The European Molecular Biology Laboratory Magazine

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EMBL etc.

Humans

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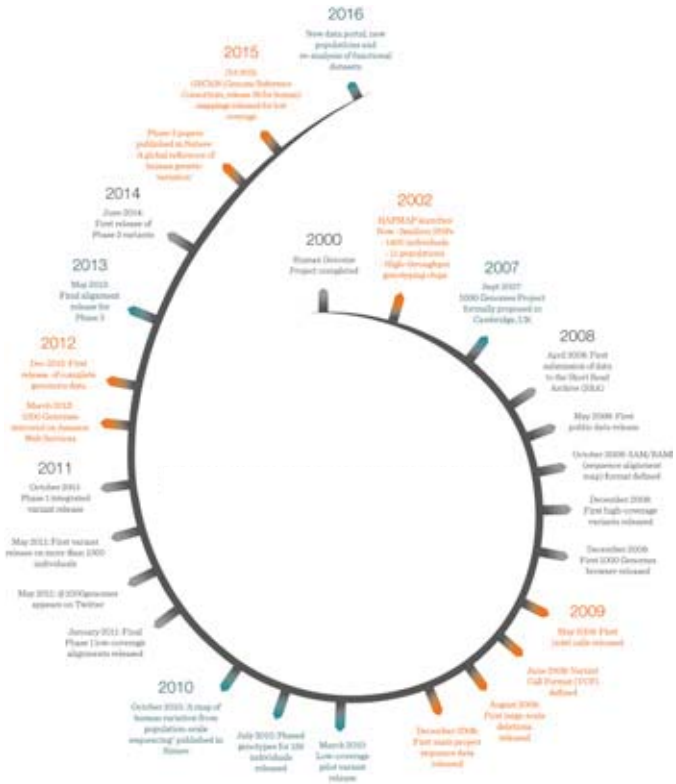

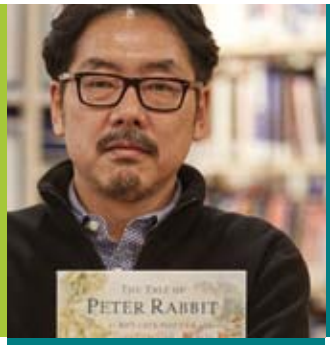

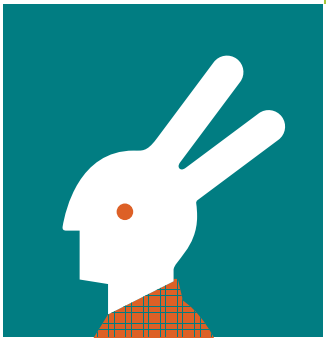

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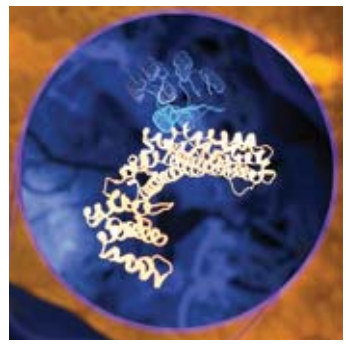

Cultures

Regulars

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Editorial

What makes us human? From when Nicolaus Copernicus set in motion his mathematical model for a heliocentric model of the solar system, to learning of the genetic language we share with gorillas, rats and flies, our concept of "humanness" continues to shift with our understanding. One of the messages I took from the recent Science and Society Symposium addressing this very question (page 41), was that while there are many things that set us apart from other mammals – such as the manner in which we cooperate, create, cook and care – identifying exactly what makes us quintessentially *Homo sapiens* requires us to reflect on many different levels. In this edition, themed on *humans*, we have invited guest authors to consider the social and scientific implications of studying human biology and how the life sciences are shifting our view of ourselves (page 26). We consider the scientific and technological legacies of the 1000 Genomes Project (page 11) and zoom into our bodies and ask what makes us human – or not (page 24). We look at other human-related aspects – from human resources (page 36) to human-themed books (page 42). And our cover story (page 15) captures a glimpse of the lives and work of some of EMBL's most important assets – the humans that drive the Lab's work across its five sites.

Adam Gristwood
Editor

Word to remember
Variant

Noun, pronunciation: /ˈvɛːrɪənt/

A form or version of a genetic sequence harboured by a person or group of people, which differs from other forms found in other people's genomes. A worldwide catalogue of genetic variants has brought insights into what makes each human unique, and left a valuable technological legacy (page 11).

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Editor-in-chief
Silke Schumacher
Director, International Relations

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

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Contact
news@embl.de

Cover photos
Marietta Schupp, Rosemary Wilson, Adam Gristwood, Mary Todd Bergman, Rodrigo Lopez

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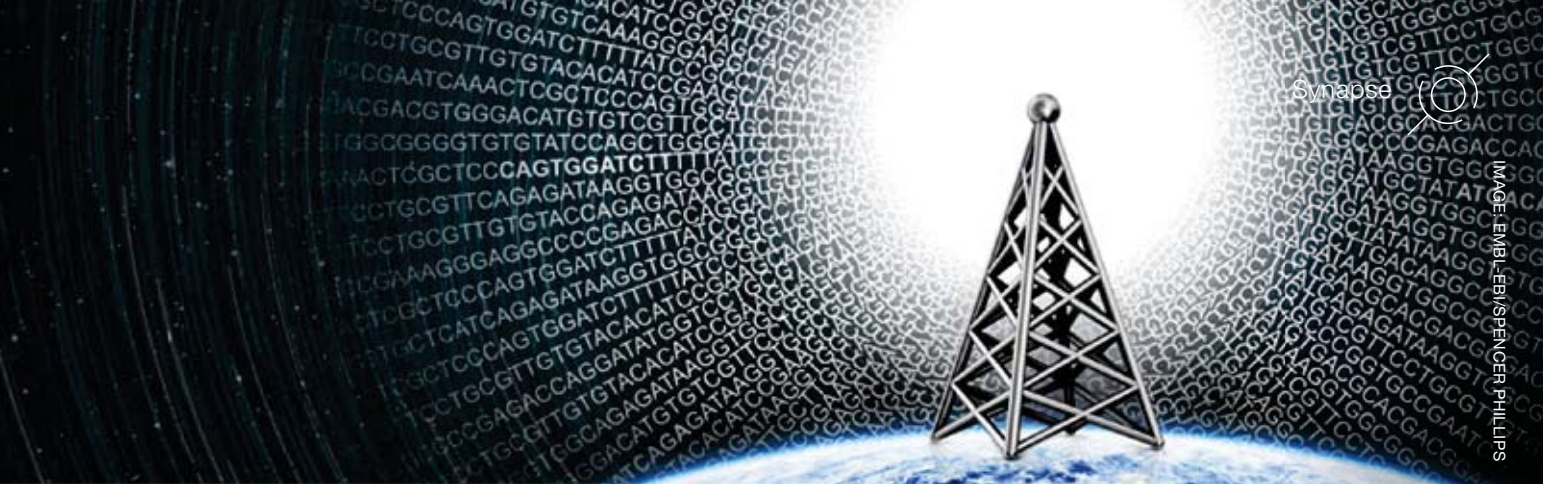


IMAGE: EMBL-EBI/SPENCER PHILLIPS

Finding links and missing genes

Missing a gene may be less problematic than you'd think. This is one of the conclusions that emerge from the most extensive catalogue of large-scale genetic changes to date.

BY SONIA FURTADO NEVES

Created by researchers at EMBL, the University of Washington, and collaborators, this reference catalogue shows how structural variations – changes in large sections of a person's DNA sequence – vary in populations across the globe, and will help guide future studies of genetics, evolution and disease.

"When we analysed the genomes of 2500 people, we were surprised to see over 200 genes that are missing entirely in some people," says Jan Korbel, who led the work at EMBL Heidelberg.

"Genome sequencing is beginning to be used for diagnostic purposes, and when doctors see that a piece of the genome is missing in a patient, there's a temptation to tie that to a diagnosis," says Evan Eichler, who led the work at the University of Washington. "We can now let clinicians know that there are certain genes that really should not be used to try to explain diseases in this way."

Many studies have implicated broadly-defined regions of the genome in common diseases. Interestingly, the large-scale changes catalogued by Korbel, Eichler and colleagues frequently occur in such disease-linked regions, implying that these structural variations are probably common risk factors for disease.

"Our work reveals that structural variations are often likely to have functional consequences," says Oliver Stegle, whose team at EMBL-EBI took part in the study. "So we can now advise on what researchers should be looking for when they're trying to understand the genetic causes of a certain condition."

The work was part of the 1000 Genomes Project, which examined genetic variation in over 2500 human genomes, with all data made available online immediately as it emerged (see page 11). Thanks to this public repository, managed at EMBL-EBI, other scientists have already begun to access and make use of the data.

"We're extremely grateful to everyone who donated their DNA to the project and made it available to use openly for research that can enable future biomedical advances," says Paul Flicek, who is in charge of the public repository of the data at EMBL-EBI. "Their generosity has not only enabled this project, but will continue to bear fruits in years to come, as many studies will make use of the data."

Sudmant PH, Rausch T, Gardner EJ, Handsaker RE, Abyzov A, Huddleston J, Zhang Y, Ye K *et al. Nature*, 1 October 2015. DOI: 10.1038/nature15394

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=5437

Ages apart

A multifaceted approach measured how cells in the brain and the liver age differently.

BY SONIA FURTADO NEVES

Age may seem like a straightforward measurement: the number of years, months, days since you were born. But for cells in different parts of your body, age can mean very different things. Scientists in Martin Beck's group at EMBL Heidelberg and collaborators at the Salk Institute and the University of California at Berkeley have now measured and compared just how ageing affects rats' liver and brain cells.

"We found that in the brain, age-related changes very often have to do with the loss of molecules that help signals to spread among neurons," says Beck. "This could explain why older rats have a reduced ability to form new connections between neurons, as well as other traits observed in the aging brain. And it is very similar to what has been found in previous studies that have looked at gene expression in humans."

The scientists compared brain and liver cells of rats in the prime of life – six months old, roughly equivalent to 18 year-old humans – to those of two year old rats. Rather than focus solely on gene expression – which genes are turned on or off – as most previous studies had done, the team employed a variety of techniques to assess several steps in the cells' protein production assembly line. They measured which parts of the genome had been transcribed into RNA, what proteins the cells had produced, what rates proteins were being produced at, and what chemical markers were added to proteins in 'post-production'.

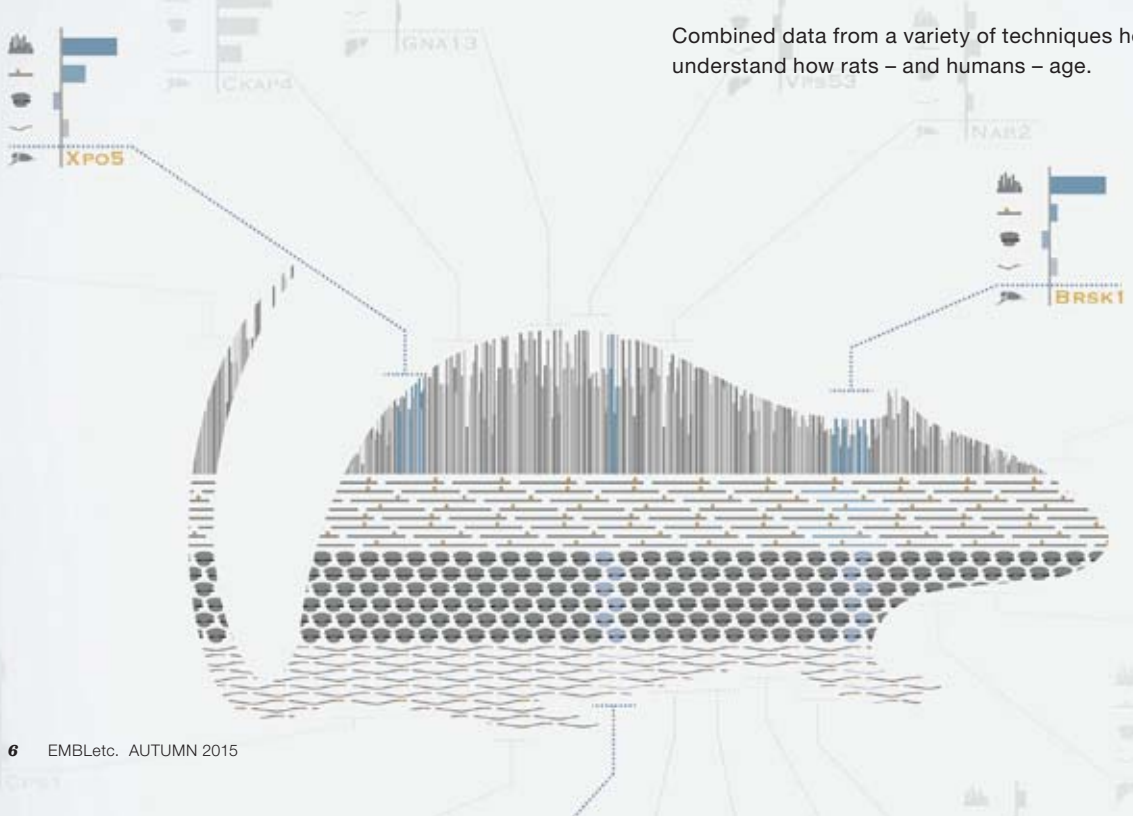
"Integrating data from different levels was crucial," says Beck. "When you see how the data sets cluster, it reveals what's actually going on. Often it was only then that we could see that a whole network of reactions is affected."

Special effects

Ageing impacted some networks equally in liver and brain – notably immune response and inflammation, and stress responses – implying that these are probably general effects of ageing, felt throughout the body. But other effects were very specific. The livers of older rats showed changes in metabolic processes – i.e. how cells process molecules – mostly at the level of regulating how the genome is 'read'. In the brain, by contrast, the tell-tale signs of ageing were mostly at the level of protein production, and mainly affected signalling processes that enable neurons to communicate with each other.

Ori A, Toyama BH, *et al. Cell Systems*, 17 September 2015.
DOI: 10.1016/j.cels.2015.08.012

FULL STORY ONLINE: NEWS.EMBL.DE/?p=5171



Combined data from a variety of techniques helps understand how rats – and humans – age.

IMAGE: BRANDON TOYAMA/SALK INSTITUTE

Mini DNA sequencer tests true

IMAGE: OXFORD NANOPORE TECHNOLOGIES

The performance of the MinION™ miniature DNA sequencing device has been evaluated by an open, international consortium, and the resulting recommendations and protocols published before peer-review on the *F1000Research* platform.

BY MARY TODD BERGMAN

The MinION, a handheld DNA-sequencing device developed by Oxford Nanopore Technologies, has been tested and evaluated by an independent, international consortium coordinated by EMBL-EBI. The innovative device opens up new possibilities for using sequencing technology in the field, for example in tracking disease outbreaks, testing packaged food or the trafficking of protected species.

The MinION works by detecting individual DNA bases that pass through a nanopore. The device was made available to thousands of laboratories all over the world, who were inspired to explore the technology and contribute to its development through the MinION Access Programme (MAP).

"The device performs well now, particularly for viral and bacterial genomes, so you can ship it anywhere and know you're going to get the same result," says Mark Akeson of the University of California Santa Cruz, a co-inventor of nanopore sequencing, consultant to Oxford Nanopore and a MAP participant. "We're looking at a democratisation of sequencing in the not-so-distant future. That is changing things for people who need to solve critical problems in challenging environments, like tracking Ebola strains during the recent outbreak in West Africa."

In this study, five laboratories in the UK, the US, Canada and the Netherlands conducted two sets of experiments for the same *E. coli* isolate (strain K-12 sub-strain MG1655) using a single, shared protocol. The accuracy and reproducibility of the data were consistent between labs and of good quality. The authors highlighted areas for improvement including molecule delivery to flow cells and software protocol clarity. The data generated in the study represents a snapshot of the MinION's performance in April 2015, with innovation now outpacing analysis.

EMBL-EBI has been coordinating the data distribution and analysis for the MinION Analysis and Reference Consortium (MARC) using the European Nucleotide Archive (ENA) to handle the raw data.

"This new device enables fully mobile sequencing with real-time data streaming, which means that with a high-speed internet connection, the first dataset could arrive 20 minutes after the DNA is loaded," says Guy Cochrane, who leads the ENA at EMBL-EBI. "We were delighted to use it as the platform for data management and sharing in MAP, so we can place the results in the public domain swiftly."

The next phase of analysis is well underway by the consortium, which is exploring ways to reduce the error rate and pushing to see how small the sample and how long the reads can be. You can join in the discussion and explore the data on the *F1000Research* Nanopore channel.

Ip CLC, *et al. F1000Research,* 12 October 2015. DOI: 10.12688/f1000research.7201.1

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=5530

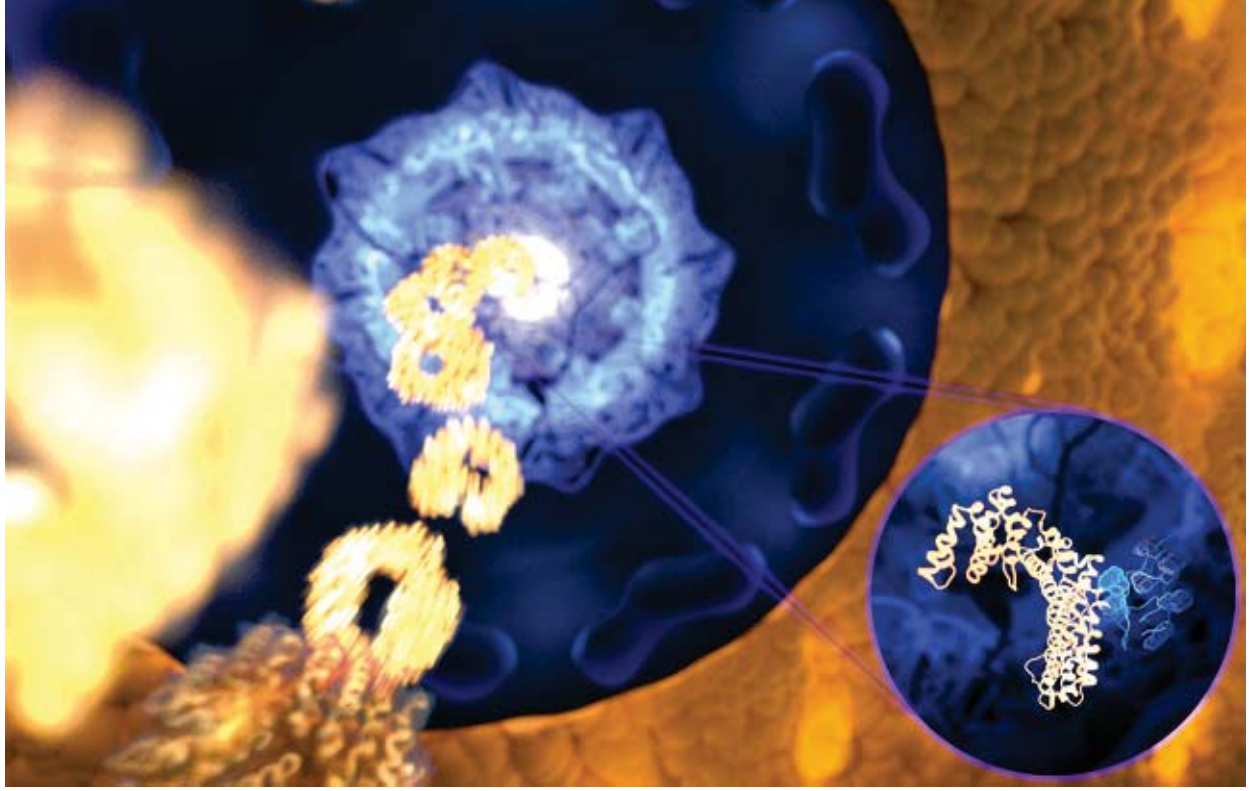


IMAGE: MERCADANTE /HITS

The ultrafast and yet selective binding allows the receptor (gold) to rapidly travel through the pore filled with disordered proteins (blue) into the nucleus, while any unwanted molecules are kept outside.

Floppy but fast

The Lemke group and collaborators discovered that spaghetti-like proteins are surprisingly effective 'keys'. BY ISABEL HARTMANN

Inside cells, communication between the nucleus, which harbours our precious genetic material, and the cytoplasm is mediated by the constant exchange of thousands of signalling molecules and proteins. Until now, it was unknown how this protein traffic can be so fast and yet precise enough to prevent the passage of unwanted molecules. Through a combination of computer simulations and various experimental techniques, researchers at EMBL Heidelberg, the Heidelberg Institute for Theoretical Studies (HITS) and the Institut de Biologie Structurale (IBS) in France have solved this puzzle.

Unexpectedly, they found that flexible, spaghetti-like proteins can be good – maybe even better than solid protein blocks – at being recognised by multiple partners. And they can do so very fast, while still retaining the high specificity the cell needs. In fact, this could be why these 'disordered' molecules are more common in evolutionarily higher organisms, the researchers surmise.

The new study suggests that many binding motifs at the surface of the spaghetti-like intrinsically disordered proteins (IDPs) create a highly reactive surface that together with the very high speed of locking and unlocking ensures efficient proof-reading while the receptors travel so fast through a pore filled with other IDPs.

Milles S, Mercadante D, Aramburu IV, *et al. Cell,* 8 October 2015 DOI: 10.1016/j.cell.2015.09.047

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=5516

Lighting the way

EMBL and its technology transfer arm EMBLEM have launched start-up company Luxendo. Funded by the EMBL Technology Fund II and Life Science Partners, the company will bring cutting-edge light-sheet microscopes to users across the globe. The technique is gaining traction as it enables scientists to observe living cells in three dimensions, for extended periods of time.

MORE ONLINE:
S.EMBL.ORG/pr141015
WWW.LUXENDO.EU

A snapshot of stem cell expression

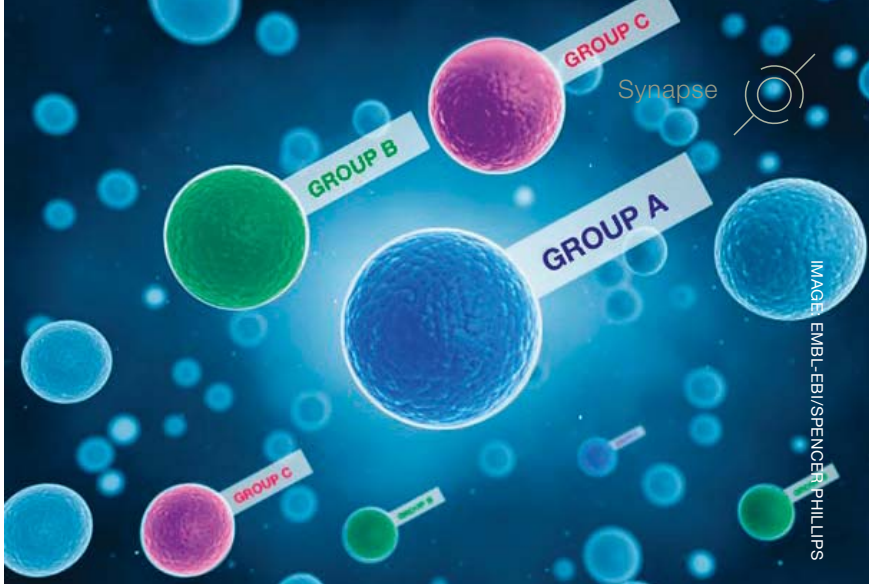


IMAGE: EMBL-EBI/SPENCER PHILLIPS

BY MARY TODD BERGMAN

What triggers stem cells to exit their 'ground' state and develop into functional cells? The spark that sets that change in motion has a lot to do with how, when and in what order the genes inside that cell are expressed (turned on or off). To understand the fundamental biology of health and disease, and to detect genetic factors that figure into a person's response to a medicine, it is essential to have a clear idea of how genes are expressed in stem cells.

In a study published in *Cell Stem Cell*, EMBL-EBI researchers used single-cell RNA sequencing technology to study the expression of thousands of genes in around 700 mouse embryonic stem cells (mESCs), and found there is a signature 'gene expression mix' that characterises different cell populations. This mix, they found, drives cellular behaviour, for instance the length of the cell cycle.

"You can take a kind of snapshot of this very dynamic process of gene expression, and infer a lot of information from it," explains Ola Kolodziejczyk of EMBL-EBI and the Sanger Institute. "It's a bit like taking a picture of a crowd in Times Square at New Year's Eve from above and ordering all of the individuals by age to get a sense of their life cycle, or grouping them by clothing style to infer which party they will go onto next."

Single-cell RNA sequencing helps researchers see what makes all the cells in our bodies take on different shapes, predict what they might do and explore the many elements that contribute to their fates. In this study, the team developed novel approaches to characterise how gene expression levels vary, stem cell by stem cell, in three different states.

"We identified new genes involved in the stem-cell regulatory network, and validated our findings using the CRISPR technology," says Jong Kyoung Kim of EMBL-EBI. "That brings us closer to inferring how the whole network is put together – and that in turn can give us insights into what keeps stem cells in a ground state and what triggers them to change."

Kolodziejczyk AA, Kim JK, *et al. Cell Stem Cell*, published online 1 October 2015. DOI: 10.1016/j.stem.2015.09.011

Enzyme research made easier

BY MARY TODD BERGMAN

EMBL-EBI has relaunched the Enzyme Portal, making it easier for researchers to explore information about enzymes and proteins with enzyme activity. Fully integrated with UniProt and the EBI Search, the portal now features comprehensive summaries, enzyme comparison, sequence search and search entry points to enzymes by disease, pathway, taxonomy and EC. The interface has been built following user-centred design methodology, and is easy to navigate. "Enzymes play a vital role in all life processes and are used extensively in biomedicine and biotechnology," says Maria Martin, who leads UniProt Development at EMBL-EBI. "The Enzyme Portal brings a huge amount of public information together in one place – it is a unique, invaluable resource for scientists and health researchers working in both academia and industry."

WWW.EBI.AC.UK/ENZYMEPORTAL

Clearing a path for cancer research

BY MARY TODD BERGMAN

A new method developed at EMBL-EBI helps researchers make better use of mass spectroscopy (MS) data to study the effects of cancer drugs on biological pathways.

Understanding biological signalling pathways is challenging because in living systems, everything seems to be happening at once. Enzymes called kinases carry out a process called phosphorylation to turn different proteins on and off, which makes them useful when phosphorylation goes haywire, for example in cancer.

The Saez-Rodriguez group created models of signalling pathways using an MS tool for studying the phosphorylation of thousands of proteins expressed simultaneously. To demonstrate that their models could be used to test the potential effect of a drug, they used data from a study of kinase inhibitors and breast cancer cells.

"Our method filters the noisy data from MS experiment and integrates the data, all in the context of what we know about kinases and their substrates, so you can see how things are connected," explains Camille Terfve, a PhD student in the group.

"You can compare what happens with the signal, for example if you use one kind of inhibitor or another. It's really exciting to have found a way to make better use of MS data, and to use bioinformatics to make cancer research more efficient."

Terfve CDA, *et al. Nature Communications*, published online 10 September 2015. DOI: 10.1038/ncomms9033

MASSIFly efficient

In September 2015, MASSIF-1 processed its 10,000th crystal, less than one year after the beamline became operational, proving its remarkable efficiency and importance to the scientific community. The first beamline of the Massively Automated Sample Selection Integrated Facility, MASSIF-1 is jointly operated by ESRF and EMBL, in Grenoble. In this fully automated service, scientists feed their experimental requirements into the beamline software while their samples enter a queuing system. The crystals are then located and screened automatically, and the data acquired without any human intervention.

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=5353

Checkpoint architecture

How can you use the same number of pieces to form two rings that fit inside each other? In the nuclear pore complex (NPC), "this geometric problem is essentially solved by flexible hinges in the Y-complex, which allows it to extend or compress a bit," says Martin Beck. His group at EMBL Heidelberg found that a specific NPC protein, called Nup358, has a key role in regulating how the Y-complexes assemble, especially in the complex's cytoplasmic ring.

von Appen A, Kosinski J, Sparks L, *et al. Nature*, 24 September 2015. DOI: 10.1038/nature15381

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=5341

One hard pull

In yeast cells, the network of actin fibres that pulls the membrane inwards to form a vesicle has to pull harder than scientists thought, François Nédélec's group in Heidelberg have shown. In a paper published in October in *PLoS Computational Biology*, postdoc Serge Dmitrieff used mechanical equilibrium theory to predict the force needed to overcome a yeast cell's internal pressure and bend its membrane inwards. Remarkably, his calculations show that the actin fibres have to exert a force that's 2500 times the cell's own weight.

Dmitrieff S, & Nédélec F, *PLoS Computational Biology*, 30 October 2015. DOI: 10.1371/journal.pcbi.1004538

FULL STORY ONLINE:
NEWS.EMBL.DE/?p=5575

A lasting legacy

What is ‘normal’ human variation? The 1000 Genomes Project, which now comes to an end, pushed knowledge forward and created technologies that will continue to be used to answer this question.

BY CLAIRE AINSWORTH

The 1000 Genomes Project, the most comprehensive fully open survey of human genetic variation ever performed, hit the headlines in October when scientists announced the final set of results from the eight-year international research effort. As well as exceeding its original aim (the team studied the DNA of more than 2500 people, instead of the 1000 originally envisaged), the project has given unprecedented insights into the genetic difference that makes each of us unique, and provided a baseline for studies into how genetic changes can cause disease.

Vital and impressive as these findings are, the EMBL scientists involved in the work say that the most important legacy of the project lies behind the headlines – in the methods and technological innovations that made the work possible. These methods have transformed how genetic and genomic research is done around the world. “With the exception of the Human Genome Project, the 1000 Genomes Project has had probably the largest impact on genomics and maybe on biology of any major project,” says Paul Flicek, senior scientist and team leader at EMBL-EBI.

Leaps and bounds

First conceived in 2007, the 1000 Genomes Project set out to catalogue the differences, or variations, in the genetic instructions, or genomes, of different people in different populations around the world. At the time, the Human Genome Project had produced the first sequence of the whole human genome, but this was based on DNA from a handful of individuals. And a project known as the HapMap Project was under way to look for common differences in single DNA “letters” between people in the hope of discovering new insights into human variation and disease. The huge expense of DNA sequencing, however, meant that the HapMap used a very different, cheaper method to hunt for these differences. While it found millions of these single changes, it didn’t have the ability to sample human genetic variation in detail.

By 2007, sequencing technology had advanced sufficiently to make >>

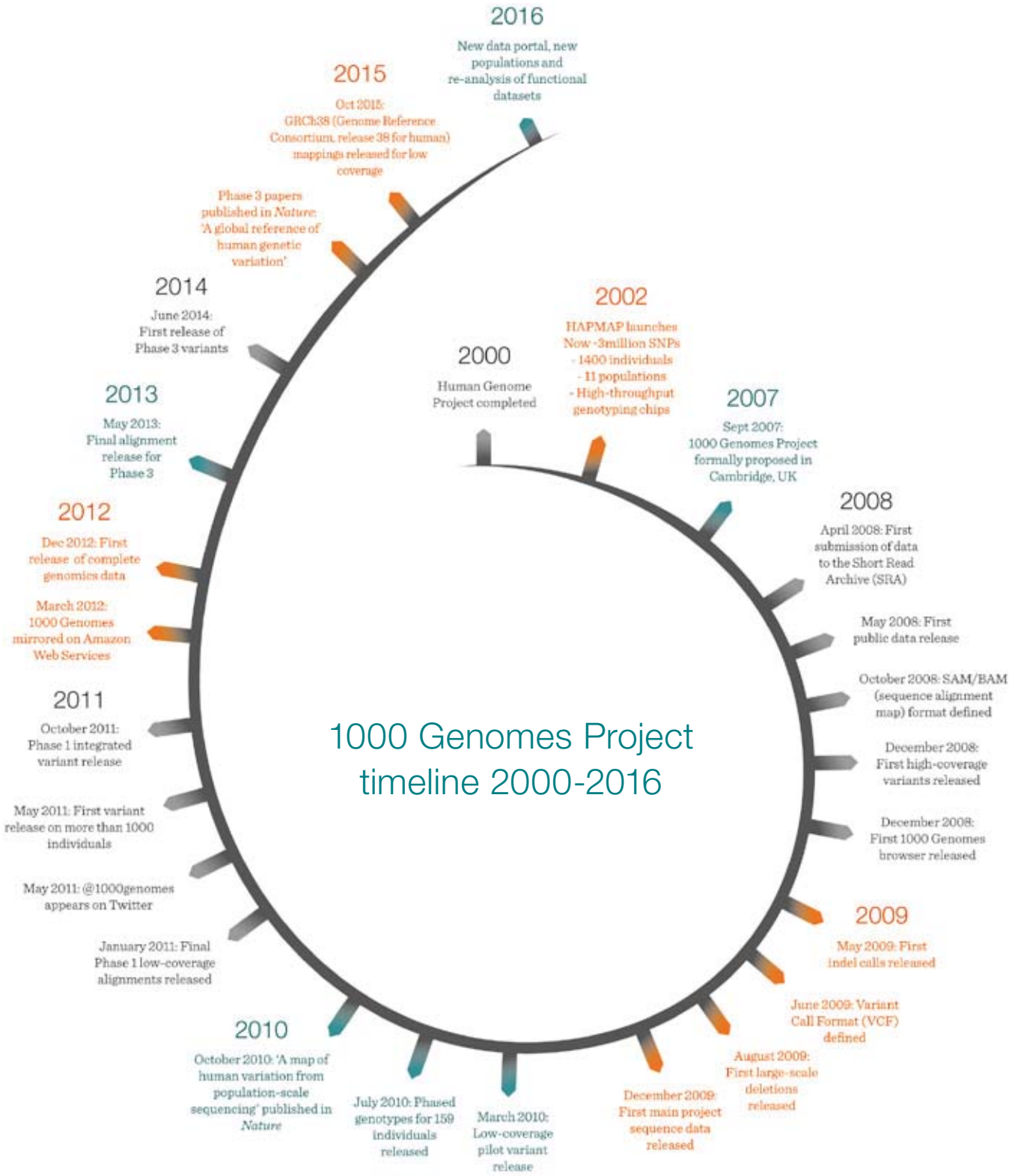


IMAGE: EMBL-EBI/SPENCER PHILLIPS

>> the mass sequencing of human genomes merely incredibly difficult, rather than impossibly expensive. Sequencing involves breaking up the genome into lots of pieces and then repeatedly reading sections of these pieces with the help of dedicated sequencing machines. Using computer software, scientists reassemble these pieces, or "reads" into the right order, by seeing how the ends of the sequences they had read overlap. This is a bit like ripping up several copies of a long, complex musical score – say, a Mahler symphony – and then trying to put the symphony back together by painstakingly reading the melody on each piece and looking for phrases at the beginning and end of each piece that match. Older sequencing technologies produced relatively long reads and enabled the Human Genome Project to complete the first draft of the whole human genome in 2000. But these technologies were time-consuming and extremely expensive. By the mid-2000s, however, new, faster and cheaper methods of DNA sequencing were being developed. Although this made the sequencing of lots of genomes feasible, the "reads" produced by the new methods were much shorter than the older ones – the equivalent of a few bars of symphonic score instead of long stretches of melody. This made assembling sequence much harder than before.

Setting standards

The first challenge for the members of the 1000 Genomes Project was to design ways of storing the sequence information in an electronic form, or file format, that would allow bioinformatics software to perform this extremely demanding computational challenge, known as alignment. Having succeeded, they then had to design a second format that would allow scientists to store and analyse the millions of differences in DNA sequences that exist between the genomes of different people. This had to be sufficiently flexible, yet also standardised, to allow researchers to make valid comparisons between them and extract meaningful information about human genetic variation.

The project came up with a file structure called Variant Call Format (VCF), which has since become the standard for all large genome projects. "Things like file formats are definitely on the un-sexy side, but they turn out to be almost as important as electricity – it's what powers everything," says Flicek. Also key was efficient logistics management by bioinformatics coordinator Laura Clarke to ensure that the deluge of data didn't overwhelm EMBL-EBI's resources.

"File formats are almost as important as electricity – it's what powers everything"

"In the long term, probably the most important thing the project did is that it largely invented all of the technologies used in large-scale next-generation sequencing and in sequencing the genomes of individual people," says Flicek. Another strength of the project was the fact that its data were publicly released as soon as it was available. "The real magic of the 1000 Genomes Project is that the data is completely open. So it can be used in all sorts of different ways," he says.

As the project progressed, it continued to innovate and respond to developments in DNA sequencing. With the help of new software developed by Jan Korbel's team at EMBL Heidelberg, as well as in collaborating institutions, the 1000 Genomes team was able to study another kind of human genetic variation, one that accounts for most of the difference between individuals and also plays a key role in diseases such as cancer and inherited disease.

This variation is known as structural variation, and involves much larger sections of the genome than the small changes that had been studied before. "It's relatively easy to identify single letter differences," says Korbel. "That is different from large-scale changes." Such changes include inversions, where long sections of sequence become reversed, deletions, where chunks of DNA are missing, and duplications, where sections of sequence are copied and inserted into the genome.

Tough to find

Even though these variations involve large areas of the genome (a page or two of musical score, instead of individual notes or bars), they are surprisingly hard to spot. This is partly down to the biology of the variations: they often occur in areas of the genome where the sequence of DNA letters is very repetitive. Such areas are notoriously difficult to sequence. What's more, the variations often result in quite complex changes in the DNA sequence at their start and end points. "There's typically some extra sequence missing, or extra sequence inserted, which makes it very, very challenging to find these things if you don't know what you're looking for," says Korbel.

Again, the length of the sequencing reads presented problems: they were too short to easily reveal complex DNA sequence changes. To overcome this, Tobias Rausch, a bioinformatician in Korbel's team, designed a new computational method called DELLY that could spot structural variation in short read data. Also key was the >>

>> emergence of a new form of DNA sequencing, called single molecule real-time sequencing, which produces longer reads. Thanks to these innovations, the 1000 Genomes team was able to identify eight kinds of structural variations and assess how often they crop up in different populations.

To understand what effects structural variants and single DNA "letter", or single-base pair, changes have on the individual, the team looked at the expression level, a measure of gene activity, of genes near the variations. This involved developing more accurate methods that could integrate different types of genetic variations to study their functional impact, a task that fell to Oliver Stegle and his team at EMBL-EBI. "There has been a community effort in refining statistical genetics technologies to fully exploit the data from the 1000 Genomes Project," says Stegle.

This revealed that structural changes were up to 50 times more likely to alter gene function than SNPs, underlining structural variation as a major factor in what makes individuals differ from each other. The complex patterns of correlation between genetic variants meant that working out whether a variant seen in a segment of DNA was having an effect, or simply happened to sit near another one that did was far from easy. "Teasing that apart has been quite a challenge," says Stegle (for more about these findings, see page 5).

"The real magic of the 1000 Genomes Project is that the data is completely open"

More to come

Such discoveries and newly developed methods will act as invaluable resources for other genomics projects searching for genetic causes of human diseases says Korbel, as it will help them work out whether a variant they observe in a patient is likely to cause disease, or whether it is part of the normal genetic variation seen in that population. Such projects include the UK's 100 000 Genomes Project, an ambitious undertaking to sequence the genomes of people with common and rare diseases, and the Pan-Cancer Analysis of Whole Genomes Project, to which Korbel and his team are contributing their expertise on structural variations and on germline genetics, to understand more about how cancers develop.

Although the 1000 Genomes Project is now officially complete, there is a need to continue to develop and add data contributed by other researchers to further expand understanding of human variation. There are yet more layers of complexity to add, including 'epigenetic' changes that affect gene activity – the equivalent of symbols added to a score to indicate how loud or soft the music should be played – and differences in gene activity between different cell types – which parts of the orchestra play which parts of the melody. All of which will help scientists build up a clearer picture of how variations in genomic themes help to make each of us unique.

MORE ONLINE:
NEWS.EMBL.DE/?p=5472

PHOTO: ISTOCK.COM/MAXIPHOTO

Humans of EMBL

Launching a new series of short stories, we dive into EMBL's universe and catch a glimpse of the lives and roles of people across the institute's five sites.

BY ADAM GRISTWOOD AND ROSEMARY WILSON

I am not a scientist by training, but I find it incredible learning how people do research, to visit their labs, and work directly with many scientists – EMBL certainly has the 'wow!' factor. Together, our Course and Conference Office team manages around 25 conferences and 40 courses in Heidelberg annually, and it is our role to ensure that events go well, providing aspects such as logistical support, managing speakers and delegates, and compiling abstract books. I have lived abroad for 10 years and hope to return to my home country Indonesia one day: research there is hugely underdeveloped and I hope I can bring some of the innovative, open and friendly culture at EMBL to an organisation there – either that, or try something completely different like running a sweet shop!

Diah Yulianti

Conference Officer, EMBL Heidelberg

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

PHOTO: EMBL/ADAM GRISTWOOD

I am celebrating a personal milestone as I joined EMBL Grenoble exactly 40 years ago in November 1975. People describe me as *le homme-à-tout-faire*, or the man who can do anything. I began as a beamline technician in charge of workshops before moving into building and maintenance: one major highlight was leading the extension of the Outstation's main building in 1993. I am also frequently asked to help out with other projects such as events or even give advice on personal do-it-yourself projects. One of the best lessons I have learned over the years is that it is important to forge close relationships with people in order to get the best out of them. EMBL is my second family and I have never felt bored with what I am doing or else I would not still be here today.

Jo Sedita

Building Manager, EMBL Grenoble

This summer, along with six other EMBLers, I took part in Roche Continents, a festival of music and drama that brings together students of arts and science to explore common grounds of creativity. I realised there are many parallels between the approaches of the two worlds: for instance, to be successful artists and scientists need to be self-critical, embrace collaboration, and give 110%. There is so much we can learn from one another as well, particularly in areas such as creative approach and communication. I also gained many other valuable insights, such as the importance of being aware of unconscious bias in our daily interactions, of adopting an open-minded approach to problems, and the benefits of taking time to have conversations and reflect on thoughts and feelings. One of the highlights was a percussion show put on by all participants, using everyday objects. I felt nervous at first, and we could not speak to each other during the performance, but I realised the importance of listening and respecting others and ourselves: when it came together, it was a beautiful moment.

Jin Wang

PhD Student, EMBL Heidelberg

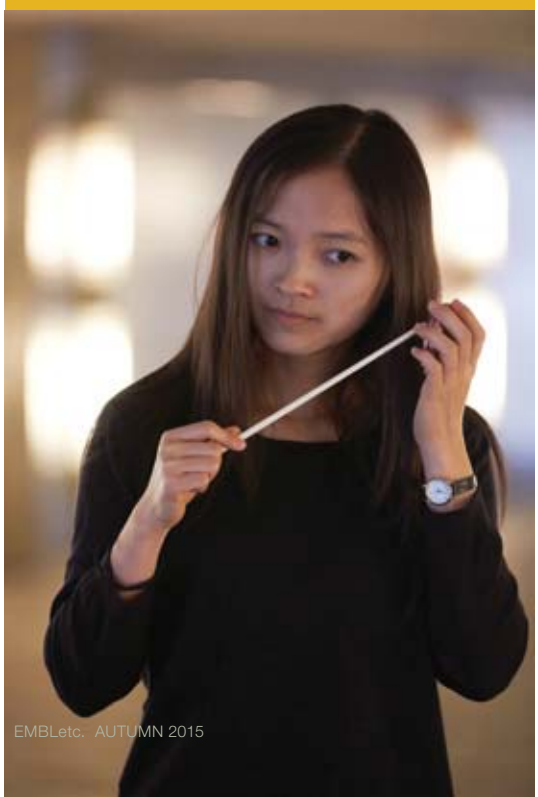


PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

PHOTO: EMBL/ROSEMARY WILSON

After about 4 months into my PhD my supervisor wrote to me and another PhD student an email saying "Okinawa?" and my colleague wrote back saying "don't you mean Chicago?", whereby my supervisor answered "both?!" When I came for the interview here I knew I would be doing a lot of travelling and teaching during my PhD but that was the start of it all. Now I have been to Chicago three times, Japan twice, Uruguay and the UK – I love it. It's such a great chance to get see so many different cultures and people. And it's not only teaching, I've been able to see several major synchrotrons for example. Usually I am teaching people who are older than me, and often they think I am also a student when I join them in the bar! I was worried in the beginning that they wouldn't respect me because of my age, but when I stand up to teach, they do. I really love being able to explain to others something I love. Wherever I go in the world I have to get a sticker for my suitcase. Quite often at airports people will look at me, then the suitcase, then back at me and say – 'have you really been to all those places?' and I will nod, and they will reply 'wow!'

Joana Pereira

PhD Student, EMBL Hamburg

I work with people from all walks of life, and when someone comes to me with a request for components or equipment, the challenge is to understand what he or she wants to achieve with it. Our team works intensively with scientists throughout the development process and if at first our solution does not work, I adapt the blueprint and we find a way – even if it ends up looking completely different to the initial concept. I have always enjoyed creating things – I was a big fan of Lego as a child – and what I like most is being involved in the full development cycle: designing, building and testing components, as well as the international ambiance.

Doris Jahn

Mechanical Technician, EMBL Hamburg

PHOTO: EMBL/ROSEMARY WILSON

I designed and manufactured a beamstop that had to be no more than 2mm in diameter: when working on such intricate projects, a major challenge is to avoid making a mistake and ending up back at the beginning. I could be drawing up a design for a new beamline component, then suddenly called to investigate a vacuum problem or to install some specialist equipment. If user operation has been interrupted due to a mechanical problem this becomes my highest priority – it can be challenging to keep on top of things, but the variety of work is hugely motivating and energising.

George Marshall

Beamline Technician, EMBL Hamburg

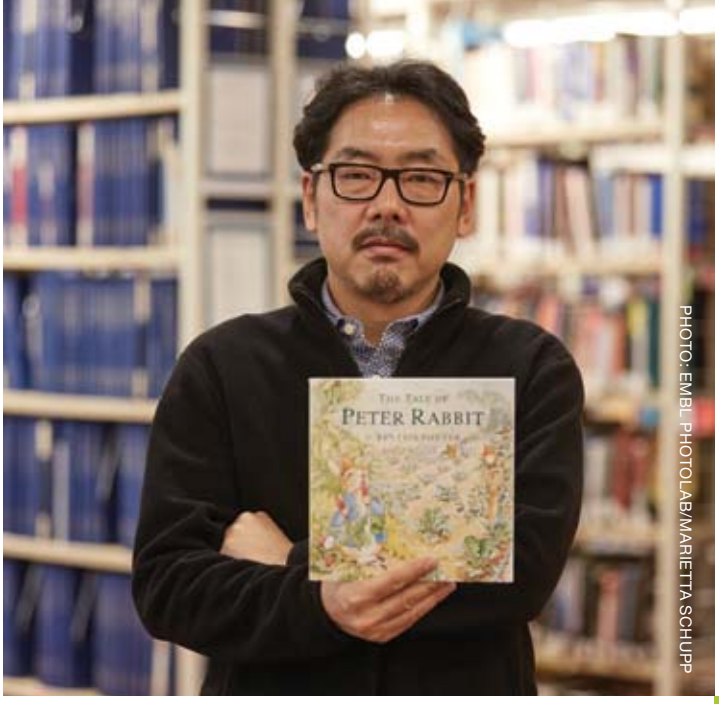


PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Albert Einstein once said: "look deep into nature, and then you will understand everything better." As a student, I went on a research expedition to a forest in Japan and realised just how important this insight was. Life science research continues to become more quantitative, with modern approaches shedding unprecedented insights into different levels and scales. However, one thing that had puzzled me was the continued application of scientific names to everything from new species, to genes and proteins, something that I associated with a 'natural history' approach to biology. My mentor, Haruko Kazama, taught me the importance of these names and classifications: I watched, awestruck, as she applied her rich knowledge of the natural world with convenience and clarity to identify and study animals, plants, and their molecular components. Standing in the forest, surrounded by thick vegetation, rain hammering on the canopy above, I stared intently at the plants around me: my knowledge of their names provided an entry point to apply my scientific knowledge and imagine the intricate molecular processes going on beneath. I felt a wonderful, overwhelming rush. For me, this demonstrated the power of science: you can understand the world at a level of detail few people fully appreciate. Professor Kazama had her own name for me: she likened me to Beatrix Potter's mischievous Peter Rabbit. We still keep in touch to this day.

Kota Miura

Visiting Scientist, EMBL Heidelberg

I have just run my first marathon: it was an amazing experience, albeit not as flat as I thought it would be! I could not walk for two days after, but I am very happy as it was on my bucket list of things to do. Most of the people in our group are sports mad and it certainly creates a great atmosphere for a healthy work/life balance.

Eugene Gbekor

Senior Technical Officer/Scientist, EMBL Heidelberg

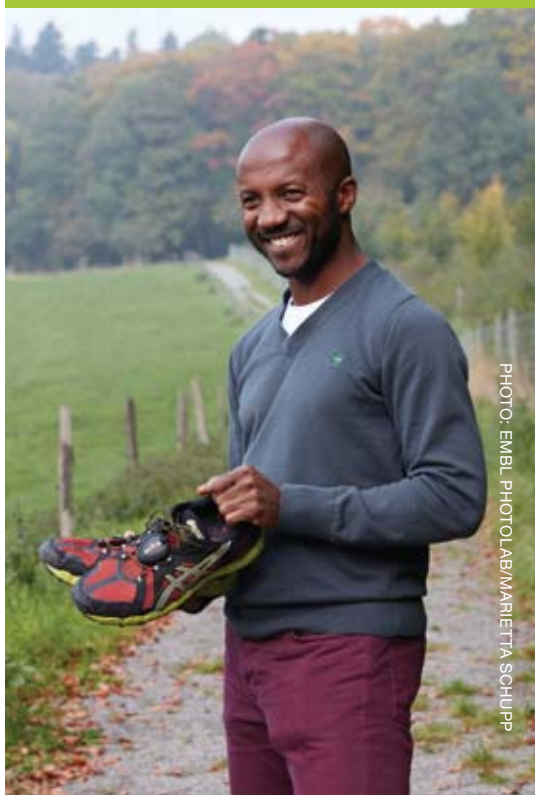


PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

We are just beginning the PhD course – there are people with so many different areas of expertise here and it is an opportunity to learn from this, to set up potential collaborations, and to make friends. Rather than being just given a PhD project, I was asked to think of my own questions. This is one of the great things about EMBL: you shape your own path. At the beginning it was terrifying, but after burying my head in journals for two months and defining what I will work on for the next three years, I felt a great sense of accomplishment.

Piotr Krzywkowski

PhD Student, EMBL Monterotondo

On a perfect workday my phone keeps on ringing, as I am a problem solver at heart. We run 25 wet lab courses per year and on each occasion the training lab has to be adapted to specific needs. Recently, during a synthetic biology course, two groups designed a new experiment and needed a rare antibody: with the help of some friendly contacts downtown my colleague Jacqueline Dreyer-Lamm was able to track it down for them – that's when you think 'yeah, this job is great!' I love creative, collaborative, hands-on work. With EMBL's Arts and Crafts Club, we visit the refugee camp in Heidelberg to run sessions on jewellery and decoration making, upcycling, and more. I am worried that the refugee crisis is impossible for politicians to manage without the help of local people. I want to show the refugees a friendly, optimistic face that knows that we, as Europeans, can handle this situation.

Yvonne Yeboah

Training Lab Technician, EMBL Heidelberg

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

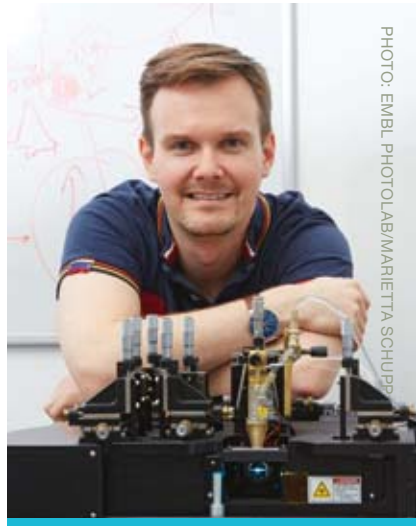


PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

I started at EMBL three months ago: it is one of the coolest places in the world to see lots of things at the same time. I already have the feeling I am constantly missing out on great seminars or other events that take place on campus! We are providing a service to people and we work with scientists on individual experiments every step of the way, defining expectations, limitations, protecting intellectual property, and exploring what we can do together to best achieve research goals.

Malte Paulsen

Manager of the Flow Cytometry Core Facility, EMBL Heidelberg

PHOTO: EMBL/ROSEMARY WILSON

Exactly two years ago I was at a microbiology conference at EMBL Heidelberg and many people were coughing and sneezing. When I got back to Hamburg I still couldn't shift the cold, but then I also discovered a lump on my neck. At first the doctors thought it was tuberculosis but after several tests and a biopsy they told me it was lymphoma. They never said cancer. Of course there were a lot of tears, but my science background really helped me focus. I could understand what the doctors were telling me about my treatment and it was actually fascinating and calming to observe and consider what was happening in my body. My belief in God was also important for me and gave me a lot of strength. I decided to stay here in Germany for my treatment – of course it was hard to be away from home, but my mum was here for more than half a year, and the doctors were great. The EMBL environment was wonderful: people I hardly knew were there for me, and have become my second family. I have always been an optimistic and upbeat person, and I believe this played a big part in my recovery. Even the doctors were amazed about how positive and calm I was throughout! I always say this was the best and the worst thing that has happened to me – it has made me stronger and changed my view on life. I want to now share some of my positive energy and have started telling my story in the hope it can help others too. I remember the first time I was allowed outside again after one round of chemo – how wonderful it was to feel the fresh air and sunshine on my face! Sometimes we forget those little joys in life.

Diana Mendes Freire

PhD Student, EMBL Hamburg

I have always been someone interested in many different things, such as psychology, teaching, and photography. I was also a very curious child and, to the frustration of my parents, I was always opening up toys to see how they were made inside. I found a career where I could combine all of these passions. As a scientist, I am doing psychology by studying how the brain works. I am teaching by working with students in the lab. I am doing photography by using light sheet microscopy. And I continue to be driven by my curiosity: our group is studying neural circuits underlying instinctive behaviour in mice – we have a big field of view, and are studying this at high resolution and we can almost see entire neural networks.

Alessandro Ciccarelli

Postdoc, EMBL Monterotondo

PHOTO: EMBL/ADAM GRISTWOOD

PHOTO: EMBL/ROSEMARY WILSON

When the users arrive at the office first thing in the morning, that's when I get my 'to do' list for the day. Maybe a user couldn't find their booking for the guesthouse when they arrived at 2am the night before, or their samples didn't get transferred to the second flight and haven't arrived yet. That's where I come in. I really love solving problems and meeting so many different people from across Europe and beyond.

Sarah Marshall

Administrative Officer, EMBL Hamburg

Our group is leaving EMBL and moving to the University of Geneva after nine years: I feel excited and scared in equal measure. In some respects it is like starting all over again, although I am in a much better position now. Coming to EMBL after my postdoc has been transformative because I could learn from colleagues and incorporate new aspects into my work from across the Lab's five sites. Our group is working with gene expression, cell biology, biochemistry, and animal models – very different to most of the groups on campus in Grenoble, which is a structural biology unit. But being here, now it is so natural for me to think about structures as well and bring this component to my research – I never felt out of place! This is typical of projects at EMBL: we use multiple techniques to address a problem and it creates a great spirit that transcends traditional boundaries. Here, I have learned the power of collaborative research and it has been amazing to see the collegial spirit between peers. EMBL is not about the machines, rooms, or buildings, but about the people: you bring together talented individuals with many interests in one place and what comes out is fantastic. Like many others before me, I will also strive to carry a bit of this spirit to where I go, and try to create a little EMBL elsewhere.

Ramesh Pillai

Group Leader, EMBL Grenoble

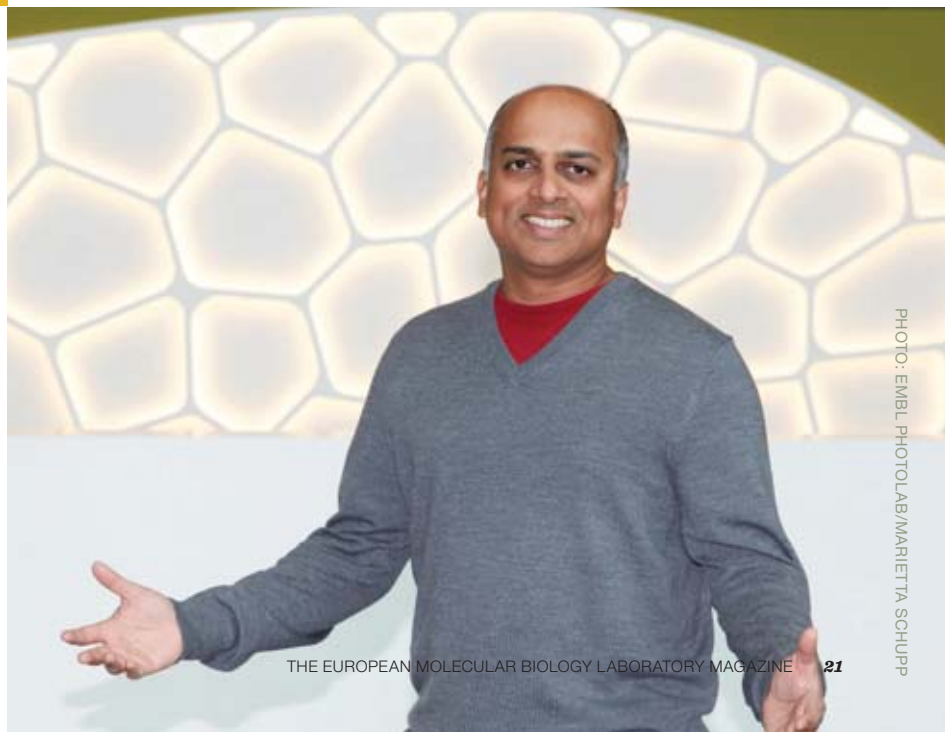


PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

I have always said I was a bit of a "methods junkie" and here at EMBL I have realised that I am driven by my passion for a method, rather than a specific scientific question. I strongly believe in small angle X-ray scattering (SAXS) as a method and what it can do for biologists and biochemists seeking to understand the bigger picture. A lot more non-specialists are relying on SAXS data now to understand their scientific questions, and I really enjoy being able to support them in achieving that and developing the method based on their needs. My first contact with SAXS was as a curious, but somewhat skeptical user here in Hamburg. But it didn't take long to convert me! I really liked the atmosphere with all these people talking and working together to run the beamline, and was immediately convinced of the benefits of the technique. So much that I jumped at the opportunity of joining the group and signed the job contract here about two months later! I really love the interdisciplinary environment here – I get to work with a great bunch of people with different backgrounds and different mindsets – engineers, physicists, software developers, biochemists and mathematicians. It's fun to see how everyone contributes their talent and knowledge to running a great beamline.

Melissa Graewert

EMBL Interdisciplinary Postdoc, EMBL Hamburg

PHOTO: EMBL/ROSEMARY WILSON

PHOTO: EMBL/ADAM GRISTWOOD

I broke my arm this year while ice climbing, standing in the wrong place at the wrong time. I had one month without pipetting in the lab, which was frustrating, but it gave me an opportunity to step back and analyse the data I had been collecting over the past year. Now after two operations I am back climbing and doing hands-on science and it feels great.

Maria Burdyniuk

PhD Student, EMBL Heidelberg

EMBL-EBI's data centres host one of the biggest collections of molecular data in the world, and when anything goes wrong in the campus data centre I am the first point of call. Petabytes of data are being accessed millions of times every month by users all over the world, and our job is to ensure the data and software are always available, 24/7. Last year we moved our public-facing data centre from two sites in London to a single centre in Hemel Hempstead. Our team was tasked with ensuring there was the room, electrical capacity and cables needed to make the transition successfully. There's nothing like having to move nearly 10 000 computers to make you appreciate the sheer scale of data we store here. My father is a mechanic and an engineer: growing up I was always in the garage with him, fixing and tinkering with cars, and that was really what I wanted to do. But it was 1979 when I left school, they just didn't hire lady mechanics. It wasn't until a few years later when, working as a secretary for a company that sold serviced computers, my boss invited me to try my hand as a computer engineer. I was a novelty, and I still don't meet many other women in my field, but I hope that will soon change – I'm very proud and lucky to be part of this.

Dawn Johnson

Data Centre Engineer, EMBL-EBI

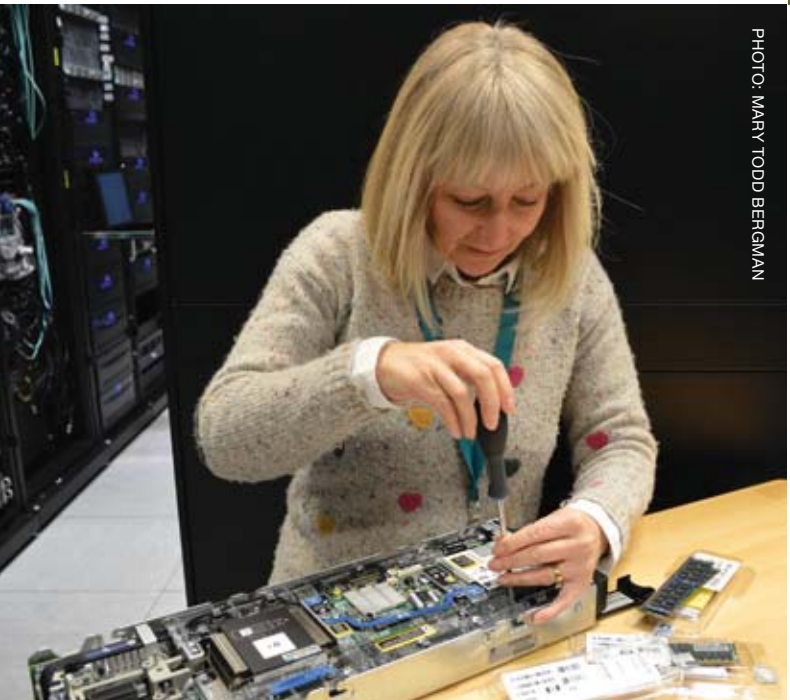


PHOTO: MARY TODD BERGMAN

Next week I am travelling to Lesotho during my vacation time to work with Kick4Life, a football initiative that aims to better the lives of vulnerable young people in the country. Over the years I have taken part in various sporting challenges to raise money for Kick4Life, which promotes sustainable livelihoods, health education, HIV testing and counselling. HIV testing can be a deeply stressful and distressing experience, and the charity is doing amazing work providing a setting that fits naturally in the community and engages people who might otherwise slip through the health-clinic net. In a country with the second highest HIV prevalence in the world, identifying undiagnosed HIV is crucial to winning the battle against the continued spread of the disease. *justgiving.com/Brendan-Vaughan*

Brendan Vaughan

Team Leader, Web Development, EMBL-EBI

PHOTO: BRENDAN VAUGHAN

What makes us human? Or not....

BY ISABELLE KLING

TRANSPOSONS

Sequences that originate from transposons, or 'jumping genes' make up approximately 50 per cent of the human genome. However, most scientists consider that most stopped jumping around 50 million years ago and 'fossilised', thus making the human genome much more stable than that of other apes. The ones that are still active are kept silent by a variety of repression mechanisms.

Transposons are often regarded as 'DNA parasites'. Viruses and transposons share some features in their genome structures and biochemical abilities, leading to speculation that they share a common ancestor.

MITOCHONDRIA

Mitochondria arose between 1 and 2 billion years ago and contributed to the emergence of animals, plants and fungi, the so-called eukaryotes. Since then, they have become important components of all eukaryotic cells, including our own. They act as 'powerhouses' that use oxygen to generate most cellular energy.

Different theories exist on the origin of mitochondria, but they all entail endosymbiosis: many years ago a host cell 'swallowed' another cell, probably similar to today's bacteria. This symbiosis co-evolved, providing both partners with physiological advantages. Mitochondria contain genes that they continue to exchange with the nucleus, constantly reinforcing their collaboration.

PARASITES

Parasites, like lice or fleas, co-existed and long co-evolved with humans. Recent research indicates that they might have had more influence on us than just provoking bad mood: parasites led to widespread grooming habits in most apes and hominids species, thus reinforcing social links and helping to establish hierarchies.

They have several pairs of legs, antennas, and feed from our blood: they are definitely not human! Parasites belong to different species that, although some might have evolved to become more specific to humans, are very far from the human genus in the evolution tree.

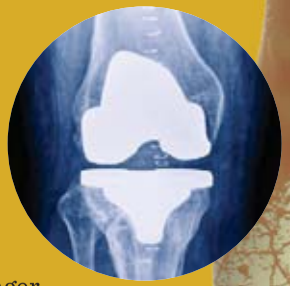
MICROBIOTA

Since our last common ancestor with apes, we lost most of our hair, adapted our digestive and nervous systems, and shaped our environment to protect us from pathogens and dangers. All these characteristics distinguish us from our hominid ancestors and make us truly human, even if bacteria are still everywhere within and around us.

According to recent studies we host more bacteria then we have human cells. They interact with almost all our main functions and are crucial to maintain our general health, help us digest, shape our immune system and maybe even our brains: we are like a bacteria-scale planet with various ecosystems hosting specific populations in constant interaction with their environment.

REPLACEMENT JOINTS

Our big brain has allowed us to devise ways to shape our environment, but also to enhance our bodies. This is a unique characteristic of humans: replacement joints are a product of our ingenious grey matter and can enable our bodies to function better and longer.



Replacement joints are usually made of very resistant ceramic material, sometimes combined with an extremely hard synthetic polycrystalline diamond surface (PCD) to give it even more resistance.

ORGAN TRANSPLANTS

Currently most organ transplants come from human donors; however, there is a shortage and researchers are looking for new sources. One tantalising prospect would be to grow organs in labs from the patients'own cells.

Surgeons are also looking to another potentially plentiful source: animals. Research into how to make animal organs compatible with the human body is currently burgeoning. Cow tendons, for example, can already be implanted to heal diseased knees in some situations.

IMAGE: SPENCER PHILLIPS/EMBL-EBI

Human minds

Special guest authors consider the social and scientific implications of studying human biology.

Using humans as a model organism

Biology is incredibly complex. Even the simplest bacteria make intricate decisions and balance different demands, all via chemical reactions happening simultaneously in what seems like just a bag of molecules: the cell.

BY EWAN BIRNEY

Larger organisms all start as a single cell and eventually become living creatures that can fly, or slither, or think – sometimes living for just a day and sometimes for centuries. Evolution has, quite amazingly, given rise to everything from uranium-feeding bacteria to massive sequoias and tax-filing, road-building, finger-painting humans.

Unpicking the complexity of biology is hard, in part because so many things are happening all at once. We've been working on it for centuries, building layer upon layer of knowledge collectively, usually relying on specific organisms with which we accumulate large amounts of knowledge on the processes of life. These 'model' organisms, for example the gut bacteria *E. coli*, are selected for their ease of husbandry and other features of their biology. Interestingly, most of them have been our companions or domesticated in some way throughout our explosive growth as a species.

To create models of animal life processes at the simplest level, we use European and African yeast. We also use the humble slime mould, which spends most of its time as a single cell but, in extremis, will band together to form a proto-organism that has given us insights into cell signalling. Taking it up a notch in complexity, we use pests that have lived off our rubbish since our earliest days in Africa: fruit flies, >>

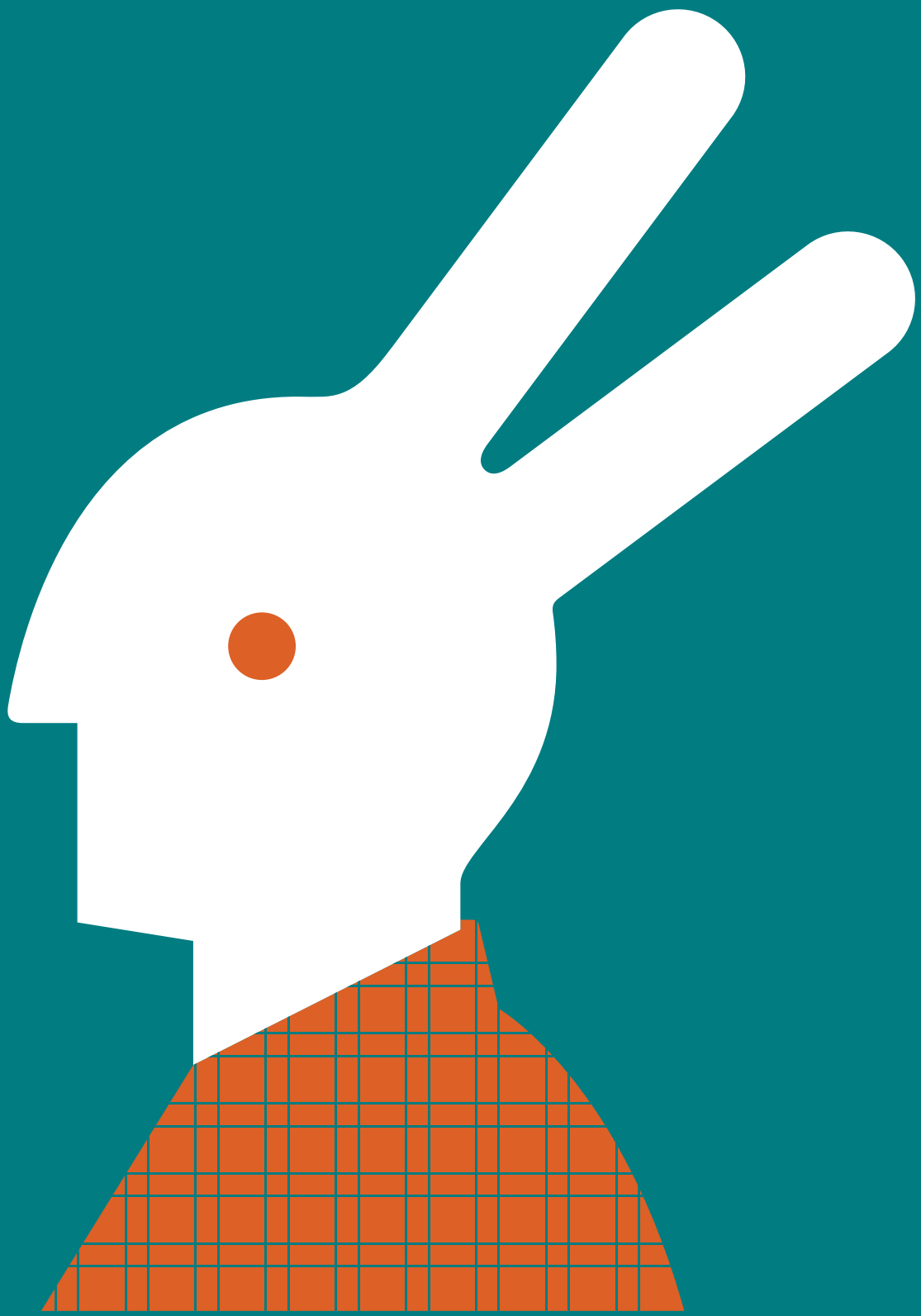


ILLUSTRATION: AAD GOUDAPPEL

>> mice and rats provide profound insights into animal life.

Each of these models has its strengths and weaknesses: the time it takes to breed generations, how easy they are to handle, the flexibility (or lack thereof) of their cellular lineage (i.e. in *C. elegans*, every individual has the same number of cells, with the same functions, created via a precisely defined set of cell divisions), and the availability of tools to observe and manipulate them in the lab. But they all share one distinct quality: they are not human.

Using ourselves?

Using *Homo sapiens* as a model species is not a new idea – it has been around since the dawn of genetics and molecular biology. Studies of human height motivated the early theory around quantitative genetics. Quite a bit of mammalian (and general eukaryotic) biochemistry and genetics was uncovered by discoveries of inborn errors in human metabolism in the 1960s and 1970s. And robust cancer-derived cell lines – most famously HeLa cells – have been used in molecular biology for decades. Using humans as a model species to understand fundamental life processes has many advantages, and some important drawbacks.

First, the advantages. At a practical level, humans are large, so we can acquire substantial amounts of material for research from consented individuals either from living people (for example, blood) or via autopsy. The human population is also extremely large, easy to access and has no ongoing husbandry costs. As a population, humans are genetically diverse, with only geography really influencing our mate choice on a global level. Many phenotyping systems are designed explicitly for humans, in some cases with a high level of automation. We can culture human cells routinely using iPSC techniques, and these cellular systems can be genetically modified

Ewan Birney, Director, EMBL-EBI

"It is possible to blend scientific approaches that have traditionally been separate"

and made into functional tissue-scale organoids.

Now for the drawbacks. There are no inbred lines for *Homo sapiens*, making it difficult to disentangle genetics from other factors. The large size and tissue complexity of this species, in particular the brain, presents significant challenges to understanding cellular and tissue behaviour. We can't keep people in a strictly defined environment, nor dictate whom they breed with. We can't make genetically modified humans, intervention studies are limited by both safety and expense, and ethical issues, which are important when studying any species, are more involved for humans – even for basic research.

Human disease

But the downsides to using humans as a model species are far fewer in number now than they were two decades ago, when the human genome was considered to be so large that a major, global consortium was required to generate it. The human genome is dwarfed in size and complexity by domesticated wheat and pine, the genomes of which are being untangled today. The cost of human genetics studies has plummeted so that large populations can now be studied (a genotyping array now costs under €50 and sequencing under €2000).

A considerable amount of money is already spent on clinical research, but the advent of inexpensive techniques to measure DNA, RNA, proteins and metabolites presents massive, new opportunities. It is now possible to blend scientific approaches that have traditionally been separate – experimental medicine and genomics, or epidemiology and bioinformatics – to exploit these measurement techniques alongside traditional clinical approaches.

Traditional models, rebooted

There is justifiable excitement around new opportunities to study humans as a model organism, but it is simply not the case that the established model organisms will become less and less relevant.

Placing too strong an emphasis on human studies could lead to inadvertently hindering research on other organisms, which would be counterproductive. Instead, we should leverage the unique properties of each model organism. For example, one remarkable paper demonstrates how a worm 'thinks' in real time, monitoring the individual firing of each specific neuron in the animal as different cues are passed over its nose. That's not an experiment that's remotely feasible in humans.

We would be very foolish to take a laser-like focus on this rather eccentric bipedal primate, however obsessed we might be with keeping it healthy, happy and long-lived. Clinical researchers might have a harder time managing this, as the necessary focus on humans to understand human disease makes it all too easy to dismiss the future impact of other organisms

on understanding human biology. But the majority of the molecular knowledge they currently deploy in their research is built on studies of a very diverse set of organisms. After all, useful and surprising insights and technologies can be gleaned from any organism.

Basic researchers, on the other hand, might dismiss the advent of human biology because it places inappropriate emphasis on applied research into the specifics of human disease. But all human studies are not necessarily translational, and in any case the interweaving between understanding biology and understanding disease makes it impossible to really separate these two concerns.

To human and back again

Over the next decade, the integration of molecular measurements with healthcare will deepen. This will almost certainly have a beneficial impact on the lives and health of many people worldwide. It also provides huge opportunities for the research community – obviously for applied research but also for curiosity-driven enquiry, as this massive part of our economies generates and manages information on ourselves. We should exploit this to its fullest so that we can understand life, on every scale, in every part of the world we inhabit.

Read the full version on Ewan's blog: genomeinformatician.blogspot.com.

Of humans and animals

From food source to objects of worship, there is a long history of complex interactions between humans and animals. BY HALLDÓR STEFÁNSSON

Since time immemorial, we have used animals for food, clothing, transportation, as beasts of burden, as well as pets and companions. And more recently, ever since science emerged in the Age of Enlightenment as a field of systematic knowledge production, various animal species have been used as objects for laboratory experiments, while along the way, science has revolutionised our understanding of the unity and contiguity of all forms of life on the planet.

But human-animal relationships have long been much more complex than that. As reflected in prehistoric cave paintings, totemic religions, and modern day pet obsessions, people have used animals in a symbolic fashion as mirrors to see themselves and as icons to render the world meaningful. Anthropomorphism is the name for a quasi-universal tendency among people to project human attributes onto animals, and thereby facilitate and intensify their emotional relationships with them. In short, "if animals are different, they are also a lot like us".

Varied viewpoints

This deep-rooted sentiment continues to infuse much of the modern, progressive and mostly praiseworthy animal welfare movement. Today, multiple well-organised lobbies and important organisations exist, both international as well as NGOs, dedicated to the enhancement of animal welfare. The European Union itself has specifically issued a comprehensive Directive (2010/63/EU) on the protection of animals for scientific purposes. And going beyond the widely shared welfare concerns, millions of animal rights activists worldwide have joined international organisations such as People for the Ethical Treatment of Animals (PETA). They commonly hold the view that non-human animals should be regarded as persons and members of the moral community whose interests deserve legal protection: to deny them that right is but a form of discrimination akin to racism or sexism.

Hence, a dilemma exists between the moral assertion that animals deserve rights and the state of affairs on the ground in our complex industrial societies. People continue to be overwhelmingly carnivorous, and animals continue to be essential (and die) for basic, clinical, pharmaceutical and toxicological research. And while most friends of animals the world over are law-abiding, peaceful people, a series of physical and verbal attacks on both research organisations and individual scientists have caused considerable consternation within the scientific community. The situation has prompted a comprehensive response, both to try to preempt such incidents happening, and also to counter the often un-nuanced, if not biased discourses propagated by the animal activist lobby.

The Basel Declaration refers to an initiative launched in 2010 by scientists from around Europe, >>


PHOTO: EMBL/ADAM GRISTWOOD

Halldór Stefánsson, Science & Society Programme Manager

>> with Rolf Zeller of Basel University, and an EMBL alumnus, as its main leader. The signatories committed to accepting greater responsibility for animal experiments and to cooperation with the public in the form of a dialogue without prejudice. At the same time, they demanded that essential animal experiments for obtaining research results remain permitted both now and in the future. With the Basel Declaration, these researchers are seeking to show that science and animal welfare are not diametrically opposed.

Proactive communication

To pursue these long-term goals the Basel Declaration Society was founded. To date, it has held four conferences around Europe to promote public awareness of the importance of animal models in experimental biomedical research, to foster communication between researchers and the public, and to enhance the acceptance of the Basel Declaration. The Basel Declaration Society also seeks to bring the scientific community together in advancing the implementation of ethical principles such as the 3Rs (Replacement – Reduction – Refinement) whenever animals are being used in research. The participants in the Basel Declaration Society unanimously hold that science must not only take a clear stance with regard to the responsible handling of laboratory animals, but also has to show greater transparency toward the public. To make the rationale and necessity, as well as the experimental procedures, for the use of animals in research more comprehensible to the public and to decision makers, the Basel Declaration researchers aim to cooperate more closely with politicians, the media, patient groups and schools in giving greater importance to the proactive and open communication of animal research and science in general.

For more information: www.basel-declaration.org

Digitally human: texting life ahead

"Typing 60 words/min, 8 hrs/day, it'd take 50 years to type the human genome. That's 78 mil #tweets". BY GIUSEPPE TESTA

This tweet I received from the Genentech account as a celebration of DNA day in 2014 exemplifies the conflation of the digital and the living that defines our times: life out of sequence, in the poignant title of a recent book on the emergence of bioinformatics[1].

The sheer possibility that our genome be computed in Twitter's metric is rooted of course in the fact that both are texts. Twitter, like many other instances of our digitised sociality, is literally a universe of texts. The genome, while literally enmeshed in the all too fleshy chemical complexity of chromatin, can nonetheless be productively understood as text. But there is more than the alignment of two textualities that emerges from this tweet. For it is not only that we make sense of the genome as text; it is the entire edifice of molecular biology, and indeed the whole enterprise of providing a molecular understanding of life, that is predicated on a genome-compatible, textual gaze that parses living phenomena in digital format. Indeed, the expansion of the life sciences into the fabric of our time is rooted in the eminent flexibility of its technological core, which entails at its most basic the following two capacities: i) that of encompassing an increasing range of biological objects and functions in digital format; and ii) that of intervening into biological objects and functions by harnessing their digital codes through a panoply of molecular switches.

Digitising ambition

Let us think, as an example, of our reframing of cell identity as a problem of combinatorial usage of enhancers, which we can now rewire through Crispr/Cas9-based epigenetic editing, a word that once more reminds us of the digital cycle of reading – and rewriting – life as text. Or let us contemplate the spectacular developments of cell reprogramming, in which cell fate is re-inscribed, inside or outside our body, through


PHOTO: GIUSEPPE TESTA

Giuseppe Testa, Professor of Molecular Biology, University of Milan; Head of the Laboratory of Stem Cell Epigenetics, European Institute of Oncology; and EMBL Monterotondo alumnus

the combinatorial usage of few transcription factors, a digitisation of cell fate poised to intersect the equally momentous digitisation of materials and shapes, all the way to the prospect of 3D organ printing. From molecules to 'omic' profiles, from cellular lineages to organs, from organisms to environments, all more or less classically defined levels of biological organisation are now amenable to the digitising ambition of the contemporary life sciences.

Quite literally, we are even redefining space and shapes through sequencing: think only of the various technologies used to probe the three-dimensional structure of the nucleus in terms of proximity of DNA stretches; or, at the other end of the spectrum, of recent successes in redefining tissue architectures and identities through the multiplexed interrogation of their single cells' transcriptomes. And even those aspects of our life that extend far beyond the sequencing of biomolecules, from medical records to credit card balances, from fMRI scans to Whatsapp conversations, are anyway all captured in digital format and hence ready to be overlayed onto the fully textualised exposition of our inner workings.

As both practicing molecular biologist and scholar in science and technology studies, I find this digital juncture particularly salient. We recently argued that scientific and social reconfigurations around the life sciences are to do with the newly found visibility they afford, with the parsing of the human condition through new units of sense-making that render it both increasingly transparent and naked: transparent, through the progressively deepening impact of our molecular gaze; and naked, once that gaze has exposed new vistas that demand choices and thereby interrogate our individual and collective sense and sensibility[2]. The next step is to realise that this molecular visibility of our selves comes in digital format, and to probe the full implications of this turn. For there is a virtually ubiquitous talk of 'big data'. Yet what has gone unnoticed so far is how seamlessly the digital representation of our selves that emerges from the life sciences can be integrated with the other digital worlds of our times. Indeed, as we recently showed, the rise of epigenetics is largely predicated on the promise to overlay 'what seemed irreducibly analogic (the social, the environmental, the biographical, the idiosyncratically human)....onto the digital genome of the informationally ripe age', with epigenomic profiles providing 'the new place holders to anchor the environment to the genome and enable the attending analogic–digital translations, conceptually as much as experimentally' [3].

Layers of humanness

The genome has thus become much more than a critical developmental resource. In its textual representation, it has taken on the role of a lingua franca, the eminently versatile digital scaffold onto which the layers of our humanness can be superimposed at distinct yet compatible levels of inquiry. The flexibility of this scaffold, of the digital core that propels the life sciences manifests itself first and foremost in the explosion of questions and contexts to which it is being applied. From mental illness to environmental pollution, from ageing to diet, from cancer to poverty, virtually all aspects of society's wellbeing are becoming amenable to biological inquiry through a multi-scale approach that illuminates these phenomena at distinct but compatible levels of analysis.

"The genome has become much more than a critical development resource"

Accordingly, our identity is also increasingly distributed and fragmented, each of us projected into an expanding repertoire of objects or representations that capture slices of our human condition with all too tangible an impact: genomes, collections of phenotypic and lifestyle information from various sources, cells and gametes stored in biobanks, avatars of our healthy and diseased tissues. And each of them often inhabits quite distinct regulatory spaces, projections (but also sources) of our selves that are invested with different legal and political meaning. The challenge is thus remarkable: to navigate the spectacular amplification of our digitised biologies governing our increasingly distributed self, and developing the necessary resources – individual and institutional alike –, to control the overlay of our manifold 'twittomes' onto our genome.

1 H. Stevens *Life out of Sequence. A Data-Driven History of Bioinformatics.* Chicago University Press, 2013
2 H. Nowotny and G. Testa *Naked Genes. Reinventing the Human in the Molecular Age,* 2011 MIT Press
3 M. Meloni and G. Testa *Scrutinizing the Epigenetics Revolution Biosocieties* 2014 doi: 10.1057/biosoc.2014.22

From side-project to valuable resource

With her PhD in her pocket, Erica Valentini is now ready to move onto the next stage of her career. But not before she has made sure the product of her PhD project – the Small Angle Scattering Biological Data Bank or SASBDB for short – is in good hands. "The project really was my baby!" she says with a wide grin. "Now it's ready for the real world and is learning to walk!"

BY ROSEMARY WILSON

As a tool for gleaning information about the 3D atomic structure of proteins, Small Angle Scattering (SAS) is gaining in popularity and importance. As life scientists realise its potential, especially in combination with other structural biology approaches such as crystallography, so the amount of data being produced is increasing. The SASBDB is a repository for SAS data and models, and is presently the world's largest database for user-friendly storage and searching of SAS X-ray (SAXS) and Neutron (SANS) data.

"This is a really useful and much-needed resource for the SAS community," explains Dmitri Svergun, head of the SAXS group in Hamburg and Valentini's PhD supervisor. "With an increasing amount of SAS data becoming available, the need for a comprehensive repository has become quite urgent," he adds. "We are pleased we could address this need and can now present the database to the SAS community." Prior to the SASBDB, several SAXS models – often submitted alongside crystallographic data – were stored in the

Erica Valentini carried out the work at EMBL Hamburg

PHOTO: EMBL/ROSEMARY WILSON

worldwide Protein Data Bank (wwPDB). Recognising that they did not have the expertise nor resources to adequately handle and curate the SAXS data, the wwPDB established a task force to draw up guidelines for a dedicated SAS data repository.

A welcome resource

A few years on, and scientists can now use the SASBDB to access and download data related to a SAXS/SANS experiment, rather than just viewing an image of the >>

"This is a really useful and much-needed resource for the SAS community"

>> model or scattering curve in a publication. Currently, the SASBDB is receiving new entries every few weeks, and slowly but surely the database is growing. "We are asking many of our collaborators to deposit their structures in the data bank and we hope that it will become standard practice, just like the PDB is standard for crystallographic data," explains Valentini. The SASBDB is now ready to receive the SAXS models that were previously stored in the wwPDB. "We have started doing tests and writing scripts to import the data," Valentini says. "We already have about 190 entries, and we are gearing up to take another 50 or so."

"Increasingly, techniques other than crystallography, NMR and electron microscopy are being used by structural biologists to study complex biological systems," says Gerard Kleywegt, who heads the PDBe (Protein Data Bank in Europe) hosted at EMBL-EBI. "Hybrid methods, where multiple techniques are used, are becoming more and more common." Kleywegt welcomes the launch of the SASBDB and the collaboration with wwPDB: "Having a major standard repository for each of these techniques is absolutely vital for scientists worldwide – as time goes on and methods develop, it is crucial that we have access to comprehensive raw data from all SAS experiments so that these can always be referred to, reinterpreted and reanalysed." If not otherwise communicated to the SASBDB team, entries will be published six months after submission.

Growing together

Remarkably, the database actually stemmed from a small side project, and put Valentini on the right path after a stumbling start to her PhD. "Our collaborators were starting a database for storing experimental data from different techniques, including SAXS, and asked for our contribution," she explains. Svergun asked if she would like to be involved by providing them with some SAXS data – having studied databases as part of her Master's degree, Erica knew that in order to store data you needed to understand the structure behind it first. "I drew a schema of what the database should look like – when Dmitri saw that I understood these things, we started to consider whether we could do something ourselves," she says. "I feel really lucky with my PhD – Dmitri really understood my strengths and pushed me in the right direction." Now in the process of making plans to leave Hamburg, Valentini has had to step back from the project and hand the reins to colleagues within the SAXS group. "It's hard to let go of your baby," she smiles, "but I am really satisfied with how it has all worked out, and I will keep on watching it grow!"

Valentini E, *et al. Nucleic Acids Research*, 28 Jan 2015.
DOI: 10.1093/nar/gku1047

Facts and figures

SASBDB is a searchable, curated repository of freely accessible and downloadable experimental data, which are deposited together with the relevant experimental conditions, sample details, derived models and their fits.

The SASBDB is maintained by the Biological Small Angle Scattering Group, EMBL Hamburg.

235 experimental data sets

350 models

350 unique visitors per month

1200 entries downloaded since its launch

17 entries in the database from well-characterised, highly purified proteins: examples of good data that can be used for teaching, learning and programming purposes.

For questions and feedback, sasbdb@embl-hamburg.de

Follow @svergungroup on twitter for SASBDB news and updates.

Cultures

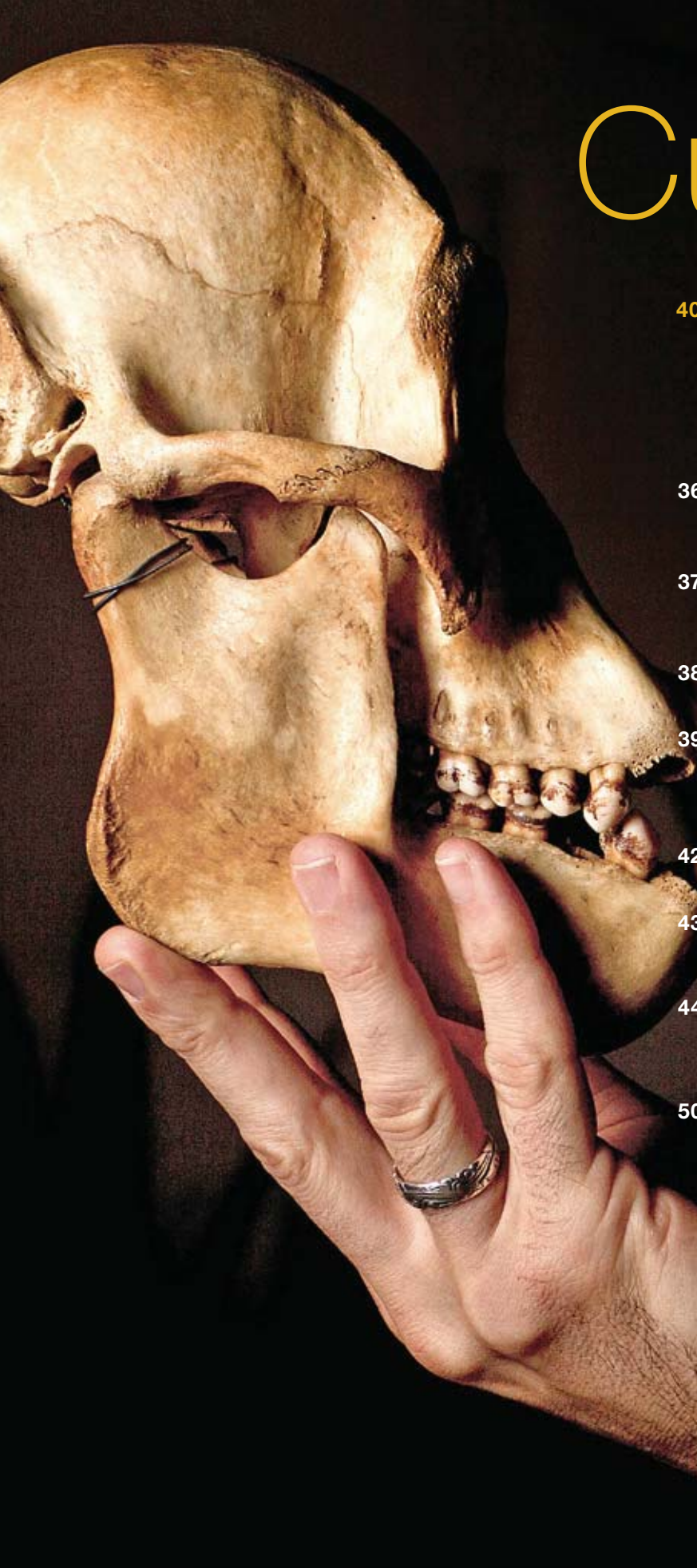


PHOTO: LAWRENCE SMITH/FAIRFAX MEDIA

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Walking the talk in HR

Rapidly approaching a year in post, Head of Human Resources Roland Block has bridged continents and reached for the stars in his three decades in the field. Composed and quietly passionate, he reveals how he's emphasising the 'human' in human resources at EMBL.

BY CHLOË CROSS

Tell us about the structure of HR at EMBL ...

Our team is close to 20 people, and that is a very reasonable ratio of around one per cent of EMBL's overall staff. Over the past 10 months we have restructured HR into sections and, in a departure from the 'generalist' approach, every team member now specialises in one or two areas, and can make a more meaningful contribution from the outset.

How do you support sites in four countries?

We had a very similar situation in my previous role at the European Southern Observatory (ESO): headquartered in Munich, with three observatories in Chile's remote Atacama Desert – slightly more challenging distances than at EMBL! All sites, regardless of geography, need to be involved in HR strategy, policy and integration. We have HR team members based at EMBL-EBI and aim to visit EMBL's outstations regularly, remaining in close contact.

What do you enjoy most about working at EMBL?

You perceive it even at your interview: EMBL is something special! The camaraderie and openness of colleagues across the Laboratory is admirable. I am impressed by the supportive attitude of all sections of the EMBL community, my colleagues in HR and Administration, the managers and the Directorate. I should also emphasise the very positive developments in relations and cooperation with the Staff Association.

What is your top recruiting tip for colleagues?

The selection panel should always take into consideration candidates' behavioural and social competencies. We all work in teams and small groups, often in close proximity – colleagues need good 'chemistry' and personalities that mesh. Alongside academic and career expertise, employees need enthusiasm, flexibility and dedication. At EMBL, an open personality and willingness to communicate and collaborate is a must, regardless of your field.

How can HR shape an organisation and its culture?

Perhaps more so than others, HR needs to walk the talk: our values and actions must reflect those of EMBL. Through recruitment, HR can also help to address specific obstacles and opportunities – such as gender equality, especially in supervisory and senior positions. How these actions combined can mould the culture of the organisation depends on the people – this I cannot foresee.

What skills do you need to be successful in HR?

You have to take complete ownership of your work – to be responsible and decisive, and open about the process with the people concerned. This is particularly necessary in academic settings, where very astute colleagues deservedly want to understand why and how decisions are implemented. Our resource is 'human' after all: HR professionals should seek to solve staff problems as if they were their own.

READ THE FULL INTERVIEW AT NEWS.EMBL.DE/?p=5676

A whole new ball game

Members of the Löw group designed and constructed a game to explain and demonstrate how proteins can transport molecules across a cell membrane for Hamburg's Night of Science event on 7 November. PhD student Yonca Ural-Blimke explains how they went about it.

BY ROSEMARY WILSON

Yonca Ural-Blimke with the game, a model of the transporter protein embedded within a cell membrane

PHOTO: EMBL/ROSEMARY WILSON

What does the game demonstrate?

Transporter proteins are anchored in, and span the entire depth of cell membranes – as the name suggests, they move molecules from one side of the membrane to the other. There are several different types of transporter proteins and mechanisms for moving molecules. We study proton-dependent oligopeptide transporters – POT for short – that move the products of digestion and certain drugs. POT proteins consist of two bundles that combine in different formations to carry molecules across the membrane. This game demonstrates the 'alternating access mechanism', whereby access by the molecule (the ball) is first into the protein, and then out into the cell once the first access point is closed.

Tell us more...

The central part of the game is a model of the transporter protein embedded within a cell membrane: the two POT bundles are represented by two polystyrene blocks positioned between plexiglass sheets decorated to represent the cell membrane. The aim of the game is to throw a small ball into the model, making the two parts of the protein move apart to let the ball cross the membrane.

How did you design and build the game?

We started playing around with the idea for EMBL's Lab Day, and discussed with various people about how to build it: How could we get two parts to move? What transparent but sturdy material could we use? After some brainstorming, I presented our idea to Mechanical Technician Doris Jahn and asked if she could help – fortunately, she said yes! We went through the workshop together and picked out some materials to test. I originally planned to build the game at home, but quickly learned that it was important to have access to the right cutting tool; moreover, the hands-on preparation of the game together with Doris in the workshop was lots of fun! An important consideration was the final size: big enough to see, but small enough to safely transport and use.

What was the most challenging part of the design?

One of the hardest issues to solve was how to get the two parts of the protein to stay in the correct conformation – it wasn't really clear until the final day how to get around it. We considered using springs to keep the parts on one side together and on the other apart, but that is surprisingly hard to get right while not obstructing the ball. The trick was to add a weight – a metal bar – to the bottom corner of the polystyrene, to keep it in the right orientation. The decorations were also fiddly and time consuming – I printed them using modelling software and yes, they are images of the real proteins!

SEE THE GAME IN ACTION: NEWS.EMBL.DE/?p=5554

Q&A What does a physicist do in a biology lab?

BY ISABELLE KLING

Making sense of data

I used to be a theoretical physicist, now I work at EMBL my research has changed significantly. My goal now is to try to make sense of biological data from a physicist's perspective. Usually biologists have a qualitative model, and their question is: is this model consistent with the numbers we get? One example of a recent study I have worked on is blood platelets' deformation. The microtubules that are part of the cells' skeleton form a ring that coils at a certain moment in the life of the platelets: we wanted to understand how this happens. We began using data from electron microscopy and light microscopy and represented this from a physical perspective. We managed to propose a model that explains the deformation of platelets in a way that makes sense from what we know biologically and physically.

A physical framework

My role is to give a physical framework to what biologists see. When cells deform or move, for me this is all about forces, mechanics and physics. For example, if we start with a model of a polyhedron and refine it, we get something more and more spherical: by this process you create something that looks like the surface of a cell. We try to make this model deform via different sorts of constraints to see if we can reproduce what we see, for example in mouse embryos. I work a lot with developmental biologists who try to understand how cells interact mechanically and how these interactions shape the development of embryos. We currently know very little about this process, so in many respects we need to start from scratch.

Serge Dmitrieff, postdoc, EMBL Heidelberg

Hervé Turlier, postdoc, EMBL Heidelberg

WATCH SERGE AND HERVÉ'S FULL INTERVIEW ONLINE: YOUTU.BE/sYw-UkHGQnQ

PHOTOS: EMBL PHOTOLAB

PHOTO: DELFT UNIVERSITY OF TECHNOLOGY

Sybrand van der Zwaag began his journey at the Cavendish Laboratory at the University of Cambridge before moving between several different projects and areas in industry and academia; he is now scientific director of the Delft Centre for Materials in the Netherlands. His efforts connecting academia and industry were honoured in 2012 with the bestowment of the title of Distinguished Professor.

Pathways
An open letter to young scientists

"And now I want to do something I have never done before!" an impatient Sybrand van der Zwaag is reported to have said at just four years of age. His talk, one of the highlights of this year's Career Day at EMBL Heidelberg on 9 July, was full of similarly adventurous advice acquired over the course of a career that has taken him to a multitude of positions in academia and industry.

BY ROSEMARY WILSON

Now scientific director of the Delft Centre for Materials in the Netherlands, where he works in areas ranging from self-healing materials to aging research, van der Zwaag gives his five top tips for young researchers thinking about their next move.

1 There really is no good or bad strategy for a career, but it is important that it fits your personal strengths. Do you prefer working alone, or in a team? Does working towards a tangible result motivate you, or do you love having the freedom to be innovative? Feel encouraged to **make your own steps** and not what you think others desire of you.

2 **Be honest about what work conditions make you happy** and persevere, but accept that the route to the holy grail may be via one or more detours. I loved my time in Cambridge and thrived in the academic culture, but my PhD topic for sure would not keep me happy for the rest of my life. Later, happy in research, I was at a place where organisational culture did not suit my character. Commit yourself to the job at hand, but make sure you can move when you are not happy. My return to academia was set in motion by an unplanned meeting with someone I did not know at all, but I was ready for it and could show quickly I had developed relevant competences and skills.

3 When weighing up new career options it is useful **to take a closer look** at a prospective workplace, including your potential future boss and colleagues. Do they seem happy? Have you spoken to staff about their experiences? What work ethics will be waiting for you?

4 It is very important to **invest time and effort into the career of your partner**. After all, a lot of your own happiness is linked to theirs: be sure to talk about it and also look into non-obvious solutions.

5 Of course there are large differences between academia and industry: hierarchy, type of rewards, team work, or individual achievements, etc. However, the **differences are overrated**. Ultimately it is a matter of your personality matching well enough with your job. Only when it matches, you can become happy – and is that not the aim of our lives?

This year's Career Day focused on intersectorial mobility and was organised by Brenda Stride, Postdoctoral Programme administrator and Helke Hillebrand, Academic Coordinator and Dean of Graduate Studies. Around 300 people registered for the event, which included a diverse programme of speakers, as well as a popular new CV-check initiative.

PHOTO: LAWRENCE SMITH/FAIRFAX MEDIA

Branches
What makes humans tick?

This question fuels Agustín Fuentes's passion for anthropology, and he shared it with the audience at the Science and Society Symposium *What makes us human?* BY JULIA ROBERTI

Let's travel back in time to the origins of human societies, a prominent feature of what we call human nature. How far would we have to go? Would 5000, 50000, 100 000 years suffice? Not even close. "When people think of deep time it often conjures up images of the pyramids of ancient Egypt, the Maya civilisation, or prehistoric cave paintings, but to understand what makes us human we need to understand the changes in our lineage starting two million years ago," explains Agustín Fuentes, a professor of anthropology at the University of Notre Dame. "We are the last hominins standing, sole survivors of a big evolutionary experiment, and we are still evolving biologically, neurologically and behaviourally. It is a complex interplay of biology and environment: this is the baseline and not the end of the story."

Defining human nature is a tricky business. Characteristics that we often associate with people, like caring for others, forming societies and looking after our young, can be observed in many other animals, such as gorillas and blue whales. What has set us apart, then? "The unique ability to coordinate, share intentionality and collaborate creatively became a distinctive pattern in our ancestors that enabled us to do all that we do today," Fuentes suggests as one answer. "An example is stone tool making. We come up with things that are not logically extractable from our experiences; no other species looked into a piece of rock and envisioned a whole different object within."

Art of teaching

Fossil evidence indicates that this know-how was passed on through direct teaching as early as 500 000 years ago, and we are the only species that share knowledge this way. "Furthermore, we create things as an expression of human imagination that we call art," Fuentes explains. "Other animals, such as non-human primates, may experience this as individuals but they do not share, teach or engage in it as we do."

Good natured

Perhaps even more surprising is the intricate interplay of traits such as competition and collaboration in determining who we are. "Conflict and violence are not opposite, but complementary to cooperation and creativity," he says. "By working together, we also developed technologies that transformed our bodies and the environment – this has huge implications for our, and other species' very survival on the planet. But while war and cruelty make headlines, we often underplay our capacity for compassion – it is amazing that the same parent-to-child hormonal and neuroendocrine responses can be observed in our interactions with strangers and even other species: this is extremely uncommon and a sign that getting along is in our nature."

PHOTO: JÖRG LANGOWSKI

If you are flicking through the pages of this magazine and reading this article, there is little doubt that you are human. We can do amazing things such as stand on two feet, manipulate objects with our hands and understand complex language. But what is it that makes us quintessentially *Homo sapiens*? Giorgia Guglielmi and Heena Khatter pick out their highlights from the *What makes us human?* symposium at EMBL Heidelberg on 20 September.

Being human beings

Only children

Ever get that feeling you are all alone? Well, for around 40 000 years *Homo sapiens* have been the only living species belonging to the genus *Homo*. "But the situation we have today, with only one species, is exceptional", explained Jean-Jacques Hublin, a Director at the Max Planck Institute for Evolutionary Anthropology. Fossil evidence exists of more than 25 species of hominids – many of which co-existed and even interbred – including the astonishing recent discovery of *Homo naledi* in a South African cave, who displays both primitive and human-like features. "Our evolutionary lineage looks more like a bush rather than a straight line: studying the timing of development and maturation in different hominids can help us to understand how they coped with different forms of social organisation and adapted to environmental challenges," added Hublin.


PHOTO: EMBL/ADAM GRISTWOOD

Jean-Jacques Hublin

BBQ masters

Fire did not only keep predators away, but it also made cooking possible. "If we consumed raw food, we would need to eat for around 10 to 12 hours each day," argued developmental biologist Alain Prochiantz of the Collège de France. The invention of fire correlated with an increase in brain size, and scientists believe that this might have been the turning point in our evolutionary history. We all experience the power of our big brain on a daily basis when we reason, judge, compute, problem-solve, and use and understand complex language – it turns out that we can do pretty remarkable things with those 1300 cubic centimeters! Prochiantz argued that by eating cooked meat, early humans could not only gain a lot of energy but also easily digest and absorb essential nutrients to feed our grey matter.

Collaborative creativity

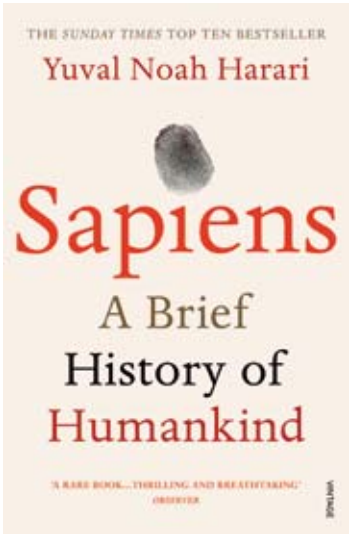
For the genus *Homo*, evolution seems to have favored teamwork over selfish motives. "Whether it was eluding predators, defeating competitors, making and sharing stone tools, controlling fire, telling stories or contending with shifts in climate, our ancestors collaborated to deal with the challenges the world threw at them," explained Agustín Fuentes (see page 40). "This baseline of creative cooperation, the ability to think, communicate, and collaborate with increasing prowess, transformed us into the beings that invented the technologies that support large-scale societies and ultimately states." Each of these features was acquired at different times during our evolutionary history, added Hublin. "While there are many things that make us human, there is no way of knowing how old the oldest human is."

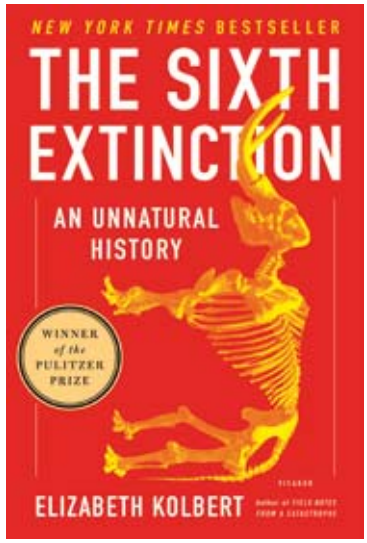

PHOTO: JÖRG LANGOWSKI

Alain Prochiantz

Reviews

Thibaut Brunet, a postdoc from EMBL Heidelberg, reflects on a pair of books exploring the unreasonable rise of *Homo sapiens*.





The past 200 000 years are a mere geological blink, but during this time *Homo sapiens* has reshaped the world. How did we rise to global domination? What does our conquest of the world mean for the species around us? What's next? The causes and consequences of human success are the topics of two of the best popular science books of last year: Yuval Noah Harari's *Sapiens: A brief history of humankind* and Elizabeth Kolbert's *The Sixth Extinction: An unnatural history*.

Sapiens: A brief history of humankind
Yuval Noah Harari

Sapiens addresses nothing less than the entire history of humankind. To many of us, the topic of history evokes memories of tedious school time litanies of faceless kings and queens fighting for abstract bits of territory on the maps of interchangeable countries that don't exist anymore – the world's longest, dullest, most repetitive sitcom. But history can be taught well, and *Sapiens* provides ample proof of it. Harari provides a fresh – and often irreverential – perspective on the main historical transitions, backed up by the latest science. The invention of writing? A mere accounting tool. The agricultural revolution? The "biggest fraud in history", making people less healthy and shorter-lived than hunter-gatherers. The key behaviour that allowed coordination of the first large human groups? The much-maligned habit of gossiping. Harari relishes in such informed reversals of conventional wisdom, and the book is full of similar gems. Weaved into a well-reasoned narrative, they build up a powerful and thought-provoking overview of human history that will convince, challenge, and sometimes puzzle – but never bore.

The Sixth Extinction: An unnatural history
Elizabeth Kolbert

The Sixth Extinction (Pulitzer Prize, 2015) also centres on the human conquest of the world, but from the perspective of the nine million other species that happen to share a planet with us. Unsurprisingly, humans are difficult to live with, and the book focuses on the mass extinction event that, according to scientific consensus, our activity is currently triggering. *The Sixth Extinction* is three books in one, each individually successful. The first is a treatise on the history of science, detailing how scientists slowly discovered the reality of past biological extinctions. The second is a field report, detailing Kolbert's eyewitness account of the sixth extinction and of the scientists studying it – from Amazonian rainforests to Australian corals. The third provides a popularisation of ecology and of what makes species vulnerable. Kolbert concludes putting forward an argument that what makes the sixth extinction so hard to prevent is that it is not the product of a single cause, but an unavoidable consequence of multiple, independently lethal ways our expansion and transformation of the world are affecting the environment. The conclusion is grim, but the demonstration is thoughtful and rigorous, and a must-read for anyone who wants to understand the current biotic crisis.

Kolbert and Harari are both wonderfully gifted writers, who manage to convey an impressive quantity of information without ever stopping to be entertaining and graceful. No ape, dolphin or robot can (yet) write such books, and their excellence stands testament to the multifarious prowess of *Homo sapiens*. Read them both, whether you are human or not, to better understand our unreasonable species.

Awards & honours

PHOTO: UNIVERSITY OF HEIDELBERG

This year's Ernst Ruska Prize, awarded by the German Society for Electron Microscopy, has been presented to EMBL Heidelberg group leader **John Briggs**. Named for the German physicist and Nobel laureate who designed the first electron microscope, the prize was jointly awarded to Briggs and Jürgen Plitzko of the Max Planck Institute of Biochemistry at the opening ceremony of the Microscopy Conference 2015 in September, in "recognition of contributions to cryo-electron microscopy of biological objects".

PHOTO: ROBERT SLOWLEY

Eric Karsenti, founder of EMBL's Cell Biology and Biophysics Unit and currently a visiting scientist, has been awarded one of France's highest scientific distinctions: the CNRS Gold Medal. "I feel very proud and grateful to have been selected by my peers to receive this award," says Karsenti. "However, I share it with all the excellent scientists from all fields who contributed to the projects I led: without their work and expertise nothing would have been possible." The award celebrates his exceptional career, marked by significant breakthroughs, pioneering interdisciplinary approaches, and efforts to push back the frontiers of knowledge as initiator of the Tara Oceans expedition.

PHOTO: EMBL PHOTOLAB

Head of EMBL Hamburg **Matthias Wilmanns** has been appointed professor of Biomedical Structural Biology at the Department of Medicine at the Universitätsklinikum Hamburg-Eppendorf (UKE). "I am very honoured to have been granted this professorship," says Wilmanns. "It is our hope and expectation that this appointment will reinforce the already successful cooperation between the UKE and EMBL, and help explore opportunities in structural biology research with important themes in molecular medicine." This appointment follows the signing of a cooperation agreement by the UKE and EMBL in April 2014, and the establishment of a joint PhD training programme.

Edward Lemke, group leader at EMBL Heidelberg, has been awarded a Young Chemical Biologist Award by the International Chemical Biology Society (ICBS). The award recognises the accomplishments of young investigators who have made ground-breaking contributions to chemical biology. Awardees give a presentation during a special 'Rising Stars' session at the annual meeting, which this year took place in Berlin, 7–9 October.

PHOTO: EMBL PHOTOLAB

Jan Korbel, group leader at EMBL Heidelberg, has been elected to the German Academy of Sciences Leopoldina, becoming the youngest member in the life sciences area. Founded in 1652, the Leopoldina is one of the world's oldest academies of science, with some 1500 members that represent world-leading scientists from across the globe. New members are invited to present a lecture at the official inauguration ceremony in May 2016. "It is a huge honour to be elected to the Leopoldina," says Korbel, whose election recognises his scientific achievements as well as his involvement with the ethical and legal self-regulation of science.

PHOTO: EMBL PHOTOLAB

Alumni

Activating alumni communities

This edition, we go behind the scenes of four recent alumni events – involving six countries from across Europe – that brought together EMBL staff, alumni and their colleagues from over 60 life science institutes, companies, government bodies and foundations. It is always great to see people benefiting from the institute's network after they move to pastures new and to hear of the new collaborations that result from these meetings. We wish all those in the EMBL community a great end to the year, and we look forward to catching up again in 2016!

Mehrnoosh Rayner
Head of Alumni Relations

PHOTO: EMBL PHOTOLAB

Science *is* collaboration

Rune Linding

Now: Professor and group leader, Biotech Research & Innovation Center, University of Copenhagen (UCPH)
At EMBL Heidelberg: 2000–2004, PhD Student Gibson Team; 2004, Postdoc, Russell Group

At EMBL...

One of the most important things I learned at EMBL, which has remained with me since, is: *science is collaboration*. Whilst it can be important to gather thoughts alone and focus on individual goals, in the end all groundbreaking life science requires intense and diverse work with other people and groups. At EMBL, one just needs to visit the Heidelberg cafeteria to feel a vibe that is present across the whole lab – the myriad of interactions between labs and people resembles an ants' nest!

Since then...

After leaving EMBL and before returning to Denmark, I trained at Mount Sinai Hospital in Toronto and the Massachusetts Institute of Technology in Boston, and then established my own lab at the Institute of Cancer Research (ICR) in London.

And now...

We are currently leading high-level, strategic, multidisciplinary studies of signalling network dynamics driving cancer metastasis in collaboration with other labs at Harvard, Yale, JAX, Memorial Sloan Kettering Cancer Center, MIT, and the University of Copenhagen. This level of collaboration is the EMBL legacy... at least one of them! We are focused on big data network biology, exploring biological systems by developing and deploying algorithms aimed at forecasting cell and tissue behavior. A strategic focus of our lab is the integration of genome-scale quantitative data we generate using mass spectrometry and genomic and phenotypic screens, with the aim to advance network medicine by identifying and targeting signalling networks associated with cancer.

Driving science in Denmark

EMBL alumni convened at the University of Copenhagen on 11 September for the first EMBL alumni meeting hosted in Denmark. The event, which followed an annual symposium held by the Core Facility for Integrated Microscopy (CFIM) in the Faculty of Health and Medical Sciences, featured an interdisciplinary programme of talks from EMBL staff, alumni, and guests, including Poul Nissen, Head of the Danish Research Institute of Translational Neuroscience (DANDRITE – the Danish node of the Nordic EMBL Partnership for Molecular Medicine) and Anne-Marie Engel, Research Director of the Lundbeck Foundation. The event, which also included social and networking aspects, was initiated and organised by alumni Laure Plantard, applications specialist at CFIM and Jutta Bulkescher, microscopy platform manager at the Novo Nordisk Foundation Center for Protein Research. Here, we catch up with two alumni who spoke at the event.

Captivating Copenhagen

Guillermo Montoya

Now: Professor, Novo Nordisk Foundation Center for Protein Research (NNF CPR)
At EMBL: 1994–2001, Postdoc, Sinning Group

After EMBL...

After leaving EMBL, I started my own lab at the Spanish National Cancer Research Centre (CNIO) in Madrid. There, the major challenge was to set up and start a new centre from scratch. After 6 years, I was promoted to senior group leader in 2007, and following 12 successful years in Spain, I was seduced by an invitation to lead a programme in structural cell biology in a young and dynamic centre at NNF CPR. I was ready for new professional and scientific challenges, and lucky to be supported by my family – there are terrific research possibilities in the city and surrounding area.

Research focus...

I am fascinated by the potential of combining different approaches, ranging from biophysics to cellular methods, to understand the gigantic chemical equilibrium that we find in the cell. In my view, many regulatory mechanisms have only so far been dissected in a very 'lineal' manner, but it is very clear that these different layers of cellular regulation are interconnected and contain important hubs that may be used to comprehend and target disease. It is therefore crucial to understand these networks from a structural and functional perspective.

Memories...

EMBL has been essential for my career: I arrived in Heidelberg as a well-trained biochemist and biophysicist. My thesis – chasing intermediate states of charge separation in photosystem II using femtosecond pulsed laser spectroscopy – enabled me to immerse myself much deeper in molecular, developmental, and cell biology. The integrative nature of EMBL makes it an excellent place for such an immersion, and it is hard to think of somewhere better anywhere in the world! The various seminar programmes were always an invaluable source of new information as well as the many opportunities for discussion over coffee or even at parties; being there was very exciting, a bit like jumping into a pool from a very high platform!

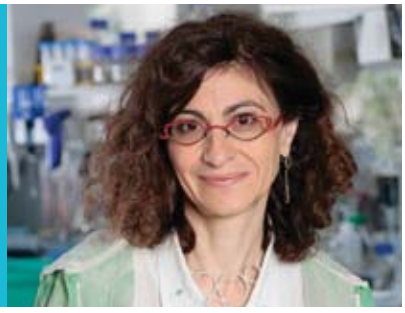
Uniting alumni at The EMBO Meeting

Staff and alumni had the opportunity to catch up over drinks, exchange information, reconnect with former colleagues and make new contacts at The EMBO Meeting on 7 September. A drinks reception was followed by dinner at Cielo's restaurant in the lively environment of Birmingham's Brindley Place. "Holding our reception at The EMBO Meeting – and its predecessor the ELSO Meeting – has been a priority for us since 2005, benefitting from an event that generally attracts the EMBL/EMBO community at large," says Matthias Hentze, EMBL Director. Here, we catch up with two members of the community attending the event.

Curi(e)ous connections

Genevieve Almouzni

Now: Research Director, Institut Curie, Paris, 2013-current
At EMBL: 2005–2010, Scientific Advisory Committee member



Relationship with EMBL...

I learnt about EMBL's role and exceptional science while serving as a member of the EMBL Scientific Advisory Committee. This has been a reference point for me ever since. I really enjoy interacting with groups at EMBL and feel I have been adopted into the community. So much happens all the time at the Lab that, as a scientist, you want to keep watching what is happening there and, as a director, you want to foster exchange at many levels to develop your own approach.

Defining qualities of the IC...

My predecessor at the Institut Curie (IC), Daniel Louvard, was an EMBL alumnus, who headed the organisation for two decades. Under his leadership, cell biology and developmental biology have really taken off, and the interface between physics and cell biology also found a fantastic springboard. Daniel went to great efforts to promote young investigators: I am living proof as the first junior group leader beginning at the institute – how time flies! My vision is to build on these areas and assets and take them further with a spirit that I call Curi(e)osity.

We have four broad programmes at the IC: biology of radiations; development, cancer, genetics and epigenetics; integrative tumour biology; and multi-scale physics-biology and chemistry. We also have connections to the hospital, which we would like to further develop. The challenges ahead are to ensure an exciting environment in which collaborative and collective efforts are rewarded, and the IC presents some unique opportunities to do this.

Researcher vs Director...

Also important are networking events, such as this one, which present great opportunities to exchange ideas – it can also lead to great collaborations, something that is key to balancing scientific activities with that of Director!

The 6th EMBO Meeting took place at the ICC in Birmingham from the 5–8 September, and there were plenty of ways for participants to network.

PHOTO: MARTYN HICKS

Integrating information

Nicolas Le Novère

Now: Group Leader, Babraham Institute, Cambridge
At EMBL-EBI: 2003–12, Group Leader

Research focus...

I organised a special interest symposium around this year's EMBO Meeting themed on the systems biology of epigenetics and cell fate. We wanted to showcase success stories of interdisciplinary research featuring computational and experimental work. An interdisciplinary approach is very much a part of my own research: since leaving EMBL-EBI and joining the Babraham Institute three years ago, I have expanded the type of bioinformatics that I do besides computational modelling, for example in the direction of lipidomics and gene expression. I find the domains of stem cells and epigenetics hugely exciting: linking cellular signalling, metabolism and epigenetics is crucial for understanding cellular reprogramming, or the basis of longevity and healthy ageing. These questions are not just biological and as a modeller they present some exciting challenges. Currently, there are many modelling approaches on many different levels and ultimately we want to integrate this information in multi-scale models to develop a global understanding of cell response to the environment.

Life at the Babraham...

The Babraham Institute is small but prestigious. Historical discoveries made here include the liposome, IP3 and PIP3 signalling and maternal imprinting by DNA methylation, and this excellence continues today. Like at EMBL, there is also a vibrant seminar series and social events that enable people to stay updated on the latest science at the institute. I did not cut all bridges with EMBL-EBI though. When I left, part of my group responsible for developing resources for computational systems biology such as BioModels, stayed behind in Henning Hermjakob's team and we maintain strong collaborations to this day.

Memories...

I nevertheless miss the family spirit of EMBL – during nine years at EMBL-EBI, I felt my office was part of my home and my co-workers were my friends. I also miss the group leader retreats – especially the discussions, the post-it note activities, and walks along the beach. Who would have thought I would ever say that?!

The next chapter

We go behind the scenes of EMBL alumni chapter meetings in Leuven and Zürich.

"For EMBL and the Benelux, I see two opportunities: Firstly to further strengthen ties between the Dutch/ Benelux scientists and EMBL in order to benefit much more from what EMBL has to offer. Secondly, to create career perspectives for scientists at EMBL, or elsewhere outside the Benelux, and searching for job opportunities back home." *Gerrit van Meer* (right)

Vera van Noort, Associate Professor, KU Leuven (EMBL Heidelberg: Staff Scientist, 2007-2013); **Gerrit van Meer,** Dean & Professor, Utrecht University, (EMBL Heidelberg: Staff Scientist, 1981-1987) and now also EMBL Council delegate for the Netherlands

More than 50 participants convened in Leuven on 23 October for an EMBL Benelux event involving speakers and participants from Belgium, the Netherlands and Luxembourg. The aim of the meeting was to offer those connected with the EMBL, and VIB institute communities to network, share and explore collaboration possibilities.

Adriano Barbosa, Research Associate, University of Luxembourg (EMBL Heidelberg: Visitor, 2006-2007); **Luis Pedro Coelho**, Postdoc, EMBL Heidelberg; **Josiane Entringer**, EMBL Council Delegate for Luxembourg; Deputy Director, Ministry of Research and Innovation, Luxembourg

"In the era of Translational Research & Big Data, I believe that the interdisciplinary and multi-center approaches to understand human diseases should be facilitated by the adoptions of standardized systems for data collection, representation and exploration." *Adriano Barbosa* (far left)

"It is enormous to envision the complexity of developing a novel drug from the beginning to the end. This is possible only with intensive joint interdisciplinary efforts and a truly collaborative spirit. Our journey of transforming science into medicine starts and ends with the patient and builds on bringing together the right ideas and people. Switzerland is the ideal place as some of the world's leading pharma companies are located here as well as top-notch academic science. Bringing these two partners together is incredibly powerful and a key step in order to maintain this sustainable world-class scientific landscape. It is great to meet EMBL alumni and to see their alternative career paths – such events are fundamentally important to make key contacts for the future, to foster new collaborations and to inspire young researchers for their path ahead." *Christoph Bieniossek* (second from left)

Matthias Haffke, Postdoc, Novartis Pharma, Basel (EMBL Grenoble: PhD Student, 2010-2015); **Christoph Bieniossek**, Senior Scientist, Roche Pharmaceuticals (EMBL Grenoble: postdoc, 2009-2013); **Michael Hennig**, Director, F. Hoffmann - La Roche Ltd. (EMBL Hamburg: PhD Student, 1990-1993); **Imre Berger**, EMBL Grenoble Group Leader

The first EMBL alumni event in Switzerland took place at the University of Zürich on 6 November, bringing together EMBL staff, alumni and their networks from academia, industry and government.

Judith Zaugg, EMBL Heidelberg group leader; **Andrea Picco**, Postdoc, University of Geneva (EMBL Heidelberg, Postdoc, 2008-2015); **Peter Blattmann**, Postdoc, ETH Zurich (EMBL Heidelberg, PhD Student, 2008-2013)

"The EMBL alumni event in Switzerland was a great opportunity to meet old friends and colleagues and to be introduced to new ones. I found it very interesting to learn about the diversity of career paths that each of us took, the histories behind each experience and how all of these relate to great science. Truly inspiring." *Andrea Picco* (centre)

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Friends in high places: A sunset rooftop soiree at EMBL Heidelberg in October was the setting to inspire conversations and connections at the first Friends of EMBL Ladies Night, where amidst a packed programme, Ailsa Mattaj, wife of EMBL Director General Iain Mattaj, presented Minister Theresia Bauer with a certificate of lifetime honorary membership.

EMBL in pictures

A snapshot of the many activities and events taking place in the world of EMBL.

PHOTO: ROBERT SLOWLEY

PHOTO: EMBL PHOTOLAB/ MARIETTA SCHUPP

PhD Students Anna Steyer and Katharina Zirngibl explore the science behind Jurassic Park, before the film was shown to more than 200 people at the second EMBL Science Movie Night on 29 October.

All aboard: Romain Trouble, Eric Karsenti, Guy Cochrane, Silke Schumacher and guests aboard Tara when the research schooner visited London in September.

Eat that! The “father of molecular gastronomy” Hervé This, of the National Institute for Research in Agronomy, Paris, serves up a surprise during this year’s postdoc retreat. The event took place 14–16 October in Alsace France, bringing more than 70 postdocs together from across EMBL’s sites. More soon on: news.embl.de.

PHOTO: EMBL/ADAM GRISTWOOD


PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

No coincidence: organisers of this year's PhD Symposium gather at EMBL Heidelberg 22–24 October for *Just by Chance? Randomness and variability shaping biology.*

PHOTO: ROBERT SLOWLEY


PHOTO: EMBL/ANGELA MICHEL

What's a typical day for an Ensembl Outreach Officer? Emily Perry shows us at EMBL-EBI Open Day 2015 on 29 October.

Light fantastic: EMBL's European Learning Laboratory for the Life Sciences (ELLS) presented practical workshops and interactive activities on 22–24 October at Science Days 2015 in Rust, near Freiburg, Germany. One of Germany's largest science festivals, the event attracted more than 20 000 visitors, and was themed on "Fascination Light".


PHOTO: DESY

Fishing for crystals at DESY Day on Hamburg's Night of Science in Hamburg on 7 November (see page 37).


PHOTO: JIN WANG

Creative commons: Seven EMBL fellows attended this year's Roche Continents festival in Salzburg 11–17 August. The event brings together 100 students from across Europe to explore music and the creative processes within arts and science. For more, go to news.embl.de.

Events

November
27

EMBL Heidelberg
EMBL Distinguished Visitor Lecture: Nicholas Proudfoot, University of Oxford


IMAGE: EMBL-EBI/SPENCER PHILLIPS

December
10

EMBL Heidelberg
EMBL Distinguished Visitor Lecture: Marianne Bronner, California Institute of Technology

January
26-29

EMBL Heidelberg
EMBO | EMBL Symposium: A new age of discovery for aquatic microeukaryotes


IMAGE: EMBO/ADITYA KUSUMA JATI

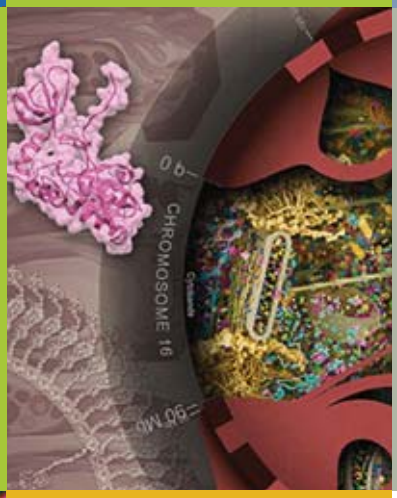
January
29

EMBL Grenoble
Science and Society Symposium: Science and religion in a globalised world: conflict or conciliation?


PHOTO: MIROSLAW LEGEZA

March
9-11

EMBL Heidelberg
EMBO Conference Series: Visualizing Biological Data (VIZBI 2016)



April
1

EMBL Monterotondo
EMBL Distinguished Visitor Lecture: Sheena Josselyn, The Hospital for Sick Children, Toronto

April
3-6

EMBL Heidelberg
EMBO | EMBL Symposium: Tumour microenvironment and signalling

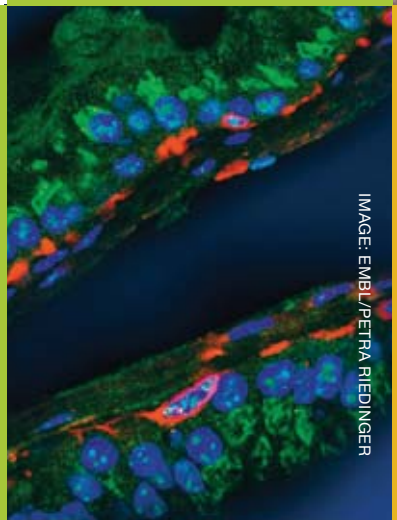


IMAGE: EMBL/PETRA RIEDINGER

Upcoming meetings
Alumni

25 November: **Stammtisch, Urban Kitchen, Heidelberg**
15 January: **Local Chapter meeting France, EMBL Grenoble**
27 May: **Local Chapter meeting Italy, Sapienza University, Rome**

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