. The first of a series of such movies, *Alien* debuted in 1979 but still has a lot to teach to modern-day sci-fi movies: A rare technique in blockbusters nowadays, Scott takes his time immersing the viewer into the setting – the cavernous towing spaceship Nostromo – before any real action begins. Nearly 25 years after its original release, *Alien* got digitally remastered, adding more detail to the visual, but mainly the sound aspect of the movie. Bottom line, *Alien* even made it to the National Film Registry of the Library of Congress, so it should definitely be on your list.

GEORGE KRITIKOS, PHD STUDENT, EMBL HEIDELBERG

UNIVERSAL STUDIOS

1985–1994
Back to the Future, Part II (1989)

There are not many movies that perfectly wrap hardcore scientific ideas into lavish entertainment or even comedy. *Back To The Future Part II*, however, is *the* movie that did it for me. Not only showing the future in an almost realistic way (I'll see you guys next year buying a Hoverboard and a flying DeLorean), this flick also threw parallel and alternative timelines at the ordinary moviegoer. I still remember my (eight-year-old) brain exploding when Doc Brown drew a very simple diagram on a blackboard explaining how a sports almanac and a cane changed the world...and after having seen it about 30 times, it still gives me goosebumps. Yep, not all sequels suck!

TIM WIEGELS, EMBL HAMBURG ALUMNUS

ALL CITY

2005–2014
Moon (2009)

Duncan Jones' *Moon* is an inventive, imaginative and original attempt to provide answers to what it means to be human – using only one actor, a sentient computer and the moon as a platform to explore philosophical and physiological themes. It was fascinating to watch the degeneration of Sam's mind, considering he only had a HAL 9000-like companion called GERTY for company for three years. Meanwhile, Kevin Spacey's anthropomorphisation of GERTY is unnerving, not least because of a disconcerting combination of monotone voice and unsettling use of smiley faces to emphasise "feelings". But it is the relationship that Sam has with his doppelganger that is what really makes the film special – you are with Sam on every step of his weird and seemingly hopeless journey.

BRONAGH CAREY, ADMINISTRATOR, EMBO

Alumni

Welcome

In this issue, we focus on valuable online resources that preserve and share information and memories for the benefit of all: crowd-based initiatives created by alumni to support life science research, like LabLore and the Life Science Network (opposite), and our most ambitious community project to-date – an online EMBL archive (below). Alumni are integral to EMBL's success (page 22) and their team spirit and continued loyalty (page 50) are testament to this very special network. We are proud to celebrate EMBL's 40th birthday with you – the community who made and make Europe's leading life science laboratory.

Mehrnoosh Rayner
Head of Alumni Relations

For the record

MR A web-based EMBL Archive – an initiative launched at the EMBL Staff-Alumni Reunion in 2010 – is beginning to take shape. The Laboratory committed two positions for an archivist and records manager earlier this year, as well as covering the costs of its infrastructure. An online donations platform for material collections and funds will be launched in July.

Key figures in the life sciences community have given their backing to this project, among them Nobel Laureate Sydney Brenner: "I'm happy to lend strong support to your initiative and wish you all success. Molecular biology is less than 60 years old and there are still some of us whose lives stretch across the entire period – it is important to have a first-hand record of this amazing saga."

"It is important to have a first-hand record of this amazing saga" – Sydney Brenner

Mark your diaries

18-19 July
EMBL 40th Anniversary Reunion and Alumni Association Board Meeting, EMBL Heidelberg

19 October
Application deadline: John Kendrew Award 2015 & Lennart Philipson Award 2015

24 October
EMBL-VIB Alumni event, VIB, Ghent

14 November
Nomination deadline for EMBL Alumni Association Board elections 2015

27-28 November
EMBL Hamburg 40th Anniversary Symposium and Celebrations and Alumni Association board meeting, EMBL Hamburg

Resourceful alumni

Seeds of collaboration and initiative take root in two alumni, each developing community-led tools to support life science research. BY CHLOË CROSS

Aurelio Teleman originally from Italy, was a staff scientist in the Cohen group, part of the Developmental Biology Unit at EMBL Heidelberg, from 1998 to 2007. For the past seven years he has been group leader at the German Cancer Research Center (DKFZ). His research interests include insulin signalling, tissue growth control and *Drosophila*.

LabLore

Like many researchers, Aurelio Teleman has all too frequently felt the frustration of building experiments and hypotheses on published data and conclusions that were not solid. Together with Thomas Horn, his solution has been to build LabLore in his spare time – a knowledge database to accompany published life science literature. "The driving force was to try to find a way for scientific work to be evaluated based not on citations, but on content," he says. Users rate papers according to reproducibility and data quality, strength and soundness of conclusions, novelty, and impact. "It's forward looking, providing a resource for people who want to design new projects and experiments based on other people's research," explains Teleman, "At LabLore you can see what experience people have had with a particular paper." Like any community-based endeavour, it relies on user participation: "Instead of putting a paper away and forgetting about it after Journal Club, document some of the thoughts and ideas that came out of the discussion on LabLore," he encourages. Comments can be voted up or down, based on their value, and the same counts for website feedback.

HAVE YOUR SAY AT WWW.LABLORE.COM.

Life Science Network

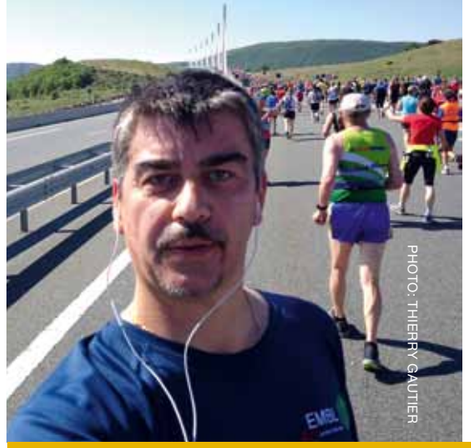
Alen Piljic has an ambitious and laudable goal as co-founder of the not-for-profit Life Science Network: "To improve the scientific process, one issue at a time, one feature at a time." His newly developed online platform combines an expanding list of tools that aim to address challenges including peer review, protocol sharing, recruitment, and communication, through community-led contributions, recommendations and comments. The various modules are built around a comprehensive directory of life science institutes, researchers and enterprises. "Behind the scenes the network is fairly complex and highly structured – triangulating location, people and content – but for the user it aims to be simple and efficient," Piljic explains. Currently in the beta stage, this free resource is a crowd-based initiative, with openness, transparency and knowledge sharing at its heart. "We built this network for the life science community," says Piljic. "The platform can be taken in any direction – if certain features aren't useful, or if users want more of one module and less of another, so it will evolve."

YOU CAN VIEW THE PLATFORM AND JOIN THE INITIATIVE AT WWW.LIFESCIENCE.NET.

Alen Piljic from Croatia, joined EMBL Heidelberg in 2002 as a PhD student, going on to become a postdoc and then research scientist in the Schultz group, part of the Cell Biology and Biophysics Unit. In 2012 he moved away from the bench to launch Life Science Network gGmbH, together with EMBL alumni Aleksander Benjak and Vibor Laketa.

Getting shirty

CC Staff and alumni getting active for fun, fitness or fundraising this year are celebrating our 40th birthday in the process. More than 300 complimentary running shirts have been sent far and wide, featuring the anniversary logo and a new public awareness motto ‘Vom Leben lernen’ (learning from life). This campaign is being piloted in Germany, but the shirts are being sported by EMBL athletes everywhere from Blenheim Palace to San Francisco Bay.



High and mighty Alumnus Thierry Gautier takes on the highest bridge in the world, the Millau Viaduct

In it to Wim it Alumnus Wim Vranken and friend before a 20K run in Brussels

Bay to Breakers Alumna Siyi Zhang celebrates completing a 12.4K race in San Francisco

All smiles, despite the miles Fellows Thomas Zichner and Maia Segura Wang run the Heidelberg half-marathon

Keeping in touch EMBL-EBI staff, alumni and friends in the Genome Campus touch rugby team

MORE GREAT PHOTOS IN THE ONLINE GALLERY: WWW.EMBL.ORG/ALUMNI/SHIRTS-GALLERY

Locus Košice, Slovak Republic

The skyline of Košice – the second biggest city in Slovakia – is dominated by the breathtaking St. Elisabeth Cathedral. Its colourful illumination was one of countless artistic performances that took place when Košice was the European Capital of Culture in 2013 (shared with Marseille).

Patricia Horosova, resource development coordination officer at EMBL Heidelberg, takes us around her home city: Košice

While visiting the city, you cannot miss Košice State Theatre – beautiful outside and in, it is an attraction in its own right. I particularly like seeing the opera here.

Every October, since 1924, thousands of professional and amateur athletes take to the streets of the city’s historic old town to run the Košice Peace Marathon. Did you know that this is the oldest annual marathon in Europe?

I am proud of the fact that my hometown was the first city in Europe to gain a royal warrant for a coat of arms, awarded by King Louis I the Great in 1369.

PHOTO: EUROPEAN COMMISSION

Events

July
17

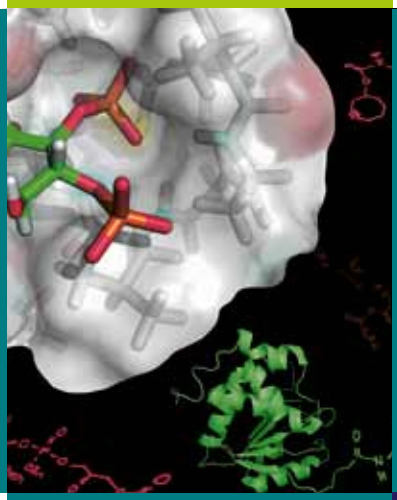
EMBL Heidelberg
Career Day

July
27

EMBL Heidelberg
Sunday Matinée: Shakespeare auf dem Kaffeelöffel – Roland Schwarz, EMBL-EBI, United Kingdom

August
20-23

EMBL Heidelberg
EMBO Conference Series: Chemical Biology 2014

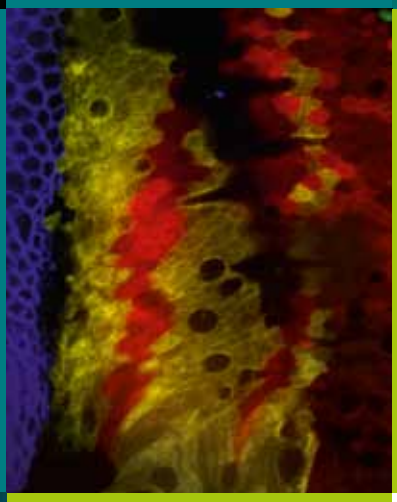


August
23-26

EMBL Heidelberg
EMBL Conference: Transcription and Chromatin

August
27-30

EMBL Heidelberg
EMBO | EMBL Symposium: Epithelia: The Building Blocks of Multicellularity

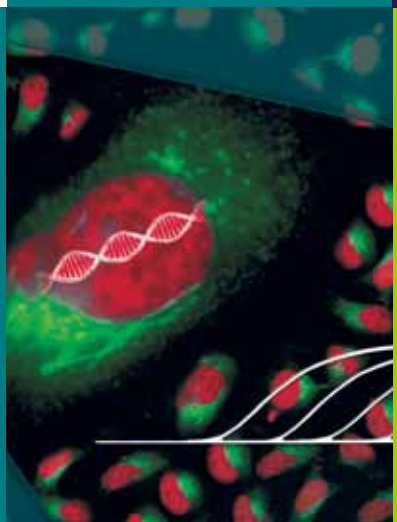


September
22

EMBL Heidelberg
Science and Society seminar: The Long History of Evolution – Rebecca Stott, University of East Anglia, United Kingdom

September
25-26

EMBL Heidelberg
EMBO Workshop: Unravelling Biological Secrets by Single-Cell Expression Profiling



September
28-30

EMBL Heidelberg
EMBL Conference: Frontiers in Fungal Systems Biology

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

IMAGES: EMBL/PETRA RIEDINGER