FUTURA

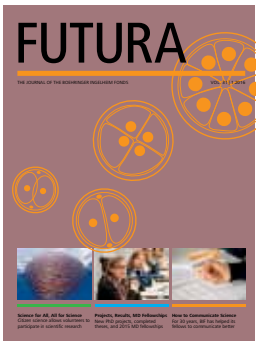
THE JOURNAL OF THE BOEHRINGER INGELHEIM FONDS

VOL. 31 | 1.2016

Science for All, All for Science
Citizen science allows volunteers to participate in scientific research

Projects, Results, MD Fellowships
New PhD projects, completed theses, and 2015 MD fellowships

How to Communicate Science
For 30 years, BIF has helped its fellows to communicate better



The cover illustration shows a simplified model of the early stages of mammalian embryogenesis up to the morula and early blastula stage. In her project, BIF fellow Victoria Rodriguez Vaello is examining how the pluripotent stem cells of the embryo transition from the naive to the primed pluripotency state, and what role alternative splicing plays in this process. Read more on page 24.

FACTS

SCIENCE FOR ALL AND ALL FOR SCIENCE

FELLOWS

NEW PHD PROJECTS, THIRD ROUND 2015

NEW PHD PROJECTS, FIRST ROUND 2016

PHD RESULTS

MD PROJECTS

FOUNDATION

THE "UNNECESSARY PIXEL ACT"

PERSPECTIVES

PROFILES

IMB AND IPP: ATTRACTING TOP TALENT TO MAINZ

PUBLISHING INFORMATION

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Stiftung für medizinische Grundlagenforschung
Schusterstr. 46–48
55116 Mainz
Germany
Tel. +49 6131 27508-0
Fax +49 6131 27508-11
E-mail: secretariat@bifonds.de
www.bifonds.de

Editor-in-Chief Dr Claudia Walther

Editors Kirsten Achenbach (BIF, executive editor), Karsten Fiehe (muehlhausmoers corporate communications gmbh)

Authors in this issue Kirsten Achenbach, Kat Arney, Bianca Gapp, Colinda Scheele, Dr Claudia Walther

Translating, copy-editing and proofreading Adam Blauhut, Dr Caroline Hadley, Dr Susan Simpson

Production muehlhausmoers corporate communications gmbh, www.muehlhausmoers.com
Project management Karsten Fiehe
Art direction Britta Siebert

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LOST IN TRANSLATION

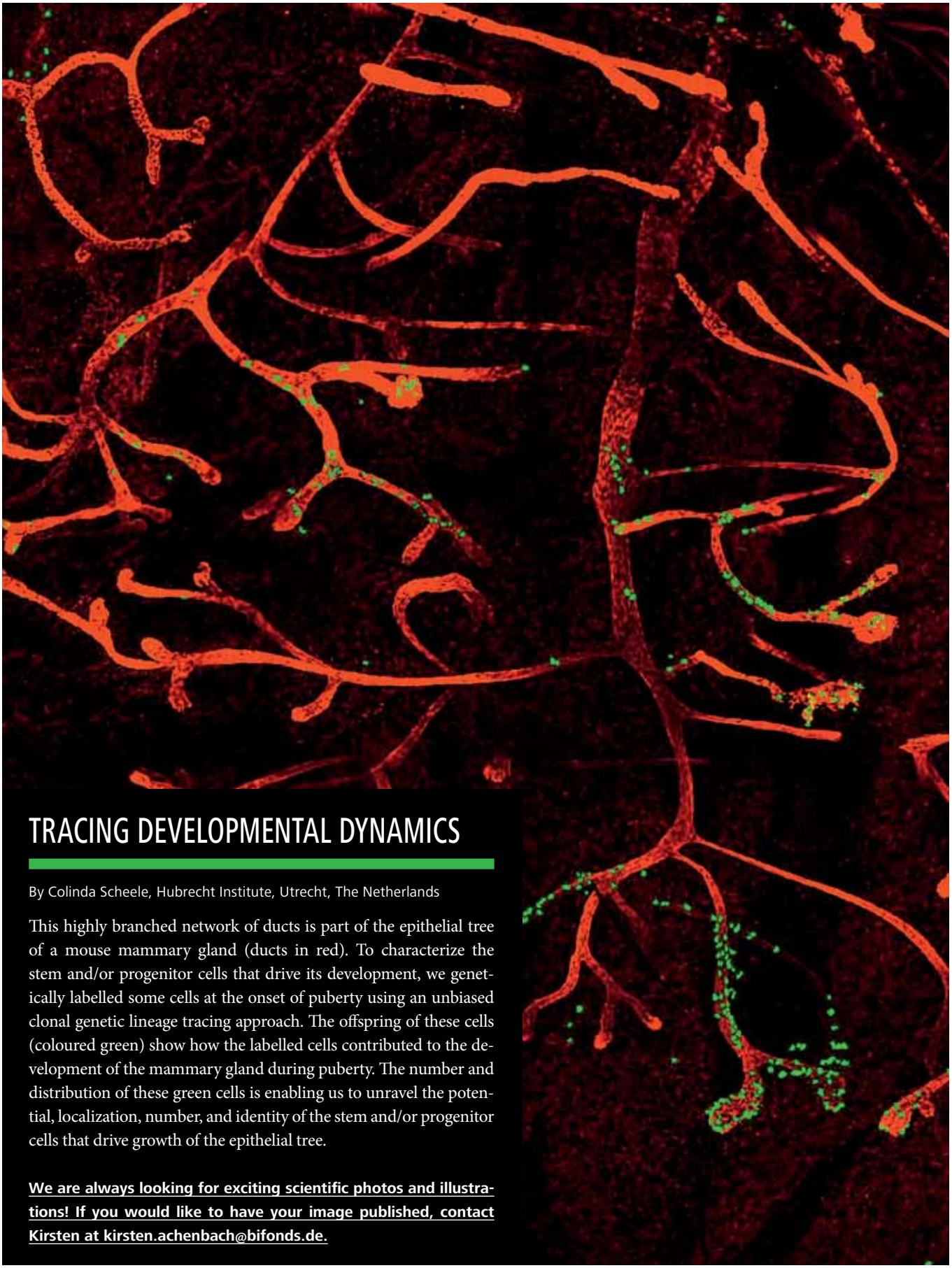
It began with a failure – at least from the perspective of scientific exchange. In the early 1980s, eager fellows presented their research projects at BIF's first summer seminar. However, many could not follow the talks of their fellow biologists or biochemists; it proved difficult to bridge the gap between even closely related disciplines. In the following year, BIF started communications training – long before "soft skills" became a familiar term in academia. This year, the seminar celebrates its 30th anniversary.

During the 5-day training, experts teach writing, graphic design, and oral presentation skills and give detailed personal feedback. Albeit using modern technology, the seminar follows the most important rhetoric theories of ancient Greek philosophers. Back then, the advent of democracy had made speeches and discussions critical to decision making. "Rules" and approaches for presenting a case convincingly were discovered, and for a long time, many cultures considered rhetoric as a part of higher education and important to personal refinement. We do not aspire to transform our fellows into Ciceros or Shakespeares – neither do we teach scientific paper writing (today offered by any serious PhD programme). We aim for the rhetoric fundamentals – relevant for all audiences and situations, inside and outside of science.

"Good communication skills have become more and more important to researchers, too."

While good communication skills are not even surrogate markers for scientific quality or a brilliant mind, they have also become more and more important to researchers: an outstanding poster, a clear talk, a convincing cover letter, a well-conducted interview, a precisely and concisely formulated abstract or grant proposal – all help to get noticed, published, read, cited, hired, or funded.

Winning the necessary support of the public and policy makers for funding and a framework conducive to basic research is even more of a challenge. BIF prides itself on supporting outstanding scientists. Shouldn't it be exactly those who inspire and spark enthusiasm for discovering new galaxies or answering intriguing biological questions? Or making research the talk of the day? Thereby, securing it the space it deserves and igniting discussions as a vital part of democracy? To those ends, scientific stories need to be told in a way that captures the audience – and, also importantly, in the native language, be it German, Spanish, or Chinese. This requires stepping out of the ivory tower fenced in by the lingua franca of the natural sciences: English. Without researchers who are willing and able to do this, no discipline will win society's support or inspire the next generation of scientists. After all, love and fascination for a subject usually bud long before a foreign language or scientific termini are learned.



TRACING DEVELOPMENTAL DYNAMICS

By Colinda Scheele, Hubrecht Institute, Utrecht, The Netherlands

This highly branched network of ducts is part of the epithelial tree of a mouse mammary gland (ducts in red). To characterize the stem and/or progenitor cells that drive its development, we genetically labelled some cells at the onset of puberty using an unbiased clonal genetic lineage tracing approach. The offspring of these cells (coloured green) show how the labelled cells contributed to the development of the mammary gland during puberty. The number and distribution of these green cells is enabling us to unravel the potential, localization, number, and identity of the stem and/or progenitor cells that drive growth of the epithelial tree.

We are always looking for exciting scientific photos and illustrations! If you would like to have your image published, contact Kirsten at kirsten.achenbach@bifonds.de.

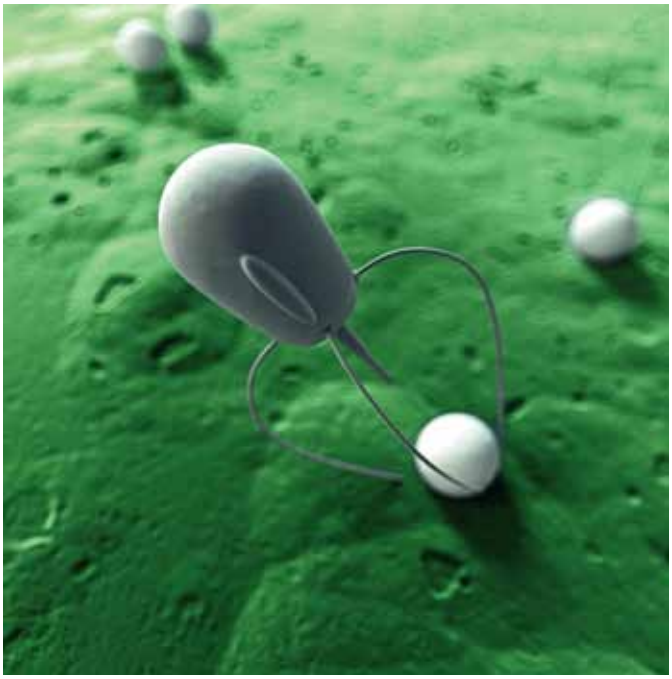
BRIGHT BUTTERFLIES, DARK MOTHS – SAME GENE

The peppered moth, *Biston betularia*, is an icon of evolution through natural selection. Countless schoolchildren have learned the story of how dark melanic versions of the insect became predominant during the 19th-century British industrial revolution, hiding on soot-covered trees while their pale cousins – previously safe on light lichen-covered trees – were picked off by predators. In another example of the power of evolution, it turns out that the gene responsible for this switch from pale to dark also lies behind the bright wing patterns of *Heliconius* tropical butterflies in South America, a world away from grimy Victorian smoke stacks. There are around 40 different species of *Heliconius*, whose brightly coloured wing patterns enable them to mimic other more toxic species and ward off would-be attackers. Through careful genetic analysis, researchers discovered that variations in a rapidly evolving gene called *cortex* – which helps to control cell division in the wings of butterflies and moths – causes their exotic patterning by determining when and where different colours appear. They also found that a mutation in *cortex*, which first arose in the mid-1800s, turns pale peppered moths into dark ones. Many hundreds of genes are involved in making a moth or butterfly's delicate wings, but one and the same helps moths to hide themselves and gets butterflies noticed.

REFERENCE

Nadeau N, Pardo-Diaz C, Whibley A, Supple M, Saenko S, Wallbank R *et al (2016)* The gene *cortex* controls mimicry and crypsis in butterflies and moths. *Nature* **534:** 106–110

ROBOTIC "ANTS" DELIVER DRUGS



The days of miniature nanovoyagers in the body delivering drugs could be closer than we think.

The idea of tiny nanorobots – one hundred thousand times smaller than the width of a human hair – travelling inside the body delivering drugs seems like science fiction, but it could one day become a reality. A key problem has been creating nanoscale machines that can generate enough power to move through blood or other fluids, which at this scale become denser than honey is for us. Scientists at Cambridge University have solved this challenge by developing tiny machines known as activating nanotransducers, or ANTs for short, made of gold nanoparticles coated with a thin polymer layer. When placed in a liquid and heated with a precision beam of light, the polymer becomes hydrophobic, causing the nanoparticles to expel water molecules and draw close together. Upon cooling, the polymer again takes up water and the particles spring apart, generating an impressive kick for their tiny size – ten to a hundred times more powerful than any existing engine or muscle cell. The researchers hope to use the repeated constriction and expansion to create a piston-like action that can power nanomachines. All the components are relatively cheap and more economical metals such as silver, nickel, or copper could also be used.

REFERENCE

Ding T, Valev V, Salmon A, Forman C, Smoukov S, Scherman O *et al* (2016) Light-induced actuating nanotransducers. *PNAS* **113:** 5503–5507

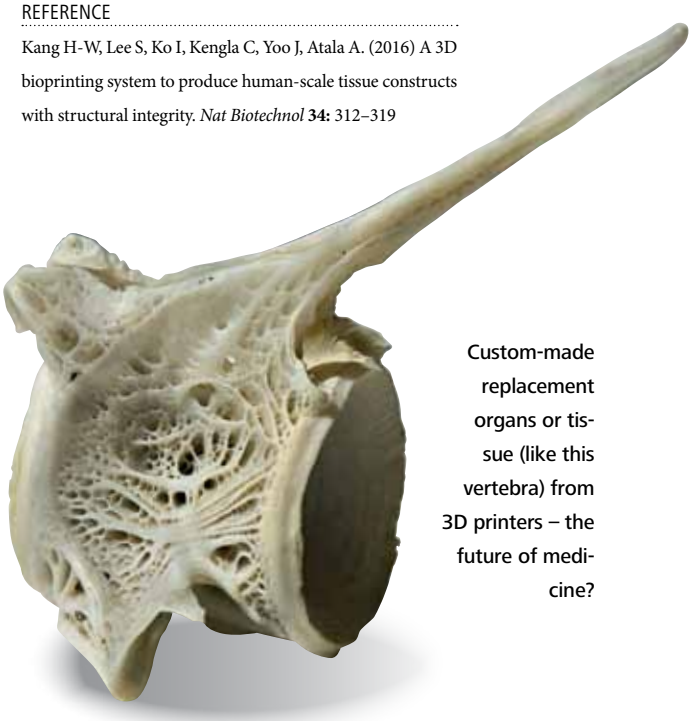
Photos: Wikimedie/Olaf Leillinger (top); shutterstock (bottom)

ORGANS PRINTED TO ORDER

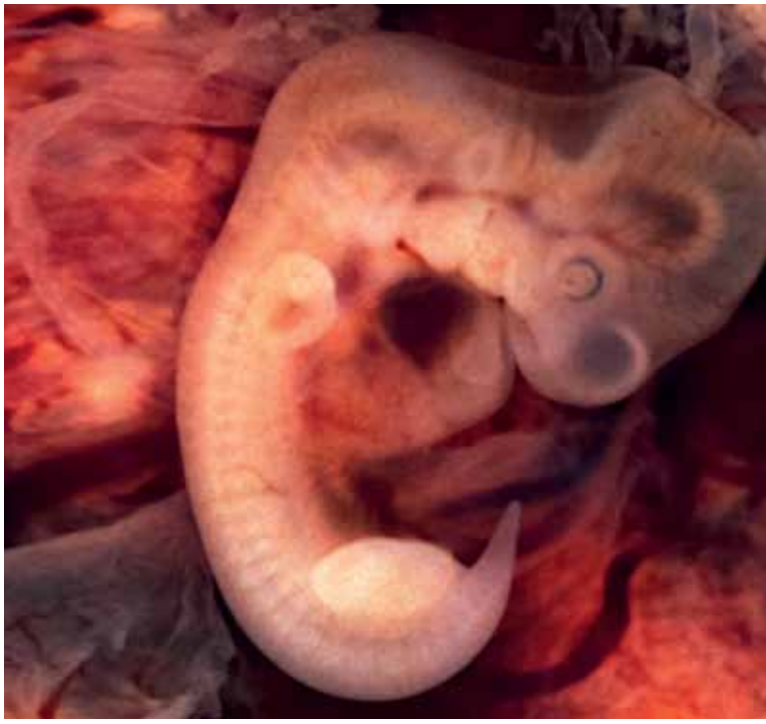
Rather than searching for a suitable donor, people could one day simply pick up replacement organs from the printers. Researchers at the Wake Forest Institute for Regenerative Medicine in the US have used three-dimensional bioprinting to create new tissues on a human-sized scale, opening the door to generating whole structures and organs for transplantation. Initially, the team used a specially modified 3D printer to create replacement pieces of skull bone and sections of muscle tissue, which were successfully transplanted into rats, quickly knitting into place and functioning. They then used the technique to print cartilage-producing cells into the shape of a human ear, based on data from a computer tomography scan. The ear grew and developed normally when transplanted onto the back of a mouse. In a final demonstration, the scientists printed a small piece of human jawbone, proving that they can create structures that have the right shape and size for transplantation. The team also aims to make implantable muscle, cartilage, and bone for human patients in the near future.

REFERENCE

Kang H-W, Lee S, Ko I, Kengla C, Yoo J, Atala A. (2016) A 3D bioprinting system to produce human-scale tissue constructs with structural integrity. *Nat Biotechnol* **34:** 312–319



Custom-made replacement organs or tissue (like this vertebra) from 3D printers – the future of medicine?

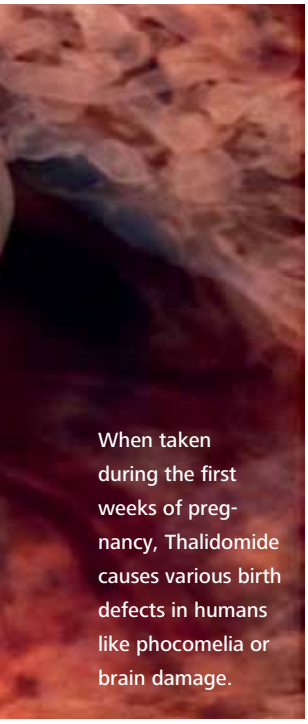


SECOND CHANCE FOR THALIDOMIDE

Notorious for having caused birth defects when given to pregnant women as a treatment for morning sickness in the late 1950s and early 1960s, the drug thalidomide has been reinvented as a cancer treatment in recent years – after it had already been shown to be effective against lepra. Two closely related drugs – lenalidomide and pomalidomide – are currently approved for tumours such as multiple myeloma, with fewer side effects than thalidomide itself. But it remained a mystery exactly how thalidomide caused its devastating effects in developing babies, or how these treatments work against cancer. German researchers have now discovered that a protein called cereblon normally brings together two other molecules, CD147 and MCT1, to create a complex that promotes cell proliferation and the growth of new blood vessels – processes that are vital for fetal development as well as the growth and spread of tumours. Thalidomide-based drugs almost completely disrupt this interaction, stopping cancer in its tracks and also causing the devastating birth defects. The hunt is now on for other drugs that can disrupt the interaction between cereblon and its partners, which could become powerful future cancer therapies.

REFERENCE

Eichner R, Heider M, Fernández-Sáiz V, van Bebber F, Garz A-K, Lemeer S *et al* (2016) Immunomodulatory drugs disrupt the cereblon-CD147-MCT1 axis to exert antitumor activity and teratogenicity. *Nat Med* **22:** 735–743



When taken during the first weeks of pregnancy, Thalidomide causes various birth defects in humans like phocomelia or brain damage.

MALARIA-MICROBIOME LINK

The bacteria living in our guts might be key to fighting malaria.

Our microbiome – the bacteria living within and upon us – is a hot topic in research. Now a new study from scientists at the University of Tennessee has revealed an unexpected link between gut bugs and the severity of malaria infection. The disease is caused by the parasite *Plasmodium*, and although there are more than 200 million cases globally every year, there's a large range of symptoms experienced by individual patients, from non-existent to life-threatening. By studying genetically identical mice, each colonized with a unique microbiological mix, the researchers discovered that animals carrying relatively high numbers of *Bifidobacteria* and *Lactobacilli* were less likely to show symptoms of malaria infection. Treating susceptible mice with antibiotics, then giving them yoghurt made from these two bacterial genera significantly reduced the burden of *Plasmodium* parasites in the animals. It's not known exactly how these bacteria are affecting malaria infection, but it seems likely that they could be stimulating the immune system to fight the parasite or combating other strains of bacteria that encourage it to grow. The results suggest that changing the microbiome might be an effective way to reduce the severity of malaria infection and potentially save thousands of lives.

REFERENCE

Villarino N, LeCleir G, Denny J, Dearth S, Harding C, Sloan S *et al* (2016) Composition of the gut microbiota modulates the severity of malaria. *PNAS* 113: 2235–2240

LIQUID CRYSTALS FIGHT FRAUD

Despite the best efforts of the public, private companies, and the police, many people will find themselves the victim of fraud, theft, or forgery at some point. Whether it's a cloned credit card, a stolen phone, or a copied passport, the personal, financial, and security impacts can be severe. It's increasingly important to have secure and reliable identification, but however carefully security devices are designed, fraudsters eventually work out a way to copy them. Now researchers at the University of Vienna have discovered a powerful weapon in this war on crime in the form of tiny microspheres made from a shell of liquid crystals, like a hollow football. These can be cheaply manufactured with a unique reflection pattern, rendering them – so far – impossible to copy but easy to "read" and verify. Like a butterfly's iridescent wings, the liquid crystals arrange themselves into structures that reflect light in characteristic but completely individual ways. Combining shells increases the dazzling diversity and the security even further. Although they are remarkably robust and can stand up to normal handling, any attempt to alter or manipulate the crystals ruins the pattern, making them tamper-proof too – hopefully for a very long time.

REFERENCE

Geng Y, Noh J, Drevensek-Olenik I, Rupp R, Lenzini G, Lagerwall J. (2016) High-fidelity spherical cholesteric liquid crystal Bragg reflectors generating unclonable patterns for secure authentication. *Sci Rep* **6:** 26840

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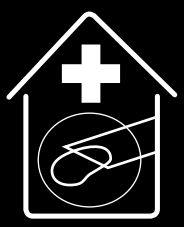
CLINICS



An alarming number of companies in the US are offering unapproved stem cell therapies, according to a new investigation published in *Cell Stem Cell*. More than 350 companies are providing treatments at 570 clinics, raising concerns that patients could come to harm, miss out on proven treatments, or lose the opportunity to take part in clinical trials.

Source: Turner L, Knoepfler P (2016) Selling stem cells in the USA: assessing the direct-to-consumer industry. *Cell Stem Cell* **19:** 154–157

Photos: flickr/cisc1970 (bottom left); Wikimedia (top middle); Wikimedia/NIAID (top right)

Just as a swarm can sample a larger volume for food, citizen science can create more data.

SCIENCE **FOR ALL AND ALL FOR** SCIENCE

By Kirsten Achenbach

Science is done by scientists. But no longer exclusively. Citizen science is a movement that calls for volunteers from the broad public to get involved in research projects that range from identifying beetles to describing art and gazing at the stars. While some projects are more about creating a wider understanding of science, others enable research that otherwise could not be done.

Hunt tigers, go on special missions, and maybe even become superheroes – these are things scientists ask ordinary citizens to do, at least if they are volunteers of "Mosquito Alert" and use its mobile device app. This citizen science project, financed by the Spanish Public Health Agency and headed by the Blanes Centre for Advanced Studies (CEAB) in Girona, was launched in 2014 to monitor the spread of the Asian tiger mosquito. Its arrival in Spain – and other parts of Europe – is alarming as it can spread viruses like dengue, Chikungunya, or Zika. From July 2014 to November 2015, the app was downloaded around 17,000 times and 5,700 tiger mosquitoes and 770 breeding sites were reported.

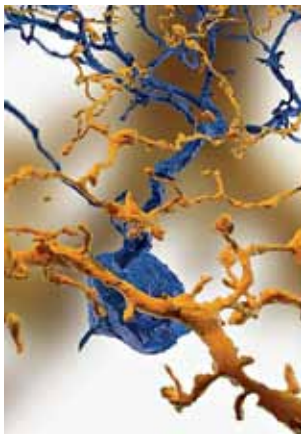
Such projects engaging ordinary citizens in the scientific process are gaining traction, especially since smartphones have made the act of sharing data a staple of daily life. The hope, according to the strategy paper of the European Citizen Science Association, is to "unleash potential for scientific research through increased data provision, better research design, and production as well as enhanced transfer of different knowledge forms." It will also teach non-scientists how science works. Several governments have picked up on and are fostering this trend – for example, the German Ministry of Science, which has launched a 4 million euro programme to finance such projects.

The scientists behind Mosquito Alert cannot even start to dream of a budget that would allow them to gather as much data as the app users generate for free. Even if they had the money, they could not always go where the citizen scientists go: tiger mosquitoes like to breed in small stagnant pools of water that are often found on private grounds – flower pots, water barrels, ornamental fountains, and bird baths. Another plus: the project raises awareness of the problem in a very direct way, encouraging people to take action. Drying out such potential breeding sites is still the safest and most efficient way to control any kind of mosquito. "So as long as we have a 'critical mass' of citizens involved, the system becomes really functional and cost-effective," explains Professor Frederic Bartumeus from CEAB, head of the project. This allows the specialists to focus on analysing the data and controlling the mosquitoes instead of searching for them.

Ensuring data quality is one of the greatest challenges when trained scientists rely on data from contributors with unknown qualifications. For Mosquito Alert, the numbers are encouraging; already in the second year of the programme, the reliability rating rose from 16% to 40% medium or high reliability. "Mosquito Alert uses two parallel validation systems," says Bartumeus. "On the one hand, pictures are validated by expert entomologists, and on the other hand, the pictures from citizens are sent out to crowdcrafting.org, where the citizens themselves can validate the pictures." Crowdcrafting exploits the power of the group, →

Photo: RGB Ventures/SuperStock/Alamy Stock Foto

WANT TO GET INVOLVED? FROM DESCRIBING THE MONA LISA TO STAR GAZING



Eyewire
In Eyewire, more than 200,000 players from 145 countries trace the 3D structure of nerve cells in electron microscopy images of the retina. The data is being used to map the retina's wiring diagram and thus the basis for information processing. The researchers also hope to teach computers this task. A further game named Brainflight is being developed to map the connections in the whole brain – the connectome.
www.eyewire.org (info at: blog.eyewire.org, English only)

Loss of the Night
This project investigates how the ever brighter night sky affects ecology, culture, and human health. With its app, people can estimate how many stars they can see and by extrapolation how bright the night sky is. More than 14,000 users downloaded the app and sent in approximately 4,000 observations. All data are shown online and some were used to calibrate satellite measurements for the "New World Atlas of Artificial Night Sky Brightness".
www.verlustdernacht.de (English, German)

ARTigo
The some 60,000 players of the browser game ARTigo tag digitalized artworks with keywords to enable art historians to find, compare, and analyse the works. The game, developed by the Ludwig-Maximillian-Universität (LMU) in Munich, Germany, so far has produced 9.5 million tags for the 150,000 images in its databanks. It is funded by the German Research Foundation (DFG).
www.artigo.org (English, German, French)

senseBox
The senseBox is a do-it-yourself kit for stationary and mobile sensors developed by the University of Münster, Germany. Citizens and schools use it to measure environmental data on climate, air quality, traffic, etc. and thus to contribute to more accurate statements about local environmental phenomena. The data from the more than 220 boxes and their 57 million measurements are visualized online.
www.sensebox.de (English, German)

whose aggregated opinion can be very close to that of an expert for certain questions – something that many episodes of "Who Wants to be a Millionaire" demonstrate. If a picture has been rated by 30 users, it appears in the map. "Running the true-expert system in Spain and a citizen's validation system that can be global will allow us to gain interesting knowledge about citizens' performances and check map reliability," says Bartumeus. As there are so many different species of mosquitos, the German citizen science project "Mückenatlas" – Mosquito Map – asks people to send whole mosquitos to the experts, not just pictures. They want to map not just two species, but, if possible, all 51 that occur in Germany today. And for that they need to see tiny details like hairs and scales on the insects' body or legs.

Other citizen science projects do not ask for the collection of specimen or new data, but for computer power to crunch data. Some probably remember the colourfully oscillating graph of one of the oldest of these projects: SETI@home, which searched for signs of intelligent life in extraterrestrial radio signals. Others go one step further and ask for minds to interpret existing data. One example is Galaxy Zoo, arguably the world's best-known online citizen science project and certainly the one with the largest number of publications based on the citizen scientists' input – 48 by 2015. It started out in 2007, when a data set with millions of galaxies was made accessible online and people were asked to categorize them into ellipticals, mergers, and spirals and — if the galaxy was spiral — to record the direction of the arms. "With so many galaxies, we as-

Photo: Alex Norton/EyeWire (top left); ARTigo (bottom left); www.verlustdernacht.de (top right); WWU/ifgi (bottom right)

sumed it would take years for visitors to the site to work through them all," the project team recalls on its website. "But within 24 hours of the launch, we were stunned to be receiving almost 70,000 classifications an hour." The volunteers' enthusiasm might also have been fired by a statement from Dr Chris Lintott, a member of the University of Oxford team who devised the project. "You get to see parts of space that have never been seen before. These images were taken by a robotic telescope and processed automatically, so the odds are that when you log on, that first galaxy you see will be one that no human has seen before." This sense of being part of something bigger than yourself seems to hold large appeal for the people giving untold hours to endeavours like this.

In a side project of Galaxy Zoo just this year, two Russian citizen scientists were not only co-authors of a scientific paper, something that happens more and more, but now have their names written in the stars: working in tandem, they discovered a rare so-called wide-angle tail galaxy more than one billion light years away containing at least 40 galaxies. Its host cluster is now known as the Matorny-Terentev Cluster. The lead author of the study, Dr Julie Banfield of CAASTRO at the Australian National University (ANU), said that the discovery surprised the astronomers running the programme. "They found something that none of us had even thought would be possible." The success of Galaxy Zoo was so overwhelming that it gave rise to Zooniverse, a platform for citizen science projects that today has 1.1 million registered users and has launched diverse projects.

While Galaxy Zoo started out asking very simple questions about shapes, FoldIt from the very beginning tasked people with figuring out which three-dimensional shape certain amino acid chains assume when they spontaneously fold themselves into a working protein. This shape is unique for every protein and is the most stable state it can adopt. Finding this shape for a given protein is a very specific scientific question with which most non-scientists would never come into contact. It is neither a trivial nor simple question, but still one, it turns out, that people can help answer without a science background. But how does a scientist even get the idea to ask ordinary people to answer such a question?

FoldIt's forerunner, Rosetta@home, started out similarly to the SETI@home project, just asking for computing power in times when the participants' computers were not in use. It also let people watch what their computer was working on. Unlike the incomprehensible radio signals of the SETI project, however, people intuitively saw solutions to how the proteins could be folded better. And they were frustrated when the computer mindlessly worked through endless possibilities. "People were writing in, saying 'Hey! The computer is doing silly things! It would be great if we could help guide it,'" remembers David Baker, HHMI investigator at the University of Washington, who developed the Rosetta algorithm and network.

Not much later, he discussed the problem with his neighbour, a computer scientist, while hiking. He suggested a project along the lines of a multiplayer game – the FoldIt project was born. His neighbour also got him in touch with Zoran Popovic, a computer science and engineering professor at the University of Washington. They added a games perspective to let people earn points, accrue high scores, build teams, or compete, build, and share shortcuts, and even chat with each other. But even more so, they fired up people's imagination. After all, why game mindlessly – even if it is fun – when you can be part of the next Nobel Prize by helping to find a cure for Alzheimer's or a vaccine against HIV?

When announcing the project in 2008, Popovic said: "We're hopefully going to change the way science is done and who it is done by. Our ultimate goal is to have ordinary people play the game and eventually be candidates for winning the Nobel Prize." The intuitive 3D problem-solving skills some players evince could very well make this possible. "Some people are just able to look at the game and in less than two minutes get to the top score. They can't even explain what they're doing, but somehow they're able to do it," Popovic added. And almost on the side, people also learn about why protein folding is important and gain whole new insights into the scientific process. →

Crowdcrafting exploits the power of the group, whose aggregated opinion can be very close to that of an expert for certain questions – something that many episodes of "Who Wants To Be A Millionaire" demonstrate.

In 2011, players were presented with a problem that had stymied researchers for over a decade: the structure of a certain protease of the Mason-Pfizer monkey virus. This relative of HIV causes an AIDS-like disease in monkeys. Knowing what its protease looks like would allow researchers to find ways of disrupting it. The challenge was part of a contest in which scientists tried to determine the best techniques for predicting 3D protein structures. The FoldIt players solved this and other complex puzzles within three weeks and bested all the scientific groups. This resulted in the first *Nature* paper with 57,000 credited authors – even if for practical reasons they were collectively named as "FoldIt players".

But the FoldIt players not only deliver results on how to fold a certain protein, they also teach scientists how to do it better, even automatically. Since 2009, the game has allowed players to write, share, and change small scripts to automate certain routines. And some of these routines can do a better job than what the scientists themselves with all their detailed understanding of the underlying science come up with. Since its release, FoldIt has attracted 460,000 players from all over the world.

The hope of the citizen science movement is to open science to parts of the population that have no direct or little contact with it. In light of the fact that most of the people playing FoldIt have no background in biochemistry, citizen science projects can achieve this goal. "We live in a society that is based on science. For people who are not in science-based jobs, citizen science can be a way to participate in this important part of our society," says Dr Katrin Vohland, vice chair of the European Citizen Science Association (ECSA).

ECSA has more than 150 members from over 28 countries across the European Union and beyond, such as the German Leibniz Network on Biodiversity, the University College London, the German Helmholtz Centre for Environmental Research, and the Spanish La Caixa research foundation. ECSA defines citizen science as "organised research in which the balance between scientific, educational, societal, and policy goals varies across projects". Where the balance lies is one of the challenges for scientists planning a project. "Data quality and management, property rights, ethical issues, proper acknowledgement of contributors, and feedback on the results are all issues that need to be addressed, but they can be resolved," says Vohland. "But in order to do so, one needs to be clear on the design of the project – what questions can we ask, how much we need to invest in training our participants, which resources we need." Help with such questions can be found on the ECSA website, which is involved in developing guidelines for projects, sees itself as a catalyst for the citizen science community in Europe, and wants to foster international cooperation.

Vohland's favourite project, "Diving for Nature Conservation", is one in which scuba divers help to map underwater plants in freshwater lakes throughout Germany. One of the results of the project will be a new water plant guide, to be published next year. With the divers' help, scientists can get their hands on much more data and thus develop better protection strategies. The project, originally planned for just two years, has had so much positive feedback, including several prizes, that it has now become a long-term collaboration between the federal association Naturschutzbund Deutschland and the Association of German Sports Divers. Although many divers are already very conscious of the impact they may have and try to minimize this impact, there still is a conflict between diving and conservation. The project tries to bridge that gap. Divers learn much more about the waters they dive in, how their ecology functions, and what impacts these waters. They also learn to see underwater plants as an important and sometimes endangered part of this system. In turn, they come to care more about its protection.

For Katrin Vohland, this project embodies the core values of citizen science. "For me, it is about people who are enthusiastic about something, about bringing different groups together, ideally resolving or lessening conflicts and teaching them about science by involving them in it. I think the strongest point of citizen science is its integrative power." But she also emphasizes the wide range of knowledge citizen scientists possess, from absolute laymen to experts. "They may not be affiliated with a research institute, but some of them are considered *the* expert in their field, for example, in the taxonomy of certain beetles."

Rush Holt, CEO of the American Association for the Advancement of Science (AAAS), also stresses the importance of involving as many people in science as possible. During the White House Citizen Science Forum in September last year, he linked the widespread misunderstandings about vaccines, climate change, and evolution to the fact that people are not evaluating evidence themselves, but instead see this as the responsibility of scientists. He points out that during their studies, scientists develop a reverence for evidence, just as people do when they become citizen scientists. "And what they learn and can communicate with their sisters, cousins, aunts, co-workers, and everyone else is that science is not just for the specialists. Science is accessible to all. It is essential that everyone practices this, at least to some extent, for the sake of our society and our policies."

Further information:

Center for Game Science at the University of Washington, http://centerforgamescience.org/

Bürger schaffen Wissen – German Citizen Science Platform, www.buergerschaffenwissen.de/

European Citizen Science Association; www.ecsa.org

Please understand that in the interest of our fellows, we publish only results online, not descriptions of ongoing projects.

Therefore, this pdf continues with the section Results.

RESULTS The Boehringer Ingelheim Fonds funds excellent PhD students who are selected as much for their academic record as for their ambitious projects. Here, they present a synopsis of their findings, which aim to push the boundaries of our knowledge of the fundamental phenomena of human life.

Shared first authorship is denoted with an *.

MAPPING SIGNALLING PATHWAY CROSSTALK MEDIATED BY LIGAND- AND RECEPTOR-GENE REGULATION

cf. BIF FUTURA, VOL. 28 | 1.2013

NOÉMIE AMMEUX († 2016)
Discipline: Geneticist, MSc
Institute: Harvard Medical School, Boston, MA, USA
Supervisor: Dr Norbert Perrimon

Cells sense and respond to their environment through the binding of ligands to receptors on their surface membrane, which then activates intracellular signalling cascades. Thus, a limited number of signalling pathways integrates the myriad of external cues to ultimately direct all cellular functions and fates. Although we lack a dynamic view of the signal interactions necessary to complete a given outcome, their integration ultimately regulates the expression of target genes, including those encoding ligands and receptors. My PhD research therefore addressed the hypothesis that ligand- and receptor-gene transcription mediates the crosstalk between signalling pathways. I first designed an *in vitro* systematic study using *Drosophila melanogaster* to screen ligand and receptor genes as targets of pathway activity. Following single and dual inductions of a pathway's receptor(s) using ligands or agonists, I measured transcript levels of individual pathway components using NanoString. This revealed several rapid variations in the transcription of ligand and receptor genes, which represent a network of sequential and simultaneous pathway interactions. I then refined these results by determining the synergies or inhibitions taking place between two stimulated pathways that dampen or enhance the responses of target genes. To investigate the underlying mechanisms I used CRISPR-Cas9 to deplete a cell line for the transcription factor STAT92E, which is the main effector of gene expression downstream of JAK/STAT pathway activity. This showed that STAT92E is required for the basal expression of genes encoding ligands and receptors as well as their response to signal integration. Finally, I validated some robust pathway-to-ligand relationships *in vivo* using mutant *Drosophila* strains to report the level of gene transcripts in the gut and the ovaries during biological processes known to activate the pathway(s) of interest. Taken together, my results reveal that changes in expression levels of ligands and receptors are essential for the efficient orchestration of the signalling network within cells. Moreover, my work serves as a scaffold for investigating more complex signalling systems in humans and for clarifying the molecular mechanisms of various diseases that are driven by improper signalling.

PUBLICATIONS

Ammeux N, Housden BE, Georgiadis A, Hu Y, Perrimon N (2016) Mapping signaling pathway cross-talk in Drosophila cells. *Proc Natl Acad Sci USA* **35:** 9940-9945

INNER NUCLEAR MEMBRANE PROTEIN TRAFFICKING IN INTERPHASE

cf. BIF FUTURA, VOL. 26 | 1.2011

ANDREA BONI
Discipline: Cell Biologist, BSc
Institute: European Molecular Biology Laboratory (EMBL), Heidelberg, Germany
Supervisor: Dr Jan Ellenberg

The nuclear envelope (NE) surrounds the cell nucleus and controls the influx of molecules through the nuclear pore complexes (NPC). The NE consists of two lipid bilayers: the outer nuclear membrane, which is continuous with the endoplasmic reticulum (ER), and the inner nuclear membrane (INM), which contains many integral membrane proteins. Although these proteins have key functions in nuclear architecture, transcription regulation, and signal transduction, how they target the INM and the molecular machinery governing this process are poorly understood. I developed a reporter system for live imaging of INM protein targeting in mammalian cells. The system facilitates the release of fluorescently tagged proteins from the ER, thereby enabling me to quantitatively measure their transport to the INM. I applied this system to the INM protein lamin B receptor (LBR) and screened a panel of candidate genes, including nucleoporins, importins, and ER membrane proteins, for their requirement in LBR targeting. Using small interfering RNA knockdowns and automated high-resolution confocal time-lapse microscopy, I compared the efficiency of LBR targeting in control and perturbed cells and scored the candidate genes based on how much they affected targeting. Using a mathematical model of INM protein targeting, I fit the kinetic signatures of LBR targeting after depletion of these genes and clustered the genes into three major phenotypic classes. These classes revealed that the number of NPCs, their permeability, and the strength of nuclear retention at the INM are critical for efficient LBR targeting. Using the same strategy with another INM protein, lamin associated poly-peptide β (Lap2β), showed that it recapitulates the phenotypes seen for LBR. My results suggest diffusion and retention at the INM as the main mechanisms for targeting of LBR- and Lap2β-type proteins in mammalian cells, rather than active receptor-mediated transport. My method can be used to systematically compare the molecular requirements for targeting of different families of INM proteins to address if mammalian cells have alternative pathways to diffusion and retention.

PUBLICATIONS

Boni A, Politi AZ, Strnad P, Xiang W, Hossain JM, Ellenberg J (2015) Live imaging and mathematical modeling of inner nuclear membrane protein targeting reveals its molecular requirements in mammalian cells. *J Cell Biol* **209:** 705–720

FUNCTIONAL INTEGRATION OF NEWBORN NEURONS INTO ESTABLISHED NEURONAL CIRCUITS

cf. BIF FUTURA, VOL. 27 | 1.2012

JONATHAN BOULANGER-WEILL
Discipline: Neuroscientist, MSc
Institute: Ecole Normale Supérieure, Paris, France
Supervisor: Dr German Sumbre

Sensory neurons assemble into circuits that interpret information about the environment and enable animals to perform appropriate behaviours. During development, these circuits acquire function by continuously recruiting newborn neurons. In the vertebrate brain, mechanisms leading to their incorporation in such circuits remain poorly understood. Indeed, as most studies have been performed at the single-cell level, a detailed description of the developmental dynamics at the circuit level is lacking. Because ageing and neurodegenerative diseases contribute to the loss of neurons, understanding this process might provide the basic knowledge to develop regenerative therapies. To investigate incorporation, I developed a genetic tool to specifically label newborn neurons in an intact and non-anaesthetized developing vertebrate: the zebrafish larva. I used calcium imaging *in vivo* to record the nascent activity of newborn neurons together with surrounding mature neuronal networks in the optic tectum, the brain's primary visual area. To describe the steps guiding the functional maturation of newborn neurons, I recorded their visually induced and spontaneous activity during their early development until maturity. My observations detail for the first time how newborn neurons incorporate into mature networks in a developing vertebrate in three sequential stages. First, they acquire intrinsic activity and connect to their pre-synaptic sensory organ, the retina, within 24 hours of differentiation. Second, they incorporate into the local neuronal circuitry and show synchronous activity with the large population of neighbouring mature neurons, which helps them to mature their sensory responses. In the third and final stage of incorporation, this synchronicity is retained – particularly with neuronal populations that respond to similar positions of the visual field. At the same time, distant connections are removed, permitting the neurons to acquire stable and robust functional responses, such as sharp receptive fields or selectivity to motion direction. Because therapies targeting neurodegenerative diseases face problems of poor survival outcomes and long-term functional incorporation, my findings may pave the way towards more efficient stem cell-based treatments for the repair of human brain function.

PUBLICATIONS

The results of this project have not yet been published.

STRUCTURAL STUDIES OF THE AUTOPHAGY RECEPTOR P62/SQSTM1

cf. BIF FUTURA, VOL. 26 | 2.2011

RODOLFO CIUFFA
Discipline: Social Scientist, MA
Institute: European Molecular Biology Laboratory (EMBL), Heidelberg, Germany
Supervisor: Dr Carsten Sachse

The aggregation of misfolded proteins interferes with cell function and is a hallmark of many neurodegenerative diseases. In autophagy, one of the two main degradative pathways in the cell, sequestome 1 (SQSTM1) recognizes and shuttles ubiquitinated proteins to the autophagosome for degradation. The goal of my PhD project was to study the structure and function of SQSTM1, a scaffold protein also known as the ubiquitin-binding protein p62. First, I focused on the SQSTM1 polymerization domain, the PB1 domain (1-102). I found that two constructs, PB1 (1–102) and an extended PB1 (1–122), give rise to flexible but structurally ordered SQSTM1 polymers. I determined the cryo-electron microscopy structures of these constructs using SPRING, software developed in the host laboratory for single-particle helical image reconstruction. I resolved the PB1 (1–102) and PB1 (1–122) structures at 10.9 Å and 10.3 Å resolution, respectively. Using electron microscopy, light microscopy, and biochemical assays, I found that the PB1 (1–102) polymer is organized in a four-stranded helix, each with 11.7 subunits per turn, whereas the PB1 (1–122) polymer is a triple-stranded helix stabilized by a new interaction surface on its C-terminal extension. Next, I purified and imaged full-length and truncated SQSTM1 based on a physiologically relevant splicing variant. In both cases, I confirmed its overall helical arrangement and describe its main secondary structures, while producing a number of preliminary reconstructions. Finally, I tested how the interaction with ubiquitin and autophagy-related protein 8 (Atg8), the two main autophagic partners of SQSTM1, alters its helical structure. I found that whereas Atg8 binds without disrupting the helical structure, ubiquitin chains are capable of inducing the depolymerization of SQSTM1 filaments. My data provide deep structural and mechanistic insight into the organization of selective autophagy and possibly into the treatment of neurodegenerative diseases.

PUBLICATIONS

Ciuffa R, Lamark T, Tarafder AK, Guesdon A, Rybina S, Hagen WJH *et al* (2015) The selective autophagy receptor p62 forms a flexible filamentous helical scaffold. *Cell Rep* **11:** 748–758

Desfosses A, Ciuffa R, Gutsche I, Sachse C (2014) SPRING – an image processing package for single-particle based helical reconstruction from electron cryomicrographs. *J Struct Biol* **185:** 15–26

MOLECULAR DISSECTION OF INFLAMMATION-INDUCED IMMUNOPATHOLOGY

cf. BIF FUTURA, VOL. 27 | 2.2012

LUKAS MAGER
Discipline: Immunologist, MD
Institute: Institute of Pathology, University of Bern, Bern, Switzerland
Supervisor: Dr Philippe Krebs

Inflammation normally serves to protect the host from dangerous pathogens. However, uncontrolled or exacerbated inflammation causes tissue damage and can lead to immunopathologies or even autoimmune diseases. Furthermore, excessive inflammation may support tumour development. In the first part of my PhD project, I unveiled a critical role of the danger signal interleukin 33 (IL-33) in the pathogenesis of myeloproliferative neoplasms (MPN), a type of blood cancer. IL-33 is an alarmin, released when cells are under stress, which amplifies inflammatory processes. I showed that IL-33 promoted disease development in two mouse models of MPN, and blood cells from MPN patients were hypersensitive to the action of IL-33. In the second part of my project, I investigated the contribution of IL-33 to colorectal cancer (CRC). To do so, I analysed samples from two cohorts of CRC patients using immunohistochemistry and performed studies in a mouse model of CRC. My data indicated that IL-33 and its receptor are upregulated in early-stage tumours in patients. Moreover, IL-33 signalling had a pro-tumorigenic effect in mice with CRC tumours. In the third part of my project, I studied the role of alternative mRNA splicing in the integrity of the intestinal barrier in mice, during either intestinal homeostasis or disease. Alternative mRNA splicing facilitates the generation of multiple proteins with similar, distinct or even opposing functions from a single gene, thus enhancing the diversity of the protein pool. I found that aberrant mRNA splicing in the intestine increased the susceptibility of mice to experimentally induced colitis and led to an abnormal immune response against commensal bacteria. In conclusion, my data revealed novel signalling pathways and molecular mechanisms for the development of certain types of blood and solid cancer, as well as intestinal inflammatory disease, thereby suggesting new potential targets for future therapeutic approaches.

PUBLICATIONS

Mertz KD*, Mager LF*, Wasmer MH, Thiesler T, Koelzer VH, Ruzzante G *et al* (2016) The IL-33/ST2 pathway contributes to intestinal tumorigenesis in humans and mice. *Oncoimmunology* **5:** e1062966

Mager LF, Riether C, Schurch CM, Banz Y, Wasmer MH, Stuber R *et al* (2015) IL-33 signaling contributes to the pathogenesis of myeloproliferative neoplasms. *J Clin Invest* **125:** 2579–2591

NOVEL SIGNALLING FUNCTIONS OF THE NEURONAL CELL ADHESION MOLECULES DSCAM AND DSCAML1

cf. BIF FUTURA, VOL. 26 | 3.2011

SONJA MARIA SACHSE
Discipline: Biochemist, Diploma
Institute: Flanders Institute for Biotechnology (VIB), KU Leuven, Leuven, Belgium
Supervisor: Prof. Dietmar Schmucker

Down syndrome cell adhesion molecule (DSCAM) and its paralogue DSCAM-like 1 (DSCAML1) are single-pass transmembrane receptors of the immunoglobulin superfamily. They both have a role in important neurodevelopmental functions including axon guidance, neurite self-avoidance, synaptic connectivity, and neuronal cell death. Surprisingly, the key mechanisms and molecular players involved in the signal transduction pathways that mediate their diverse functions are largely unknown. The aim of my PhD project was to identify signalling partners of DSCAMs using the mammalian protein–protein interaction trap (MAPPIT) technique. This high-throughput assay allowed me to screen approximately 10,000 cytoplasmic proteins in the human ORFeome collection for their interaction with DSCAMs. Among the proteins that specifically interacted with both DSCAM and DSCAML1 in the assay was importin 5 (IPO5), which is a beta-importin that mediates nuclear protein import. This prompted me to investigate whether DSCAMs undergo proteolytic processing and subsequently function directly in the nucleus. I showed that mouse DSCAM and DSCAML1 are cleaved *in vitro* and *Drosophila* Dscam1 is cleaved *in vivo*, resulting in the release of C-terminal intracellular domain (ICD) fragments. Moreover, I found that the ICDs of DSCAMs contain nuclear localization signals that form the binding sites for IPO5 and are required for the nuclear import of the ICDs upon their expression in cell lines and primary neuronal cultures. I next performed RNA-seq experiments on cell lines stably expressing the ICDs of DSCAMs and found that the nuclear translocation of these proteins results in distinct differential expression of genes that have a role in nervous system development. In particular, I identified differentially regulated gene clusters associated with axon guidance, neurotrophin signalling, and neuronal cell death. I have also performed some preliminary overexpression experiments that suggest that nuclear translocation of the DSCAML1 ICD impairs neurite outgrowth in primary mouse cortical neurons. Taken together, the results of my PhD point to a novel membrane-to-nucleus signalling mechanism by which DSCAMs regulate the transcription of neuronal gene networks and may ultimately explain how DSCAMs affect the morphology and function of neural circuits.

PUBLICATIONS

The results of this project have not yet been published.

INDIVIDIAL GUT MICROBES CAN SHAPE THE PHENOTYPE AND FUNCTION OF REGULATORY T CELLS

cf. BIF FUTURA, VOL. 27 | 2.2012

ESEN SEFIK
Discipline: Immunologist, BSc
Institute: Harvard Medical School, Boston, MA, USA
Supervisors: Prof. Christophe Benoist and Prof. Diane Mathis

Colonization of the gastrointestinal (GI) tract by the natural gut flora requires immunological tolerance, which is established by regulatory T cells (Tregs) that express the transcription factor FoxP3. We know that intestinal Tregs can be induced by various pools of microbes. To study whether single microbial species can impact the immune system as well, we performed a large-scale screen on mice lacking live bacteria in their GI tract. They were colonized with individual microbes from a panel of bacterial strains selected from human GI tract microbiota. Overall, the screen covered 5 phyla, 29 genera, and 52 species. To our surprise, 43% of these microbes were able to independently induce colonic Tregs comparable to levels in mice with normal or conventional flora, which may imply a degree of redundancy in the microbes' ability to induce Tregs. We next dissected the effect of the microbes on colonic Tregs and found that they induced the expression of the transcription factor Rorγ. This was puzzling given that Rorγ is an antagonist of FoxP3 *in vitro* and has an inflammatory role in innate and adaptive immunocyte differentiation, for example, by controlling the production of cytokine IL17. However, we found that colonic Rorγ$^+$ Tregs do not produce IL17. Interestingly, the loss of Rorγ in Tregs increased production of inflammatory cytokines by other T cells in the colon, suggesting that Rorγ$^+$ Tregs have an immunosuppressive function. In a chemically induced colitis model, mice lacking Rorγ$^+$ Tregs were more severely affected, as reflected in their overall colitis score and their histopathology. The results of my PhD therefore show that microbiota-dependent expression of Rorγ potentiates Tregs in the GI tract and promotes colonic homeostasis. Deciphering how microbe-derived Rorγ ligands specifically induce colonic Rorγ$^+$ Tregs but not other inflammatory Rorγ$^+$ T cells may be useful for the identification of effective therapeutic targets in various intestinal or systemic inflammatory diseases.

PUBLICATIONS

Sefik E, Geva-Zatorsky N, Oh S, Konnikova L, Zemmour D, McGuire AM *et al* (2015) Individual intestinal symbionts induce a distinct population of RORγ+ regulatory T cells. *Science* **349:** 993–997

Morton AM, Sefik E, Upadhyay R, Weissleder R, Benoist C, Mathis D (2014) Endoscopic photoconversion reveals unexpectedly broad leukocyte trafficking to and from the gut. *Proc Natl Acad Sci USA* **111:** 6696-6701

NOVEL MOUSE MODELS TO DEPLETE DENDRITIC CELLS *IN VIVO*

cf. BIF FUTURA, VOL. 27 | 3.2012

JANNEKE VAN BLIJSWIJK
Discipline: Biologist, MSc
Institute: The Francis Crick Institute, London, UK
Supervisor: Prof. Caetano Reis e Sousa

Dendritic cells (DCs) are key players at the interface between innate and adaptive immunity and are the main antigen-presenting cells in the body. Much of our knowledge of DC biology has come from transgenic mouse models in which DCs can be inducibly or constitutively ablated. However, these models have a number of drawbacks, mainly because other cells of the immune system are unintentionally targeted. To overcome these limitations, the goal of my PhD was to develop novel mouse models in which the DCs are specifically depleted. I exploited the fact that DC precursors can be manipulated via genetic editing of the *Clec9a* locus, which encodes the C-type lectin receptor CLEC9A (also known as DNGR-1). My initial approach involved crossing Clec9a-Cre mice with a strain engineered to express the diphtheria toxin receptor (DTR), ROSA26-DTR. The injection of diphtheria toxin into the resulting mice should deplete their DCs. However, these mice unexpectedly suffer from lymph node hypocellularity and reduced frequencies of DCs in lymph nodes, even before diphtheria toxin injection. In an alternative approach, I engineered mice that express the diphtheria toxin alpha subunit (DTA), which is acutely toxic to cells, under the control of the *Clec9a* locus. These Clec9a-DTA mice should lack all DCs owing to the expression of DTA in the DC precursors. Unfortunately, these mice still harboured DCs and only showed partial reduction of one DC subset. In summary, although manipulation of the *Clec9a* locus is an excellent way to target DCs, the mice I generated showed unexpected characteristics that limit their use for studying DCs *in vivo*. Producing Clec9a-DTA mice via a different genetic targeting approach or the use of an alternative depletion system based on inducible suicide genes may lead to the successful generation of mice with depleted DCs in the future.

PUBLICATIONS

Schraml BU, van Blijswijk J, Zelenay S, Whitney PG, Filby A, Acton SE *et al* (2013) Genetic tracing via DNGR-1 expression history defines dendritic cells as a hematopoietic lineage. *Cell* **154:** 843–858

van Blijswijk J, Schraml BU, Reis e Sousa C (2013) Advantages and limitations of mouse models to deplete dendritic cells. *Eur J Immunol* **43:** 22–26

van Blijswijk J, Schraml BU, Rogers NC, Whitney PG, Zelenay S, Acton SE *et al* (2015) Altered lymph node composition in diphtheria toxin receptor-based mouse models to ablate dendritic cells. *J Immunol* **194:** 307–315

MD FELLOWS 2015

With its MD fellowships, the Boehringer Ingelheim Fonds helps outstanding medical students to pursue an ambitious experimental project in basic biomedical research. Candidates study in Germany and change their workplace (institution and city) for at least ten months to join an internationally renowned laboratory. Here, we present the ten fellows who were granted an MD fellowship in 2015.

NINA HARDER

The influence of lifestyle modifiers on hematopoietic niches during atherosclerosis

KATJA HASSLER

Functional characterization of the coronin actin interaction of the human malaria-causing pathogen *Plasmodium falciparum*

RAINER KAISER

The impact of RNA-binding proteins on the cellular response to hypoxia

KRISTINA LANGEMACK

Mitochondrial impairment in glial cells of the central and enteric nervous system: implications for Parkinson's disease

JANA LEONHARDS

Characterization of HIV-specific NK cells in HIV-infected individuals and HIV-exposed seronegative individuals

CHRISTINA SCHROETER

Quantitative proteomic analysis of the Par3B interactome

LEON SEIFERT

Characterization of the ETS-family transcription factor ELF1 – a novel antiviral protein

BJÖRN STOLTE

The role of protein phosphatase 2A in Ewing sarcoma

REBECCA WICKLEIN

Pathogenic mechanisms of SHANK3 mutations in human neurons

CHRISTOPH WIEST

Neural circuit mechanisms underlying major depressive disorder (MDD) in zebrafish brain

THE INFLUENCE OF LIFESTYLE MODIFIERS ON HEMATOPOIETIC NICHES DURING ATHEROSCLEROSIS

NINA HARDER

Duration: 09/15–08/16

Project at: Harvard Medical School, Massachusetts General Hospital, Boston, MA, USA

Supervisor: Professor Filip K. Swirski, PhD

Home University: University Heart Center Freiburg

FUNCTIONAL CHARACTERIZATION OF THE CORONIN ACTIN INTERACTION OF THE HUMAN MALARIA-CAUSING PATHOGEN *PLASMODIUM FALCIPARUM*

KATJA HASSLER

Duration: 08/15–06/16

Project at: Imperial College London, Faculty of Natural Sciences, London, UK

Supervisor: Dr Jake Baum

Home University: Heidelberg University Hospital

THE IMPACT OF RNA-BINDING PROTEINS ON THE CELLULAR RESPONSE TO HYPOXIA

RAINER KAISER

Duration: 02/16–01/17

Project at: Uniklinik Köln, Cologne, Germany

Supervisor: Priv.-Doz. Dr Roman-Ulrich Müller

Home University: Heidelberg University Hospital

MITOCHONDRIAL IMPAIRMENT IN GLIAL CELLS OF THE CENTRAL AND ENTERIC NERVOUS SYSTEM: IMPLICATIONS FOR PARKINSON'S DISEASE

KRISTINA LANGEMACK

Duration: 11/15–09/16

Project at: Karolinska Institutet, Department of Neuroscience, Stockholm, Sweden

Supervisor: Dr Dagmar Galter

Home University: Heidelberg University

CHARACTERISATION OF HIV-SPECIFIC NK CELLS IN HIV-INFECTED INDIVIDUALS AND HIV-EXPOSED SERONEGATIVE INDIVIDUALS

JANA LEONHARDS

Duration: 10/15–09/16

Project at: Harvard Medical School, the Ragon Institute of MGH, MIT and Harvard, Cambridge, MA, USA

Supervisor: Dr Stephanie Jost

Home University: Heinrich Pette Institute

QUANTITATIVE PROTEOMIC ANALYSIS OF THE PAR3B INTERACTOME

CHRISTINA SCHROETER

Duration: 07/15–04/16

Project at: Uniklinik Köln, Zentrum für Molekulare Medizin Köln (ZMMK), Cologne, Germany

Supervisor: Priv.-Doz. Dr med. Paul Brinkkötter

Home University: University Witten/Herdecke

CHARACTERIZATION OF THE ETS-FAMILY TRANSCRIPTION FACTOR ELF1 – A NOVEL ANTIVIRAL PROTEIN

LEON SEIFERT

Duration: 09/15–08/16

Project at: Rockefeller University, Laboratory of Virology and Infectious Disease, New York, NY, USA

Supervisor: Professor Charles Rice, PhD

Home University: University Hospital Muenster

THE ROLE OF PROTEIN PHOSPHATASE 2A IN EWING SARCOMA

BJÖRN STOLTE

Duration: 06/15–05/16

Project at: Dana-Farber Cancer Institute, Boston, MA, USA

Supervisor: Professor Kimberly Stegmaier, MD

Home University: Universitätsklinikum München

PATHOGENIC MECHANISMS OF SHANK3 MUTATIONS IN HUMAN NEURONS

REBECCA WICKLEIN

Duration: 03/16–02/17

Project at: Stanford University School of Medicine, Howard Hughes Medical Institute, Stanford, CA, USA

Supervisor: Professor Thomas C. Südhof, MD

Home University: University of Freiburg

NEURAL CIRCUIT MECHANISMS UNDERLYING MAJOR DEPRESSIVE DISORDER (MDD) IN ZEBRAFISH BRAIN

CHRISTOPH WIEST

Duration: 03/16–02/17

Project at: Kavli Institute for Systems Neuroscience, Center for Neural Computation, Trondheim, Norway

Supervisor: Professor Emre Yaksi

Home University: Heidelberg University

THE FOUNDATION The Boehringer Ingelheim Fonds (BIF) is a public foundation – an independent, non-profit organization for the exclusive and direct promotion of basic research in biomedicine. The foundation pays particular attention to fostering junior scientists. From the start, it has provided its fellowship holders with more than just monthly bank transfers: seminars, events, and personal support have nurtured the development of a worldwide network of current and former fellows.

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The Banbury Center at the Cold Spring Harbor Laboratory on Long Island, NY, USA, hosts the US seminar.

THE "UNNECESSARY PIXEL ACT"

In 1986, with BIF just three years old, it did something very unusual for the time: it invited its fellows to a three-day seminar on how to communicate better. This was sparked by another BIF seminar the year before, the summer seminar, where students presented the progress made in their scientific projects.

By Kirsten Achenbach

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After noticing what a hard time the students had had during the progress reports by their fellow biologists, the then managing director Hasso Schröder famously exclaimed: "They do not understand each other, we have to have communication training."

Today, 30 years, 40 seminars, and a considerable evolution process later, the communication seminars are a fixed part of BIF's calendar. In 2005, with rising numbers of fellows and their internationalization, BIF started to organize yearly training, not only in Germany, but also in the USA. BIF being BIF, the setting for both seminars has a strong connection to science: the German seminar takes place in Lautrach Castle, near Ulm in Germany, where Karl von Frisch, Albert Einstein, Richard Willstädter, and the like met, and the overseas seminar at the Banbury Conference Center of Cold Spring Harbor Laboratories near New York City, USA.

»My skill set has improved much more than I thought possible in just five days.«

Matthew Paul, fellow

»I now understand the enthusiasm of other BIF fellows about the seminars – it feels like family.«

Maria Placentino, fellow

Now, during the five-day seminars, experts teach writing, rhetoric, and graphic skills. Theoretical lectures are kept to a minimum and exercises with detailed feedback from trainers and other participants make up most of the seminar. The training is intense, starts early, and often lasts until late in the evening. "It is not simply about writing scientific papers – we aim to convey the fundamental communication skills important to science and other areas of life," says →

1 ***The Elements of Style*** has helped people to write well since 1918.

2 **Fellows usually work with laptops,** but for some exercises paper and pen are the better option.

3 **William Tansey,** one of our trainers in the USA, during the video analysis.

4 **Writing is only one part –** analysing, editing, and giving feedback are also taught.

5 **One afternoon is reserved** for a well-deserved break.

6 **Looking in from the outside –** the seminar room at Banbury Center.

»Being allowed to teach the concepts and practices of good design to the inquisitive minds of BIF fellows is a pleasure – every year the discussions continue late into the night.«

Joachim Schreiber, graphic designer and trainer for the European seminar

Photos: Background: iStock 1, 3: Constance Brukin; 2, 4: Orla Connolly; 5: BIF, Kirsten Achenbach

7 **A picture is worth** 1,000 words – if it is the right one.

8 **Fellows Alessia Deglincerti and Johannes Haushofer** make the best of the tight schedule – combining fresh air with work on the assignment.

9 **Fellow Christoph Wiest** discussing the writing assignment.

10 **Guess what?** Guess where?

Claudia Walther, managing director of BIF. The main messages repeated again and again in all parts of the seminar are simple: first, consider your audience, second, find and hone your story to their needs, third, be clear and concise. Include the neccessary essentials and nothing else. As simple as this sounds, getting it right takes training, training, training. And as Steve Jobs once said, "Simple can be harder than complex: You have to work hard to get your thinking clean to make it simple."

This is repeatedly emphasized by William Tansey, professor at Vanderbuilt University in Nashville, USA, in his quest to convince students to unclutter their slides and long-winded presentations. Tansey teaches the oral presentation part of the USA seminar

»Young researchers should especially be aware of the impact different aspects of rhetoric have on the convincing communication of their subjects: precise language, appealing presentation, and the scientists' manner, including posture, facial expressions, gestures, and voice.«

Dr. Andrea Merger,
rhetorics trainer, European seminar

»The BIF communication seminar each year is the highlight of my teaching calendar.«

William P. Tansey, PhD, Ingram Professor at the Vanderbilt University School of Medicine

and coined the phrase of "unnecessary pixel act", or, as a physicist would put it, "reduce noise to get signal across".

And if you want to stay on the good side of Nikki Le Brasseur, the overseas writing trainer, never again use phrases such as "shed light on" or "plays a role in". If you cannot say what something does in more precise terms, it is not worth writing about.

In those early seminars, all text and graphics were done by hand, no PowerPoint slide in sight, although the first seminar already incorporated a talk about the "new possibilites to express science through computer graphics". In 1990, a video camera started to show the fellows how they presented themselves and their science and what effects they had on their audience. Today, it is the norm for every student to have a high-powered laptop capable of running professional graphics software. But as much as the technical side of presenting science may have changed over time – such key aspects of communication as clear logic, the right words, body language, and voice control are still the same since the birth of rhetoric in ancient Greece.

Photos: 6, 7, 9: Constance Brukin; 8: Orla Connolly; 10: BIF, Claudia Walther

PERSPECTIVES

SCIENCE IN ACADEMIA AND INDUSTRY

After a long career in science, Johannes le Coutre decided to work for Nestlé to "add translatability" to his scientific endeavours. FUTURA talked to Johannes about his decision to leave academia, how to stay innovative, and why BIF has been key to happiness in his private life.

INTERVIEW WITH DR JOHANNES LE COUTRE, NESTLÉ RESEARCH CENTER IN LAUSANNE, SWITZERLAND

Photo: private

Johannes le Coutre studied biology in Regensburg, Germany, and finished his PhD at the Max Planck Institute for Nutritional Physiology in Dortmund in 1995. For his postdoctoral training, he moved to the Howard Hughes Medical Institute at UCLA in Los Angeles, USA. In 2000, he returned to Europe to work at the Nestlé Research Center in Lausanne, Switzerland, where he has been head of Perception Physiology since 2004. During his career, his chosen research field of nutrition science has evolved from "uncool" to hot topic, with the vast influence of nutrition on diseases such as diabetes, Alzheimer's, and even depression becoming increasingly evident.

What made you leave for industry?

After about 15 years of purely academic science, I got the feeling that a lot of science is being conducted merely for getting papers published. In 2000, I decided to add translatability to my scientific endeavours. Right now, while we do publish a lot, the science ultimately needs to prove purposeful.

You've worked in Germany, Switzerland, and the USA. Have you noticed differences in the relationship between academia and industry?

In Germany, it seems to me that academia can still improve its relationship with the private sector, while industry is eager to invest – even in high risk science – and funds are available. In the USA, with its more entrepreneurial climate and higher availability of venture capital, many successful scientists build a second career by founding start-up companies. In Switzerland, big companies, but also many smaller ones, traditionally invest in collaborations with universities, making high risk exploratory projects feasible within short time frames for the benefit of both sides. At times, the government also matches private funds for academic research.

You're head of an industrial research group, lecturer at the École Polytechnique Fédérale de Lausanne (EPFL), founding and chief editor of *Frontiers in Nutrition*, and visiting professor at the University of Tokyo, Japan – what do you take from each role?

Innovation happens at the interface. All scientific institutions have their opportunities and limitations. My focus is the pursuit of meaningful new concepts and ideas. Within the field of nutrition science, you find different mindsets and cultures. Embracing these differences and trying to extract an alloy of key insights is elementary to driving innovation in all sectors.

What would be your dream issue for *Frontiers in Nutrition*?

If we could have Melinda Gates, Jamie Oliver, Jeffrey Friedman, and Jeffrey Gordon talk about nutrition in the context of rigorous science, global health, and wellness – that would be something …

What does BIF mean to you personally?

For those matured BIF alumni who are reading this: My lovely wife, Ronit, who was a BIF PhD fellow herself, and I are the BIF dream team no. 1! We remain grateful to BIF for making this very important contact. Our network of BIF friends remains strong and sustainable and we try to meet whenever possible. Of course there is more to it: we follow the meetings at Schloss Gracht and try to participate. Being a dedicated reader of FUTURA, it also gives me pleasure to see that more than 20 years after my fellowship, BIF is strong and going in the right direction.

PROFILES

Dr Andreas Bergthaler,
Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna, Austria
Fellowship: 2004–2006

Andreas Bergthaler has been granted an ERC Starting Grant for his project "Crosstalk of Metabolism and Inflammation". He will analyse the metabolic and inflammatory processes in a mouse model of chronic viral hepatitis to better understand how they interact with each other and what influence this has on the outcome of viral infections.

Prof. Daniel Braun,
Institute of Neural Information Processing, Ulm University, Ulm, Germany
Fellowship: 2006–2008

Daniel Braun has been appointed professor at Ulm University, starting in July 2016. His group will study the interactions between sensory input and the adaptation of movement. For this he has also been granted an ERC Starting Grant to develop a mathematical framework for the description of movements and motion sequences.

Dr Ines Drinnenberg,
Nuclear Dynamics, Institut Curie, Paris, France
Fellowship: 2007–2010

Ines Drinnenberg now heads the group "Evolution of Centromeres and Chromosome Segregation" at the Institute Curie, studying how centromeres evolved through time and species. By studying the effects of changes that occur over millions of years, such as the natural loss of genes or pathways, she is seeking an alternative method to gain insights into centromere function.

Dr Jan Ellenberg,
Cell Biology and Biophysics, EMBL, Heibelberg, Germany
Fellowship: 1995–1998

Dr Michael Sieweke,
Centre d´Immunologie de Marseille-Luminy, France
Postdoc fellowship: 1991–1992

The ERC has awarded Advanced Grants to Jan Ellenberg and Michael Siewecke. Jan's project is titled "Cell Division and the Origin of Embryonic Aneuploidy in Preimplantation Mouse Development", while Michael will use the grant to study "Macrophage Aging and Rejuvenation". The Advanced Grants make it possible to pursue ground-breaking, high-risk projects. They are given to researchers working in Europe who have already established themselves as top independent research leaders regardless of nationality and age.

Dr Sylvia Erhardt,
Centre for Molecular Biology of Heidelberg University (ZMBH), Heidelberg, Germany
Fellowship: 1999–2001

Group leader Sylvia Erhardt has been awarded a 1.9 million euro ERC Consolidator Grant for her five-year project "The Role of RNA in Centromere Biology and Genome Integrity". Starting in April 2016, she will explore how epigenetic mechanisms connected with RNA assure the correct splitting of chromosomes during cell division. At the end of 2015, Sylvia was also awarded the 100,000 euro Hella Bühler Prize for the implications her research has for cancer. The award has been endowed by a Heidelberg dentist and aims to support young cancer researchers in Heidelberg.

Dr Martin Etzrodt,
Biosystems Science and Engineering, ETH Zurich, Switzerland
Fellowship: 2008–2011

Martin Etzrodt has been awarded one of the newly established Career Seed Grants of the ETH Zurich which provide up to 50,000 Swiss francs. He will use it to continue his postdoc project "Single Cell Analysis of Hematopoietic Stem Cell Responses to Inflammation and Stress" at the Department of Biosystems Science and Engineering. These grants support postdocs in establishing their own record of independent research and cover running and material costs.

Prof. Dennis Kätzel,
Institute of Applied Physiology, Ulm University, Ulm, Germany
Fellowship: 2008–2011

Dennis Kätzel has been appointed tenure track assistant professor at Ulm University. His appointment has been supported by a grant of 110,000 euros from the Else Kröner-Fresenius Foundation, which assists German universities in attracting excellent medical scientists from abroad. His research focuses on understanding the neuronal mechanisms that lead to schizophrenia.

Photos: Bergthaler: CeMM; Braun: private; Drinnenberg: Aida de la Cruz; Ellenberg: EMBL; Sieweke: Jean-Marie Huron, CIML; Erhardt: Universität Heidelberg; Kätzel: private

FROM THE BIF NETWORK

Professor Hidde Ploegh, BIF trustee and member of the Whitehead Institute for Biomedical Research, Cambridge, USA, has been elected to the National Academy of Sciences (NAS) in recognition of distinguished and continuing achievements in original research. His research focuses on developing innovative tools and techniques with which to explore the complexities of the immune system and its response to antigens, including those from invading pathogens and cancer cells. NAS membership is considered among the highest honours that can be accorded a US scientist or engineer. The 84 newly elected members bring the total number of active members to nearly 2,300.

Professor Reinhard Jahn, BIF trustee and director at the Max Planck Institute for Biophysical Chemistry, Göttingen, Germany, has been honoured with the Communitas Award of the Max Planck Society (MPG). This annual prize recognizes extraordinary commitment to the MPG, in Professor Jahn's case his enduring and energetic pursuit of better structures and conditions in science, especially for young scientists.

BIF'S SISTER FOUNDATIONS

IMB AND IPP: ATTRACTING TOP TALENT TO MAINZ

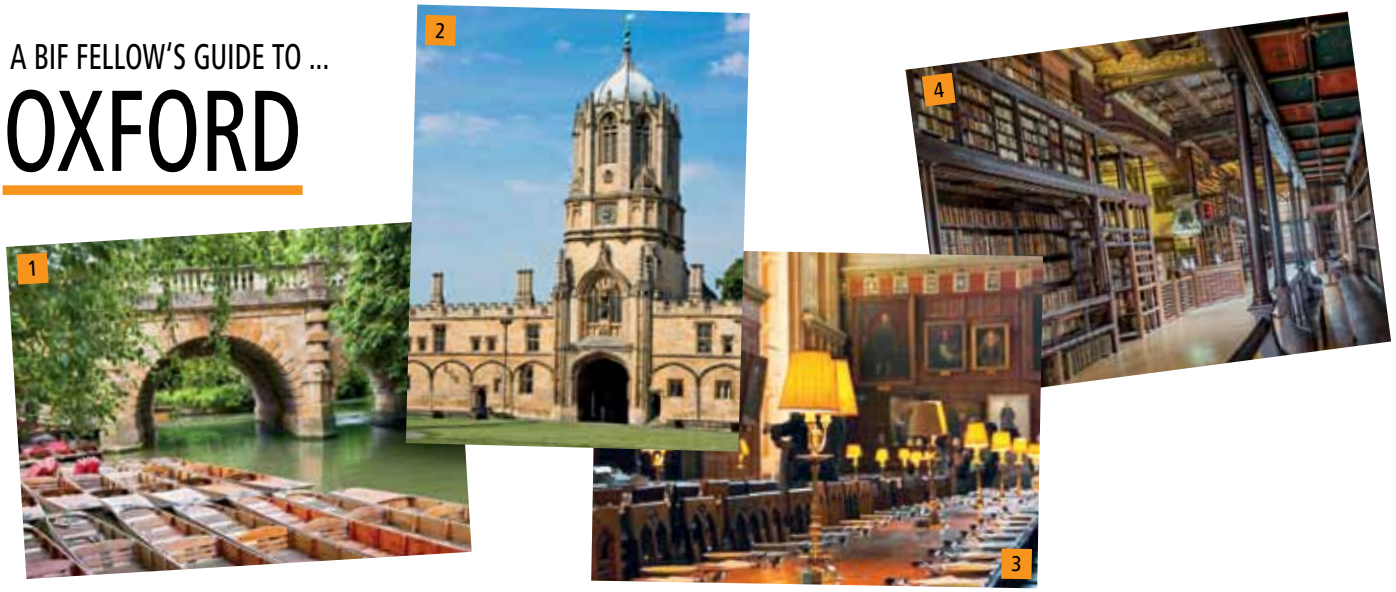
BIF's sister foundation, the Boehringer Ingelheim Foundation (BIS), funds the scientific operation of the Institute of Molecular Biology (IMB) in Mainz, Germany, with a total of 100 million euros over 10 years. It also provides the core funding for the International PhD Programme (IPP) of the University Medical Center Mainz and the IMB, coordinated by the latter. Both endeavours were evaluated in fall 2015 and received much praise. The evaluation committees, comprised of internationally known scientists, attested them to be driving forces for the development and rising international visibility of the life sciences in Mainz, attracting excellent scientists in all career stages. The IMB evaluation committee commended the institute for its research, convincing concept, and very impressive development since its inauguration in 2011. Above all, they agreed that IMB is well on its way to becoming what it set out to be: a top international institute for the life sciences. The IPP evaluation committee stated that the programme has already significantly contributed to collaborations between the participating institutions and that its quality is on par with the best PhD programmes in Germany.

More than 200 staff and 17 groups investigate cutting-edge biomedical questions at the IMB.

Photos: Ploegh: Whitehead Institute/Chris Sanchez; Jahn: Irene Böttcher-Gajewski/Uni Göttingen; IMB: Ule Ruhland, Adler & Olesch

A BIF FELLOW'S GUIDE TO ...

OXFORD



Travelling is fun – especially if you get insider tips from locals! In each edition of FUTURA, one fellow shows you around his or her city. In this edition, your guide is Bianca Gapp. She reports from Oxford, UK, the city best known as the home of the second oldest university in the world.

FACTS & FIGURES

Country: United Kingdom
Population: Around 158,000
Area: Roughly 46 km²
Students: Roughly 22,000
Famous for its university tradition, pubs, rowing, and punting
Websites: www.oxfordcity.co.uk

WHERE TO STAY

Malmaison: Former Victorian prison converted into a sleek hotel; located next to Oxford Castle.
Oxford rooms: You can sleep inside historic university colleges and have breakfast in the grand hall.
Central Backpackers: A friendly budget option right in the centre of the town.

NIGHTLIFE

Turf Tavern: Historic pub in the centre of Oxford. Definitely worth a visit but usually quite crowded.
Freud: Former church converted into a cocktail bar. Great location!
The Mad Hatter: The Hatter offers the maddest of tea parties. Be prepared to answer a riddle on the way in!

RESTAURANTS

Cherwell Boathouse: Boathouse and restaurant on the River Cherwell, delicious food at a reasonable price.
Magdalen arms: Gastropub offering solid dishes like the traditional Sunday roast.
Dosa Park: Don't expect service or atmosphere but fantastic cheap Indian food.

ACTIVITIES

Punting 1**:** Hire a punt at the Magdalen Boathose for an essential Oxford experience; punts are available from March to October.
College tour: Walk around the city centre and check out some of the historic colleges. My favorite: Keble College. 3
Themed tours: There are several themed tours available, including Alice in Wonderland, Harry Potter, Inspector Morse, and Oxford ghost tours.

BEST SIGHTS

Christ Church College 2**:** The largest of all colleges in Oxford. Served as inspiration for the Hogwarts dining hall in the Harry Potter films.
Duke Humfrey's Library within the Bodleian Library 4**:** One of the oldest public libraries in the world.
Oxford Union: Legendary member society, famous for its feisty debates.
Ashmolean Museum: Claims to be the first public museum in the world, founded in 1683.

Contributors wanted! If you would like to introduce your city to the readers of FUTURA, send an e-mail to Kirsten.Achenbach@bifonds.de.

Bianca Gapp

Name Bianca Gapp
Nationality Austrian
Age 30
University University of Oxford, Ludwig Cancer Research Institute
Supervisor Dr Sebastian Nijman

Photos: Thinkstock; 4: Wikimedia

PROFILES

Prof. Stefan Kochanek,
Department for Gene Therapy, Ulm University, Germany
Postdoc Fellowship: 1988–1990

Priv.-Doz. Florian Kreppel,
Department for Gene Therapy, Ulm University, Germany
Fellowship: 1999–2001

For their work on how to use viruses to fight cancer, Florian Kreppel and Stefan Kochanek have been awarded the 2016 Innovation Prize of the BioRegions of Germany, a network of 30 regional initiatives promoting business applications of modern biotechnology. It is known that viruses preferentially multiply within cancer cells, a process which destroys them and exposes tumour markers to the immune system. Florian, Stefan, and their team have developed a molecular bath cap that allows viruses to swim through the blood to the cancer cells without being attacked by the body's immune system themselves. They hope that this mostly ideational prize will help them to attract investors for their biotech start-up Ad-O-Lytics.

Prof. Kai Papenfort,
Faculty of Biology, LMU Munich, Germany
Fellowship: 2007–2008

Kai Papenfort has moved back to Europe again: he has accepted a junior professorship for micro-biology at LMU Munich's Faculty of Biology. His research focuses on the molecular mechanisms of bacterial communication. He has also been elected to the Young College of the Bavarian Academy of Sciences and Humanities. This includes a three-year fellowship.

Dr Marion Silies,
European Neuroscience Institute, Göttingen, Germany
Fellowship: 2006–2008

Marion Silies received the Bernard Katz Lecture Award for her work on unravelling the circuits that compute visual motion in the brain of the fruit fly. She first built genetic tools that theoretically allow cell type-specific access to any neuron in the fly visual system. She then used this toolkit to identify neurons that are critical for motion detection and characterized their specific circuit function. The annual award was established by 1991 Nobel Prize Laureate Bert Sakmann with part of his prize money. It is alternately awarded to young German and Israeli scientists who will travel to the other country to give a lecture.

Priv.-Doz. Sven Thoms,
University Medical Center, Göttingen, Germany
Fellowship: 1998–2000

In March, Sven Thoms was congratulated for receiving the 2016 Eva Luise Köhler Research Prize for Rare Diseases by German Federal President Joachim Gauck and the former president Horst Köhler and his wife, Eva Luise, at the Konzerthaus in Berlin. Together with the research group for neuromuscular diseases in Göttingen, he was awarded this prize for a research proposal suggesting a bioinformatics-supported approach for the treatment of genetic diseases caused by premature stop codon mutations. He and his colleagues will use the prize money of 50,000 euros to evaluate treatment options for dyferlinopathies, a group of rare muscular dystrophies.

UPCOMING EVENTS

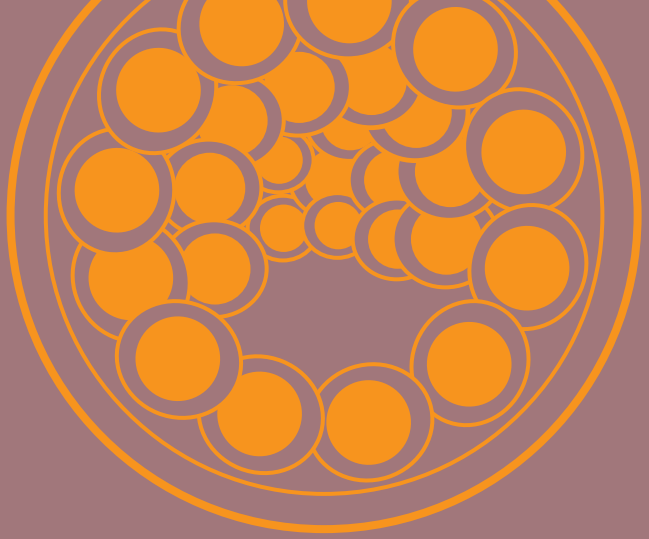
11–12 NOVEMBER 2016
Meeting of BIF's Board of Trustees
The trustees decide on the allocation of fellowships, review the proposals for the International Titisee Conferences, and settle all the foundation's matters of fundamental importance.

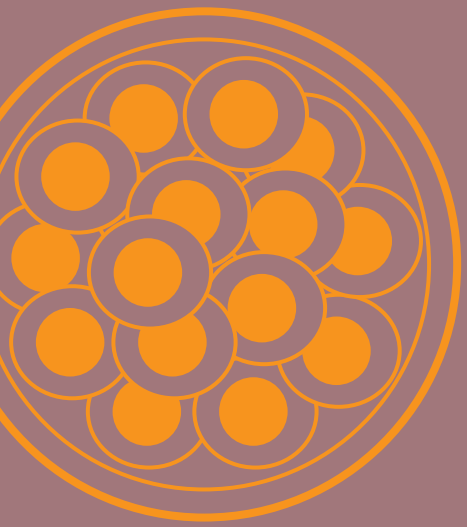
16–20 NOVEMBER 2016
114th International Titisee Conference
"The Molecules and Mechanisms of Magneto-, Thermo-, and Mechanosensation" is the title of the 114th ITC at Lake Titisee, Germany. It will be chaired by David A. Keays, Institute for Molecular Pathology, Vienna, Austria, and William R. Schafer, MRC Laboratory of Molecular Biology, Cambridge, UK. Guided by the behavioural repertoire of animals, this conference will discuss the underlying biophysical mechanisms and molecules of magneto-, thermo-, and mechanosensation.
Participation is by invitation only.

16 DECEMBER 2016
BIF Christmas Party
Christmas is coming round again – and with it BIF's Christmas party. It takes place on 16 December and starts at 6 pm. All fellows and alumni are invited to celebrate with the BIF team. Food and drink will be provided and floor space for people wanting to stay overnight will be available.

Need an update on upcoming events? Check our website at www.bifonds.de.

Photos: Kochanek: Jan Sobott; Kreppel: Kreppel; Papenfort: private; Silies: private; Thoms: E.L. u. H. Köhler Stiftung





Boehringer Ingelheim Fonds
Stiftung für medizinische
Grundlagenforschung

Schusterstr. 46–48
55116 Mainz
Germany
Tel. +49 6131 27508-0
Fax +49 6131 27508-11
E-mail: secretariat@bifonds.de
www.bifonds.de

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