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Editorial

As this issue of EMBO Encounters goes to print, the British Parliament is preparing for the delayed vote on the Brexit agreement that will determine the future relationship between the UK and the EU.

At this point, we cannot be certain what the effect of any of the possible scenarios will be on science in Europe. But it seems highly likely that Brexit will have an impact on UK-European scientific exchange and collaboration.

Back in September 2018, we wrote to Dominic Raab, who at the time was the UK's Secretary of State for Exiting the European Union, about concerns that Brexit will damage the scientific ties between the UK and the rest of Europe.

In the letter, which I co-signed with EMBO Council Chair Carl-Henrik Heldin and Secretary General Sir Paul Nurse, we made the case for international mobility of scientists and called on the UK government to protect the freedom of movement for all citizens between the UK and the EU. We also asked for protection of the UK's access to the funding and transnational networks offered by the EU Framework Programmes.

Scientists' mobility across Europe has been central to EMBO and its activities since the organization's very beginning. This will not change and the UK will remain part of all of our programmes and activities.

EMBO receives its funds from the EMBC, an intergovernmental funding body made up of 30 Member States, which include the UK. This means that we will continue to support scientists coming from and going to the UK. EMBO Courses & Workshops can continue to take place in the UK, postdoctoral and shortterm fellows can still exchange between the UK and the EU, and EMBO Members based in the UK will remain an integral part of our community.

Maria Leptin Director, EMBO

Open does not equal 'for free'

EMBO responds to European Open Access mandate 'Plan S'



On 4 September 2018, a coalition of eleven national research funders, with the support of the European Commission, announced that all scientific studies supported by their grants must be published Open Access.

he initiative, referred to as Plan S', was developed by Science Europe and the Commission's Open Access Envoy Robert-Jan Smits. It mandates that from 1 January 2020, scientists who receive funding from the European Research Council or certain public funders in Austria, France, Ireland, Italy, Luxembourg, the Netherlands, Norway, Poland, Slovenia, Sweden and the UK, i.e. the members of 'cOAlition S', publish their work in journals or on platforms that offer immediate Open Access. Since the initial announcement a second Swedish funder, Finland's national research funder, the Wellcome Trust in the UK and the Bill & Melinda Gates Foundation in the USA have joined the initiative.

Science Europe announced 'cOAlition S' alongside the publication of the coalition's tenpoint 'Plan S' that outlines the principles of Open Access publishing supported by the initiative.

EMBO response: quality must not be sacrificed

EMBO responded to the publication of 'Plan S' with the following statement by EMBO Director Maria Leptin.

"We welcome the plan, which echoes some of the recommendations EMBO has made within the Commission's Open Science Policy Platform, and through individual discussions with Robert-Jan Smits and other European Commission representatives.

"We are pleased that 'Plan S' acknowledges the importance of quality in the publication process. In working towards a complete and immediate Open Access goal, we must make sure that we do not sacrifice this quality as a result of equating 'open' to 'for free'.

"The coalition aims to standardize and cap publication fees across Europe. It is important that a cap on Article Processing Charges (APC) is not below the cost for assessment and processing per accepted article at quality journals. Otherwise there is a risk that openness and quality will be traded off against one another."

In the preamble to the announcement, the coalition also highlighted its commitment to changing the way research is assessed and rewarded.

"We welcome the coalition's desire to use the San Francisco Declaration on Research Assessment (DORA) as a starting point to move away from the journal impact factor as a measure of research output.

"It is important that changes in scientific publishing are accompanied by changes in the institutional and funding systems such that researchers are not judged by the impact factor of the journals in which their work is published."

Further developments

The publication of 'Plan S' has resulted in intense debate, particularly over the ban of hybrid journals (i.e. those journals that charge subscription fees but also offer Open Access publishing in return for an APC) in 'Plan S'.

On 27 November 2018, cOAlition S published a more detailed guidance document in which the group responded to some of the criticisms of 'Plan S'. According to these guidelines, authors will be able to follow one of three Plan-S-compliant publication routes: (1) publication in an Open Access journal or on an Open Access platform, (2) publication in a subscription journal provided the accepted manuscript is immediately made openly available in a repository, (3) published in hybrid journals that have signed agreements (by the end of 2021) to change to full Open Access publishing.

EMBO's next steps

EMBO will continue to seek conversations with those who are pushing the development and implementation of 'Plan S' forward. In addition, the organization will analyze what the future in Open Access publishing might hold and think about this topic in light of the 'Plan S' mandate.

EMBO is also looking to consult with the life science community about their views and how they see Open Access and Open Science being adopted more widely. "We are always looking to represent the community, acting at the interface between scientists and policymakers," explains Maria Leptin. "But it is clear to us that there are questions relating to Open Access and the 'Plan S' mandate that EMBO cannot simply answer on behalf of scientists."

Do scientists value journals that are highly selective or would they be willing to sacrifice selectivity in favour of cutting costs? Would scientists be put off paying a higher price for publishing in a journal that offers additional features? Would authors prefer to pay individual APCs per article or for their institutes to negotiate deals with publishers? These are the type of questions that EMBO would like to look into. If you would like to provide feedback, please get in touch at communications@embo.org

Further information

Documents and information published by cOAlition S can be found at: scienceeurope.org/coalition-s/

Also of interest: Head of Scientific publications at EMBO, Bernd Pulverer's, editorial on Open Access and 'Plan S' http://emboj.embopress.org/content/ early/2018/12/03/embj.2018101215

Welcome to the EMBO Young Investigators of 2018

26 group leaders to be supported in establishing their first lab

EMBO has chosen 26 life science researchers within their first four years as group leaders to become EMBO Young Investigators. They join an active network of 102 current and 314 past Young Investigators and will gain access to opportunities for funding, training and networking for themselves and their lab members (see box).

"The accepted candidates have all shown outstanding promise in their early careers and impressed our selection committee with both the quality of their current work and their proposals for future research," said EMBO Director Maria Leptin. "We look forward to supporting them in establishing their own research groups."

The 2018 group of Young Investigators comprises scientists based in 11 countries, including two EMBC Associate Member States: India and Singapore.

Support for the appointed scientists lasts for four years with financial and practical assistance for career development and collaboration during the important early stages of founding an independent research group.



Polly Leilei CHEN Understanding RNA editing in human cancer: causes and functional consequences, *Singapore*, SG



Ananthanarayanan Quantitative biology of the cytoskeleton and associated proteins Banaalore. IN



Alan Cheung Molecular mechanisms of chromatin coactivator complexes London, GB



Taco Kooij Malaria parasite biology and intervention strategies during host switching *Nijmegen, NL*



Nicole Joller

Andrea Pauli The germline-to-embryo transition – from fertilization to embryogenesis Vienge 4T



ZIV SNUIMAN Cellular dynamics of the antibody immune response Rehovot, IL



Martin Pilhofer Multiscale models of macromolecular machines mediating cell-cell interactions Zurich CH



Manuel Valiente Metastatic colonization of the brain Madrid ES



Thomas Baden Evolution of feature computation in the vertebrate retina Brighton, GB



Sebastian Deindl Mechanisms and regulation of protein machines at the single-molecule and atomic level Uppsala, SE



Yanlan Mao Mechanical regulation of tissue growth and regeneration London, GB



Anthony Roberts Building the cilium with ATP-driven molecular motors London, GB



Sven van Teeffelen Physical cell biology of bacteria – cell shape, cell size and growth Paris, FR



Emmanuelle Bayer The function of membrane tethering in plant intercellular communication Villengue d'Ormon FR



Xiaoqi Feng Epigenetic reprogramming in plant germlines Norwich, GB



Ivan Matic Proteomics and ADP-ribosylation signaling Cologne, DF



Nathalie Rochefort Neuronal processing of visual information in the mouse visual cortex Edinburgh, CB



Julie Welburn Cooperation of microtubul motors, cargos and their tracks Edinburgh, CB



Studying and fighting pathogenic bacteria with the help of CRISPR



Meritxell Huch Understanding liver regeneration and its implication in liver cancer



Hind Medyouf Role of the bone marrow microenvironment in hem topoietic malignancies Frankfurt. DE



Peter Sarkies Transgenerational epigenetic inheritance and evolution London, CB



Hyun Youk Distinguishing longterm dormancy from death: Principles of restarting life



Mathieu Brochet Signalling in malaria parasites _{Geneva, CH}



Mechanism and contr of DNA repair in immu nity and oncogenesis Oxford, GB

The programme at a glance

During their four-year tenure, EMBO Young Investigators receive a range of benefits:

upport for Young Investigato

- → 15,000 euros award
- → Up to 10,000 euros additional funding
- Childcare support
- → EMBO Research Leadership course

Support for their labs and lab members

- → Young Investigator PhD course and local courses
- → Meeting grants and Nobel laureate meeting
- ➔ Visits to other labs
- Access to EMBL core facilities
- → Lab retreat and creativity facilitation
- → Listing of job vacancies

Networking opportunities

- → Annual Young Investigator meeting
- → Sectoral meetings
- → Institute visits
- → Support for European networks of junior PIs
- → Joint group meetings

Helping the Young Investigators get noticed

- → Lecture grants
- → Conference support for organisers
- Listing of awards and publications in print and on social media
- → Inclusion in the EMBO directory and an online database
- → EMBO Press publishing fees covered

More information:

embo.org/funding-awards/young-investigators

A space to learn and reflect

First EMBO Young Investigator Programme retreat took place in Italy

w do I choose the best people? How do I negotiate a deal with my university? And how do I set a clear vision and goals for my research and prioritize my own and the group's time?

These are just some of the questions that researchers moving into their first group leader position face. And often they have received little to no training during their PhD and postdoc in how to answer them. The list only gets longer as the group grows, including questions about improving the team's effectiveness and ensuring that multiple projects stay on track and support the lab's overall goals.

The EMBO Young Investigator Programme offers its participants a range of opportunities to develop the skills to address these questions. These include participation in the EMBO Lab Leadership Courses, opportunities for mentoring by an EMBO Member, and exchange with other young group leaders at the annual Young Investigator Meeting.

Time away to learn and reflect

This year, the programme extended the support on offer by introducing a Young Investigator retreat, which took place in September at Villa Vigoni, a centre for promoting scientific exchange funded by the German and Italian governments, located at Lake Como in Italy. Programme Head Gerlind Wallon explains: "We hear first hand about the different challenges that scientists face when they first transition to leading their own group. With the retreat we wanted to offer them an opportunity to attend a range of soft-skills training courses with the goal of providing a set of knowledge and tools to address these questions."

"Instead of offering a week-long course, we decided to develop a programme that allowed attendees to pick and choose the sessions most relevant to them," continues Wallon. In addition, this meant that the participants could also use the retreat to spend time away from the daily demands of the lab to work on grants or write manuscripts.

Learnings that apply to everyday scenarios

49 Young Investigators attended sessions during the week-long retreat. The programme included and different courses from the EMBO Lab Leadership portfolio. In addition, the participants were able to take part in several new courses that were being piloted, including Portfolio Management, Self-Leadership in a mixed gender group and Design Principles. The feedback obtained from the participants will help EMBO to further develop the courses into something that is useful for the life science community.

Jan-Willem Veening from the University of Lausanne, Switzerland, attended the retreat to have some time away from the demands of the lab and family life in order to reflect and to use





joint meals to connect with other young group leaders.

He also joined the 'Applying design principles to schematic figures' workshop to get tips on how to create powerful schematic figures. He not only enjoyed the workshop, but was also able to immediately put his learnings to use on return to the lab. "I am working on a manuscript for which I needed a schematic to introduce the experiments and idea of the study," says Veening. "I made a rough sketch of the main components and wrote the figure legend. Then, as we learned in the workshop I let my team come up with ideas for the figure in pairs, which we discussed afterward. Once I showed them my own design, we implemented the best concepts."

He adds: "As a team we made a great figure. And we now plan to do this for all our schematic figures in the future – it is super effective and utilises everyone's creativity."

Space for own discussions

The retreat also enabled participants to bring their own suggestions for discussion sessions. Several Young Investigators had previously suggested topics they would like to discuss among this group. These were integrated into the retreat as informal evening discussions. The topics included how to hire the best people into a relatively new lab, the pros and cons of a using a'sandpit approach' to encourage free thinking in order to generate new scientific ideas, and the usefulness of an advances statistics course for PIs.

One of the hosts of such a session was Ana García-Sáez, a group leader at the University of Tübingen, Germany, who wished to tap into the expertise and experience of her peers. Her session offered a forum in which she and one other participant could practice their European Research Council grant proposal presentations and receive feedback from the audience.

"I thought it would be useful to rehearse my presentation in front of people that I am not familiar with," explains García-Sáez. And the session seemed to have hit a nerve. With this being scheduled at the end of the retreat, she did not expect many participants. But, she says, most Young Investigators joined and "had very good suggestions in terms of format and style, but also from the content point of view, which helped me make the presentation clearer."

García-Sáez says she "considered my session a success." Overall feedback from the attendees was very positive. "It was great to hear that the participants felt the retreat was time well spent," says Gerlind Wallon. "We are already thinking about a repeat event in two year's time."

embo.org/funding-awards/young-investigators lab-management.embo.org/

Welcoming new EMBO Members

n May last year, 62 life scientists were elected as EMBO Members or Associate Members, L joining the group of more than 1,800 outstanding life scientists. At the annual Members' meeting in Heidelberg in October, the new Members were welcomed. "This meeting is packed with science at its best", EMBO Director Maria Leptin said. EMBO Members are leading scientists working across all of the life sciences. They strengthen the research community in Europe and beyond

through their international collaborations and connections.

The EMBO Members are actively involved in the execution of the organization's initiatives by serving on EMBO Council, Committees and Editorial Boards, by evaluating applications for EMBO funding, by mentoring young scientists and by providing suggestions and feedback on activities

CSABA PÁL

L. S. SHASHIDHARA

New EMBO Associate Member



ingadahalli Subrahmanya Shashidhara uses Drosophila as a model system to answer two fundamental questions: What is the mechanism by which cells, tissues and organs - a network of actin, myosin are positioned in the body? And how are shape and size of different organs determined? His lab is studying molecular and morphogenic events downstream to Hox genes, which play critical roles in the elaboration of segmental identities in all bilaterian animals.

the Indian Institute of Science Education & Research (IISER) in Pune, India. "I am very happy to be one among such accomplished biologists. I hope to benefit from interactions with the EMBO community, particularly in the domains of science policy and science management EMBO Member," she said. practices", he said.

www.iiserpune.ac.in/~ls. shashidhara/



EWA PALUCH

The focus for Ewa Paluch is to understand how animal cells control their shape. She investigates how the mechanical properties of the cell cortex and associated proteins that lies under the plasma membrane and gives most animal cells their shape - are determined by its molecular components and how these properties are regulated to drive cellular deformations.

Ewa Paluch, of the MRC Laboratory for Molecular Cell L. S. Shashidhara is heading Biology at University College London will be moving her laboratory to the Department of Physiology, Development and Neuroscience at the University of Cambridge in 2019.

"I look forward to further promoting interdisciplinary approaches in biology as an

www.pdn.cam.ac.uk/directory/ ewa-paluch

EMBO Member

saba Pál's research targets central issues in evolution with medical importance. He and his lab develop novel methods in microbial genome engineering with the aim to study antibiotic resistance with unprecedented detail. Another focus of his group is microbial evolutionary genomics, studying dosage balance hypothesis, compensatory evolution and the role of phenotypic heterogeneity. Csaba Pál heads the Synthethic and Systems Biology Unit at the Biological Research Centre of the Hungarian Academy of Sciences in Szeged.

"EMBO Membership is an amazing opportunity to foster new collaborations, to catalyze research opportunities for talented students, and to popularize our achievements to a broad audience," he said at the meeting.

group.szbk.u-szeged.hu/sysbiol/

Open Access: To be free or not to be?

At the EMBO Members' meeting, Bernd Pulverer, Head of Scientific Publishing at EMBO, talked about requirements for implementing Open Access in publishing

 $B^{y\ 2020,\ 'Plan\ S'}$ by the so-called cOAlition S will mandate free access to research published by scientists funded by the European Commission or by the funders who are signatory to the plan. (see page 3) " 'Free' must not be confused with 'at no cost', if quality is not to be compromised", Pulverer said. "Journals are charging for an important service that ensures the selection of reliable research results that are worth sharing."

He provided insight into the cost structure of the five journals published by EMBO Press. Two of them are hybrid journals: The EMBO Journal and EMBO Reports are subscription-based, but offer authors the choice to make their papers fully Open Access (also called 'Gold OA') by paying a fee. The other three are fully Open Access: Molecular System Biology, EMBO Molecular Medicine and Life Science Alliance. The fees charged e.g. by Molecular Systems Biology and EMBO Molecular Medicine for OA are substantial as the journals select for quality as well as for interest and importance of the work. Only 12% of submitted papers are published, raising the unit cost. "To put the cost in perspective, one also needs to consider the total budget that underlies the average bioscience research paper," Pulverer said. The limited data available suggest that spending on publishing are in the order of 1-3% of the overall research spending.

He explained that flipping all five EMBO Press journals to Gold OA would require author fees above the cap anticipated from Plan S signatories, "except if the journals would reduce their selectivity. This is not what we intend to do with our journals". Moreover, publishers will have to be able to provide additional value to journals beyond OA in order to make the research re-usable and to encourage reproducibility, Pulverer concluded.

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Peer Review Week 2018

Encouraging diversity and inclusion in the review process

Peer review is a crucial component of scholarly publishing to optimize the quality of the published research. To recognize and celebrate peer review and the scientists acting as reviewers, a group of organizations introduced Peer Review Week in 2015.

Peer Review Week took place once more between 10 and 15 September 2018 and focused on the topic of 'Diversity and Inclusion'. Bernd Pulverer, Head of Scientific Publishing at EMBO, took the opportunity to outline some of the initiatives to increase diversity in peer review at the EMBO Press publications.

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We ask for referee recommendations from established colleagues and require that co-referees be identified.

Diversity in peer review is not something that is always easy to achieve. At the EMBO Press journals, for example, the proportion of authors from Asia is much larger than that of referees from the same continent. Early-career researchers also remain underrepresented, while established referees are increasingly overburdened.

One of the ways in which the editors of *The EMBO Journal, EMBO Reports, EMBO Molecular Medicine* and *Molecular Systems Biology* are addressing this is by taking into consideration gender and geographical diversity as well as career stage when inviting scientists to join the editorial boards of the journals and when selecting referees. In order to identify a wider range of suitable reviewers, we ask for referee recommendations from established colleagues and require that co-referees be identified.

Another step we take to ensure that we use as many different reviewers as possible is to aim for a combination of scientists who have previously refereed for our journals and first-time reviewers. We also encourage senior scientists to include postdoctoral fellows as co-referees, and to mentor them in refereeing. The EMBO Press transparent process means that referee reports, author responses and editors' decisions are all published alongside papers (also see 'Transparent peer review' on this page). This enables new referees to train themselves to review optimally by analyzing the editorial process on published papers in their area of research.

Named co-refereeing not only helps to identify and train early-career researchers as reviewers. It also ensures those scientists who did the work can receive credit for this crucial contribution to the scientific process. Taking this further, we hope to work directly with funders to ensure that refereeing can be taken into account as a scientific output in research evaluation.

Finally, our commitment to involving earlycareer researchers in our publishing activities

Transparent peer review

EMBO Press co-signs open letter to support publication of peer review reports

E MBO Press is among more than 20 signatories of an open letter that expresses their commitment to the publication of the peer reviews associated with scientific papers. Those who signed the letter but had not yet implemented this step pledged to do so. In addition, the goal is to encourage other journals and publishers to do the same to establish the publication of peer reviews as a standard in scholarly publishing.

The letter is the outcome of a meeting between editors, publishers, funders, and researchers to discuss innovations in peer review that took place at the Howard Hughes Medical Institute in Chevy Chase, USA in February 2018. It was coordinated by ASAPbio, a community initiative in the biological sciences that promotes transparency and openness in science communication. A majority of participants at the meeting agreed that publishing all of the content of peer review, whether anonymized or not, and the author responses would benefit the research community by increasing transparency of the assessment process. These benefits include:

- increased reviewer and editorial accountability,
- opportunities for learning and self-training,

extends beyond co-refereeing of papers. *Life Science Alliance*, which EMBO Press publishes in partnership with Rockefeller University Press and Cold Spring Harbor Laboratory Press, specifically focuses on engaging both established and emerging leaders in their fields as editors, on the editorial board and during peer review.

More information:

embopress.org/transparent-process peerreviewweek.wordpress.com

- enhancing readers' understanding of the article in the context of the field, and
- a pathway to providing credit for peer review. *The EMBO Journal* introduced the publication of Review Process files, which include the referee comments, authors' responses and the editorial decision letter, in 2009. The other EMBO Press journals, *EMBO Reports, EMBO Molecular Medicine* and *Molecular Systems Biology* followed suit in 2010, and the publication of these files is a central component to EMBO Press' transparent process.

Head of Scientific Publishing at EMBO Press, Bernd Pulverer, says about the letter: "It is great to see that other journals are adopting policies to publish peer review reports, author rebuttals and editorial decision letters. Together with the letter's signatories, I encourage other publishers to join this initiative so that it can become a standard in publishing after a decade of unequivocally positive experiences with this process at EMBO Press. Referee cross-commenting, named co-referees, avoidance of confidential referee comments and transferable referee reports add to make for a more informed and fair publishing process."

Letter and a list of signatories: asapbio.org/ letter

Additional information: *Nature*, doi: 10.1038/ d41586-018-06032-w

More information about the transparent process at EMBO Press: doi: 10.1038/ emboj.2008.250 and 10.1038/emboj.2010.307



Setting the wheels in motion

Three co-organisers report on the impact of the EMBO research integrity courses at their institute or university

W T've been approached by people asking for the next steps. There is a call for action." Eirikur Steingrimsson's testimonial of EMBO's research integrity workshop shows that starting a conversation about the topic of responsible conduct of research can result in furtherreaching action.

In addition to being an EMBO Member, Steingrimsson, of the University of Iceland in Reykjavik, currently holds the position of vicepresident of the European Molecular Biology Conference (EMBC), EMBO's intergovernmental funding body. It was at an EMBC meeting that he first heard about the research integrity workshops EMBO has been delivering at institutes and universities in EMBC Member States. Feeling that researchers at the University of Iceland would also benefit from such a workshop, he approached the EMBO Science Policy Programme, which then organised a workshop that took place in Reykjavik in April last year.

Raising awareness of the subject

EMBO initiated the workshops – initially as a pilot – in 2016 to raise awareness of the importance of conducting research in a responsible way and to contribute to fostering responsible research practices in Europe. Programme Head Michele Garfinkel and Programme Officer Sandra Bendiscioli have since visited ten institutes in nine countries, working with an EMBO Member as local co-organiser to deliver tailored workshops on research integrity to up to 30 participants at a time.

The feedback from the approximately 25 postdocs and young group leaders who participated in Reykjavik was overwhelmingly positive, says Steingrimsson. "They were really happy that the university was thinking about this subject and to have the opportunity to hear and talk about it."

In addition to leaving an impression on the participants, the workshop led the university to look at how awareness of responsible conduct of research could be further increased to ensure the workshop wasn't just a one-off event. "After the course we brought together the administrators and people organising the graduate programme to talk about where the university stands," he says. "There are things happening: for example, everyone in the graduate programme is required to take a research ethics course since last year. But unfortunately I'm not yet aware of anything similar for more senior scientists."

A focus on data management

The importance of following up the workshop with concrete steps is something that EMBO Member and Council Member Claudio Sunkel echoes. He co-organised the EMBO research integrity workshop that took place at the i3S Institute in Porto, Portugal, in January 2017.

"The workshop was excellent," he recalls, "people came out with a very clear view on what is proper research conduct and what it is not. And because parts of the workshop were open to everyone, we were able to bring that message across to lots of people."

The institute already has an ombudsperson to deal with research matters, but, Sunkel says, it is also looking to hire someone whose full-time position is dedicated to research integrity and ethics. For now the i3S has integrated the topics of research ethics, misconduct and responsible research data management into the training for PhD students and postdocs and has also embedded research integrity into some of their career development courses.

Sunkel explains: "We want to make people aware that they need to be very conscious of what they do with data and how they manage them." However, he adds, it would be helpful to also have something in writing, such as a booklet summarising the most important points, to distribute to all staff and encourage discussion to ensure that everyone at the institute is on the same page.

The importance of strong mentorship

The second element he stresses is the importance of mentorship to transmit the values of responsible research practices and the knowledge necessary to work responsibly. Following the EMBO workshop, the participants began sharing what they learnt, making others aware of the types of questionable practices that might occasionally be followed but that one is not supposed to use. "That also reflects on the importance of mentorship," says Sunkel. "It's important to mentor the mentors, because you have people coming out of a postdoc, starting to run their own lab and they know very little about these things."

Strong mentorship is also something that Claire Hivroz at the Institute Curie considers crucial in establishing responsible research practices at all levels. Together with EMBO Member Geneviève Almouzni, Hivroz co-organised an EMBO research integrity workshop at the institute in Paris, France in June 2017.

"Following on from the workshop and discussions with Michele and Sandra, we have organised four sessions for young PIs this year," says Hivroz. She explains that the sessions were structured more broadly around wellbeing in a research group but also included research integrity, adding that "these things are linked. When people have confidence in their supervisor, they also feel much more confident to ask questions and are clear on what is expected of them."

Finding the best way to train

Another activity put in place at the Institut Curie is a three-hour session on research integrity for all new PhD students. Delivered by two group leaders or a group leader and a postdoc, these workshops give participants the chance to think about the subject, to ask questions and to participate by telling their own stories.

"These sessions are mandatory for all PhD students," explains Hivroz. "But the real challenge is that with 60-70 new students and a participant limit of around 15, we have to organise quite a few sessions a year." She says the institute also thinks about offering online training in research integrity through a massive open online course. However, she says, "some of the feedback from those who already followed such a course has been that people end up 'click-clicking' without thinking about the subject. So we really need to find the right mix."

Listening to all three co-organisers, it becomes clear there is a need and desire to discuss research integrity issues. The EMBO workshops have had an impact in raising awareness and triggering additional activities. Yet for many researchers and institutes the challenge remains how to best and most efficiently foster responsible research conduct. As Steingrimsson puts it: "It's a live issue that doesn't go away. It needs be kept alive and one of the most important questions is 'how do we do that'?"

embo.org/science-policy/research-integrity For more information about the workshops, contact policy@embo.org

Lab exchanges

EMBO Short-Term Fellowships fund laboratory visits for up to three months. Here, four recipients talk about how such an exchange influenced them professionally and personally.

By Kathy Weston

Arie-Steph Aschtgen, a postdoc in Birgitta Henriques-Normark's lab at the Karolinska Institute in Sweden, studies Klebsiella pneumoniae. She works on virulence factors, the weaponry that bacteria use to subvert or elude host defences. Specifically, she is interested in a molecular machine called the type 6 secretion system (T6SS), which forces bacterial proteins into neighbouring cells using a phagelike injection system.

Finding a biofilm expert

While T6SS has an important function in hostpathogen interactions, it's also a major player in inter-bacterial relationships. Bacteria normally live in biofilms that are resistant to stresses such as antibiotics. So Aschtgen was intrigued to discover that one of her clinical isolates of *K. pneumoniae* had a T6SS mutant that prevented biofilm formation. However, there was a problem: her home lab had no expertise in biofilm work.

Fortunately, Henriques-Normark is a visiting professor in Singapore, and put Aschtgen in touch with Scott Rice at Nanyang Technical University. His lab is devoted to biofilm development, and he was happy to help. "Scott has an awesome microscopy facility and grows bacteria in biofilm conditions, which we couldn't do in Sweden", says Aschtgen. But visiting Singapore was going to be very expensive, she realised: "I needed to spend at least a month in his lab, so I applied for an EMBO Short Term Fellowship." Aschtgen had the added complication of being a new mother, but she simply solved that problem by bringing her partner and eight month-old daughter with her.

From one-off project to long-term collaboration Rice's lab went out of their way to help: "The lab were really welcoming," says Aschtgen. "I didn't expect to be able to get through all the experiments we'd planned, but Scott assigned a PhD student and post-doc to help me, and they were fantastic. I was able to work almost from day one." She also did some networking, setting up meetings with faculty with complementary interests.

As with all good projects, Aschtgen's lab work didn't turn out quite as expected: her clinically



From Stockholm to Singapore

isolated T6SS mutant bugs were indeed miserably bad at forming biofilms in monoculture, but when mixed with different types of bacteria, they actually performed better, outcompeting other species of *K. pneumoniae*. One of Rice's PhD students is now working on the project, too, and Aschtgen plans to return, helped by further funding from EMBO.

Aschtgen thinks the short-term fellowship was a vital component of the project's success: "Because of the fellowship, it's become a real collaboration that will continue for a long time. I don't know if that would have been possible otherwise."

Plants are increasingly put under stress, for example by environmental challenges such as global warming and pollution. Pramod Sivan, a young investigator at the Rubber Research Institute of India in Kerala, is interested in the mechanisms by which plant cell walls resist stress.

An intensified working relationship

Sivan's work, on the role of the cellwall polymer lignin in conferring mechanical strength and aiding resistance to stress, uses tobacco plants

as a model. Over the years, he has had a lot of advice from Ewa Mellerowicz of the Swedish University of Agricultural Sciences in Umeå. So when Mellerowicz suggested he applied for an EMBO Short-Term Fellowship to come to Umeå for three months, Sivan jumped at the chance. "The Umeå lab has facilities that aren't available in my home institute, and the opportunity to learn a whole new set of techniques in such an environment was irresistible."

Any apprehension about spending time so far from home vanished almost as soon as Sivan



arrived in Sweden. His plane from Stockholm to Umeå had been cancelled, but a friendly local helped him sort out what to do next. And his flatmates in the apartment he shared were lovely: "They found out it was my birthday just after I arrived and surprised me with a nice celebration," he says. "I felt like a family member by the time I left."

Sivan's project in Umeå used transgenic aspen plants to see how changes in cell wall composition affect the biosynthesis of the cuticle. Mutation of the enzyme pectate lyase unexpectedly turned out to have profound effects on cuticle formation during cell wall maturation. "I'm hoping to return to Umeå to carry on the collaboration," says Sivan, "as it's a very interesting idea that pectin and other polymers are so heavily involved in cuticle development."

Experiencing another lab culture

As well as a successful scientific stay, Sivan had a valuable insight into the workings of a different lab. He

particularly liked the communality: "People were trained really well on the equipment, and could move freely between different labs to access the facilities," he reflects. The flat hierarchy was also appealing: "Everyone's opinion was listened to, and weight was given to knowledge, not position," Sivan says. "This visit was a great opportunity to learn many things personally and professionally and it will definitely help in making better future plans." Dietary factors are likely to play a part in the development of bladder cancer, and there is mounting evidence that vitamin A, and its metabolite retinoic acid, can decrease the cancer risk. However, the mechanism of action is unknown.

Daša Zupančič is an associate professor at the Institute of Cell Biology at the University of Ljubljana, Slovenia, and has been studying bladder cancer for several years using histopathology and microscopy. Her institute has an excellent track record in microscopy, but Zupančič found that it lacked the capacity for more molecularlyoriented studies. This hampered her ability to get to grips with the molecular mechanisms of bladder cancer development and the link with vitamin A.

Trading microscopy for molecular biology

Zupančič had wanted to take a sabbatical to learn some molecular biology for a number of years, but life outside of work intervened. She got married and gave birth to four children during and after her PhD. With her youngest child now attending school, and the older three being able to help at home, she revisited the idea.

One of the most important experimental tools for bladder cancer research is the BBN (N-butyl-N-(4-hydroxybutyl)nitrosamine)-induced mouse model of bladder carcinogenesis, and Zupančič already had a working relationship with the lab of Janoš Terzić at the University of Split School

Drosophila rely heavily on a sense of smell to navigate the world, but how do they classify scents into meaningful categories? An odour such as carbon dioxide can signal the presence of fermenting fruit (good) or a group of very stressed fellow fruitflies (bad). And an incoming fly must choose the appropriate behavioural response – feeding or leaving the scene as quickly as possible.

The answer seems to lie in the mushroom body, a higher brain region in flies that 'reads' the aversive input and balances it with a 'reward' input

from dopaminergic neurons sensing other odours, emitted, in this case, by 'good' food sources. Such contextual modulation of behaviour has a relevance extending far beyond a humble fruitfly's desire to find rotting fruit; it may yield insights into how mammalian brains make analogous decisions.

Taking a chance

Nicolás Fuenzalida-Uribe, a recent PhD graduate in Jorge Campusano's lab at the Universidad Católica de Chile in Santiago, works on a twist to the *Drosophila* olfactory story: how ageing affects contextual modulation. During his PhD project, Fuenzalida-Uribe showed that older flies have an altered response to benzaldehyde,

of Medicine in Croatia, where the model is in routine use. A collaboration looking at the role of vitamin A in BBN-induced carcinogenesis, where Zupančič traded her expertise in microscopy for the Terzič lab's proficiency in molecular biology seemed a perfect match, and EMBO awarded her a three-month short-term fellowship to get the project off the ground.

"I didn't even know that EMBO existed," says Zupančič, "but Janoš told me about the Fellowship Programme. I was very happy to find such a great opportunity!"

Jelena Korać Prlić in Terzić's laboratory gave Zupančič a crash course in RNA purification, cDNA synthesis and PCR, and she set to work preparing and analyzing samples from BBN-treated animals fed either a vitamin A-rich, or a control diet. After more than a decade spent teaching undergraduates, with only a little time for research, Zupančič was in heaven: "Having three months' uninterrupted time in the lab was like being a PhD student again," she says. For the first time in years, she also had some free time, which she used to read and to explore Split and its surroundings with new friends she made in the lab.



Bringing new ideas back home

Zupančič was impressed by the level of collaboration and equipment-sharing between labs in Split, and hopes to implement something similar back in Ljubljana. "Money is short, and it makes so much more sense to share resources," she says. She already agreed a deal with another department, whereby the other researchers can use her department's microscopes in exchange for time on a new scanner for Western blots.

The vitamin A project itself had such promising results, showing that vitamin A hinders the development of urothelial dysplasia in BBN-treated mice, that Zupančič and Korać Prlić are continuing to collaborate. They are in the process of writing up a paper and applying for further funding.



which like carbon dioxide, is another contextdependent feed-or-flee-stimulus. To dissect the physiology of this behaviour in more detail, he decided to use calcium responsiveness, a proxy for neuronal activity, to see if Kenyon cells, the specialised olfactory neurons in mushroom bodies, change their neural activity in response to benzaldehyde as flies age.

Unfortunately, the very expensive two-photon microscope he needed to do this work wasn't available in his home lab. Undeterred, Fuenzalida-Uribe did an internet search for groups with the right microscope together with expertise in Drosophila olfactory bulb imaging, and came up with Ilona Grunwald Kadow's lab at the Technical University of Munich, Germany. He emailed her, and was delighted when she suggested he could come for a visit. As a source of funding, Grunwald Kadow suggested he applied for an EMBO Short-Term Fellowship.

The beginnings of a postdoctoral project?

Having arrived in Munich Fuenzalida-Uribe's first task was to set up crosses of the flies he'd need, so that they'd be appropriately aged towards the end of his three-month visit. He was taught how to use the two-photon microscope by Siju Kunhi Purayil, a postdoc in the

lab, and by the end of his time in Germany, had successfully shown age-dependent differences in calcium dynamics, which can potentially be used as physiological markers for the aging process. He now hopes to be able to return to Germany as a postdoc to continue the project.

In addition to working hard Fuenzalida-Uribe managed to do a bit of sightseeing: "The lab organised a trip to the oldest continuously working brewery in the world," he says, "and they also helped me test some of the beer in Munich!" However, his favourite trip was to Prague: "I really like Franz Kafka, and one of my dreams has always been to visit the place he was from," he says. "That was very special."



Spotlight on EMBO Courses & Workshops

he organizers of EMBO Courses and Workshops play an important role in making these events successful. Through their connections and knowledge of the field they create up-to-date programmes and identify the most suitable speakers – whether the event is part of a recurring series or a first in line representing an emerging field. Below, the organizers of a course and two workshops report on how their events came about, what made them a success and which topics drew the most intense discussions.

A FIRST FOR COMBINING NEUROSCIENCE AND BIOPHYSICS

Between 8 and 12 May 2018, biophysics met neurobiology at the first EMBO Workshop on molecular neurobiology that took place on the island of Crete in Greece. The meeting was designed to foster interaction and discussion between rapidly growing yet traditionally distinct fields, with approximately 120 structural biologists, biophysicists, and cellular biologists attending.

Here, two of the organizers, EMBO Member Rob Meijers, EMBL, Hamburg, Germany, and EMBO Young Investigator Elena Seiradake, Oxford University, UK, explain their motivation of bringing together scientists from such diverse fields.

With technological and methodological advances, structural biology has evolved into an important contributor in analyzing biological molecules in all their complexity. At the same time, imaging techniques now make it possible to follow single molecules in individual cells and in tissues. And genetic tools have become so sophisticated that different developmental stages can be monitored. These parallel developments provide unprecedented possibilities to study fundamental problems in neuronal development and pathology.

The meeting showcased data acquired by different state-of-the art techniques, and presented a 'hot spot' for pushing boundaries and forging cross-disciplinary collaborations. New X-ray crystallography and electron microscopy data revealed molecular level insights into axon guidance systems, adhesion molecules, and ion channels, illustrating how these techniques can be used to analyze ever more complex and physiologically relevant molecular assemblies. Animal models, live-cell and super-resolution microscopy revealed protein localization properties, receptor dynamics and a picture of how the nervous system works at the molecular, cellular and tissue levels. Structure-based mutants and genetics emerged as tools of choice for analyzing how multifunctional proteins perform their specific roles in tissues, while tomography and advanced fluorescence-based methods bring structural biology into the cell.

In summary, the meeting highlighted where and how biophysics and neurobiology are converging. It is always difficult to predict where a field is moving, but we asked some of the presenters to reveal their 'dream experiments', outlining scientific and methodological goals. The emerging theme was the ability to visualize proteins at high resolution, in action and in the context of the entire cell. As EMBO Member and meeting attendee Poul Nissen of Aarhus University, Denmark, put it: "The field is aiming for biophysical models of life."

FIELDWORK COMPLETES MOLECULAR GEOBIOLOGY COURSE

Researchers with interests in areas as diverse as astrobiology, the origins of life, and the way organisms adapt to extreme environments, came together at the European Molecular Biology Laboratory (EMBL) in Heidelberg from 26-31 August 2018 for the EMBO Practical Course 'Molecular Geobiology'.

This was the first EMBO course on geobiology and the first to involve an element of fieldwork, with participants travelling to the Ries impact structure in Bavaria, Germany to take rock samples and test them for the presence of microbial species. The Ries impact structure is a crater 24 km in diameter, thought to have been formed by a meteorite impact around 14.5 million years ago. Kiran Patil from EMBL, one of the organisers, says that the fieldwork aspect of the course came out of discussions between himself and co-organiser Haley Sapers, of the California Institute of Technology and NASA Jet Propulsion Laboratory, USA. "We'd been talking about collecting samples from the Ries crater to see if we could identify



Course attendees collecting rock samples at the geobiology course.

the microbes there and analyse their DNA, which had not been done before, he says.

Preparing the course, Sapers came to EMBL and, along with Patil, Sonja Blasche and Yongkyu Kim from Patil's group, and Vladimir Benes from EMBL's Genomics Core Facility, drove to the Ries crater to collect some rocks that were formed by the meteorite impact. After some effort from Blasche and Benes, the group succeeded in getting good quality DNA sequences from these rocks and eventually isolated some of the microbes that are likely to be new species – this is, in fact, now an ongoing project.

Patil explains: "We thought it was an extremely rewarding and fun exercise and one that other people might benefit from. The subsequent discussions led to the idea of the course, which we thought would be incomplete without actually going to the field. Only then can one understand the whole picture."

ANNIVERSARY WORKSHOPS

Several of the EMBO Courses and Workshops are long-standing meetings that have been taking place for several decades, bringing together scientific communities at regular, usually two-year, intervals to discuss the latest research in their respective fields.

The EMBO Workshop on the molecular and developmental biology of *Drosophila* is one example, having run for over four decades. The meeting took place in Crete, Greece for the 21st time in June this year. Another is the cell signalling workshop in Cavtat, Croatia, which celebrated its 20th anniversary this year.

Another workshop that celebrated an anniversary this year is the EMBO Workshop 'Lymphocyte Antigen Receptor Signalling'. Between 25 and 29 August 2018, the conference took place for the tenth time in Siena, Italy. Organizer and EMBO Member Cosima Tatiana Baldari says: "This conference continues to be extremely popular. This year we had nearly 500 applications for just over 100 places, and we had a unanimous request to organize it again in two years' time in the same location." This year's workshop aimed to present and discuss the most recent advances in understanding the nature and interplay of the signals that drive lymphocyte activation, development and differentiation; the outcome of their alterations on immunerelated diseases; and their exploitation for creating therapeutics. It combined talks by invited speakers, selected short talks by young participants and a poster session. "We have always put great

emphasis on encouraging interaction between all participants," explains Baldari. "We held the poster session in the afternoon of the second day to give it full exposure, and it was very well attended." In addition, she says, the fact that all participants stay on site and share extensive coffee breaks and all meals at the venue in the Tuscan hills favours discussions and interactions.

Baldari continues: "The conference was a success, both in terms of its superb scientific standards and for its unique features of liveliness,



participation and friendliness, which make it stand out compared to similar initiatives." She highlights that a majority of data presented were unpublished and triggered lively discussions; and points out that the conference has helped to propel the field forward. "The format of the conference truly supports the formation of collaborations. And over the course of two decades I have seen it help the scientific development of many young scientists who have now become leaders in the field."

Responding to community needs

ast year, 250 organizers of EMBO Courses and Workshops offered feedback through a survey. How did their responses influence the programme?

Scientific meetings are central to the sharing and discussing of scientific knowledge. As the largest funder of scientific meetings in Europe, the organization supports over 90 practical courses and workshops, which are proposed by researchers. Reflecting the needs of the scientific community, these events bring together more than 11,000 participants from a diverse range of fields in the life sciences each year.

In addition to funding, EMBO provides organizers with administrative and communications support, such as the provision of a website with registration system and the creation of an event poster. The scientific programme, invitation of speakers, selection of participants and event organization, however, remain entirely in the hands of the organizers.

In order to ensure that the support EMBO provides meets the needs of the life science community, EMBO asked those scientists who had applied to the Courses & Workshops Programme during the last three years to provide feedback through a survey.

"We were pleased that, on the whole, the feedback was very positive," says Courses & Workshops Programme Head Gerlind Wallon. "But of course it is the comments on where we could improve that will help us better tailor the programme's offering to the community's needs."

On funds and registration

EMBO funds more than half of the applications it receives. One purpose of the survey was to find out whether the organizers' whose applications EMBO rejected found alternative means to fund their meetings. "We were positively surprised that more than 70% of workshops still took place," says Wallon, "but it was a very different picture for practical courses, where only 38% took place without EMBO funding."

At present, a maximum of 38,000 euros core funding are available per event. Nearly half of the organizers felt that this was not sufficient to fund a workshop without additional funding, although of these more than three quarters were able to source such support through other means. The core funding had been increased in 2017 to the current level from 30,000 euros.

"There are many different factors that determine the final cost of a scientific meeting," explains Wallon. "Considering, for example, that most organizers fully cover speaker costs and that it is difficult to predict how many participants a meeting will attract, i.e. how much income is generated via registration fees, the funds might not always be sufficient."

EMBO caps the registration fees at its workshops. Nearly 40% of survey respondents felt these were too low. "It is interesting to hear that such a large proportion of organizers would favour higher registration fees. However, this is not something that we are likely to change. The money for the EMBO Workshops comes from the 30 Member States of EMBO's intergovernmental funding body, the EMBC, and they expect that scientific meetings remain affordable."

Working with and for the community

Eight of ten organizers said that they made use of EMBO's offering of website and registration system support, and of those that did, 96% were satisfied with the support they received. One of the items that organizers commented on was the lack of a payment tool that was directly integrated into the website. "Nearly two thirds of organizers said they were willing to pay a supplier to provide this," says Wallon. "And they now have the option to install a payment system via the website."

In response to the survey EMBO also made some adjustments to the application procedure. Wallon explains: "Overall the feedback we received was that the application procedure is straightforward, and we want to make sure we maintain the balance between ease of application and the information needed by the committee to make an informed decision. It is something we continue to work on with the committee. And we will of course continue to use the feedback we receive from our community – through the survey and otherwise – to ensure the programme meets scientists' needs."

More information: embo.org/funding/ courses-workshops

Application deadlines: 1 March and 1 August

Predicting the LifeTime of a cell

ifeTime is a pan-European initiative that aims to improve healthcare by tracking and understanding human cells during disease. The consortium, lead by EMBO Members Nikolaus Rajewsky at the Max Delbrück Center in Berlin, Germany, and Geneviève Almouzni at the Institut Curie in Paris, France, has successfully applied for a Coordination and Support Action (CSA) published by the EU Horizon 2020 Future and Emerging Technologies (FET) Flagship programme. The CSA is scheduled to start in May 2019 and will run for one year. It will deliver the blueprint for the proposed large scale research initiative. A scientific conference, planned to take place between 5 and 7 May 2019 in Berlin, will mark the start of the CSA.

LifeTime's goal is to quantify, model and predict cell trajectories in tissues and whole organisms. In the long term, the initiative wants to provide tools to medical doctors to assess the molecular history and current state of a patient's tissues in real time, making it easier for them to



diagnose a disease and effectively intercept its progression.

The project is driven by 65 founding members from across Europe, 34 of which are also part of the EMBO Membership. As leaders in a wide range of fields such as single-cell biology, computer science, mathematics, pathology, imaging and physics, LifeTime members will focus on bringing individual expertise together. For example, single-cell genomics will be integrated with smart imaging to deliver clinical-grade single-cell pathology with high spatial resolution. Other approaches will include the combination of computational models with artificial intelligence analyses of gene function, or profiling organoid technologies at single-cell resolution.

Australia's Walter and Eliza Hall Institute focuses on ubiquitin

n November 2018, EMBO Member David Komander joined the Walter and Eliza Hall Institute in Melbourne, Australia, where he will head a new research division focusing broadly on ubiquitin biology.

The institute wishes to broaden its research into healthy ageing and development to supplement the current research on cancer, immunity and infection. Komander says that the institute's multidisciplinary research expertise offers an ideal environment to progress his work in understanding how proteins can distinguish between and respond to different forms of ubiquitin modifications in the cell.

"The Walter and Eliza Hall Institute has successfully shown it has the capability to applying expertise in structural biology, medicinal chemistry and clinical translation to progress new therapies for cancer, immune disorders such as arthritis and inflammatory bowel disease, and malaria," Komander adds. "I'm excited to be joining the institute where there is the opportunity to progress, and eventually translate, our research into the links between ubiquitin signalling, inflammation and neurodegenerative disorders."

Agricultural information for Africa

MBO Member and former EMBO Council Chair Chris Leaver, Emeritus Professor at the University of Oxford, UK, is among a group of scientists, educators and communicators that run Biosciences for Farming in Africa (B4FA). The independent not-for-profit initiative provides balanced, scientifically-based information on best practice, innovation and entrepreneurship to support African farmers.

"The need to encourage African farmers to embrace modern agricultural developments in order to provide food security is clearly recognized", explains Leaver and emphasizes the importance of good communications between scientists, farmers and decision makers to achieve this goal. B4FA has provided training to more than 160 print and broadcast journalists in Ghana, Nigeria, Tanzania and Uganda to increase their understanding of biosciences and modern plant breeding techniques. Leaver says: "Growing out of these and other concerns expressed to us by scientists and journalists alike, we saw a need for an on-going, accurate, unbiased and up-to-date source of information for all those working to improve African agriculture and food security."

This has led to the B4FA Newswire: through social media, a weekly newsletter and a website updated daily, B4FA reaches more than 10,000 policymakers, scientists, journalists, educators, students, and farmers each month. It is the only medium that consolidates and amplifies information specifically for and about sub-Saharan Africa. "The importance of spreading this information was brought home to me recently at an Alexander von Humboldt Foundation conference in Akure, Nigeria," adds Leaver. "I gave a lecture on unlocking agricultural potential to achieve food security and sustainability for 9.7 billion and learned how relatively isolated many scientists and researchers in Africa felt from developments across their continent."

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More information: b4fa.org twitter.com/B4FA

Frankfurt Cancer Institute announced

he establishment of a new interdisciplinary cancer institute in Frankfurt, Germany, has been announced. The focus of the Frankfurt Cancer Institute (FCI) will be on the molecular mechanisms underlying tumour development and therapy resistance with the aim to, ultimately, develop new diagnostics and therapies that can be directly and quickly translated into clinical applications.

EMBO Member Ivan Dikic, Goethe University Frankfurt, serves on the leadership team together with Florian Greten, Georg-Speyer-Haus and Goethe University Frankfurt, and Hubert Serve, University Clinic Frankfurt. Representing, respectively, basic research, preclinical research and clinical application, they will drive the translational focus of the work at the FCI.

Warsaw to host Centre of Excellence for Neural Plasticity

HBO Member Leszek Kaczmarek and Ewelina Knapska from the Nencki Institute of Experimental Biology, Warsaw, Poland have received funding to establish 'BRAINCITY', a new Polish Centre of Excellence in Neural Plasticity and Brain Disorders.

The focus of the centre, which will be located at the Nencki Institute of the Polish Academy of Sciences in Warsaw, will be on studying the complex mechanisms of brain plasticity. "Our knowledge of neurobiology, brain functions and dysfunctions has increased exponentially in the recent years. This is largely due to the breakthroughs currently being observed in experimental techniques and research methods," says Kaczmarek. "All these substantial technological and methodological achievements will be utilised in BRAINCITY, and the overriding goal of our activities will be to develop new solutions improving the prevention, diagnostics, monitoring and treatment of diseases and pathologies related to neuroplasticity.

As part of BRAINCITY, The Nencki Institute plans to establish six scientific laboratories. The project's international strategic partner, the European Molecular Biology Laboratory (EMBL), will support the selection of the principal investigators of these research groups. With the involvement of partners from EMBL, BRAINCITY will also gain access to state-of-the-art genetic engineering technologies, genome-editing technologies, and bioinformatics databases relating to diseases linked to human-genetic variation. The FCI's vision is a close connection between bench and bedside. Clinicians and scientists aim to mechanistically understand why some patients respond to existing therapies and others do not. Tumour material of patients will be analyzed using a range of approaches

including molecular profiling, organoid models and drug screening to test for new therapeutic approaches. It is hoped that the close collaboration between doctors and researchers will result in bringing new drugs to the market more quickly.

Construction of the building are estimated to cost 73,4 million euros. Funds have been made



available by the German and Hessian governments, the German cancer charity 'Deutsche Krebshilfe' and other cooperation partners. In addition the German federal state of Hesse has committed 23,6 million euros for four years within its LOEWE programme to carry scientific and administrative costs.

BOOK REVIEW

Introducing stem cell biology

In *The Science of Stem Cells* EMBO Member Jonathan Slack, University of Bath, UK, provides those interested in studying stem cells with the cell and developmental biological concepts that inform the field.

The book is for advanced undergraduate and graduate students studying stem cell biology, regenerative medicine and tissue engineering. In eleven chapters, Slack covers topics ranging from an introduction to what stem cells are and how they can be identified to their roles in development, body plan formation, organogenesis, regeneration, wound healing and cancer.

"The central message of the book is that there is nothing magic about stem cells. In fact, it turns out that stem cell behavior is more important than the stem cells themselves," says Slack. Explaining his motivation to write the book, he adds: "In the long term, stem cell biology does have huge potential for generating novel therapies. This will be realized most easily when all students and practitioners can become masters of the science of stem cells."

The book contains numerous illustrations, including a 16-page insert of coloured photos and illustrations. These and additional supplementary material can be downloaded from the accompanying website (www.wiley.com/go/ slack/thescienceofstemcells).



The Science of Stem Cells Jonathan M.W. Slack Wiley Blackwell | November 2017 onlinelibrary.wiley.com/doi/ book/10.1002/9781119235293 Doi:10.1002/9781119235293

Transforming science into art

ooking Glass – Photographic Essays on the Mechanisms of Life (De Gruyter (Edition Angewandte), 2018) is a publication that resulted from a collaboration between the Institute of Molecular Biotechnology (IMBA) and the University of Applied Arts in Vienna, Austria. EMBO Member Josef Penninger and the university's Gerald Bast are the two chief editors.

Describing the idea behind the project, Penninger says: "For me the process of creating something new in science and in art is very similar. One has to have the courage to get oneself lost in a dark forest – like Dante in the Divine Comedy – a forest that can be very dark and scary, and then you find a guiding spirit to find your way out."

For the book IMBA scientists, including the labs of EMBO Members Josef Penninger, Jürgen Knoblich, Daniel Gerlich, Julius Brennecke, Kikue Tachibana and EMBO Young Investigator Stefan Ameres, paired up with artists. Their exchange and dialogue formed the basis for the artistic representation of molecular mechanisms using applied photography. The result is a collection of photo galleries visualizing the findings in 15 IMBA publications. In the book, the photos are presented together with the scientific abstracts and lay summaries of the papers, bringing art and science even closer together.





Josef Penninger and colleagues

Osteoclast differentiation factor RANKL controls development of progestin-driven mammary cancer (Schramek et al., 2010, Nature) RANKL/RANK control Brcal mutation-driven mammary tumors (Sigl et al., 2016, Cell Research)

Jürgen Knoblich and colleagues

Cerebral organoids model human brain development and microcephaly (Lancaster et al, 2013, Nature)



Kikue Tachibana and colleagues

A Surveillance Mechanism Ensures Repair of DNA Lesions during Zygotic Reprogramming (Ladstätter et al., 2016, Cell)

BOOK REVIEW

A microbiology revolution

How have the developments in molecular and cell biology, genomics and bioinformatics influenced the study of microbes and microbiology? In her book, The *New Microbiology: From Microbiomes to CRISPR*, EMBO Member Pascale Cossart, Institut Pasteur, France, provides an overview of how the field has changed.

Cossart describes the objective of the book "to illustrate that very important discoveries and new concepts have come to light in the last few decades. The field of microbiology has undergone a bona fide revolution and that the amazing renaissance that is taking place can have wide-ranging consequences."

Beginning with a short history of the study of infectious diseases and the first descriptions of bacteria, Cossart takes readers on a tour through bacteriology. Virology, parasitology and mycology are also mentioned, but are not the main focus of the book. The book is divided into four parts: new concepts, sociomicrobiology, the biology of infections and bacteria as tools.



The New Microbiology: From Microbiomes to CRISPR

Pascale Cossart American Society for Microbiology | 2018 www.asmscience.org/content/ book/10.1128/9781683670117 Doi: 10.1128/9781683670117 ISBN: 978-1478918806

Poster Prizes

Through our journals, we sponsor a number of poster prizes at various conferences. The recipients include:

Sebastian Bänfer

Philipps-Universität Marburg, Germany Recruitment of galectin-3 into multivesicular bodies for polarized exosomal secretion Presented at the EMBO Workshop "Transducing glycan information into function: Lessons from galectins" Mandelieu-la-Napoule, France. 27 November–1 December 2016

Agathe Dubuisson

INSERM, Paris, France New development of anticancer monoclonal antibodies targeting death receptors Presented at the European Association for Cancer Research Conference "A Matter of Life or Death" Amsterdam, 1-3 February 2018

Irene Fernandez-Duran

MRC Institute of Genetics & Molecular Medicine, Edinburgh, UK Investigating the activation of the non-canonical inflammasome in senescence Presented at the European Association for Cancer Research Conference "A Matter of Life or Death" Amsterdam, 1-3 February 2018

Esther N. Arwert

Francis Crick Institute, London, UK Heterotypic Interactions Between Cancer Cells and Fibroblasts Modulate Immune Recruitment and Oncolytic Virus Efficacy Presented at the EMBO Workshop "Perspectives on skin cancer prevention" Les Diablerets, 8-11 April 2018

Awards of Excellence

EMBO MEMBERS

Breakthrough Prize in Life Sciences

Associate Members Angelika Amon, Massachusetts Institute of Technology and Howard Hughes Medical Institute, USA, and Xiaowei Zhuang, Harvard University and Howard Hughes Medical Institute, USA, are two of the five recipients of the 2019 Breakthrough Prize in Life Sciences. Amon receives the prize for determining the consequences of aneuploidy. Zhuang is honoured for discovering hidden structures in cells by developing super-resolution imaging using stochastic optical reconstruction microscopy (STORM), Each receives a prize of three million US dollars

FEMS-Lwoff Award and Heinrich Wieland Prize

Pascale Cossart, Institut Pasteur, Paris, France, received the 2018 Heinrich Wieland Prize. It honours outstanding research in chemistry, biochemistry and physiology and is endowed with 100,000 euros. In addition, the Federation of European Microbiological Societies awarded Cossart the FEMS-Lwoff Award. The award recognizes microbiological work that helps to address today's societal problems.

Sir Hans Krebs Medal and Thomson Medal Award

Albert Heck, Utrecht University, The Netherlands, received two honours for his work analyzing protein interactions with mass spectrometry. The Federation of European Biochemical Societies awarded Heck the Sir Hans Krebs Medal, a prize that is awarded for outstanding achievements in biochemistry, molecular biology or related sciences. Heck also receives the British Institute of Physics' Thomson Medal and Prize, which recognizes research in atomic or molecular physics.

Balzan Prize

Eva Kondorosi, Hungarian Academy of Sciences, Szeged, Hungary, was awarded the Balzan Prize for Chemical Ecology for her contributions to chemical ecology. The prize, which is endowed with 750,000 Swiss francs, recognizes Kondorosi's work on the symbiosis between legume plants and nitrogen-fixing bacteria. Tang Prize for Biopharmaceutical Science

The Tang Prize for Pharmaceutical Science was awarded to EMBO Associate Member **Tony Hunter**, Salk Institute, La Jolla, USA, together with Brian Druker, Oregon Health Sciences University Knight Cancer Institute, USA, and John Mendelsohn, MD Anderson Cancer Center, USA. They receive the prize for the discovery of protein tyrosine phosphorylation and tyrosine kinases as oncogenes. The prize is endowed with 50 million Taiwanese dollars.

Cloëtta Prize

Johanna Joyce from the Ludwig Institute for Cancer Research and the Lausanne University, Switzerland received the 2018 Cloëtta Prize. The 50,000-Swissfrancs-prize is awarded by the Swiss Cloëtta Foundation to researchers who have distinguished themselves medical research fields.

Royal Medals

Two of the three Royal Society's Royal Medals were awarded to EMBO Members. Lewis Wolpert, University College London, UK, received the honour for his research on morphogenesis and pattern formation. **Shankar Balasubramanian** shares the award with David Klenerman (both University of Cambridge, UK) for their co-development of DNA sequencing techniques transforming biology and genomic medicine.

Croonian Medal

The Royal Society awarded its Croonian Medal and Lecture 2019 to **Kay Davies**, University of Oxford, UK, for her achievements in developing a prenatal test for Duchenne muscular dystrophy and her work on characterizing dystrophin related proteins. She will receive a medal and a gift of 10,000 pounds Sterling.

Buchanan Medal

Adrian Bird received the Royal Society's Buchanan Medal for his discovery that the MeCP2 protein silences transcription of methylated DNA and can reverse established Rett Syndrome in MeCP2 deficiency, demonstrating that such neurodevelopmental diseases are curable. The award is endowed with a prize of 2,000 pounds Sterling.

Canada Gairdner International Award

Azim Surani of the Gurdon Institute, Cambridge, UK, received the 2018 Canada Gairdner International Award together with Davor Solter of the Max Planck Institute of Immunobiology and Epigenetics, Freiburg, Germany. They receive the award, which recognises seminal discoveries or contributions to biomedical science, for their discovery of mammalian genomic imprinting that causes parent-of-origin specific gene expression and its consequences for development and disease.

EMBO YOUNG INVESTIGATORS

AstraZeneca Young Researchers Award

Cuadalupe Sabio from the National Center for Cardiovascular Research in Madrid, Spain, won the Astra Zeneca Young Researchers Awards in the Type II Diabetes and Obesity category for her work on the role of p38MAPK in the development of obesity and associated diseases. She received 20,000 euros to develop her research.

Good Read – Publications from the EMBO community

Bacteria in the ageing gut: did the taming of fire promote a long human lifespan? Antoine Danchin (EMBO Member) Environmental Microbiology | 4 May 2018 Doi: 10.1111/1462-2920.14255

Feedback inhibition of actin on Rho mediates content release from large secretory vesicles Benny Shilo (EMBO Member) and colleagues Journal of Cell Biology | 7 May 7 2018 Doi: 10.1083/cb.201711006

The Microglial Innate Immune Receptor TREM2 Is Required for Synapse Elimination and Normal Brain Connectivity Michela Matteoli (EMBO Member) and colleagues Immunity | 15 May 2018 Doi: 10.1016/j.immuni.2018.04.016

Codon usage of highly expressed genes affects proteome-wide translation efficiency Yitzhak Pilpel (EMBO Member) and colleagues PNAS / 22 May 2018 Doi: 10.1073/pnas.1719375115

HotSpot Wizard 3.0: Web Server for Automated Design of Mutations and Smart Libraries Based on Sequence Input Information

Jiri Damborsky (former EMBO Installation Grantee) and colleagues Nucleic Acids Research | 23 May 2018 Doi: 10.1093/nar/gky417 Clobal maps of ProQ binding in vivo reveal target recognition via RNA structure and stability control at mRNA 3' ends Jörg Vogel (EMBO member) and colleagues Molecular Cell | 24 May 2018 Doi: 10.1016/j.molcel.2018.04.017

Identification of MOSPD2, a novel scaffold for endoplasmic reticulum membrane contact sites

Bruno Klaholz (former EMBO Installation Grantee) EMBO Reports | 1 June 2018 Doi: 10.15252/embr.201745453

Altered p53 functionality in cancer-associated fibroblasts contributes to their cancersupporting features Yosef Yarden, Benjamin Geiger, Moshe Oren (EMBO Members) and colleagues Proceedings of the National Academy of Sciences | 4 June 2018 Doi: 10.1073/pnas.1719076115

A Bacterial Growth Law out of

Steady State Uri Alon (EMBO Member) and colleagues Cell Reports | 5 June 2018 Doi: 10.1016/j.celrep.2018.05.007

Safety and efficacy of human embryonic stem cell-derived astrocytes following intrathecal transplantation in SOD1C93A and NSG animal models Michel Revel (EMBO Member) and colleagues Stem Cell Research & Therapy | 6 June 2018

Doi: 10.1186/s13287-018-0890-5

Epigenetic Control of Expression Homeostasis during Replication Is Stabilized by the Replication Checkpoint Naama Barkai (EMBO Member) and colleagues Molecular Cell 14 Jun 2018 Doi: 10.1016/j.molcel.2018.05.015

Photochemistry beyond the red limit in chlorophyll fcontaining photosystems Bill Rutherford (EMBO Member) and colleagues Science 15 June 2018 Doi: 10.1126/science.aar8313

Bacterial Adaptation to the Host's Diet Is a Key Evolutionary Force Shaping Drosophila-Lactobacillus Symbiosis Francois Leulier (EMBO Young Investigator) and colleagues Cell Host & Microbe | 28 June 28 Doi: 10.1016/j.chom.2018.06.001

Single-cell mapping of the thymic stroma identifies IL-25producing tuft epithelial cells Ido Amit (EMBO Member) and colleagues Nature | 18 July 2018 Doi: 10.1038/s41586-018-0346-1

Structural Lipids Enable the Formation of Functional Oligomers of the Eukaryotic Purine Symporter UapA George Diallinas (EMBO Member) and colleagues Cell Chemical Biology | 19 July 2018 Doi: 10.1016/j.chembiol.2018.03.011 Secretory Vesicle Polar Sorting, Endosome Recycling and Cytoskeleton Organization Require the AP-1 Complex in Aspergillus nidulans George Diallinas (EMBO Member) and colleagues Genetics | 1 August 2018 Doi: 10.1534/genetics

Quiescin sulfhydryl oxidase 1 (QSOX1) glycosite mutation perturbs secretion but not Golgi localization Deborah Fass (EMBO Member) and colleagues Glycobiology | 1 August 2018 Doi: 10.1093/glycob/cuy044

Heteromeric RNP assembly at LINEs controls lineagespecific RNA processing Jernej Ule (EMBO Member) and colleagues *Cell* | 2 August 2018 *Doi:* 10.1016/j.cell.2018.07.001

Target-Based Discovery of an Inhibitor of the Regulatory Phosphatase PP1R15B Anne Bertolotti (EMBO Member) and colleagues Cell / 23 August 2018 Doi: 10.1126/science.aar8313

Genetics of hearing loss in the Arab population of northern Israel

Karen Avraham (EMBO Member) and colleagues European Journal of Human Genetics / 23 Aug 2018 Doiorg/10.1038/s41431-018-0218-z A mutant p53-dependent embryonic stem cell gene signature is associated with augmented tumorigenesis of stem cells Varda Rotter (EMBO Member) and colleagues Cancer Research / 28 August 2018 Doi: 10.1158/0008-5472.CAN-18-0805

Cells alter their tRNA abundance to selectively regulate protein synthesis during stress conditions Madan Babu (EMBO Member) and colleagues Science Signaling | 4 September 2018 Doi: 10.1126/scisignal.aat6409

Post-Antibiotic Gut Mucosal Microbiome Reconstitution Is Impaired by Probiotics and Improved by Autologous FMT Eran Elinav and Eran Segal (EMBO Members) and colleagues Cell | 6 September 2018 Doi: 10.1016/j.cell.2018.08.047

Neutralizing Gatad2a-Chd4-Mbd3/NuRD Complex Facilitates Deterministic Induction of Naive Pluripotency Jacob Hanna (EMBO Member) and colleagues Cell Stem Cell | 6 September 2018 Doi: 10.1016/j.stem.2018.07.004

Small RNA sequences derived from pre-microrNAs in the supraspliceosome Ruth Sperling (EMBO Member) and colleagues Nucleic Acids Research / 8 September 2018 Doi: 10.1093/nar/gky791

EMBO EVENTS

Practical Courses

DE-Dresden | 5-13 February 2019 | A.

Hyman Methods for studying phase separation in biology

DE-Heidelberg | 25–29 March 2019 | S. De Renzis **Optogenetics: From design to cell**

signalling to tissue morphogenesis

IT-Procida | 30 March–6 April 2019 | V. Colonna **Population genomics: Background,**

tools and programming

DE-Heidelberg | 7–12 April 2019 | M. Schorb

High-accuracy CLEM: Applications at room temperature and in cryo

ES-Barcelona | 7–13 April 2019 | M. Lluch Senar The 2019 whole-cell modeling

summer school

TR-Izmir | 8–12 April 2019 | E. Karaca Research to service: Planning and running a bioinformatics core facility

DK-Odense | 2–10 May 2019 | M.R. Larsen

Characterisation of post-translational modifications in cellular signalling

DE-Heidelberg | 5–10 May 2019 | J. Krijgsveld Quantitative proteomics: Strategies and tools to probe biology

DE-Heidelberg | 12–18 May 2019 | Q. Deng

Single cell omics

JP-Nagoya | 21–30 May 2019 | A. Maizel Functional live imaging of plants

DE-Heidelberg | 2–7 June 2019 | A.

Hendrix Extracellular vesicles: From biology to biomedical applications

UK-Didcot | 10–19 June 2019 | N. Burgess-Brown

High-throughput protein production and crystallization

CZ-České Budějovice | 10–20 June 2019 | J. Nebesarova Advanced methods of electron

microscopy in cell biology

DE-Heidelberg | 12–19 June 2019 | J.E. González-Pastor **Microbial metagenomics: A 360°**

approach IT-San Michele all'Adige | 16–30 June

2019 | C. Donati Bioinformatics and genome analyses

NL-Wageningen | 1–5 July 2019 | C. Welte

Breathless microbes: Techniques and theory in anaerobic microbiology

UK-London | 7–20 July 2019 | C. Kiecker Developmental neurobiology: From worms to mammals

FR-Paris | 8–13 July 2019 | M. Nilges Integrative and cellular structural biology

DE-Garching | 26 July-2 August 2019 | M. Sattler

Structure, dynamics and function of biological macromolecules by NMR

Workshops

CL-San Pedro de Atacama | 10–12 January 2019 | M. Allende **Exploring genomic landscapes**

IN-Bangalore | 4–7 February 2019 | H. Ghosh

Molecular neuroscience: From genes to circuits in health and disease

ES-Salamanca | 8–11 March 2019 | A. Borkhardt

B-cell development and leukemia

DE-Heidelberg | 13–15 March 2019 | S. O'Donoghue

Visualizing biological data (VIZBI 2019)

ES-Sant Feliu de Guixols | 23–27 March 2019 | R. Erdmann Current advances in protein

translocation across membranes UK-Oxford | 1–5 April 2019 | J.

Rehwinkel Pathogen immunity and signalling

CL-Santiago | 2–5 April 2019 | M.

Bridging cell and tissue mechanics to fate specification in development

IL-Herzliya | 7–11 April 2019 | Y. Shiloh Genome dynamics in neuroscience and aging

ES-Chiclana de la Frontera | 8–11 April 2019 | G. Sabio **Organ crosstalk in energy balance**

and metabolic disease

CN-Xiu Ning | 11–14 April 2019 | J. Hu Membrane shaping and remodeling by proteins

CL-Villarrica | 14–18 April 2019 | C. Gonzalez-Billault

Emerging concepts of the neuronal cytoskeleton

UK-Windsor | 15–17 April 2019 | S. Helaine

Toxin-antitoxin systems in bacteria

CL-Santiago | 22–25 April 2019 | E. Schirmer

Integrative biology: From molecules to ecosystems in extreme environments

ES-Costa de la Calma | 28 April–3 May 2019 | B. Bukau

Protein quality control: From mechanisms to disease

DE-Heidelberg | 1–4 May 2019 | A.

Chromatin and epigenetics

GR-Heraklion | 7–10 May 2019 | F. Bradke

Cell biology of the neuron: Polarity, plasticity and regeneration

PT-Cascais | 11–15 May 2019 | L. Jansen

Editorial

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Print & web layout Igor Jukic

18 EMBOencounters | Winter 2018/2019 | communications@embo.org

Chromosome segregation and aneuploidy

DE-Heidelberg | 3–6 July 2019 | F.

Mechanical forces in development

DE-Heidelberg | 10–13 July 2019 | A.

New approaches and concepts in

IN-Chennai | 10–13 March 2019 | R.

Regulatory epigenomics: From large

IN-New Delhi | 15-17 April 2019 | A.

Sensing and signalling in plant stress

IN-Kalyani | 9–12 November 2019 | S.

Human microbiome: Resistance and

GR-Spetses Island | 23-31 May 2019 |

Molecular mechanisms of tissue

injury, repair and fibrosisGlobal

IT-Venice | 26–30 August 2019 | J.

Mechanism in development and

Global Exchange Lecture Courses CL-Las Cruces | 5–13 April 2019 | J.

For a complete and up-to-date

list of EMBO events please go to

Small brains, big ideas

events.embo.org

Next issue

The next issue of EMBO

Encounters issue will be

February 2019.

dispatched in April 2019. Please

UPCOMING DEADLINES

Courses, Workshops and Global

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Exchange Lecture Courses

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India | EMBO Symposia

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evolution

Sierralta

India | EMBO Symposia

data to useful models

Lecture Courses

EMBO | FEBS Lecture Course

Exchange Lecture Course

EMBO | FEBS Lecture Course

Venice summer school 2019:

FR-Le Pouliguen | 12–16 May 2019 | C. Lamaze

Translating structural principles and dynamics into function

CZ-Prague | 15–18 May 2019 | P. Svoboda

Awakening of the genome: The maternal-to-zygotic transition

GR-Athens | 19–23 May 2019 | G. Kollias Mesenchymal cells in inflammation.

immunity and cancer IL-Rehovot | 19–24 May 2019 | J.

Abramson ThymE: T cell and thymus biology

JP-Tokyo | 20–22 May 2019 | P. Carninci Single cell biology

GR-Kyllini | 20–24 May 2019 | A. Papantonis

The genome in three dimensions

IT-Baveno | 25–28 May 2019 | L. Tamagnone **Neural guidance molecules in**

development and disease

ES-Sant Feliu de Guixols | 26–31 May 2019 | S. Iden Cell polarity and membrane dynamics

FR-Paris | 30 May-2 June 2019 | A.

Hosmalin Antigen processing and presentation

10 (APP 10) SE-Lund | 9–12 June 2019 | T. Den

Blaauwen Bacterial cell division: Closing the gap

CZ-Nové Hrady | 23–28 June 2019 | J. Carey Synergy of experiment and computation in quantitative systems

biology ES-Barcelona | 2–5 July 2019 | J. Sharpe Limb development and regeneration: New tools for classic model system

UK-Norwich | 14–18 July 2019 | T. Mock The molecular life of diatoms

ES-Barcelona | 14–19 July 2019 | J. Ayte Fission yeast

GR-Chania | 22–26 July 2019 | G. Christophides Molecular and population biology of mosquitoes and other disease vectors

Symposia

EMBO | EMBL Symposia

DE-Heidelberg | 17–20 March 2019 | S. De Renzis Synthetic morphogenesis: From gene

circuits to tissue architecture

DE-Heidelberg | 31 March–3 April 2019 | J. Krause

Reconstructing the human past: Using ancient and modern genomics

DE-Heidelberg | 10–13 April 2019 | L. Rondi-Reig Probing neural dynamics with

behavioural genetics

DE-Heidelberg | 15–18 May 2019 | H. Kaessmann The identity and evolution of cell types

EMBO Molecular Medicine



Targeting senescent cells

Senescent cells are not dead, but irreversibly stop dividing to restrict the propagation of cellular defects, while still secreting cytokines and growth factors that activate the immune system to induce repair. Although this is, generally speaking, a good strategy, senescence underlies ageing and several diseases, leading to chronic inflammation and fibrosis. Eliminating senescent cells is therefore regarded as a promising therapeutic approach.

Daniel Muñoz-Espín, EMBO Member Daniel Serrano and their colleagues have now developed a strategy to specifically deliver drugs to senescent cells. Their approach takes advantage of the fact that senescent cells have high levels of lysosomal β-galactosidase activity. To specifically target drugs to senescent cells, the researchers encapsulate them with galacto oligosaccharides, so-called GalNP beads. The beads are taken up by cells within the diseased tissue, but only senescent cells with high β -galactosidase activity can digest the coating on the beads, allowing the drug to be released into the cell. As a proof-of-principle, the researchers demonstrated the therapeutic efficacy of their system in mouse models of pulmonary fibrosis and cancer.

A versatile drug delivery system targeting senescent cells Daniel Muñoz-Espín et al.

Read the paper: embomolmed.embopress.org/content/10/9/e9355

EMBO *reports*

A gene behind addiction

Cocaine can have a devastating effect on people. It directly stimulates the brain's reward center, and can induce long-term addictive behaviors. De Backer *et al.* have now uncovered that a gene called Maged1 plays a crucial role in controlling these pathological changes. This finding opens the door to further investigate the molecular mechanisms underlying addiction-associated adaptations in the brain.

De Backer *et al.* observed that mice lacking Maged1 did not show any response to cocaine, such as addictive behavior or drug sensitization. In normal brains, cocaine leads to a dopamine surge that over-activates the reward circuitry and induces long-lasting changes in the brain, eventually leading to addiction. A closer look at the role of Maged1 in the brain revealed that it is required in the prefrontal cortex for the development of cocaine sensitization and dopamine release.

Only very few mutations are known to induce a complete lack of behavioral response to cocaine. Other members of this small group, in contrast to Maged1, are established components of the reward system. Maged1 thus serves as a promising new entry point into the analysis of the mechanisms underlying drug addiction.

Deletion of Maged1 in mice abolishes locomotor and reinforcing effects of cocaine

Jean-François De Backer et al. Read the paper: embor.embopress.org/ content/19/9/e45089



Binding disordered domains

Many eukaryotic proteins contain so-called intrinsically disordered regions that do not adopt defined structures, but are nonetheless functionally important. While function, in general, can be deducted from the three-dimensional structure of a protein, understanding the role of these disordered regions has been challenging.

Post-translational modifications, on of which is arginine methylation, cluster within intrinsically disordered regions. Using a systems approach, Woodsmith *et al.* found clustered methyl-arginine arrays within disordered protein sequences of many proteins and examined the potential role of such arrays using one candidate, a heterogeneous nuclear ribonucleoprotein family member called SYNCRIP.

Specifically, the researchers generated a large set of SYNCRIP mutants and investigated how well they associated with two different partners that bind unmethylated and methylated arginine, respectively. The researchers observed that in both cases, binding increased with arginine content in the disordered region. However, while unmodified arginines are preferred in continual stretches, their methylated counterparts function in concert irrespective of their position within the structurally disordered array.

Interaction modulation through arrays of clustered methyl-arginine protein modifications

Jonathan Woodsmith et al. Read the paper: life-science-alliance.org/ content/1/5/e201800178

Rhythm without clocks

systems

molecular

biology

A number of biological processes, such as sleep patterns in animals, follow a daily cycle. Circadian clocks are biochemical processes that coordinate such cyclic behaviors with the earth's solar day. According to current models, circadian rhythms are driven by feedback loops, where so-called clock genes inhibit their own transcription to drive the oscillation of the biological clock. In Drosophila melanogaster, the clock genes period and timeless have been regarded as the major pacemakers. Guilleaume Rey et al. have now uncovered that there are circadian oscillations in Drosophila cells that are not driven by clock genes.

The researchers used Drosophila Schneider (S2) cells, a cell line that does not express circadian clock genes and have thus far have been viewed as 'non-rhythmic'. After synchronizing S2 cells with daily temperature cycles for a week, they sampled cells at three-hour intervals in constant conditions, and analyzed the samples using a multi-omics approach. They revealed that hundreds of genes and proteins oscillate in a 24-hour cycle, among them, most notably, components of core metabolic pathways. The results suggest a reconsideration of existing models of the clockwork in Drosophila and other eukaryotic systems.

Metabolic oscillations on the circadian time scale in Drosophila cells lacking clock genes

Guilleaume Rey et al.

Read the paper: msb.embopress.org/ content/14/8/e8376

Starving resistant cancers

EMBO JOURNAL

Cisplatin is a common therapeutic drug with a 40-year history in treating numerous human cancers. However, tumour cells often develop resistance against the drug, which ultimately triggers a relapse. Florine Obrist *et al.* have now discovered potential co-treatments that may prevent relapse.

The researchers around EMBO Member Guido Kroemer first determined that cisplatin-resistant tumor cells are highly sensitive to nutrient depletion when they discovered that the cells died when cultured in nutrient-free medium. Moreover, mice with cisplatinresistant cancers survived longer when they fasted periodically, suggesting that fasting-cycles could help to prevent relapse in humans, as well.

Next, the researchers investigated the nutrient sensitivity of cisplatinresistant tumors in more detail, and found that the effect of fasting is mediated by glutamine. Glutamine is involved in a number of cellular processes, but in cisplatin-resistant tumors it is mostly required for nucleotide biosynthesis.

Accordingly, the researchers tested agents that target nucleotide synthesis pathways, such as 5-fluorouracil or clofarabine, and showed that cisplatin-resistant tumor cells were particularly sensitive to these substances. These drugs might therefore be potential candidates for co-treatment with cisplatin.

Metabolic vulnerability of cisplatinresistant cancers Florine Obrist *et al.* Read the paper: emboj.embopress.org/ content/37/14/e98597

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Bart de Strooper VIB-KU Leuven, Belgium; UCL London, UK

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