

Issue 4 July 4<sup>th</sup> 2014

# Lab Times

News  
for the  
European  
Life Sciences

Issue  
No.

50

The image shows a stack of 'Lab Times' magazines. The top cover is dark blue with a glowing, textured number '50' in the center. The number is composed of many small, bright orange and yellow particles, giving it a shimmering, almost crystalline appearance. The background of the cover is a dark, abstract pattern of blue and black. The text 'Issue No.' is printed in a bold, sans-serif font above the number. At the top right, the issue information 'Issue 4 July 4th 2014' and the subtitle 'News for the European Life Sciences' are visible. The magazine is resting on a light-colored wooden surface.



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# Do you remember...

... the summer of 2006? It was an eventful year that saw the 6,500,000,000<sup>th</sup> earthling born on our overcrowded globe and the last Chinese river dolphin (*Lipotes vexillifer*, if any paleoecologists are present) leading his species to extinction. Among the illustrious lives brought to a conclusion were those of Polish science fiction writer, Stanisław Lem (aged 84), Pink Floyd founding member, Syd Barrett (aged 60), and Galápagos tortoise Harriet (aged 175). Some claim that Harriet was a good friend of the young Charles Darwin, who allegedly met her in 1835 on the volcanic archipelago in the Pacific Ocean and took her with him to England on the *Beagle* (whether true or not, a touching story).

A few political dinosaurs also disappeared from the landscape in 2006, for example, Cuba's "Máximo Líder" Fidel Castro, and Italy's political heavyweight, Silvio Berlusconi (at least until 2008, when the controversial media tycoon was elected Prime Minister for the 4<sup>th</sup> time). Tony Blair announced his approaching resignation as the United Kingdom's Prime Minister, too, while, in a world first, the identical Kaczynski twins, became Heads of Government and State in Poland. You remember?

Two other political dinosaurs proved their madness in 2006: Mahmud Ahmadinedschad of Iran, and Kim Jong-il of North Korea. Both congratulated themselves on becoming members of the nuclear weapons club and their hard-won ability to blow the globe into smithereens.

Let's shift to more pleasant topics. In May 2006, the Human Genome Project published its final chromosome sequence (paradoxically it was #1, the largest human chromosome, that was last to be finished). Shortly after, the FIFA World Cup in Germany ended, after four weeks of thrilling competition, with an Italian victory (a nailbiting 5:3 over France after penalties). At the same time, the testosterone-fuelled US rider Floyd Landis won the Tour de France (and was stripped of his title four days later after a positive doping test).

Allowed to keep their 2006 titles were Stanford biochemist, Roger Kornberg (Nobel Prize in Chemistry, for his studies on the molecular basis of eukaryotic transcription), and the biologists Andrew Fire and Craig Mello, (Nobel Prize in Physiology or Medicine, for their discovery of RNA interference). Another scientific genius, mathematician Grigori Perelman, refused the prestigious Fields Medal in the same year. After having proved the Poincaré conjecture, a theorem that leading experts had failed to solve for over 100 years, Perelman not only renounced the award but also abandoned mathematics due to, "the low ethical standards of the discipline and its conformism".

The Russian eccentric is not entirely wrong. Inadequate ethical standards in science, whether in regard to plagiarism, data manipulation or honour authorships, are in fact a major problem that remains to be solved. Especially in biomedicine where countless finger-wagging reproofs have been made but little action taken.

Scientific abuse has long been an important topic for *Laborjournal*, too. Founded in 1994 as a German grassroots magazine for life science researchers ("written by scientists for scientists"), and from the beginning produced by a committed team of enthusiastic scientists who turned to journalism after their final uni-



April 2006: The first issue of *Lab Times*

versity degrees, *Laborjournal* quickly became ubiquitous in German-speaking labs thanks to its independent investigative reporting of controversial issues. Soon requests mounted, mainly from foreign-language guest scientists at German institutes, for the translation of *Laborjournal* articles into English.

"Nice idea, but an enormous and expensive undertaking. And if we actually did it, why limit distribution to Germany, Austria and Switzerland?", we asked ourselves.

So, slowly an idea took root, and, as the year 2005 turned into 2006, we decided to do it properly. Within just a few months, we had developed a concept for a second magazine, *Lab Times*, a pan-European, English-language scientific journal that would be the source of information for European researchers and completely different to existing magazines (with the exception of *Laborjournal*). We wanted to create a "lab bench-focussed" magazine, written for professors and PhD students, for postdocs and lab assistants; a magazine that would be of interest to any European life science researcher from Reykjavik to Lisbon and Athens to Riga.

So we contacted and engaged freelance journalists with scientific backgrounds from the United Kingdom, France, Spain and other European countries; we investigated topics of interest; we hired native English speakers; we established an extensive distribution system, making sure that each of the 25,000 copies printed per issue reaches its reader, whether in the shadow of Eyjafjallajökull in Iceland or in an office at Exeter College in central Oxford. A new website for the new magazine was also constructed, of course.

As mentioned above, the new kid on the block was called *Lab Times – News Magazine for the European Life Sciences*. The first issue was published in April 2006, and, after eight eventful years, issue number 50 is lying in front of you.

To celebrate this milestone, we decided to produce a very special edition of *Lab Times*. We met with scientists, researchers and bioentrepreneurs all over Europe to talk about their visions and their hypotheses, their technological developments and research, their desires, fears and concerns and their daily work.

So turn the page and enjoy our interviews with thirteen protagonists of the European life sciences!





Karin Hollricher spoke to EMBO Director, Maria Leptin, about the past, present and future of the most important life sciences organisation in Europe (p. 16).



Florian Fisch met EPFL President, Patrick Aebischer, in his office to talk about the Human Brain Project and increasing cooperation between universities and industry (p. 26).



Steven Buckingham talked to computer scientist, Ross King, who is pursuing the idea of an artificially intelligent "robot scientist" that autonomously executes research (p. 38).



Steven Buckingham had an appointment with 85-year-old Geoffrey Burnstock, who is still active in research and full of new ideas and hypotheses (p. 54).

## Celebrating the 50<sup>th</sup> Issue of *Lab Times*

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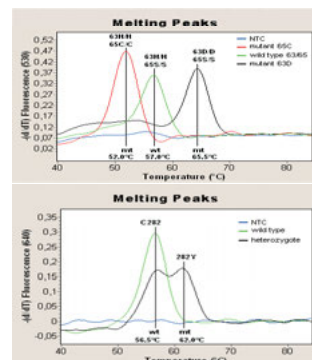
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*A conversation with Sir Tim Hunt, emeritus professor, London Research Institute*

# “I Believe in Giving Power to the Young”

A few years back, *Lab Times* received an email from Tim Hunt, in which he confessed, “I like your magazine”. Now, we ask what the recently retired Nobel laureate thinks about the current research scene in Europe.



Photo: BioMed Central

Sir Tim Hunt started his research career in 1964 at the University of Cambridge (UK) working on haemoglobin synthesis under the supervision of Asher Korner. After obtaining his PhD in 1968, he spent a few years at the Albert Einstein College of Medicine in New York (USA) working with Irving London, until he returned to Cambridge to teach and establish his independent research career, studying translational control.

In the late 1970s, he began teaching a summer course at the Marine Biological Laboratory, Woods Hole (USA), where he began working with sea urchin and clam eggs. These experiments eventually led to the discovery of cyclins, a family of regulatory proteins that partner with cyclin-dependent kinases (CDKs) to control the transition between cell cycle phases. For this breakthrough, Hunt was awarded the Nobel Prize in Physiology or Medicine in 2001, together with Lee Hartwell and Paul Nurse for their work on CDKs in yeast.

He is currently member of the Scientific Council of the European Research Council (ERC), the Advisory Council for the Campaign for Science and Engineering (CaSE), and of the Selection Committee for the Shaw Prize in Life Science and Medicine.

**“Biology is still pretty small science that has to be carried out by committed individuals focusing on particular problems.”**

*Lab Times:* You have recently retired from a long and prolific research career. How different is it to pursue a research career now, compared to when you started, or even just a couple of decades ago?

**Hunt:** I always like to joke that I am glad that I am not 20 something years old today because I think it is much harder than when we started. When I started as a PhD student in 1964, our department didn't have a Xerox machine, there were no calculators, you had to go to the library to read things and it was virtual-

ly impossible to analyse individual proteins because the SDS gel had not yet been invented. The tools were very blunt and the questions you could ask were correspondingly limited; now the two are exceedingly sharp and the analytical procedures are absolutely awesome.

When you look back at the papers of that era, they were pretty simple, easier to understand in many cases. There was only so much you could do. I am appalled sometimes at some papers today: they are so data-heavy and I don't think that makes them better papers.

In terms of publication, there is just much more competition these days because the biosciences have been so successful; they consume about 2% of the gross national product in the US and the result is

that there are thousands of competing young scientists. My generation is just on the point of retirement and, in the meantime, we have all trained dozens of doctoral students and post-

docs, each of which has trained their own students and postdocs, so this exponential growth is what caused all the problems, I would say.

*Where do you think all this is heading?*

**Hunt:** I really don't know... Somewhere between 1990 and 2000, many of the outstanding problems of cellular, molecular and developmental biology were effectively solved. You do kind of wonder: how many really important problems are there in biology that remain? Of course, there are hundreds of details but the last great frontier is how the brain works, there you have a very primitive partial understanding of most of it. It is a pretty difficult problem.

*Is the European Union currently taking the right measures to move European science forward?*

**Hunt:** The old investigator-led grants are excellent and much better than top-down collaborative network grants, which are quite good fun but I don't think it is a terribly good mechanism to hunt for the

best science because the people aren't really working together. When you really work with somebody you see them everyday and, here, the idea is that you see one another once a year, or perhaps four times a year; it just doesn't work. There are projects that might work, like these huge projects to sequence the human genome, the big science, but mostly I think that biology is still pretty small science that has to be carried out by committed individuals focusing on particular problems. I don't know very many things that require that kind of effort.

*What are the strengths and pitfalls of the European research community, when compared, for example, with research in the US?*

**Hunt:** I think things have improved tremendously in Europe in the last few years. For example, in my field, the European Molecular Biology Laboratory (EMBL) has trained lots of people, not only in how to do science but also on how to manage science and how to choose scientists.

I believe very much in giving power to the young and not putting them under. I





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was given full autonomy and authority at a very young age, at 27 years old. I wasn't running my own lab, I had friends around to help and I liked that.

There is much more internationalisation in Europe, good practice [of science] is much more diffused throughout. In the former communist countries, Poland, Bulgaria and places like that, they still have a long way to go but it is difficult to feed because any new talent that arises, very quickly migrates abroad. At the ERC we think about that a lot but we haven't really taken steps to deal with it because it is against our principles. We say excellence only and that rules most of those people out; hence, it is understandable, they don't have a good science base and it is hard to see how they can build one.

*What do you think of big science prizes like the Breakthrough Prize? Some people claim that junior scientists should receive this type of prize instead of established scientists.*

**Hunt:** I don't know to be honest. You have to find a compromise. If you are a granting agency, you really do need to try to identify people who are successful and clever, and who will make good use of the money.

There are a lot of funding agencies and in the past you feel that every person had to get a little piece of the cake, and in general, that meant that the food is spread too thinly. So, I think that a bit of concentration is a good idea but that then raises the question: how do you identify the good people? That is when the problems begin, because now we start talking about impact factor and things like that, and everybody knows there are problems with that but nobody has found a satisfactory solution.

We are good at judging science retrospectively but we are not good at judging science prospectively, because the future is always very hard to predict. The ERC does the best it can. We like

to keep things very simple, so in judging grant applications you give half the marks to the track record of the ap-

plicant and half the marks to the project they propose. I think that is a pretty good ratio. You can't just give money to people who have been successful in the past and say, "Do whatever you'd like". I don't think that sort of view is responsible, although in some cases it will be fine. And likewise, people can propose very fancy and clever research projects but when you look at their

productivity, you see that they are much better at writing grants than actually carrying out research. Somewhere between those two extremes lies the compromise.

*How can we change the way scientists (and science) are perceived by the public?*

**Hunt:** I don't know, I think that is a very difficult question to answer. People always say that scientists must be encouraged to go out and explain what they are doing. I'm all for that; I try to do a little bit:

I go and talk in schools, and so forth. But nothing ever really comes close to the experience of actually doing science, which is usually a rather peculiar random walk, mostly failure and the occasional few successes. But it doesn't really explain why it is so wonderful and such good fun to do because, in order to understand it, you have to usually have first done a PhD in the subject and most people haven't.

I would find it difficult to explain to a quantum mechanics expert what I was doing and why I thought it was interesting. Science is really just a way of finding things out. You pursue a lot of false clues, you get misled and misinterpret things. And that is very hard to convey and, unfortunately, I think the teaching of science in school is very delusive... They make it sound as if there are some geniuses out there that figured everything out and then wrote it down in textbooks; all you have to do is learn what it says in the textbooks and you will be a brilliant scientist but we all know that textbooks are actually wrong in a lot of places. And the alternative to that, of course, is: ok we won't teach the kids what is known, we will let them find it all out for themselves. But if you have to find everything out for yourself, it takes an awfully long time to discover anything. It is really important to have practical experience but it is very difficult

*"This emphasis on translation research is very foolish. It implies, we know everything and that is not true."*

*Do you think scientists are pressured to focus their research on 'hot' topics, like cancer or neuroscience?*

**Hunt:** I think they are. It is the money issue; people tend to migrate in that direction because they have no choice. I don't think it is a very sensible way to spend the money. I am a tremendous believer in fundamental research. When I look at the great breakthroughs, like the discovery of penicil-

lin – that wasn't produced by doctors wanting to make antibiotics; none of them realised it was possible. It was a tiny handful of basic researchers who were curious and figured out how to do it.

I think this emphasis on translation research is very foolish because it implies, we know everything that we need to know

*"We are good at judging science retrospectively but we are not good at judging science prospectively."*

and that is not true, obviously. A good example is the case of gene therapy, which is much needed to treat genetic diseases and it doesn't work very well because much more biological engineering is required.

I think most biological fields are well populated and if a breakthrough occurs, they won't fail to exploit them.

*How would you explain to someone in one sentence that it is important to fund and encourage more basic research?*

**Hunt:** I wouldn't know how to begin! I think it is extremely difficult to justify because what you are really saying is "just pay me to have more fun" and that works much better than paying me to do something I have no clue how to do.

*In your opinion, why are women still under-represented in senior positions in academia and funding bodies?*

**Hunt:** I'm not sure there is really a problem, actually. People just look at the statistics. I dare, myself, think there is any discrimination, either for or against men or women. I think people are really good at selecting good scientists but I must admit the inequalities in the outcomes, especially at the higher end, are quite staggering. And I have no idea what the reasons are. One should start asking why women being under-represented in senior positions is such a big problem. Is this actually a bad thing? It is not immediately obvious for me... is this bad for women? Or bad for science? Or bad for society? I don't know, it clearly upsets people a lot.

*What research area excites you at the moment?*

**Hunt:** I am very excited by stem cell biology. I think the advances that have been made are just fantastic and I really hope this is something that will lead to people growing pancreas in a test tube and using them to cure diabetes, for example. I think that those advances have been absolutely spectacular; very, very interesting.

INTERVIEW: ISABEL TORRES



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A conversation with Martin Fenner, Public Library of Science

# “People only Care for Quick Answers”

Originally interested in finding treatments for patients with germ cell tumours, renal cell carcinoma and prostate cancer, Martin Fenner recently moved his scientific focus to an issue that is just as hotly debated as cancer research – publication metrics.

**M**artin Fenner obtained his Doctor of Medicine from the Free University Berlin in 1991. After starting a residency in internal medicine at Hannover Medical School in 1992, he was a postdoc at Massachusetts General Hospital Cancer Center from 1994-1998. Then he worked as a medical oncologist at the Charité Universitätsmedizin Berlin and the Hannover Medical School Cancer Centre.

He started his own blog, ‘Gobbledygook’, in 2007 on the *Nature* Network blogging platform that was launched a few months earlier by Nature Publishing Group. His blog is “about how the

*“Using the Journal Impact Factor to assess the performance of individual researchers is complete nonsense from a bibliometrics perspective.”*

internet is changing scholarly communication”. It moved to the PLoS Blogs network in 2010, and, in 2013, to a self-hosted platform

where he cannot only write about technology but also experiment with the blogging platform ([blog.martinfenner.org](http://blog.martinfenner.org)).

He has been associated with ORCID (the ‘Open Researcher and Contributor ID’ project that aims to solve the name ambiguity problem in research), serving on the ORCID board from 2010-12. He is a member of the ORCID outreach steering group.

Since 2012, Martin Fenner has been working for the *Public Library of Science* (PLoS) as the Technical Lead on their Article-Level Metrics project. He is responsible for technical decisions in the context of the larger Article-Level Metrics team at PLoS, doing most of the software development work, holding presentations and working with other software developers.

*Lab Times:* In your article ‘What Can Article-Level Metrics Do for You?’, PLoS Biol, 11(10): e1001687 you compare the difference between article-level metrics and new uses of alternative metrics. A lot of people are worried about failings in the traditional system but do you really think the new system has proved itself yet?

**Fenner:** That’s a good question. The National Information Standards Organization (NISO) is trying to address this in its Alternative Assessment Metrics project; I am the chair of the steering group. This started in July 2013. In its first year, we collected input from the community about these new alternative metrics and how we can move forward with developing standards and best practices to make the data comparable, for example, when counting Mendeley bookmarks or Twitter tweets.

The position of many people we talked to is that there is a conflation, an overlap of different uses of alternative metrics,

namely discovery, online post-publication discussion and research assessment. Of course, research assessment is important but that is only one of several things you can do, and I think it will be many years before these newer metrics can be routinely used for tenure and promotion decisions. But there are exceptions where people have already presented newer research outputs, such as datasets in a tenure package, then used alternative metrics to demonstrate their impact.

Currently, the real value I see in alternative metrics is as a discovery tool. Before we can use alternative metrics for research evaluation, we need to resolve a number of issues, including decisions on which research outputs to evaluate, the specific metrics to be used, the data quality of these newer metrics and the relative role of metrics vs. peer evaluation.

The main driver of the discussion is the misuse of the Journal Impact Factor to assess the performance of individual researchers, a practice that unfortunately is increasingly common in Europe and elsewhere but that is complete nonsense from a bibliometrics perspective.

*In your chapter, ‘Altmetrics and Other Novel Measures for Scientific Impact’ [from ‘Opening Science: The Evolving Guide on How the Internet is Changing Research, Collaboration and Scholarly Publishing’, a SpringerOpen book available online for feedback and updates at [book.openingscience.org](http://book.openingscience.org)], you say that before we can use altmetrics as an evaluation tool, we first need to answer the question, “Can numbers reflect the impact of research, across disciplines and over time?”*

**Fenner:** Of course they can’t. You have to be very, very careful with any kind of metric for evaluating research. There is a really excellent chapter in the same book on this theme.

*“Currently, the real value I see in alternative metrics is as a discovery tool.”*

*You’re referring to the chapter by Mathias Binswanger: ‘Excellence by Nonsense: The Competition for Publications in Modern Science?’*

**Fenner:** Yes, he has his own position on this but I really like this chapter and I also read his book, ‘Sinnlose Wettbewerbe’ [ISBN 978-3451303487] that discusses similar problems in other areas, e.g. education. I believe the big problem is that people think that because you can attach a number to something it actually reflects quality. For example, in *Lab Times*, each issue presents citation rankings by discipline. You can take this as an informative overview of important papers and researchers in a



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field. But the problems start when you take the actual numbers too seriously. The ranking is discipline-specific but defining what papers belong to that particular discipline is a problem. The next one is aggregating citations by author. Can we actually do that? And how do we account for the different roles an author had in a paper – the position in the list of author names is a very crude measure. The fundamental problem is the assumption that the number of citations of a paper reflects quality. It's a very dangerous idea. It's like going to a classical music concert and saying that it scores 8.2, so it's better than the one I heard last week, which had a score of only 7.8. That sounds hilarious but I don't think it's so different.

**“Too much time is spent in trying to get published in relationship to doing the research.”**

publication in “high-impact” journals? It is not really about what kind of research you do or whether you've found something interesting. Just that you've managed to publish it in a particular journal. But publishing in a high-profile journal means that the manuscript has been circulating for one or two years before it sees the light of day, before other people can read it and can do research building on the results.

*Does the use of metrics for evaluation create undesired incentives?*

**Fenner:** Of course! To me, this is the biggest problem, at least in biomedical research. What is increasingly driving research is the

In the end, you waste so much time and many resources. Perhaps the paper that is eventually published in *Nature* is better than the first submitted manuscript – but there is this undesirable incentive. Too much time is spent in trying to get published in relationship to doing the research.

**“The fundamental problem is the assumption that the number of citations of a paper reflects quality. It's a very dangerous idea.”**

*The introduction to the book discusses the idea that with the Internet and the departure from traditional printed journals, scientists could effectively publish and present their data almost as soon as it arrives, on a daily basis. Altmetrics seems almost to be encouraging people to go too fast when they are presenting the information.*

**Fenner:** This is an interesting idea, and a number of people are experimenting with this approach, usually in the context of open notebook science, but I don't see this becoming mainstream any time soon.

What I personally like, but unfortunately I don't think it has a high chance of success in the life sciences, is the ‘arXiv’ physics/mathematics pre-print model. Everybody can read the results and people know that they can publish as soon as they're ready. Two pre-print archives for biology launched last year (PeerJ Preprint and BioRxiv from Cold

## Article-Level Metrics and Altmetrics

Altmetrics are new metrics proposed as an alternative to the widely-used journal impact factor. Altmetrics is the creation and study of new metrics based on the Social Web for analysing and informing scholarship. Only about one in 70 users who download a PDF of the paper will cite it. But many more will engage with it in other ways and some of this activity can be captured with altmetrics.

Article-level metrics (ALM) provide a wide range of metrics about the uptake of an individual journal article by the scientific community after publication. They include citations, usage statistics, discussions in online comments and social media, social bookmarking, and recommendations. Article-level metrics collect and provide metrics for individual articles, rather than aggregating them per journal.

Altmetrics and article-level metrics are sometimes used interchangeably but there are important differences: Article-level metrics also include citations and usage data, while altmetrics can also be applied to other research outputs, such as research data.

PLoS (the *Public Library of Science*) has played a prominent role in promoting

these new metrics, based on the belief that “research articles should primarily be judged on their individual merits, rather than on the basis of the journal, in which they were published”. In March 2009, PLoS inaugurated a programme to provide article-level metrics on every article across all journals. On the PLoS site, you can select ‘Metrics’ for each article that give statistics corresponding to the following ALM classifications. These are placed in order of “increasing engagement” with the research article:

**VIEWED:** Activity of users accessing the article online. “Article views” are provided as an aggregate metric or broken down, month-by-month, in graphical format.

**SAVED:** Activity of saving articles in online bibliography managers, which helps researchers organise papers for themselves as well as share them with others. This includes data from common, online reference management services – CiteULike and Mendeley – to indicate how many times the research article in question has been bookmarked by individual researchers or research groups.

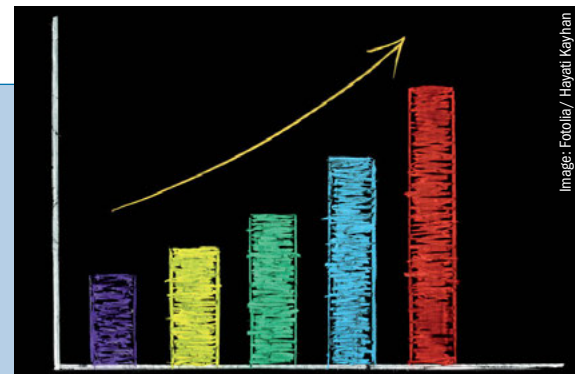


Image: Fotolia/ Hayati Kayhan

**DISCUSSED:** Discussions of the research described in an article (ranging from a short comment shared on Twitter to more in-depth comments in a blog posting). E.g. *NatureBlogs*, *PLoS Comments*, Wikipedia, Twitter, Facebook.

**RECOMMENDED:** Activity of a user formally endorsing the research article (via a platform such as an online recommendations channel). E.g. F1000 Prime, which is a directory of recommended articles by their expert team of scientists and clinical researchers in biology and medicine.

**CITED:** Formal citation of an article in other scientific journals. PLoS provides citation data on each article from third-party citation measuring services: Scopus, Web of Science, PubMed Central and CrossRef.

(“Altmetrics in Evolution: Defining and Redefining the Ontology of Article-Level Metrics”, J. Lin and M. Fenner (*Information Standards Quarterly*, 2013).



Spring Harbor Laboratory) and have each published about 400 pre-prints, so far. Alternative metrics are a good fit for this publishing model.

But we have to be aware that even in high-energy physics, where basically 100% of the content is published in arXiv, there are still journals. The pre-prints are used to quickly disseminate the information but the journals are needed for reputation building. This is why the high-energy physics community has worked very hard to launch SCOAP3 (the Sponsoring Consortium for Open Access Publishing in Particle Physics that started in January 2014), a project that aims to turn the majority of high-energy physics publications into Open Access.

*You also spoke in your chapter about information overflow: "Information overflow has become a major problem, and it has become clear that relying on the journal as a filter is no longer an appropriate strategy. Altmetrics have the potential to help in the discovery process. The advantage over citation based metrics is that we don't have to wait years before we can see meaningful numbers."*

**Fenner:** In scientific publishing, everything is now based on the Internet. Right now, all altmetrics providers focus on showing a number next to an article to make the author happy. He feels good because he can see how many times his article has been cited or downloaded. But that's not really helpful if you want to discover something, to search through a whole new research area with particular keywords. You have hundreds of thousands of search hits and you want help to figure out, which ones are the most interesting. Altmetrics can help with this discovery process but for the most part, these kinds of tools are still missing. It is one of the things that is on our development roadmap for the next 12 months.

*PLoS ONE publishes about 3,000 papers a month. Even if you filter by subject area, you cannot read a table of contents that long. One way to improve this is to use article-level metrics as a filter, to generate a table of contents small enough for people to read it every week.*

*At PLoS ONE, you're saying you're suffering from information overload?*

**Fenner:** Absolutely. *PLoS ONE* publishes everything that is solid science and doesn't pay any attention to the perceived impact a submitted manuscript will have. One consequence is obviously that *PLoS ONE* publishes a lot of papers, another one that it publishes good papers, excellent papers – but also not so good papers. *PLoS ONE* makes it easier for the author to publish but it makes it more difficult for the reader to find the most relevant content – a reader can't read all papers he finds interesting in *PLoS ONE*, he needs tools to help him find the most relevant papers.

*Which leads to the problem of how people are going to evaluate what is better or worse in terms of all this research that has been presented to them?*



**Fenner:** There's a big difference between using these tools to search the literature and research evaluation, where you should be much more stringent. For evaluation, you hope that people still read the papers and listen to the presentation that the candidate is giving, and pose the right questions. But there is a danger that we just look at the numbers.

*Do the currently available altmetrics really measure impact or something else?*

**Fenner:** The problem with altmetrics in this regard is that it is a mixed bag of totally diverse things. Social media metrics are a good example of something that reflects attention much more than impact. Other, newer metrics are probably much better at reflecting impact, e.g. the number of citations in clinical practice guidelines.

*How can we standardise altmetrics?*

**Fenner:** In the NISO project, we discussed whether we are ready for standardisation and best practices, and what would be the areas where we would start. We came up with a list of 25 potential action items for further work and in the next few months we'll decide, which ones to work on.

*The Altmetrics Manifesto was published in 2010 (altmetrics.org/manifesto). In the aftermath, there were many questions about how much research is going to be needed to prove the value of altmetrics. Has there been a lot of progress in the last four years?*

**Fenner:** Two years ago, it was all very new and people were sceptical but I think that now it has become more mainstream, at least for publishers and funders, although not so much yet for researchers. But there still needs to be more research to better understand what these metrics mean, how they correlate with each other, etc. The 'Altmetrics14' conference at the end of June is a conference focussed on research into alternative metrics and there was also a lot of altmetrics research presented last year at ISSI (the International Society of Scientometrics and Informetrics), the main bibliometrics conference.

*"I personally like the 'arXiv' physics/mathematics pre-print model but, unfortunately, I don't think it has a high chance of success in the life sciences."*

*What is your opinion of post-publication peer review? Michael Eisen, one of the founders of PLoS, has been pushing this as a solution.*

**Fenner:** Mike is very much of the opinion that you should make publication as easy as possible and then let other people work out, which publication is interesting for them, and why. Article-Level Metrics try to collect everything that talks about an article post-publication – comments in PubMed Commons are on our list of sources to add. Some of it is just numbers, like number of Facebook likes or Mendeley readers, but we also capture a lot of sometimes detailed discussion around a paper. Unfortunately, this deeper public discussion of *PLoS* articles via journal com-

ments, blog posts, F1000Prime evaluations, etc., still only happens for a minority of articles.

*Often, we read articles but we are not inclined to write a comment?*

**Fenner:** Publishers, such as *Frontiers*, are trying to improve this by building a discussion platform on top of their publishing platform. There are technical challenges to do this right but the bigger problem seems to be that people, in general, and life sciences researchers in particular, don't feel inclined to make a comment.

**“PLOS ONE makes it easier for the author to publish but it makes it more difficult for the reader to find the most relevant content.”**

For example, the problem in molecular biology, where doing the experiment can be relatively easy, is that once you have the idea, you know what you're doing. So you try to keep your stuff secret until you have published it. This is very different from other fields. Imagine high-energy physics – there are only a few places in the world where you can do the experiment, so it's really hard to cheat on each other. The same is true for other fields where research depends on complex equipment or scarce samples: the Mars Rover team will not get scooped on their research. Clinical medicine is also an area where you can't cheat because clinical trials have to be registered in a public database before you even see the first patient, years before you publish your results.

*Although clinical medicine is one of the domains that has suffered from the rise of impact factors?*

**Fenner:** That is true. But at least the fear of getting scooped is much lower and that means that presentations at medical conferences are where you first hear about new research, not from the published article. In biology, many presenters tend to be much more cautious, only presenting published results, stuff that everybody already knows about, unless it's a very small meeting, or you are particularly famous.

*Another area of altmetrics that doesn't pass by the Internet?*

**Fenner:** Yes, that is very unfortunate. Although some conference abstracts make it into centralised databases, overall this is a very fragmented and sometimes even closed system that makes it very hard to track metrics, e.g. to find the most discussed or cited abstracts.

*You mentioned the problem of information overload with the internet. Do you feel that there is a loss of capacity to personally organise all this information?*

**Fenner:** The way that people expect to search for stuff is completely dominated by Google. It is an easy search engine. We have specialised databases for scholarly content, such as PubMed, that allow us to do very complex searches but no researcher is using

**“Not using the Journal Impact Factor but instead looking at citations for an individual article would make a big difference.”**

these advanced features. I think it is a little sad that people only care for quick answers but it also means that we have to adjust our tools. In a world of Google, everything that is not on the first results page is totally ignored. So, when you do a search, it is really highlighting the popular stuff. And everybody is reading that. One consequence of this information overflow is the loss of variety in what people are read-

ing. There used to be the serendipity of people randomly looking through the table of contents and saying, “Oh, that looks interesting, let's look it up” but that is happening far less now because there is just too much content out there. People are now doing specific searches and just looking at those articles.

*Do you think we need new search guidelines?*

**Fenner:** No. Something that is happening in other areas, but not quite yet in science, is the move from the Google World to the Facebook World. The Google metaphor is where we are now. But

## Bibliometrics – The Tyranny of the Journal Impact Factor

Most researchers in universities and research institutions, especially those working in the life sciences and medicine, are well aware of the tyranny of journal-based bibliometrics. Their ‘worth’ as a scientist and the perception of their productivity as a researcher are frequently reduced to a crude numerical assessment of their research publications. The scientific content of the articles is often considered less important than where the article has been published.

According to Peter Lawrence, changes in the publication process during the last 30 years have had a very bad effect on the health of science. These have been driven by the demands of journal-based bibliometrics: “We've got into a situation where the measurers drive the science, rather than the measurers being there to quantify the scientific effort or achievement.” (*LT 2-2011 p.24-31*. This interview received an ‘Article Recommendation’ from F1000Prime, one of the alternative metrics included in the *PLoS Article-Level Metrics*).

In May 2013, the Declaration on Research Assessment (DORA) focussed on the disastrous effects for the research community of allowing the citation rate of a scientific journal to become a dominant measure of the value of all scientific research: “Impact factors warp the way that research is conducted, reported and funded” (*LT 05-2013 p.18-23*). Supported by many senior academics, journals and research organisations, DORA makes 18 recommendations for changes in the “scientific culture at all levels”. The overall aim is to reduce the dominant role of the Journal Impact Factor in evaluating research and researchers, and instead to focus on the content of primary research papers, regardless of publication venue ([am.ascb.org/dora](http://am.ascb.org/dora)).

DORA's recommendation No. 17 exhorts us to “Use a range of article metrics and indicators on personal/supporting statements, as evidence of the impact of individual published articles and other research outputs.” As an example of these alternative measures of scientific value, it points to altmetrics.

In December 2013, on the day before he received his Nobel Prize in Stockholm, Randy Schekman, one of the instigators of DORA, announced that he would no longer submit any research articles from his lab to the ‘luxury journals’, in particular *Science*, *Nature* and *Cell*. Schekman protested that these journals have distorted science through their publishing practices and that something has to change if the health of science is to improve (*LT 1-2014 p.16-21*).



what you really want is from the people you trust, to be in your friends' network, to see what they are reading, what they are recommending. This is, of course, a very strong and effective filter, which also creates all kinds of biases but I think that is the direction things are taking.

*I notice you are active on Twitter.*

**Fenner:** For me, Twitter, on a small-scale, is where I hear for the first time about a lot of articles, blog posts, papers, etc. I think a lot of people use Twitter for that; not because it is a great discussion platform, because it is horrible for that, but really as an alerting system, where you can then decide who to follow and what to do.

*When we talk about Google, Facebook, Twitter, do you think anything has changed as a result of the revelations about the NSA (US National Security Agency) and the extent to which the Internet is being spied upon?*

**Fenner:** I think this is very relevant but I'm not sure how much this has had an impact on science communication. There are problems of privacy. There's a very simple one, which totally annoys me – the fact that every paper you publish has your email address on it, so everyone gets a lot of spam emails asking to submit to journals, or conferences, or to order lab reagents. But that is more of an annoyance than a privacy issue. A scientist who is publishing work is a public person, similar to musicians, politicians, etc. You have to publish in science and so you have to reveal a bit of information about yourself.

*In DORA (the Declaration on Research Assessment), there was a call to use altmetrics to find alternatives to the Journal Impact Factor because there is a feeling that funding organisations are still looking at these bibliometric numbers when making decisions.*

**Fenner:** I don't agree. Talking to many funding organisations, I find that they don't care about impact factors. Sometimes, they are more progressive and specifically state that they won't allow their use in evaluation. Using the Impact Factor for assessing individuals is really a bad idea. If you took the same approach to the science that you do, you would immediately lose your job.

It's not pressure from the outside, it's the scientific community itself that has decided to misuse the Journal Impact Factor. Of course, it is about taking short-cuts – if you have 100 applicants for a position, you can just filter out by, say, looking at only those who publish in *Science* or *Nature*, and then take it from there. But the funding organisations are not to blame. The publishers, some of whom live well from this system, have no reason to change it. But at the end of the day, it's really the researchers who are to blame. That is why I like DORA because it involves a lot of academic editors, experienced researchers themselves, who have spent time thinking about this.

*It would be nice if more researchers actually admitted that there is a problem.*

**Fenner:** This is definitely an area where altmetrics is not doing a good job because for the most part they are not yet used and discussed by researchers. Even taking a small step – not using the Journal Impact Factor but instead looking at citations for an individual article – would make a big difference, even without any additional newer metrics. There is still a lot of work to do in this area.

INTERVIEW: JEREMY GARWOOD

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*A conversation with Maria Leptin, EMBO, Heidelberg*

# “EMBO Should Speak for all Biologists in Europe”

Maria Leptin was happily doing research at the Cologne University when she was asked to become EMBO's Director General. She accepted and has been heading the organisation since 2010. She also runs two labs, one in Cologne, the other in Heidelberg. Karin Hollricher talked to her about work load, EMBO and science in Europe.



Photo: EMBO

About 250 kilometres separate Heidelberg from Cologne, Maria Leptin's two places of work. Her research topics are, at first sight, just as wide apart: *Drosophila* development and zebrafish immunology. Her first scientific love was immunology. In 1983, she received her PhD from the Basel Institute for Immunology for her work on B-cell activation. Shortly after, she got more interested in fruit fly development, when she became a postdoctoral fellow in Michael Wilcox's lab at the Medical Research Council Laboratory for Molecular Biology in Cambridge,

UK. In 1989, Leptin enjoyed a short stint at the University of California, San Francisco before returning to Europe and leading a research group at the Max Planck Institute for Developmental Biology in Tübingen, Germany. Since 1994, she has been a professor of genetics at the University of Cologne and since 2010 director of EMBO, with a second research group at the EMBL, Heidelberg. Her research focuses on cell shape determination in *Drosophila* and the genetics of pathogen resistance in zebrafish.

*Lab Times:* Why did you accept this busy job as the EMBO Director? Weren't you fully engaged with research?

**Leptin:** Of course I was – but not only with science, since at the university you also have many other, non-research

duties – teaching, administration and so on. So it's not as if I went from a job spending all my time doing research to one that was only administration. Also, at this time, my children were about to leave home, so I had more free time to dedicate to the new job and was able to increase my working hours again to the level they were at before we had kids. This means that not all of the extra time spent on EMBO work had to come out of research time.

*You didn't give up science, yet you have two groups working in two cities. Aren't you occupied with this director job?*

**Leptin:** Of course the EMBO directorship is a demanding task that needs a lot of concentration. But I would not have considered the position if it had meant giving up research. Council and the Secretary General had made a clear decision that they wanted an active scientist as the Director. I think this is really important and I personally feel that this is a good situation, too. I can retain a close connection with the community, go to meetings, be engaged with the active community as one of them rather than as an administrator. And hear the needs of the community directly from the grassroots.

*If you would have to name three aspects: what's best about EMBO?*

**Leptin:** That's easy. First, the community of EMBO members and the wider EMBO community: the best researchers in the life sciences in Europe, clever, innovative, entertaining; willing to put in an effort to support the EMBO programmes. The members help with everything. They do the selection of the postdocs, they do the assessment of courses and workshop programmes, they often give us advice on ideas and plans. They counsel, supervise what we do and advise at what we do. That takes them a lot of time.

*Second point?*

**Leptin:** Second, the EMBO staff in Heidelberg: highly professional, intelligent, well-informed, fantastically dedicated.

*“I can retain a close connection with the community, go to meetings, be engaged with the active community as one of them rather than as an administrator.”*



There's an extremely good atmosphere with everyone working toward a common goal. This is really special. I do not want to trash German universities but our staff is very, very good. They earn good salaries, so the best apply and we get excellent people. Our administration is very small, some 20 people who run the whole show.

*And your third point?*

**Leptin:** The mission of EMBO.

*That is?*

**Leptin:** To generally support the life sciences through money, workshops, training, fellowships to create a situation in Europe where life sciences can achieve top-notch work. We are building networks between researchers; for example, with our Young Investigator Programme we have created a cohort of some of the top people, who we've fund-

ed from an early stage, when they started their independent research careers. They know each other, support each other across research fields. That really enriches European life sciences. I'd also like to add that we have made significant improvements in our journals, making them more author-friendly.

*Author-friendly? We were not aware that editors, generally speaking, are committed to the idea of such a service.*

**Leptin:** [laughs] Okay, I'll give you an idea. We try to be fast. We are totally transparent. The referees' reports are published. So, referees have to make an effort and think carefully about what they write. The referees communicate with each other before the editors make the decision. This means that a referee with unjustified demands can be stopped at that stage. Also, an uncritical referee can

be stopped. Additionally, referees are asked not to make 'confidential remarks' to the editor. Everything they say about the paper should also be visible to the authors. We also cancelled that idiotic thing that a publication will be stopped only because somebody else publishes similar data at the very same time. Once you have submitted your paper to one of the EMBO journals, it will go its way. Our editors are always reachable, we don't hide their phone numbers. They attend scientific meetings, they know their communities and the community knows them.

*Sounds good. How do the authors react?*

**Leptin:** We receive a lot of positive feedback, they really appreciate what we do.

*Did you have any particular ideas of implementing new projects or changes in EMBO, be it either scientific or administrative, when you started out?*

**Leptin:** Some, of course. I wanted to establish better contacts with scientists and

*"We also cancelled that idiotic thing that a publication will be stopped only because somebody else publishes similar data at the very same time."*

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science management in the countries outside Europe that have begun successfully to build up their own science base of cutting-edge life science research. We are also working on improving our connections with policy makers in Brussels and elsewhere. And I intend to further expand the membership to include all of the modern life sciences.

*This means the membership expansion that EMBO started along with its 50<sup>th</sup> anniversary in 2014?*

**Leptin:** Right. EMBO was founded as an organisation for molecular biology only. For many years, it was small, consisting of about 200 members. Now, molecular biology is present everywhere in the life sciences, including, for example, forensics or food chemistry. But some fields are under-represented, such as neurobiology, hard core evolution or ecology. We felt it was not wise to insist on staying with the core only; EMBO should cover the whole breadth of the life sciences and speak for all biologists in Europe. So we assembled a group of experts to identify the leading scientists in these under-represented fields. A list was created, which was presented and those people were elected.

*Now, looking back, did you succeed in implementing your intentions?*

**Leptin:** The first two are still ongoing, both being goals that cannot be achieved overnight but require patience and consistent work. Regarding the widening of the membership, we have made the first big step. With regard to world-wide interactions, we have successfully established cooperation agreements with several Asian countries. I also started the Science Policy programme because I think, with its 1,500 expert scientists, EMBO is in an excellent position to provide analyses for European policy makers that are unbiased by national interests, and because it is becoming increasingly important that someone speaks up for the needs of researchers. The programme has run several workshops and produced analyses on a number of issues.

*Most likely you have gained deep insight into the European scientific community and its science administration as a whole. Can EMBO influence political decisions in Brussels regarding science?*

**Leptin:** We certainly hope so! We have established many close connections with policy organisations and individuals, in Brussels and elsewhere. In fact, we believe that in one instance we did help. EMBO is part of the ISE...

*The Initiative for Science in Europe.*

**Leptin:** Right. Building on an open letter sent by Nobel laureates, we recruited two of those laureates, who were also EMBO members, et cetera. A long list of signatures went to Brussels. Result: The sci-

*“It takes a long time to build up a top-notch research culture and infrastructure, and almost no time to destroy past achievements.”*

**Leptin:** It's painful for many countries. In some, researchers have had to take up to 30% income reductions and fellowships for PhD students have been reduced or suspended. It is painful to see this because we know that it takes a long time to build up a top-notch research culture and infrastructure, and almost no time to destroy past achievements. While one can understand that some government expenses appear more important to citizens than research,

it is very unfortunate that even some politicians seem to see research and education as a bit of a luxury that one can take or leave, rather than a critical investment for the future.

*If you'd have to decide to fund one of two equally excellent projects – would the economic situation of science in the respective European countries be a criterion for your decision? In other words: would you tend to fund the project in the “poorer” country?*

**Leptin:** All funding decisions are made by committees made up of EMBO members and they look at excellence of proposals first. However, they are always sympathetic to the situation of their colleagues in poorer countries. In some programmes it would be inappropriate to make ‘political’ or strategic decisions that would not favour the best applicants. For example, postdoctoral fellowships should only be awarded based on the quality of the applicant and his or her proposal. In general, there really has to be a careful balance and we try to achieve that.

While it is important to help the poorer countries to achieve more, there is no point in directing funds for advanced research into a place where there is no political will to actively build up an excellent infrastructure and to support research, in such a way that it will eventually become competitive with that going on in richer countries. This does not only require a financial investment by the country but also a willingness to change administrative structures and the distribution of power in decision-making. A country or institution has to offer young researchers total intellectual and economic independence for their research, if they want to attract the best scientists.



In 2012, Maria Leptin visited the Beijing Genomics Institute, BGI, according to them, “the world’s largest genomics organization”. During her stay, she had “heated scientific exchanges with BGI delegates”.

*“I also started the Science Policy programme (...) because it is becoming increasingly important that someone speaks up for the needs of researchers.”*

ence budget in Horizon2020, including that for the ERC, was better protected than it might otherwise have been. Here, I'd like to remind you that EMBO was initially responsible for even starting the ERC. But the Science Policy programme does many other things, too. We obtained grants from the Bosch foundation and ESF, to support workshops on gender quotas and human sequence data usage. EMBO has written up studies on genetically modified organisms that resulted from a workshop.

*What impact had and still has the economic recession in European countries on the respective science?*



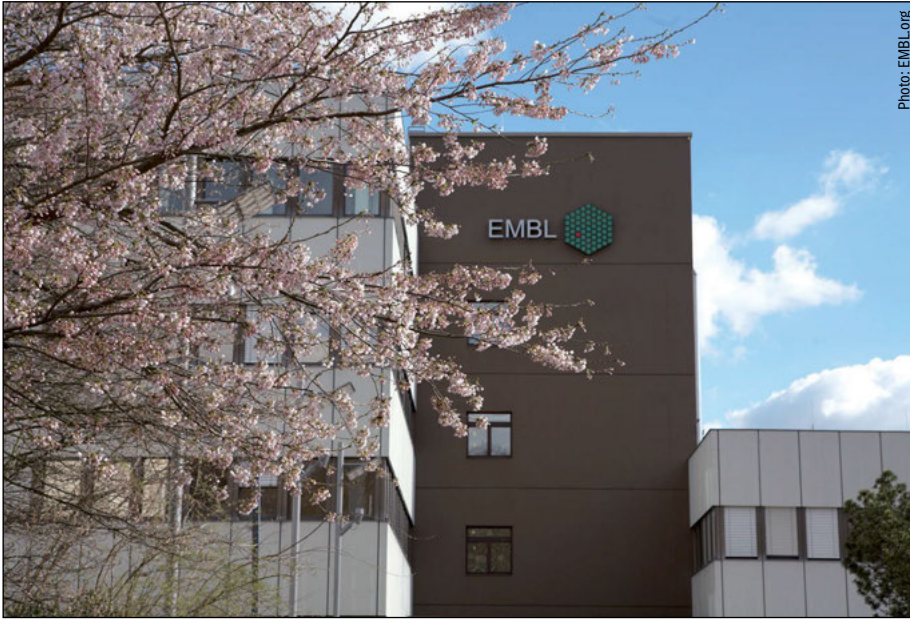


Photo: EMBL.org

**EMBL in romantic Heidelberg**

Fortunately, many countries want change and are willing to make commitments; EMBO has a programme, the Strategic Development Installation Grants, that is one of our contributions to solve that special problem. It helps these countries to recruit the best young people to set up independent labs in their country and to create an environment for these researchers, in which they can accomplish their scientific goals. The government of the country makes a significant financial contribution and positions in this programme can only be offered to young scientists, who have been selected in a rigorous, highly competitive selection process run by EMBO.

*You're a woman on a director's chair, so we feel obliged to ask at least one question regarding women in science: you are definitely female, successful in science and science policy; so you can be considered as one of the role models that in official reports are so important for young female scientists. Do you really sense that?*

**Leptin:** I personally never thought of myself like that. I just did what I did and it didn't occur to me that it mattered what my sex was. Nowadays, it is of course impossible not to notice because we are constantly told about gender. I am not entire-

***"While it is important to help the poorer countries, there is no point in directing funds into a place where there is no political will to actively build up an excellent infrastructure."***

***"Both research and the job at EMBO are completely different: new and interesting problems that need creative solutions every day."***

ly convinced that this is always good. We need a little less agonising and a bit more of a naïve approach; of just going for it and not thinking too much about all the potential problems one might face in one's career. That's just off-putting. The only way one can face the stress of a scientific career – and I wouldn't dream of saying there is no stress – is not to think about it.

*In another interview you said "I only decided to become a scientist when I realised that I couldn't stand the idea of having to go to school for another 40 years!" Please guess: How long can you stand the idea of being EMBO Director?*

**Leptin:** The reason I couldn't face teaching is that it looked to me to be too repetitive and I would have to be doing the same thing over and over again. Both research – whether at universities or research institutions – and the job at EMBO are completely different: new and interesting problems that need creative solutions every day. So, for neither job – here at EMBO or back in my lab in Cologne – is the question how long can I stand it but how long will I be allowed and how long will I be mentally capable of doing them.

INTERVIEW: KARIN HOLLRICHER

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A conversation with Carl-Henrik Heldin, Ludwig Institute, Uppsala

# “The Success of the ERC in Itself Presents a Challenge”

Molecular biologist by day, Vice-President of the European Research Council and Chairman of the Board of the Nobel Foundation by night – Carl-Henrik Heldin is a busy man. *Lab Times* talked to him about the latest developments at the ERC as well as about the research funding situation and internationalisation efforts in Sweden.



**B**orn in 1952 in Växjö, Southern Sweden, Carl-Henrik Heldin has remained true to his home country throughout his life and career. In 1980, he completed his PhD studies at the Department of Medical and Physiological Chemistry at the University of Uppsala, working on “growth factors for human cultured cells”. Since 1986, he has directed the Uppsala branch of the Ludwig Institute for Cancer Research. His research on mechanisms of signal transduction by growth regulatory factors has so far culminated in over 400 research papers, numerous patents and close to 60,000 citations. His most cited paper about TGFbeta signalling through SMAD proteins, from 1997, collected over 2,000 citations alone (*Nature*, 390(6659):465-71). As a successful

scientist, Heldin has been in great demand to provide his scientific advice to academic institutes like the European Molecular Biology Laboratory in Heidelberg, Germany, and the European Institute for Oncology in Milan, Italy. In 2011, he accepted the position as Vice-President of the ERC.

*Lab Times:* With a budget of close to €80 billion, Horizon 2020, the new research and innovation funding programme of the European Commission, was launched earlier this year. A hitherto unprecedented emphasis has been placed on excellent science, in which the European Research Council (ERC) plays a vital part. How did you become involved in the ERC?

**Heldin:** In 2005, I was asked to serve on the founding ERC Council, consisting of 22 members from different research fields and different countries.

What functions do you have as a Vice-President of the ERC?

**Heldin:** As Vice-President, I take part in five meetings per year with the ERC Council, during which we discuss and decide on overall strategies for the ERC. I also take part in ERC Board meetings every month in Brussels together with the President, the other Vice-Presidents and the senior staff at the ERC Executive Agency. During these meetings, we discuss operational problems, etc. I also act as Coordinator for the Life Sciences, which involves a lot of work related to the recruitment of members to our evaluation panels.

*“The ERC is a wonderful opportunity but if we fail, we will not get another chance.”*

Do you remember the beginnings of the ERC and what have been your expectations and worries?

**Heldin:** Certainly! I think all Council members felt a lot of responsibility to get things right; the ERC is a wonderful opportunity but if we fail, we

will not get another chance. We all felt that it is of utmost importance to create an efficient, non-bureaucratic ERC with excellence as the only evaluation criteria. To achieve this, a certain independence from the Commission is important.

A major review of the ERC was performed by an external panel in 2009. What were the major conclusions of the evaluation?

**Heldin:** The external evaluation committee recommended several of the things that we in the Council had been striving for, including increased independence for the ERC. Their recommendations were of great help for us.

In response to the external review and in prospect of Horizon 2020, a Task Force with current and previous members of the ERC, the ERC Executive Agency and various Departments of the European Commission was set up. What have been the major recommendations?

**Heldin:** The most important recommendation was to establish a position as ERC President, employed near full-time and living in Brussels. At the same time, the position as Secretary General, who previously served as the Council representative in Brussels, was disposed of. With a President continuously present in Brussels, the interactions between the Council and the Executive Agency and EU Commission will be more efficient.

In comparison to FP7, the previous Framework Programme, the ERC budget has increased from €7.5 billion to over €13 billion in Horizon 2020. Please give a comment.

**Heldin:** We are glad for the increased budget, which means that the ERC will be able to continue to play an important role for European research. However, the ERC could use even more money; the gradual in-



crease of the budget during the first seven years – a similar year-by-year increase will also occur during Horizon 2020 – means that the budgets for 2014, 2015 and 2016 are actually lower than that of 2013.

*The ERC continues to support ground-breaking high-risk/high-gain research in any scientific discipline. Have there been any changes at the start of Horizon 2020?*

**Heldin:** No, not really. The ERC is committed to a bottom-up procedure, encouraging a high-risk/high-gain type of research, with excellence as the only evaluation criteria.

*You have been a member of the ERC Working Group on Gender Balance. What have been major outcomes and what will be major topics for the future?*

**Heldin:** A problem we have experienced is that in each of the first 12 ERC calls, the success rate for women has been slightly, but significantly, lower than for men. We have taken this observation very seriously and within the Gender Balance Working Group have done our utmost, to investigate what may be the reasons for this discrepancy. The most important question is whether this has to do with the evaluation procedure at the ERC, or whether it has to do with factors outside of the ERC. We do not yet have any conclusive evidence to explain the discrepancy but we continue to investigate this issue.

*Are you able to provide some hints on major topics that are currently discussed within the ERC and on upcoming modifications with respect to funding and structure?*

**Heldin:** I think that we have a consensus in the Council that the calls for Starter, Consolidator and Advanced researchers are at the core of the ERC's funding mechanism. These are large grants for five years to individual researchers, which give the grantees the possibility to take on ambitious research projects. We have also had very good experience with the Proof of Concept grants, which gives ERC grantees the opportunity to get an extra 150,000 euros to develop a discovery towards application. For 2012 and 2013, we also had calls for Synergy Grants, which are grants for two to four researchers, who will work together to

*“Many times, when ERC grant holders complain about bureaucracy, it turns out that their host institute has caused the problem.”*

*“A clear philosophy for the ERC is to keep a simple, bottom-up principle, without any predefined research areas.”*

address a common research problem, preferentially adopting a multidisciplinary approach. The advantages and disadvantages

of this grant type, compared to the individual grants, are now being investigated. Depending on the outcome, there will, or will not, be additional Synergy calls, maybe from

2017. No other types of calls are discussed for the moment. A clear philosophy for the ERC is to keep a simple, bottom-up principle, without any predefined research areas.

*What are the main, future challenges for the ERC from your view as Vice-President?*

**Heldin:** The success of the ERC in itself presents a challenge, since the ERC is overwhelmed with increasing numbers of applications and the success rates have, therefore, decreased year-by-year. In 2013, it was well below 10% for the Starters and Consolidators. We, therefore, had to tighten the re-submission restrictions, which means that if someone submits an application, which is not successful, he/she may not submit another application the coming year or two (depending on the scores the evaluation panel gave the application). This was a painful but necessary decision; it seems to have worked, since the number of applications actually decreased somewhat from 2013 to 2014. Another challenge is to assure a suitable independence of the ERC from the Commission.

*What may be further improvements at the ERC from your view as a researcher?*

**Heldin:** We continuously strive for efficiency and flexibility of ERC grants, as well as for fairness and the highest possible quality of the evaluation procedure.

*What about the current burden of bureaucracy for the individual ERC-supported scientist and his home institution?*

**Heldin:** We are very anxious that the ERC bureaucracy should be minimised. We have made some progress but there is more to do. It should be mentioned, however, that many times, when ERC grant holders contact us to complain about bureaucracy and we look into the problem, it turns out that, in fact, their host institute has caused the problem.

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What type of criticism – if any – is made of the ERC by the scientific community as well as by national policy makers and funding agencies?

**Heldin:** Support for the ERC is generally overwhelming from scientists, other funding organisations and universities. There are, of course, some differences of opinion about details but there appears to be a consensus about the general principles the ERC has adopted. Unsuccessful applicants are sometimes unhappy but most people realise that the major problem is a lack of appropriate funds making it very difficult to get an ERC grant. Some countries that have not been so successful are also not happy but most often they still back up the policy of excellence as the only evaluation criteria.

Besides having a high-profile Scientific Council how does the ERC stay in touch with the scientific community in Europe and beyond?

**Heldin:** Members of the Scientific Council and the staff of the Executive Agency often participate in information meetings in different countries inside and outside of Europe, as well as give information about the ERC at large scientific meetings. Other members of the Council and I are also often contacted by scientists, who have questions or express opinions about the ERC.

One might argue that without the support of the ERC, many of the excellent scientists would tap domestic funding sources and even be successful with respect to research output.

**Heldin:** In most countries, ERC funding comes on top of the national funding, which in most European countries is modest. ERC grantees very often contest that their funding from the ERC really makes a difference.

How do you judge the impact the ERC has on Horizon 2020 and the European research landscape?

**Heldin:** The ERC gets 17% of the Horizon 2020 budget, up from 15% during Framework Programme 7. The ERC nicely complements other types of EU funding for research. We are glad for the increased ERC budget but could easily find good use for more money. I think that there is a consensus that the ERC contributes in a crucial manner to the “excellence pillar” of Horizon 2020.

What, in your opinion, are necessary steps to achieve the European Research Area (ERA) with a free circulation of scientists, knowledge and technology as put forward by the European Commission?

**Heldin:** I think we already have a rather good free circulation of scientists, knowledge and technology in Europe. What remains to be improved are practical things, like help when scientists move with families, housing, some flexibility with regard to salaries, flexible and movable pension systems, etc.

There are growing concerns that sooner or later the European Commission will intervene more directly with national research pol-

is not perfect. Basic research would need some more money and we would need a better career path for young scientists.

Have there been any major changes or novel, noteworthy programmes in the Swedish funding landscape?

**Heldin:** The Research Council just stopped their programmes of positions for young and mid-term scientists, claiming that recruitment is the responsibility of the universities. Whereas this may sound logical, the consequence is that too few positions are now being advertised, which is a problem for young scientists. On the positive side is new funding in the form of Science for Life Laboratory, which includes support for infrastructure in the life science area.



Photo: © The Nobel Foundation/Alexander Ljungdahl

icies by EU-wide legislative measures. How might the highly varying needs and necessities of individual countries regarding the completion of the ERA be balanced against national priorities and independence?

**Heldin:** Many EU countries have well-functioning research funding mechanisms and a longer experience than the EU in this regard. They will rightfully protest if the EU interferes in an inappropriate manner. The EU needs to learn from the best-functioning countries, while a balance and a sensible division of roles and responsibilities between national and European efforts need to be found.

How do you judge the current funding situation for biomedical research in Sweden?

**Heldin:** The funding situation in Sweden is rather good, however, our system

In more than a few countries there has been a significant shift to more applied research and experimental development in expense to basic and blue sky research over the last years. How is the situation in Sweden?

**Heldin:** This is a continuous discussion everywhere, including Sweden. However, I think that there is still a general agreement in Sweden that basic research is important. Most scientists realise that without strong basic research there will be no high quality applied research, and that we need to support both basic and applied research.

What about the career perspectives of young Swedish scientists, in general?

**Heldin:** As I said above, we do not have a good career system for young scientists. However, some private foundations, includ-

*“ERC grantees very often contest that their funding from the ERC really makes a difference.”*

*“In Sweden, we need to be able to convince young people that research is interesting and something worth trying.”*



ing the Wallenberg and Söderberg foundations, have programmes offering generous support to young scientists; in the absence of sufficient university-supported positions, these programmes are very important.

*What, in your opinion, are the necessary mid- and long-term steps and measures to advance science in Sweden further?*

**Heldin:** The future standard of research in Sweden stands and falls with our ability to recruit brilliant scientists. On the one hand the basic school system of Sweden, which used to be excellent, needs substantial improvement following its continued deterioration over the last 20-40 years. Moreover, we need to be able to convince young people that research is interesting and something worth trying. We also need to make Sweden attractive for foreigners to come and work here.

*Have there been any major changes in Sweden recently with respect to incoming or outgoing scientists?*

**Heldin:** Swedish people are often not so mobile. Many undertake a postdoc period abroad, which is good, and then come back to the same university where they did their training. This is understandable, since Sweden is a small country that does not have so many high class universities. Sweden does recruit some scientists from abroad, however, many of the best often move on to even more prestigious places outside Sweden.

*Can you elaborate a bit on funding possibilities for scientists from abroad wishing to establish a career in Sweden?*

**Heldin:** Scientists who want to move to Sweden need a start-up package from their host university, since it takes some time to get into the system and to get grants from Swedish and European sources. Many progressive universities understand that this is necessary for successful recruitments but this can be improved further.

*Are you, yourself, engaged in different programmes to obtain funding by international sources?*

**Heldin:** I have been involved in EU-funded Networks of Excellence, Integrated Projects and other funding mechanisms in the past but not at the moment. For conflict-of-interest reasons, I am not allowed to apply for ERC grants.

*What have been recent major discoveries by your research group in the field of signal transduction?*

**Heldin:** We have elucidated molecular mechanisms, by which TGFbeta induces epithelial-mesenchymal transition and invasiveness of cancer cells, and demonstrated the importance of PDGF for the stromal compartment of solid tumours.

*Did you make any progress with respect to the clinical use of signal transduction antagonists?*

**Heldin:** We have used signal transduction inhibitors in cell culture assays and animal models only but others have used different types of signal transduction inhibitors in clinical trials and a few drugs have been approved for clinical treatment of certain tumour types.

*In December of last year you, as the newly elected Chairman of the Board of the Nobel Foundation, gave the opening address at the Nobel Prize Award ceremony. Please tell us about this experience.*

**Heldin:** This was an interesting, exciting and gratifying experience for me, who has never done anything similar before.

*What is the exact role of the Chairman?*

**Heldin:** The Board of the Nobel Foundation does not take part in the selection of the Nobel Laureates. Each of the Prizes has a special committee, as specified in the will of Alfred Nobel. However, the overall responsibility rests with the Board, which also has the responsibility for the Nobel Museums in Stockholm and Oslo, and Nobel Media. Other important tasks include making sure that the Nobel Fund money is wisely invested and overseeing the building of a new Nobel Centre in the middle of Stockholm.

*Do you still have some leisure time in light of your many activities in domestic and international organisations and boards?*

**Heldin:** It is true that I devote a lot of time to research at my institute and to many outside duties. However, I live in a small town – Uppsala has 200,000 inhabitants – where life is easy and where it is possible to be very efficient. Moreover, I live close to the major airport of Sweden. All this helps to make room for other activities, including spending time with my family and friends, and different forms of physical exercise.

INTERVIEW: RALF SCHRECK

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A conversation with María Blasco,  
Spanish National Cancer Research Centre, Madrid

# “Science Should always be **Exciting!**”

Cancer and ageing are one of the most pressing health challenges, the developed world is facing. María Blasco took up the battle. As a woman scientist in an economically recessed country, she didn't make it easy for herself.

as primer for the replication of the viral genome. My PhD thesis was to do a structure-function analysis of the polymerase by mutating the most conserved residues. By that

I saw the radiograph showing that we had generated mice without telomerase.

*Are you still a big believer in this model system, despite growing critics on using mice to model human disease?*

**Blasco:** I continue working with mice. I think it is still the best animal model for understanding human disease. The telomerase-deficient mouse served to prove that telomere shortening to a critical length caused chromosomal instability and premature ageing and disease, and helped to unveil the molecular mechanisms by which this occurred. This was years before humans with telomerase mutations were actually found. The mouse work provided the first solid genetic evidence for the role of telomeres and telomerase in cancer and ageing, and it paved the way to understand these human diseases, known as telomere syndromes. My group has more recently demonstrated that mice also suffer telomere shortening with

ageing, like humans do, and that if we delay telomere shortening by expressing telomerase in the adult organism we can delay disease and extend longevity.

The telomerase deficient mouse model also served to show that telomerase inhibition could be effective in ceasing cancer growth.

*How did moving to the US for you as a postdoc change the way you approached science and your research?*

**Blasco:** Being at the Cold Spring Harbor Laboratory was fantastic. It was an exciting environment where more postdocs like myself were thriving to make important discov-

time, I had heard of telomerase, an enzyme discovered by Elisabeth Blackburn and Carol Greider that was postulated to be key in the solution to the “end replication problem” in higher organisms, and was also suspected to have a role in cancer and ageing. I immediately decided that I wanted to specialise in telomerase. Because Carol was in Cold Spring Harbor Laboratory, which to me was the “Mecca” of Molecular Biology, I decided to apply to Carol's lab.

*During your postdoc in Carol Greider's lab, you generated the first mouse knock-out of telomerase. How important was this work for understanding the many functions of telomerase and of telomeres?*

**Blasco:** When I arrived in Carol's lab, the genes of the mammalian telomerase were unknown, only the *Tetrahymena* telomerase RNA component had been cloned by Greider herself. To demonstrate a role for telomerase and telomere length in cancer and ageing, it was essential to clone the mammalian genes. That was my project when I arrived: to clone the telomerase RNA component in mice and to generate a mouse without telomerase, to demonstrate its importance in cancer and ageing. One of the most exciting days of my postdoc was when

*“Hopefully [the economic crisis] will pass soon and Spain will continue to grow in excellence in science and innovation.”*

**M**aría Blasco is director at the Spanish National Cancer Research Centre (CNIO) and former member of the EMBO Council. After completing a PhD with Margarita Salas at the University Autónoma of Madrid (Spain) in 1993, she moved to the Cold Spring Harbor Laboratory (US) to work with Carol Greider, one of the laureates of the 2009 Nobel Prize for Physiology and Medicine for the discovery of how chromosomes are protected by telomeres and the enzyme telomerase. In 1997, Blasco moved back to Spain to set up a research group at the Spanish National Biotechnology Centre (CNB) in Madrid and a few years later she moved to the CNIO. Amongst her many important scientific contributions, Blasco cloned the RNA component of mammalian telomerase and also produced the first telomerase knock-out mouse, which was fundamental to establishing a role for the ribonucleoprotein in cancer and ageing.

*Lab Times: Your research career began in the laboratory of Margarita Salas working on a DNA polymerase involved in bacteriophage replication. What made you decide to change to a murine model and focus on telomere biology?*

**Blasco:** With Margarita Salas I was working on the “end replication problem” of the bacteriophage. In that case, this problem was solved by using a terminal protein





eries. You could sense that feeling of discovery and leading edge research. In Europe in general, scientists are a bit more relaxed, although this is changing and certainly in my group at the CNIO I try to convey that science should always be exciting!

*Given the current economic crisis and the affect it has had on research, what is it like to be a researcher in Spain now, compared to when you started?*

**Blasco:** I returned to Spain because I got a permanent position at the Spanish Research Council, which secured my salary, together with a good offer to set up my own laboratory in a new and very well, privately funded Department. I had enough space, personnel and money to do my research.

This made it very easy for me to start my own laboratory and, in no time, I was already contributing with my own research to the telomere field. This

was back in 1997, since then Spain has undergone an amazing transformation with the creation of new research centres like the CNIO or CNIC in Madrid or the CRG and IRB in Barcelona. These institutes are excellent and comparable in their scientific production to the best places in the world. The economic crisis is, unfortunately, affecting Spanish science more than we all wish; hopefully this will pass soon and Spain will continue to grow in excellence in science and innovation.

*There is an ongoing debate about whether funding agencies should encourage more (or less) 'clinically relevant' research, rather than fundamental research. Do you think basic research gets the short end of the stick?*

**Blasco:** I think it should not be a matter of basic versus clinically relevant science; it should be a matter of funding top-notch excellent science. If science is truly groundbreaking and provides answers to relevant questions, it will be always of interest for society and very likely to result in innovative ideas and products.

*You have been supervised by two successful female scientists during your PhD and postdoc. Did this inspire and encourage you in your own research career?*

**Blasco:** Definitely, Margarita Salas and Carol Greider have been role models for me. It is amazing to what extent we are influenced by our mentors and this is why it is so important that there are more women in

mentoring and decision-making positions, so they can help other women and serve them as role models. I am very worried about the fact that we still have not reached gender balance in the Group Leader or Programme Director positions. Mounting evidence indicates that there are strong "gender schemas", largely outside of our awareness, which ensure that women and men are not treated equally in terms of mentoring and opportunities. Small differences in opportunities accumulate over the very long scientific career and can result in big differences at the end.

In 2012, we started the Women in Science (WISE) Office at the CNIO, to make the necessary changes to prevent "gender schemas" and to facilitate gender balance, as well as to facilitate networking between women scientists at the CNIO but also with other women outside of the CNIO

or the science field. I believe that only having more women in decision-making positions will help break these walls, to facilitate that others make it.

*Coming back to telomerase. You have shown that overexpression can delay ageing and expand life-span in cancer-resistant mice but will we ever be able to increase life-span in humans by tweaking with telomere length (e.g. with gene therapy)?*

**Blasco:** I believe so because of the nature of the gene therapy vectors that we used. We purposely used Adeno Associated vectors, which are non-integrative. This means that if a cell, transduced by these vectors, proliferates more than normal, owing to oncogenes or loss of tumour suppressor genes, it will also lose telomerase expression. We think that is why this strategy did not lead to more cancer in mice, indeed mice treated with telomerase showed cancer at later ages. I think it is only a matter of time until we have efficient strategies to activate telomerase for the treatment of telomere syndromes or even for the treatment and prevention of ageing-associated diseases.

*What project in your lab excites you more at the moment and what do you plan to focus on in the future?*

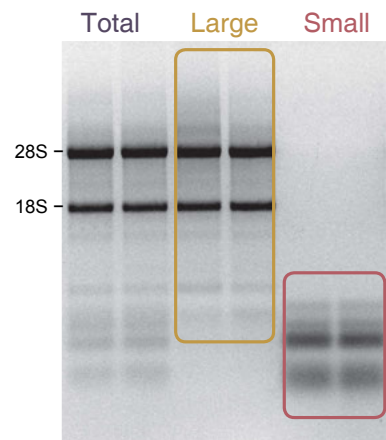
**Blasco:** All projects have to be exciting in order to start them at the lab. What happens is that, with time, some become even more exciting than others!

INTERVIEW: ISABEL TORRES

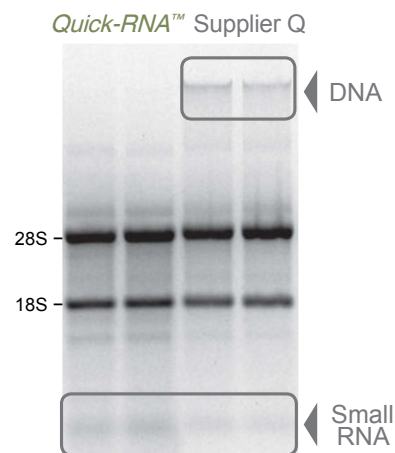
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A conversation with Patrick Aebischer, EPF Lausanne

# “Competition is Inherent to Science”

If you have heard of the Swiss Federal Institute of Technology in Lausanne or the Human Brain Project this is most probably thanks to Patrick Aebischer. The neuroscientist gives his view on governing a university and the role of big science.

to Aebischer, who started his academic career as a medical student in Geneva in the late 1970s. From the mid-80s to the early 90s, he worked at Brown University, USA, and returned to Switzerland in 1992. As a researcher, his studies revolve around understanding and treating neurodegenerative diseases, such as Parkinson’s disease and Alzheimer’s disease.

Most people agree that Aebischer has achieved a lot with the EPFL. Competitors from Zurich say that Aebischer would prefer to destroy a project rather than give way to others. Surprisingly, the president’s office is on top of one of the old buildings. The grey-haired Aebischer gives a paternal impression and amidst presidential advertisements, he is also open for banter.

*Lab Times: Being president of a university, is it more like managing a company or like managing a government office?*

**Aebischer:** It’s neither. You certainly cannot run a university like a company. My 380 professors can do and say whatever they want without having to fear any sanctions. Academic freedom is unique about a university. But as a president you have to set the ambition, the culture of the institution, which is what I did when I became president of the EPFL: I said

that I wanted to transform this good engineering school into a world class technical university. This is different from government. You cannot be the best government.

*“Being a university president is not like a conductor of an orchestra but rather like an organiser of a jam session.”*

*“In the ideal world, we should cease the salami tactics and publish less but more important papers.”*

*How much influence does the president really have in such a process?*

**Aebischer:** We have much more influence than we think. Most importantly, it is our responsibility to nominate professors.

Up until now, I have nominated more than 80 percent of the faculty. This is key for the quality. Probably, the most important reform we undertook at the EPFL was setting up an assistant professor tenure track system

for young scientists. This has attracted the brightest scientists and engineers because they know they can become independent early on in their career. The tenure track system is the strength of the USA compared to Europe. It was an experiment to adapt the US system to European conditions.

*Did it not create resistance from older professors?*

**Aebischer:** There was quite some resistance at the beginning. But with time, the faculty saw the advantage at being surrounded by the best, to be able to collaborate with them. That’s the secret of good research institutions.

*So you mainly determine the composition of your professorate?*

**Aebischer:** You can also influence the areas of research. When I arrived at EPFL, I thought that it is important to have life sciences at a technical university. Apart from that, you also have the responsibility to ensure that the infrastructure is up to the level of the expectations

and that you attract funds from both the public and the private sector. This allows you to modulate an institution. Being a university president is not like a conduc-

**W**hen Patrick Aebischer became President of the Swiss Federal Institute of Technology in Lausanne (EPFL) in 1999, the Swiss university landscape changed forever. The professor of neurosciences started by upgrading the little sister to the grand ETH in Zurich, by opening a school for life sciences. The well-known and highly debated Human Brain Project became the flagship of the EPFL with the rock star scientist, Henry Markram, at the helm.

Under the presidency of Aebischer, the EPFL took over mathematics, physics and chemistry from the neighbouring university of Lausanne, and enlarged the campus by adding many new buildings, like the fancy library (Rolex Learning Center) and the SwissTech Convention Center, to name but only two prominent examples. Other rectors and presidents look grey and dull next



tor of an orchestra but rather like an organiser of a jam session. You put the best musicians together and you give them the beat.

*You are said to have a strong hand, having made some enemies. Is it necessary to show aggressiveness as a president?*

**Aebischer:** If you want to apply major changes, you need a strong hand, yes. At the beginning you have to break eggs to make an omelette. We, the presidents of the Swiss Federal Institutes of Technology in Lausanne and Zurich, are in a special position because we are not elected by the faculty but appointed by the federal counsel [government cabinet]. You could say parachuted. You still have to be accepted by the institution because otherwise you will never be able run it. The advantage of not being elected is that you don't have to please everybody. I closed all 13 departments, for example, in order to create five Schools. At the beginning, I would never have passed an election but today – maybe I'm wrong about his – I think I would have a chance.

*One of your tough changes was to increase competition between Swiss universities. Most people probably agree that competition is necessary for progress. But was it maybe too much?*

**Aebischer:** I don't think this is what I have done. I never said that I want to compete against Zurich. The ETHZ is a great institution. It's just that we were considered to be second-class and when my generation of scientists came back from the USA, we did not see ourselves as second-class. I am not doing this against anybody, I am just trying to attract the best scientists. Before, there was one world-class technical university. Now there are two. This is good for Switzerland and good for Europe as well. By the way, that's also how you attract the best students. Competition is inherent to science. It happens automatically between labs and even within labs – maybe too much so. You compete for funds and for publications.

*There are worries that too much competition corrupts science. Many studies are not replicable, for example.*

**Aebischer:** Yes, this is an issue that academia will have to deal with.

*Is there something you can change as a president?*

**“You cannot continue to accumulate data lab by lab. Some industrialisation of data gathering is necessary.”**

**Aebischer:** Yes, I think we need a broader perspective for our promotion criteria because that's what the faculty responds to. Before, it was one lab, one ego. Today, science is much more collaborative. The evaluation of publication has to change, the teaching and the technology transfer have to be taken into consideration as well. We have to get away from this publish or perish concept. In the ideal world, we should cease the salami tactics and publish less but more important papers. It's maybe a utopian idea but I suggest to our promotion committee not to look at the total number of publications but to take the five best and read them.

*Are they doing it?*

**Aebischer:** [laughs] I think they try. It's difficult to change the system all by yourself. The journal editors have vested interests as well. So yes, in many areas there is too much pressure to publish.

*You are the godfather of the Human Brain Project, the best-known flagship of the EPFL. Is this sort of big science a model for science in the future?*

**Aebischer:** Yes, it is. In the past, big science was the speciality of physics. CERN is a very good example in Geneva. Why did physicists do big science? Because they needed the big infrastructure. Life sciences started to become big with the Human Genome Project. The reason is that with all the omics technologies we are generating a gigantic amount of data. Of course, the hypothesis-driven investigation in your own lab will have to continue as well. The community has to learn to find the right balance between these two, the structured goal-oriented research and the hypothesis-driven approach. There has to be a little more top-down, more organisation in life science. Of course, the people doing the regular thing are afraid of big science.

The US National Institutes of Health (NIH) pumps about six billion dollars a year into neuroscience. The Human Brain Project costs 100 million euros a year. So this is certainly not putting the whole of neuroscience into disarray. You cannot continue to accumulate data lab by lab, some of it not being difficult to reproduce and not compa-

ble. Some industrialisation of data gathering is necessary. That's exactly what the Human Genome Project did. Now, people would have a hard time to do human genetics without the results of the human genome database.

*Isn't there a big difference between the Human Genome Project, which was organised by different leaders in the field, and the Human Brain Project, a one-man-show with Henry Markram?*

**Aebischer:** The Human Brain Project is not a one-man-show. Henry Markram has a lot of visibility like Francis Collins or Craig Venter with the Human Genome Project. You always need people who think out of the box. Today, the Human Brain Project has 13 Principal Investigators with Henry Markram as the spokesperson. It's a highly coordinated and goal-oriented project, very similar to the Human Genome Project.

*But the difference is...*

**Aebischer:** There is a big difference. The goal set by the Human Genome Project was well-defined: read the three billion base pairs. The Human Brain Project is more open. Its ambition is to use the enormous amount of data generated by neuroscientists across the world to perform a simulation. There are more than 100,000 neuroscience papers published in a year. Somebody needs to integrate and normalise these data, to use them in order to understand the function of the human brain, so the generation of data that we can compare and use for the simulation is a first, well-defined goal. And very importantly, all this data will be shared with all interested scientists. It's not that we will fully understand the brain in ten years but I hope that in five years we will have better-defined goals to go to the next step.

**“The goal set by the Human Genome Project was well-defined: read the three billion base pairs. The Human Brain Project is more open.”**

*So you need to invest 500 million euros just to define the right goals?*

**Aebischer:** The goals are clearly defined. But every so often you refine them as you move along.

*One critique of the Human Brain Project is that, due to its size, it has to be a success. Is that compatible with the values of science, where you should honestly report negative results, too?*

**Aebischer:** For the Human Genome Project, people said: we are going to cure all

the diseases. Later, critics said: now we have the sequence and nothing has changed. But now it is impossible to think of cancer therapy without the sequencing capabilities. The Human Brain Project will become a platform, accessible to do neuroscience simulation. I see potential application to simulate deep brain stimulation [for Parkinson's disease], where we have no idea, how it works. We are used to thinking in two to three year terms. When you ask people to think in ten year terms, you get into a catch-22 situation between ambition and feasibility.

*It's clear that the sheer number of published papers doesn't give more insight. But doesn't a healthy diversity of papers from different groups create better ideas than one single project?*

**Aebischer:** Take ion channels as an example. We have to apply industrial scale approaches, like the Allen Institute has done with the connectome, so as to really understand how they interact. With comparable data you can simulate because it is reproducible at the macro-level.

*One of your achievements was to involve industry much more at the university. This collaboration is no doubt necessary for innovation. Do you see a limit on how much industry should be involved?*

**Aebischer:** Yes. That's an advantage in Europe that the state is involved in education and basic research. No company can afford that anymore. The Bell labs and similar institutions have all disappeared. So the public sector clearly has to support basic research. But then you need to pass the baton. We have the responsibility that our technology is going to be utilised. We need the patents and the people at the interface because at university we cannot develop drugs by ourselves. We also need to put things into perspective: industrial funding is less than ten percent of research funding at the EPFL.

*So why can't the contracts be made publicly available?*

**Aebischer:** They are; we were forced to hand them out. But I think this is problematic. In the case of research contracts, a company wants to sponsor some research

in return for patents or licenses from it. If you tell everybody what the research is all about, the company will hesitate twice before collaborating with academia. It gives away their competitive advantage. Granting agencies are facing the same problem. If you don't collaborate with industry you'll end up doing academic engineering. We would never ever sign a contract, if the professor were to lose his or her academic freedom. And it would be naive to think that an industrial partner could dictate to Henry Markram what to do.

*Why can't you publish the general conditions of a research contract without disclosing the topic?*

**Aebischer:** The conditions are always the same. We give them maximum three

get something directly they need a separate research contract.

*I see that calling your library the Rolex Learning Center is not problematic for academic freedom. But don't you feel it's strange to call it that? Why don't you go ahead and sell the EPFL name as a whole?*

**Aebischer:** It would be too expensive. [laughs] I wouldn't for the institution but for a mere building, I don't see the problem. We are Swiss and want to be proud of our watch industry. You know, who pays us? It's the taxes. We need a flourishing economy, otherwise there will be no taxes. Money doesn't grow on trees! Swiss-German journalists seem to be more sensitive to the issue. You are all thinking in the same box. I wish you would be more interested in talking about the 90 ERC grants we have received, since the launch of the programme.

*I'll stay in my box: Is it necessary for you to be on the board of Nestlé Health Science and Lonza?*

**Aebischer:** Would you put the same question to the president of Stanford?

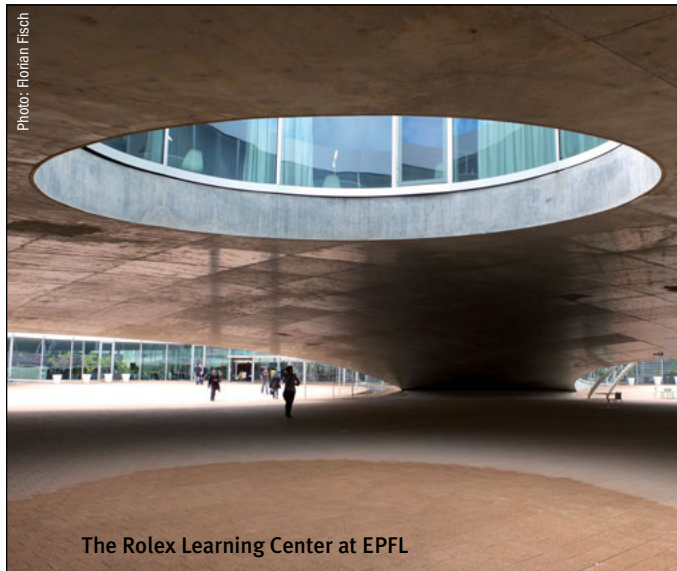
*Yes, absolutely!*

**Aebischer:** We have the responsibility to help the companies to contribute to the wealth and development of Switzerland. Here, we have a very big company called Nestlé; why should they invest in a research centre in Beijing instead of Switzerland? If they ask me to join the board, I have no problem with that.

*Nobody wants to stop you from advertising the EPFL at these companies. But being on the board and being paid by Nestlé comes with special responsibilities that also make it difficult for you to take a decision necessary for the EPFL but harmful to Nestlé. This results in a conflict of interest.*

**Aebischer:** Is there anything in life without conflict of interest? If you do not have conflict, it means you are not doing anything that is interesting. I do not believe that I have ever been exposed to a conflict of interest since I have been on the boards. It may come, of course. What's important is how you manage them. I would not do this for a Chinese or an US-American compa-

*"If you do not have conflict, it means you are not doing anything that is interesting."*



The Rolex Learning Center at EPFL

months – usually one month – before publication of the results, so they can file a patent. Everything we do will end up in the public domain. Otherwise we do not collaborate with industry. It is important for our graduate students and postdocs to be able to publish. Sharing knowledge is at the root of academia.

*What does a company get in return for sponsoring a chair?*

**Aebischer:** Nothing. The name of the chair. Of course, they can talk to the professor and, indirectly, they get more people doing research in their area. If they want to

*"It is difficult for scientists to fight populism. For us, the ends don't justify the means."*



ny, even though there would be fewer perceived conflicts of interest. I want to be sure that the Swiss companies thrive. When I see Novartis closing down neuroscience in Basel and moving to Cambridge, I am worried as a Swiss citizen. When the majority of the managers of large companies are non-European, I start to be worried. When we have a popular vote on Europe, who speaks out publicly? Putting too much emphasis on the fear of conflicts of interests could be problematic for the country. You increase the risk of delocalisation by having top managers that are not rooted in the area you live in. Now, you and I will not be there but our children and grandchildren will live through this. I try to choose the fields where Switzerland can thrive and align the EPFL with the Swiss DNA. When I came to the EPFL 50 percent of the Swiss GDP was not represented in research. There was no life science and no finance. We have to align our interests. Maybe we've gotten too wealthy and we forgot how we got there.

*If you are as worried as you say, why did you not speak out more against the popular initiative against mass immigration in February? There was only one small manifesto passing/slipping under the radar of most mass media.*

**Aebischer:** Sure, we could have done more. Unfortunately, I was in Africa on a sabbatical, on massive open online courses at the time. The vote was not about research collaboration and it's always easier to judge afterwards. In addition, it is difficult for scientists to fight populism. For us, the ends don't justify the means. It's a delicate issue that worries me a lot. Being outside of the research programme Horizon 2020 and being submitted to contingents of scientists would be the end of Swiss science at the world level. This, for me, is much more an issue than links to industry.

*What can you and your president colleagues do about it?*

**Aebischer:** Let me first remind you that all the cantons from the French speaking part of Switzerland voted against the initiative. I did quite a bit since coming back from my sabbatical. We invite people to the campus and we try to show how openness is key. Switzerland was not only split between the French and the German parts but also between town and countryside. The influence

of the EPFL on the German part is modest. It is the duty of our colleagues in Zurich to engage in trying to change the mentality about the fear of immigration.

*Antonio Loprieno, the rector at the University of Basel, said that it is difficult for publicly-funded institutions to speak on political issues.*

**Aebischer:** It's true and we even regularly receive directives by the government that we shouldn't get involved. I honestly just ignore it.

*Are you admonished for this?*

**Aebischer:** No. [laughs] I think we should have this autonomy, despite being part of the federal administration.

*You are appointed by the government and you are on the ETH council that governs the Swiss Federal Institutes of Technology in Lausanne and Zurich. So, you are sort of a political figure yourself. How do you have to function on this level, in order to be successful?*

**Aebischer:** All university presidents are scientists to start with. I kept my position as a professor. Yesterday, for example, I was in the lab and last night I corrected a paper. Without this I could not survive.

*How do you behave with the politicians?*

**Aebischer:** You have to be there, explain what we do. Several times a year I go to speak in parliamentary committees. They ask questions – often related to risks. It's perfectly normal as they provide us with the necessary funds. What is remarkable in the Swiss system is that we are highly autonomous. The interference from the executive branch is extremely limited. There have been very few cases in my 15 years as president.

*When does it happen?*

**Aebischer:** I typically interact with our federal councillors during trips abroad. It gives us the opportunity to talk in an informal manner. I have never had a federal counsellor calling me to do something or not to do anything, compared to France, for example, where they sometimes receive "directives". We are highly independent. The autonomy is probably the biggest strength of the Swiss system. We are protected from direct intervention by the ETH board.

INTERVIEW: FLORIAN FISCH



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*A conversation with John Ioannidis, Stanford School of Medicine, California, USA*

## “I am Happy to Find My Own Errors”

John Ioannidis is the epitome of conscience for scientific endeavour. For years, the medical doctor has addressed the flaws and failures in science. So, one could be forgiven for expecting an embittered activist – but far from it!

If you want to know why most published research results are false, John Ioannidis is the right man to talk to. Ioannidis is professor of Health Research and Policy at Stanford School of Medicine and director of the Stanford Prevention Research Center. Born in 1965 in New York City, he was raised in Athens, Greece and studied medicine at the University of Athens Medical School, graduating in 1990. His research career then led him to Harvard Medical School, Johns Hopkins University School of Medicine and Tufts University Medical School, before he returned to Greece in 1999, chairing the Department of Hygiene and Epidemiology at the University of Ioannina until 2010.

When your *Lab Times* reporter learned that Ioannidis was to give a talk on the subject of “Funding research: Impact, Conformity and Reproducibility” at the Swiss National Science Foundation (SNF), he immediately knew he had to go along. Seeing how this good-humoured professor in his late 40s with his mischievous look tells the intelligentsia of the SNF that “the citation profile of academic technocrats in governments is dismal” had a highly refreshing effect.

Ioannidis addresses the problems of science upfront: be it unfounded claims of significance, empty promises of innovation, funding of conformers rather than innovators, false positives and exaggerations leading to irreproducibility of studies or biases influencing the statistical outcome, he lays everything that ham-

pers scientific progress on the line. His conclusion: “Funding practices can influence the legacy of the scientific endeavour”.

Luckily, Ioannidis spontaneously agreed to give an interview to the unprepared but opportunist *Lab Times* reporter. It was a truly fascinating experience.

*Lab Times:* You are studying biases of scientists. How do you leave out your own?

**Ioannidis:** [laughs] I am sure I have tons of biases in every single project that I do. Much of the time, the stimulation I get to probe into some of these problems are errors that I have made myself earlier on. We are all part of the same scientific process. What we do is not unrelated to science; it's part of our everyday scientific experience. There are two ways to think about biases: one is to try to forget about them and the other is to try to be sensitised about them. I prefer the latter and to amend them rather than hiding things under the carpet.

*So, you're not disappointed when you discover your own biases?*

**Ioannidis:** No, I am very happy. There are two types of errors. There are the ones that are recognisable, which means you can correct them in the future. This is great news. However, there are others that you cannot even recognise. This is bad news because you continue repeating the same error again and again.



*Ideally, you enjoy finding errors in your own research. But in the end it tells you that something you have done before is wrong. It diminishes the value of your previous research. That is not easy to take, is it?*

**Ioannidis:** Why does it diminish the value of your previous research? If it was done with the best intentions and you thought as well as you could about it, then making a mistake is perfectly fine. Science is never perfect. The ideal study with the perfect results is even incongruent with science, which is an effort to improve, correct and come closer to more accurate estimates of reality. If you take a broad perspective, disappointment is part of the process.

*Nevertheless, you draw quite a bleak picture of science. Discovering that most published research findings are false is clearly shocking. How do you evaluate science as an activity overall?*

**Ioannidis:** I don't see the bleak message. Science is the best thing that has happened to humanity and it's the noblest endeavour that I can think of. The fact that it has this potential for falsification makes it so important. Without this potential it would be dogma, politics or religion but certainly not science. Exactly the fact that there is such great effort invested, that it is so difficult to do and that it has evolutionary improvement over time is what really gives it value.

*This is difficult to see for outsiders...*

**Ioannidis:** If we try to convey a picture of science as being related to impressive discoveries, successful all the time, bringing major progress, getting rid of cancer and reaching out to the galaxies, people will get the sense that everything is so easy and that science is omnipotent. This is very unrealistic. Despite spending years and years, sometimes nothing emerges. In reality, the effort that led to nothing and the one that led to the Nobel Prize belong to the same family. They all share the same glory and satisfaction.

*But science communication should be honest. If you believe that the science is the best that has happened to humanity, you also need to ensure that the public keeps funding the science. Often, they don't share your enthusiasm but want to see tangible results instead.*

**Ioannidis:** I agree. This is tricky. There are again two paths one could try to follow. One is to try to promise that research will deliver. You give me money and I will give you back more money. I have seen that thinking being adopted by leading scientists in big scientific agencies, who are under a lot of pressure trying to justify their activity to politicians, the public or the taxpayers. And it is definitely true that the entire scientific enterprise is cost-effective in the long run. But I am a little worried that when we enter this type of justification for science, we will run into unethical competition. There will be many other endeavours that will make the case with spurious data arguing it is better to invest in what they do. Take sports, for example. They make even more money, get more visibility and have a bigger impact in the media. Scientists are not good at this game and blanket promising is incongruent with scientific thinking. We want to be cautious and critical. We want to avoid being misled and fooled. We would be abandoning what we are good at to fight a different discipline on a different type of terrain. This is problematic.

***"If it was done with the best intentions and you thought as well as you could about it, then making a mistake is perfectly fine."***

***"Science is the best thing that has happened to humanity and it's the noblest endeavour that I can think of."***

*What can we do instead?*

**Ioannidis:** We should take the most honest line and make a case that the public and government should continue to fund research generously because we really have no other way of understanding what's happening in and around us. We have to make a case that this is very difficult. We cannot promise the cure to cancer but we should say, "This is very difficult. Thousands of the brightest people have been working on it for years. We are making progress and to be honest, we don't know where the next big progress is going to happen." Otherwise the public will notice sooner or later that the cure for cancer is not going to be found in two years.

*The problems of science, like the current reproducibility crisis, are deeply engrained into the scientific culture and extremely hard to change.*

*While everybody agrees with you, in principle, not many agree on how to solve it. What's your approach?*

**Ioannidis:** I wouldn't be so pessimistic about it. Many scientific fields do find ways to solve their problems with efficiency and reproducibility. There are different stages of tackling the problem: first is realising that there is a problem, then comes identifying how big it is and how it manifests itself, in the end it has to be worked out what causes it and how we get rid of it. Things can be done and many fields have taken steps in the right direction. Sometimes the solution is more replication. In other cases replication is taken as a condition sine qua non for publication for some type of results.

*Lately, it seems that we are far away from replication being a condition sine qua non for publication?*

**Ioannidis:** Take genetics, for example. If a genetic association study hasn't been replicated extensively by multiple groups, papers will not be accepted by the major journals. They have very stringent criteria for significance. Many other fields are adopting more transparent standards. Measures, protocols and reporting are standardised. Dozens of study reporting guidelines have been widely adopted, even within a few years. Many journals are adopting policies of transparency, data sharing and openness. Now, there is routine registration of protocols for clinical trials that was unheard of ten years ago. Registration is indeed a sine qua non for publication of clinical trials in any major journal.

*Ok, the guidelines are there. In reality, unregistered trials still get published. Even the International Committee of Medical Journal Editors (ICMJE) admits that the problem is yet to be solved.*

**Ioannidis:** It can always be improved. The top journals have adopted the principle and are following it. Of course, there are hundreds of journals ready to publish a trial without registration but they have much less influence. I agree that registration is not the end of the story. Even when you have a registered protocol, maybe the protocol is incomplete, the analysis will be distorted or the results will be non-replicable in other ways. It still is a major step forward because in the past we did not even know about the existence of certain trials. Now, if we see that some get published, we can ask how many we haven't seen yet. If we could manage to get a broader picture of what is happening, maybe some of the good practices could be adopted in other fields to achieve multiplicative impact.

What do you think of publishing the methods instead of the results?

**Ioannidis:** It would definitely make sense to put more emphasis on methods. Currently, many journals publish reduced versions of methods in fine print that make it very difficult to understand what exactly has happened. It would be useful to improve transparency of methods for others to be able to understand what exactly has happened in each step. Many of the reporting standards are taking care of that. They are explicitly asking for information on the major aspects of the methods for each type of study design. But results are still very important. I would argue that results should be in the public domain and people should be able to see them.

*But aren't the methods key when judging the value of a publication? The results could be released to some database after a project has been finished.*

**Ioannidis:** The methods are certainly more important than the results. Some journals have said that they are willing to accept submission of protocols. People may submit their protocols and get pre-decisions on the publication based on the protocol alone. The journals that have offered to do this, found themselves in a difficult position. *Lancet*, for example, was one of the first to adopt this as a practice but realised that some results were eventually not interesting, considering their impact factor of 35.

For the 99 percent of journals just wanting to publish good science, this is a very workable solution. However, it's still possible for the methods to seem okay whereas the conduct of the study may not be so great. So, I want to be a little bit cautious. It also depends on the type of research. There is research where the methods can be explicitly anticipated, like a computer code that can be run. Other research proceeds by exploratory iterations that cannot be fully anticipated. Half way down the road, you have to improvise and change direction. This does not necessarily mean that this is bad research. What matters is to be transparent about what has happened and not pretend that this convoluted path was pre-specified in one's mind right from the beginning.

*You said that funding agencies should accept that most effects in biology are small effects. That sounds extremely honest. Isn't that a problem for the whole of biology. If effects are small, are they really worth studying?*

**Ioannidis:** If it turns out that nature is full of small effects, yes certainly.

*Are the small discoveries still meaningful for our lives?*

**Ioannidis:** Information is meaningful, no matter how small

*"It's still possible for the methods to seem okay whereas the conduct of the study may not be so great."*



*"Science is worth pursuing irrespective of whether the [observed] effects are big or small."*

the effects are. As long as it is trustworthy information, that's what it is. However, applying the information to change our lives is different. Most of the time we shouldn't make any changes to our lives just because of some new discovery of some small effect. I don't see what should be bad about this. It would be horrible if there were a zillion things to have to change in our behaviour, or if an average healthy person had to take one million different pills to improve their health.

*When I read about research results I often think: So what?*

**Ioannidis:** Very nice question.

*Is it still worth pursuing this science?*

**Ioannidis:** Science is worth pursuing irrespective of whether the effects are big or small. I get the impression that most effects are small. Maybe that even makes sense in biology. If biology were composed of huge effects, maybe we would be monsters, very uneven beings. We have very concrete equilibria and soft differences in evolution. Documenting these is perfectly fine. If this is how it looks, then we have to be honest, not do anything but sit back and say: interesting!

*If you had the chance to re-design how the ERC decides about who gets funded, how would it look?*

**Ioannidis:** I think the ERC is doing a great job, the way it is now. Clearly, compared to contesters, mostly national funding agencies, it does much, much better. It has an outlook towards selecting excellence and innovation and people who are the best and also trying to have the best possible panel to appraise that. My personal bias is that I would like to obtain some experimental evidence on research funding processes. I

feel uneasy with the fact that we're funding science without having any science about how to do this. Isn't that a paradox? We want science about anything around ourselves but when it comes to appraising science we don't want scientific methods or experiments. I would only suggest that leading funding agencies should consider experimental studies comparing different modes of appraisal.

*Isn't that problematic? We can easily conduct science on things we can measure but these are not the important factors. What we really want to fund is qualitatively good research. Citation figures only give us a proxy of quality, while the judgement of quality is entirely subjective.*

**Ioannidis:** I am not sure whether I would agree with that. For any scientific question the issue is to have rigorous outcomes. For example: Do we have measures for pain that are good enough? We can just ask the patients how much pain they feel. We can also



ask physicians about how much patients are screaming. Is that objective? Maybe we should measure the nerve impulses on all pain fibres. There is always a surrogacy issue: we are measuring something that may not be the most concrete or complete outcome of what we want to measure. But I would argue that we have outcomes that we can measure. Citation impact, quality, reproducibility, sharing and translation are things we can measure. I mean papers and citations clearly are measurable.

You can have age-adjusted indices or co-authorship-adjusted indices and many other fancy metrics. Whether someone is publishing data or keeping it in the file drawer, registrations of trials and translations to application are all measurable. You have to wait some years or measure a surrogate outcome earlier on. I am not saying that these measures capture everything. But unless we start thinking about this and running the studies, we will not be able to use the best possible metrics to improve upon. It's an iterative learning process.

*That all sounds nice. But how do you measure the quality factor?*

**Ioannidis:** There are ways to appraise quality. We should ask: what are the hallmarks of a good study. No one would contest that randomisation and blinded assessments are crucial in animal experiments – yet, most animal studies still ignore them. I would feel better, if one could really think about the rules rather than trust that an expert panel, which often includes scientists with minimal impact or failed quality standards in their own work, selects the best people. It doesn't sound very scientific to me.

*Some people say that there are too many bad scientists and that we would do better by cutting their number by half.*

**Ioannidis:** I've heard that, too. This is a dangerous intervention. Depending on who decides and where we cut, it can be a real mess. Science is growing without a masterplan but some rational interventions do happen as well. At least, this should be subjected to studies. What happens if you try to strengthen a more credible core? We don't know. But it doesn't sound right to me to just cut the number of scientists in half by some arbitrary dictatorial selection. [laughs]

*You ask for the right incentives. Where would you put them?*

**Ioannidis:** Incentives appear on all levels of scientific and academic coinage: at the level of publication, funding and promotion. You only need to give the right ones. If you ask for statistically significant results for publication you will get statistically significant results. If you ask for reproducible research to get funding, people will generate reproducible research. If scientists get promoted because they share their data, they will share their data. [laughs] They would be making phone calls at midnight saying, "I want to share my data."

*It seems to me that these changes don't happen because people setting the incentives are part of the same crowd as the people following them.*

**Ioannidis:** Well, the crowd is made of people. If the scientific community agrees that these criteria are important, then they should reward the scientists following them.

*"I feel uneasy with the fact that we're funding science without having any science about how to do this. Isn't that a paradox?"*

*"In my career I usually have had no clue where I would be in five years. One has to be receptive and responsive to new ideas and possibilities."*

*Your research often contains heavy mathematics that is not easy to understand for average biologists like me. Is there a way to make it more accessible?*

**Ioannidis:** I think that there could be simplified versions. I enjoy both mathematical reasoning in terms of theory and empirical evaluation of hypotheses. Some of the messages are easier to convey to a wider public than others. I have been pleasantly surprised by the level of understanding that these issues have achieved.

To me, many seemed esoteric without the potential to reach a wider sphere. But apparently, there is a lot of interest both within science and in the rest of society.

*Do you get enough PhD students to work with you?*

**Ioannidis:** I have lots of brilliant people who come to me physically and electronically and they want to collaborate to work on some of these ideas. There are thousands of people around the world that I feel are part of my scientific team. It's a virtual lab scattered around the world that is different from that of many scientists who know that their lab is on the third floor, has four benches and four PhD students and assistants. I am really humbled by the interest of the number of people who have approached me to brainstorm on different projects. It's an opportunity to learn from them, as many of them come from fields that I am not familiar with. They have different practices and problems and they have thought differently about overcoming them.

*Have your findings changed the way you do your own research?*

**Ioannidis:** Absolutely, yes. There have been striking changes in almost everything that I do. In my career I usually have had no clue where I would be in five years and what I would be doing then and how. One has to be receptive and responsive to new ideas and possibilities. This is one reason why I feel uneasy about modes of appraisal where you ask scientists to tell you exactly what they will deliver in five years from now. Some types of projects may be amenable to this, for example, when you have a randomised clinical trial. But many other fields are so live and vibrant, so many interesting ideas arise that you don't want to abandon them, especially ideas that bridge different disciplines. If you could combine plant science with astrophysics, that would be wonderful. The question is how to do it.

INTERVIEW: FLORIAN FISCH

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A conversation with Kai Simons,  
MPI of Molecular Cell Biology and Genetics, Dresden

## “There Are No Easy Solutions”



Photo: MPI-CBG

Kai Simons has been doing research for 50 years. He knows the many problems of modern science all too well – from the reproducibility issue to lack of funding and the outmoded publication system. Was doing research much better or easier in the past?

Having graduated from the University of Helsinki in 1964, Kai Simons spent his postdoc years at the Rockefeller University, New York, went back to Finland and, in 1975, gained a group leader position at the European Molecular Biology Laboratory in Heidelberg, Germany, working on lipid rafts in the cell membrane. A rather controversial topic as it turned out.

From 1998 to 2006, Simons directed the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden, Germany. And he hasn't retired yet. At 76, he has more than enough panache to manage his own company called Lipotype, specialising in li-

pid analysis. We thought, with a biography like his, he might have one or the other story to tell about the good old and modern days of science and research. Apart from that, he also had a hand in the foundation of *Lab Times*.

*Lab Times:* This is now the 50<sup>th</sup> issue of *Lab Times*. I heard that you were involved with the magazine in the beginning.

**Simons:** Yes, ELSO was involved. ELSO was the European Life Scientist Organization that I founded, to fill a gap in the European research scene. There

was, of course, FEBS, Federation of European Biochemical Societies, and EMBO, European Molecular Biology Organization, but, in fact, there was no meeting that could catch the excitement of cutting edge research in the same way as the American Society for Cell Biology, ASCB, did at its annual meeting. And there were no big exhibitions either, where all the new methods and equipment were presented like at the ASCB meeting. The ASCB was also a very strong political lobby group for the life sciences.

So, we wanted to copy that. I had been a member of the ASCB council and I wanted to see if we could also do the same in Europe. And why shouldn't we? So we started ELSO and we organised an annual meeting. In the beginning we had 1,500 to 2,000 people. It was quite a big success. And then we thought we could have a newsletter with advertisements [which actually ended up in *Lab Times*]. I don't remember exactly how it went but I think [LT's designated chief editor], Ralf, came by and we started discussing the idea of a *Laborjournal* [the successful German-speaking life science magazine, the *LT* team has been publishing since 1994] for Europe. The idea was to do something in this direction. We thought, let's have ELSO support it because you wanted to make it for free and you already had your distribution system in Germany but not yet in Europe. ELSO could help here. This was the idea to begin with.

*What happened to ELSO?*

**Simons:** 'We' were only Ingeborg Fatscher, Carol Featherstone, Konrad Müller and me. So, we were four people. And of course, everyone was doing something else as well; it was only a side job for all of us. We had no-one, who was working full-time. And, at some point, ELSO became a nuisance for me [laughs] and I persuaded EMBO to take over and start organising our annual meeting. EMBO did so and I was very surprised that they did not manage to get more people to the meeting than we did. I don't understand why. I know some of the problems: they started again from scratch and did not build on our established

base. We already had a following; we could get 1,000 people together, no problem. But it was too much work for our small team. To get all the funding together

was also a huge problem. We managed in the end without ELSO making a loss – and for this I'm very happy. We have Kon-

**“There are so many problems in research today. It's very important that such issues are discussed and that people read about them.”**



rad Müller and the Klaus Tschira Foundation to thank for this.

*Now there's a new ELSO, the Extracorporeal Life Support Organisation...*

**Simons:** Yes, they existed then already but now they have our brand name. We sold it to them. I don't remember if we got any money for it.

*Coming back to Lab Times, what were the original ideas you were discussing with Ralf?*

**Simons:** We thought it could be an organ for the European life scientists and, in this way, also have a political influence on European funding, for example. The ERC was an enormous achievement and ELSO was very much involved with promoting the ERC funding project in the early phase. Much more could be achieved if life scientists and other scientists worked together to promote new projects.

*Do you still browse through the magazine occasionally?*

**Simons:** Yes, I do. There's this citation ranking that you're doing. It's, of course, popular for everyone to follow, who is most cited in each field. And then, there are so many problems in research today and *Lab Times* covers them. For instance, fraudulent science that seems to be on the rise or the general problem of reproducibility in research. If as the pharmaceutical companies claim that less than 30% of what we do is not reproducible, then we have a huge problem before us. It's very important that such issues are discussed and that people read about them. And of course, it is also important to report about basic research that is helping to establish companies and in this way shows how our work can become useful for society. I think that *Lab Times* has been a success and I hope that you can continue along these lines.

*"Now is an exciting time for young scientists, who are creative and innovative because they will show the way to the future."*

*I hope so, too. Next, I would like to talk with you a little bit about the old and new times of science and research. What changes or differences have you noticed over the years?*

**Simons:** Sure, I'm a senior [laughs]. I think the biggest change is the numbers game. There are now more scientists, there are more publications, there are more institutes, there's more money, there are more positions, there's more of everything. But, the fact that there are so many more scien-

tists also makes the world so much more complicated, on many different accounts. If you look at the life sciences, they are thriving, there's no end to the projects, to the goals... And we still know so little. But we are in a paradigm shift. Just think about my own area, membrane trafficking. In the beginning, when I gave a lecture on membrane trafficking, one single membrane protein was known, clathrin. Today, of course, you know... in every area we are confronted with thousands of proteins. That's a big, big shift. We are facing complexity now but, we're still using yesterday's methods. Scientists are doing one gene after another and so forth and we know it is too slow. Then you try to put them into high-throughput... all these high-throughput papers, where most of the work is irreproducible. The problem is, nobody is responsible for the data. In the lab, when we work on one protein, we look for the optimal conditions; for example, when you want to do pull downs and identify interaction partners. However, we are trying to study thousands of proteins at once – using the same conditions for everything. It is obvious that there will be so much error. We have to come up with technological solutions to face the complexity.

*How can this be done?*

**Simons:** There are no clear, easy solutions. There are many, many, many ways of doing research but there are no easy solutions. Now is an exciting time for young scientists, who are creative and innovative because they will show the way to the future with new solutions. The life sciences remain exciting but, of course, young scientists are also facing other problems, such as funding and positions.

With so many people out there looking for jobs and funding, the issue is: how will we be able to provide enough opportunities for everyone who is really qualified. In France, there has been more funding for positions but not for grants to do the research. There has to be some kind of a compromise. There will be a limit to how many researchers we can fund and to how much money can be spent on biological research. We are training too many PhDs for the number of research positions available. Every group is training many more than one, so that's a

hell of a number of PhDs. And most of them will not become professors or research leaders in their areas. So, we should face that.

When Bruce Alberts was president of ASCB, he proposed that we should have two streams: one for hardcore science-researchers and another one, where you aim at a career outside of academic research. In the second stream you, of course, have a research project but not as ambitious as in the first stream and you also acquire soft skills through courses provided by the university. So, you are already making a decision early on that you're not going to become a professor. Of course, you can move up again, if you want to and you think this is worthwhile.

We should try to prepare people more for their future career paths. In Germany, for instance, there are now many more group leaderships for young scientists. A lot of them. That's a big, big improvement. But what happens after they leave the non-tenured position that they now have as group leaders? That's still a problem. You have to have a system that allows side-moves before you get into trouble. But it's still very clear that if you have a good training in the life sciences, there are many job opportunities. It's an area where you have great chances to get a position but perhaps not to do exactly what you dreamed about when you started your training.

*Many ailments plague modern science and research. What do you think should be tackled first?*

**Simons:** I think the publication system is the one that we have to come to grips with, better sooner than later, because the logic of having to publish in high impact journals is not clear. It does not work because getting a paper into the high impact journals has become a lottery. I think we need an even bigger spectrum of journals. If you look at the publication system in the last five or ten years, it has changed dramatically. And it will change even more. There's a project coming up from my side but I can't talk about it yet [laughs].

*Ok, I'll come back later...*

**Simons:** Yes, come back later. It's not a project for solving the whole problem; of course, it will never be solved completely. It has to be solved by different scenarios. *eLife* is a good complement to the journals that already exist but it hasn't changed the

culture. So, we need more solutions. Right now, lots of new journals are being founded but they are mostly useless. They are there only to make some money but this cannot be the reason for scientific publications.

*Was it easier to publish papers in the 1960s/70s?*

**Simons:** Maybe it was more pragmatic; it was also difficult to get into *Nature* and *Science* back then but today it is more of a lottery. It's very difficult to predict the outcome when you submit because they are not publishing many more papers than they did before. So, the queue is much longer. Therefore, it was easier before. And going one level down, you got your paper in without too many problems. One question is whether there are many more young scientists today giving up because they get frustrated and say they don't want to be tortured until they retire by the system, by grants and publications. Earlier, this frustration was not very common.

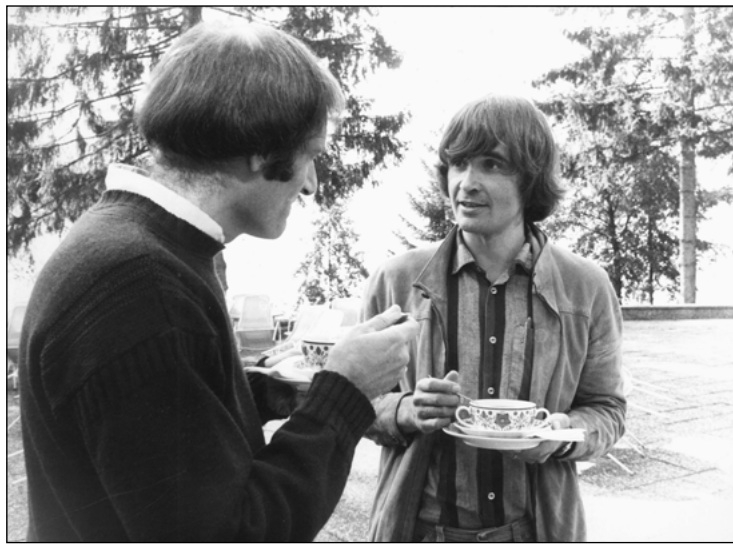
*Comparing again, old and new times. How was the research atmosphere 30 years ago? Was there as much competition as there is today?*

**Simons:** I think we thought less about these things. We thought less about positions, we thought less about pensions. We thought less about research careers in general. We were not so bound by all these career prospect problems. When I started off in Finland as a biochemist, I could only imagine having a professorship in biochemistry at the University of Helsinki. I looked at the list of professors and saw that they were very young and, clearly, I wouldn't get a professorship before I was too old. So my only hope was... there were always these graduation events. The whole university or the different faculties would have a festivity, where they awarded PhDs and honorary doctorships during a pompous celebration. They also had a big party on a steamship out on the sea, outside of Helsinki. My hope was that there would be an enormous storm [laughs], the whole ship would go under and then there would be some professorships vacant. That's what

I thought. But I didn't think about this seriously and, in the end, the whole world was open.

I don't think we were as worried as the present generation. In fact, there are many more opportunities today but also more worries. We also had good reasons to worry but we didn't [laughs]. It was a bit of a different attitude then but whether the research atmosphere was different? I don't know. I think very few places anyway have a very supportive research atmosphere. I've

*"There are many more opportunities today but also more worries."*



Sometime in the 1970s: Kai Simons (right) and Martin Raff, discussing science over tea and biscuits.

worked in places where this has been the case. And, of course, it's a big boost to everyone who works there. But most laboratories are full of internal issues and problems, which do affect the research atmosphere. This means that the young scientists there cannot make use of the opportunities that exist everywhere. If the professors don't talk to each other, the people in their labs don't talk to each other either. And that's really the worst. Why can't people be pragmatic and understand that science can be promoted by symbiotic efforts?

*"Most laboratories are full of internal issues and problems. Why can't people understand that science can be promoted by symbiotic efforts?"*

*Let's move on to equipment now and back then.*

**Simons:** Well, we needed less equipment before. The equipment we used was cheap. Biology was cheap. The cell biology programme at the EMBL ran on one million euros for around 10-12 groups. That's nothing

today! So, it was much cheaper, everything was much cheaper. That's another thing where the numbers are much higher today. More money is needed for infrastructure, for all the methods we use, they are so much more expensive. Take imaging: before we had normal microscopes, now we have a spectrum of different imaging methods available that cost millions. For any lab to keep abreast of the changes and the new technologies, it's almost impossible. Of course, imaging has undergone a revolution and is unravelling cellular features and processes that we could not see before. Fantastic! But the microscopes are expensive!

*Another important aspect of modern science is internationality. You're originally from Finland...*

**Simons:** I was first working at the EMBL in Heidelberg, which was very international. But our institute here, the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden, is also very international; we have over 50% of foreigners. In a world class institute today, you're going to see many more foreigners than you saw before. In the past, Europe had very little exchange; most people went to the United States to do their postdoc. Today, you also do your postdoc in Europe. That is an enormous change compared to before. Science is much more international everywhere. Of course, there were international places before as well but they were few.

*Why did you decide to go to Germany back then?*

**Simons:** I got this offer to go to the EMBL. It was an offer you could not refuse [laughs].

*And if you could choose a country today?*

**Simons:** I would go to Germany. The funding here is still much better than elsewhere. One cannot really complain. The government understands the need for research and they also give enough money for research to thrive. All these Excellence Initiatives for the universities, billions of euros are pumped into the university system. Of course, more would be needed for the uni-



versities to be really competitive but Germany is a great place.

*How about the UK?*

**Simons:** The UK is worse because they have less money. They have big problems with funding at the moment.

*And Finland?*

**Simons:** Finland has spent a lot on research and improved its research base enormously. But now they are also starting to make cuts. They are losing their nerve, they should just continue as they did before. When the wall came down in 1989-1990, Finland's trade with the Soviet Union collapsed and the unemployment rate rose to 20%. During that time, the government decided to increase the money for research and education. *Increase.* They did it and it worked. Now, if all the countries in Europe were to do the same, they would certainly be in a better state in ten years time. But unfortunately, they don't have the foresight that would enable them to do that. But they should.

*Changing the subject again. In our last issue, we had an article about personalities in the lab. What character traits are essential for a modern scientist, especially if you have to fight for your research results, as in your case.*

**Simons:** Everything new you find is, in a way, controversial. Especially membranes are difficult because you have to integrate lipids and proteins into a functioning whole. So, either you're a protein person or a lipid person. And today, there are very few lipid people. Understanding membranes as a system has been difficult and also technologies have not been available. With imaging and other new technologies like mass spectrometry, we can now analyse lipids with fantastic and convincing precision but this was not the case before. Earlier methodology was a bit crude, too crude, perhaps. If you put "lipid raft" into the abstract of your paper, it would be editorially rejected right away. So, you had to be strong to survive – and I was [laughs].

*Do you have any advice for young scientists, who are in a similar situation?*

**Simons:** I think young scientists should seek advice from mature scientists. They should really try to establish good relations with one of their seniors. If you are in a place where the seniors are not at all sup-

portive, you have less of a chance to make it. That's one thing that is important, to be in the right environment. The second thing is to try to find friends on the same level as you. If you are a young Principal Investigator, find another PI that you can team up with. Have journal clubs together, lab seminars together. To have someone you can talk to and a shoulder to cry on when things don't work. The other person can

*“People spend too little time establishing intimate networks, which they need to be strong enough to survive.”*

do the same to you. You should not continuously complain to your bosses, to the people in your lab, or to your spouse about all the problems that you encounter in your work. You have to find mates that you can talk to. I think people spend too little time establishing these intimate networks, which they need to be strong enough to survive. If your paper is rejected again, you just go out for a beer with your mate. I think that people underestimate the value of good communication and good networks. Not only networks all around the world but really the local networks. And if these local networks don't work, if they are against you, then you have to leave. You have to find another place.

*You are now the boss of your own company, Lipotype. Are you still doing some research?*

**Simons:** My lab is closing this year. There are still some people there but it's closing down. Now, I'm mostly focused on my plan B, this Lipotype company. Lipotype, phenotype, lipid signatures, biomarkers. Together with Andrej Shevchenko, we have developed a new technology for lipid analysis, which is called shotgun mass spectrometry. We have now moved this technique into high-throughput but at the same time our method is totally quantitative. We add internal lipid standards and so we can get absolute quantification of the lipids.

Proteomics was also trying to identify biomarkers but they were not quantitative so they had little luck. You need to quantitate, otherwise you cannot get signatures. So, we now screen large populations to get the normal values for the blood lipidome (more than 400 lipid species) and then find out how these normal lipidomic signatures change in different diseases. One day we want to have our lipotypes introduced into

clinical practice. Another area for lipotypes is the food industry. They have a big problem. They are producing food that causes disease – obesity, diabetes type 2, cardiovascular diseases. If you think about how the obesity epidemic is increasing around the world, it is clear that we have to do something to stop this menace. And why has it come so far? Because people eat the wrong things. This fast food, I mean... The number one food in the United States is potato chips. You can become almost addicted, it's like a drug. And the food industry? They don't want to stop selling their money-makers but now they want make new products that they call nutraceuticals. These are food products, which alleviate or prevent disease. However, they need evidence and lipotypes could be a good way to get that. You have a pathological diabetes type 2 signature and then you normalise it by eating the right food. So this is the Lipotype strategy. I am sure that it will work.

*Final question. Would you say it's good or even better to be a scientist right now?*

**Simons:** I would say that if you look at it generally and you compare to how it was 50 years ago, it's not better and it's not really worse. There are many more people but there are also more jobs. And there's more money. Of course, we are complaining and we are tortured by the system, and we are crying about all the problems that exist but they existed before, as well. I think we have some serious issues that require change. The publication system is badly in need of change. I don't think we can expect there to be much more money, so we will have

*“We have to accept the fact that we also have to train life science PhDs for other jobs than being a scientist.”*

to think about limits for the research establishment. And then we will train less people for hardcore science. We have to accept the fact that we also have

to train life science PhDs for other jobs than being a scientist. But we do have to emphasise that the life sciences are full of excitement today. It is indeed fantastic what we can do with all our fancy equipment: to observe what happens in live cells and tissues in real time. It's incredible, what we can do and what we have achieved. And this excitement will continue! So, I would say, things are pretty good today, even if young scientists look around and say I would like to have been there 50 years ago.



Photo: Private

*A conversation with Ross King, Professor of Machine Intelligence, Manchester, United Kingdom*

## “There is Little Real Theory in Biology”

This man has a vision that many would call a wacky pipe dream: Ross King is striving for the automisation of science, going far beyond the robots that manage simple lab tasks. Much more than that, the computer scientist from Manchester is pursuing the idea of an artificially intelligent “robot scientist” that autonomously executes high-throughput hypothesis-driven research.

**W**hen do you think the idea of automating science was first proposed with any seriousness? You know that I wouldn't ask unless it was really early. In the 1960s? The 1930s? Still not early enough? The late 19<sup>th</sup> century?

Far from it.

The answer will surprise you: German mathematician and philosopher Gottfried Wilhelm Leibniz first mooted the idea of automating science in the late 1600s. He argued that what philosophers want is a device that automatically separates truth from error – what we today would call automation. He also argued for a special mathematical language for philosophers, and claimed to have worked one out (the *characteristica universalis*), though, inconveniently, he never wrote it out in detail. But the point he was making was that we need to put an end to uncertainty, and the only way to do that is to talk and write in a way that, as we would say today, a machine could understand.

Leibniz, of course, could not have conceived of thinking machines, but if he had,

I have little doubt he would be the first to say “make machines to do the thinking”.

### **Making machines do the thinking**

Most of us today would call that somewhat ambitious, to say the least. Along with artists, composers and lawyers, we scientists have never thought of our jobs as being under any serious threat from automation. Even so, automation of some sort is standard in most laboratories, and has become so ubiquitous that we often don't even notice it.

It is a bit like the old dream of self-driving cars. Ten years ago it would have seemed impossible. Instead, automation crept in bit by bit. First, of course, there was the automatic transmission. Then came engine-controlling chips, that quietly took the day to day maintenance of our precious motors out of our hands. Own up – how many of you actually check the oil these days, and how many just wait un-

til the on-board computer politely tells us that we need a top-up? Then came those park-assist cars, which take over the tricky job of inching into a tiny parking space. To top it all, the latest models (am I giving my age away here?) have dashboard computers that watch our facial gestures for the tell-tale signs of falling asleep at the wheel, or warn us when we stray out of lane.

You know where this has been going, don't you? This is simply preparation for the inevitable: Self-driven cars. I hear that a certain well-known search-engine (no science fiction writer ever predicted *that*) is already testing one as I write.

### **Self-driven devices**

Now here's the scary bit. Lab work has been going the same way. OK, those of you with experience of clinical testing will not be at all surprised by this. Large-scale automation is standard in the lab, and it was

*“I got disillusioned with bio-chemistry, because, to put it simply, it was more chemistry than bio – it was all about mashing things up into a soup and destroying the living thing.”*



here that automated machines first came in, with the “Autoanalyzer1”, which was based on continuous flow analysis. Then came Laboratory Information Management Systems (LIMS), originally designed to automate billing but quickly extended to cover whole workflows, tracking samples, recording measurements and generating reports. Like Vortigern’s (the legendary British 5<sup>th</sup>-century warlord) Anglo-Saxon tribes, they were brought in to do a simple job, then ended up taking over the whole show.

But that’s not what I am talking about here. Just about every example of automation you can find today is either a single, whole machine running a preset workflow, or a combination of such machines being served by robots – think of automated pipetors that dispense samples into microtitre plates then load them onto a plate reader.

This is nothing. It is the lab equivalent of automatic transmission and park-assist. Where are the Google cars of the laboratory?

### Adam and Eve, the artificial scientists

This is where Ross King comes in. Ross is Professor of Machine Intelligence at the University of Manchester’s School of Computer Science, and he has automated not just a laboratory process, but the whole scientific cycle. He has developed the idea of a “robot scientist” – a, “physically implemented computer/robotic system that utilises techniques from artificial intelligence to execute cycles of scientific experimentation” (as he explains on his website). This synthetic scientist even has a name, Adam (on the right photo you can see his sister Eve), and automatically, “originates hypotheses to explain observations, devises experiments to test these hypotheses, physically runs the experiments and interprets the results”.

By doing this, King maintains, Adam has discovered new scientific knowledge. Recently, he created Adam’s sister, Eve, to automate drug discovery to a degree never seen before.

The computer scientist, King, is also interested in the fine arts. Together with musician, Colin Angus, of Scottish psychedelic electronic dance music band, The Shamen, he developed an algorithm for converting DNA sequences into melodic tone sequences, called “PM – Protein Music”. The resulting sounds were immortalised in 1996

in the “protein song”, S2-translation (Ross King and Colin Angus, PM-Protein music. *Comput Appl Biosci* (1996) 12 (3): 251).

Steven Buckingham met with King in Manchester, where he moved from Aberystwyth University in January 2012. They chatted about Ross’s – alarming? Exciting? Over-ambitious? – attempts to close the robotlab loop.

*Ross, let’s start with you telling me about how you got into a career in science.*

**Ross King:** I was keen on insects when I was a boy. So why didn’t I set off on a career in insects? Well, I realised it was going to be hard to make a living as an entomologist. I also developed a more general interest in biodiversity. And I got interested in biochemistry because of trouble with lichen.

*Sorry . . . ?*

**King:** The book, *Trouble with Lichen*, by John Wyndham. It is a story about a compound that made people live longer. When

*So how did you get into computer science?*

**King:** I did an MSc in computer science. It was a one-year course with the last six months as a sort of conversion course. It went really well.

*But why did you do that?*

**King:** The reason was all because of a final year project for my degree course. We all had to select a project, and there was one that no-one wanted to do. It

was on mathematical modelling. Because no-one wanted to do it, we ended up having to draw straws – and I got the short straw. In the end the project worked out really well. It was about growing bacteria on beads and in a culture medium. We were measuring the amount of nitrite, which is a measure of the number of cells. It was all ordinary differential equations and fitting models to data. But I discovered something about biologists. You know, most of the time, biology students aren’t really learning science – they are learning about the results of sci-

*“We all had to select a project, and there was one that no-one wanted to do. It was on mathematical modelling. Because no-one wanted to do it, we ended up having to draw straws – and I got the short straw.”*



**Eve, the artificial scientist, going about her daily work.**

Photo: Private

I read that, I thought, “well, the future is biochemistry”. That was when I was about 15 years old or so. But I got disillusioned with biochemistry, because, to put it simply, it was more chemistry than bio – it was all about mashing things up into a soup and destroying the living thing. Take away structure, and you take away the life.

ence. They don’t have to do that much original thinking, at least not as an undergraduate. But a fundamental thing with computer science makes it quite a different matter, because you have to do the programming and the software has to work. It is really very creative. You know, there is so little real theory in biology. ▶▶

Tell me about your PhD years.

**King:** I did my PhD at the Turing Institute in Edinburgh in the late 1980s. There was a lot of money for artificial intelligence at the time. Basically, the British and American governments were worried about what was happening in the Far East. The Japanese economy was booming and they were making huge strides in computer engineering – there was talk about them developing 5<sup>th</sup> generation computers.

What was the atmosphere at the Turing Institute like?

**King:** It was excellent – it was the best institute I have ever worked in. It was mostly because of Donald Michie [a British artificial intelligence researcher, 1923-2007], who had worked with Alan Turing at Bletchley. It is hard to put a finger on what made that place so special but I guess it was something in the atmosphere. There were a lot of smart people there, it was a nice building and there were plenty of resources. We were pretty much left to our own devices. We were not spoon-fed there like so many graduate students are today.

Do you think it is a bad thing then that we look after our students so well these days?

**King:** I suppose it depends on the student – but let's face it, we can't fail students any more and that can't be good, can it? I even think sometimes that the role of student and supervisor has almost reversed – soon we'll have to do the project for them!

OK, so tell us about Adam, the lab robot.

**King:** The basic idea behind Adam is to automate the entire cycle of scientific research. Let's think about the input end first. You start off by telling it about an area of science in a formal way and the computer will understand the corpus. So you have to represent the body of knowledge in a semantically clean way.

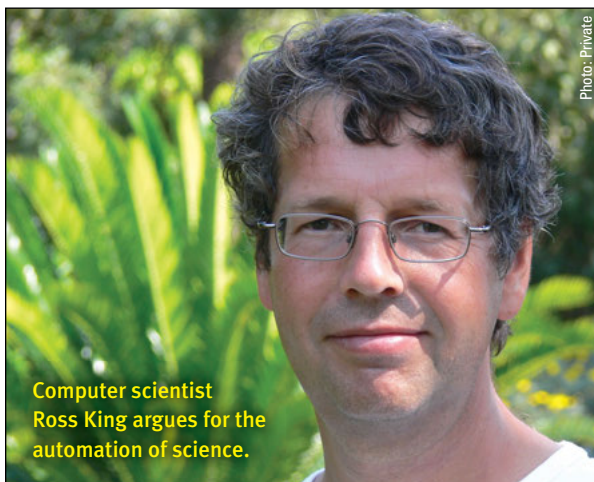
Isn't that a lot of work? Can't you get Adam to read natural language?

**King:** That's not realistic at the moment – there have been a lot of advances in text mining but we are nowhere near there yet.

That problem is a really hard one. Actually, I don't think the problem is with Adam, I think it is with us. I think we should attack the problem the other way around – we should compel people to write their papers in a way that can be machine-readable.

I wonder if you are trying to conceal one of Adam's weaknesses here. Are you telling me Adam can only handle the simple concepts? Surely, the really interesting concepts in biology, the ones that are worth writing home about, are going to be the very subtle, complex ones?

*“Actually, I don't think the problem is with Adam [the lab robot], I think it is with us. I think we should attack the problem the other way around – we should compel people to write their papers in a way that can be machine-readable.”*



Computer scientist  
Ross King argues for the  
automation of science.

**King:** I don't agree at all. I maintain that if you can't express a concept rigorously, you don't understand the concept. And this isn't a new idea either. Back in the 17<sup>th</sup> century, Leibniz argued that we need a special language for rigorous philosophy – what we today would call an ordered ontology or a markup language.

*“I even think sometimes that the role of student and supervisor has almost reversed – soon we'll have to do the project for them!”*

OK, so back to Adam

...

**King:** Adam takes this input and uses old-fashioned, traditional logic to infer new scientific hypotheses. But the point is that he does it efficiently, by which I mean in terms of both time and money. Then he runs the experiment, and interprets the result. Of course, that generates new knowledge which gets added back to the original stuff we fed in, and so the cycle continues. That is what I mean when I say that Adam is the first case of automation, filling the whole scientific loop.

So what projects has Adam run?

**King:** He has two main application areas. The first area, in which Adam could do the whole cycle, was specific to yeast functional genomics. As you may know, some 10% of yeast genes have no known function. So we told Adam all we knew about proteins whose enzymatic activity was known.

Adam then worked out hypotheses, then went ahead and thawed out strains from his freezer (or ordered them if he didn't have them). He took care of the thawing, monitoring their recovery, and all the pre-growing procedures as well.

The second area is in drug discovery. We have automated the whole Quantitative Structure Activity Study (QSAR) cycle. The robot tests a library of compounds, works out hypotheses relating structure to function, then tests those hypotheses, telling us to run out and buy compounds as needed. Actually, it was a second generation Adam that did this. We called it Eve, of course.

I have three favourite personal questions I like to ask my interviewees. The first is, which scientist, living or dead, has influenced you most?

**King:** That has to be Donald Michie, who sadly died just a few years ago. He was the first world-class scientist I knew, and although I rarely, if ever, spoke to him face-to-face, he left his mark on the Institute. I remember the talks he gave very well.

The second question is, if you hadn't done that MSc, what would you be doing now? (If it helps, my answer to this question would be train driver!)

**King:** Oh, I am really not sure. I was into rock music when I was younger, and have a close friend in music . . .

The final question is, what would you most like to be remembered for? Adam?

**King:** I haven't had an answer for that until recently. All I can tell you is that I am moving onto other things now, which takes me beyond Adam . . .

Can you tell me?

**King:** . . . No!



A meeting with Klementina Österberg and Lorna Fletcher, technology transfer specialists, Gothenburg, Sweden

# “Some Researchers Have All the Skills to Do Great Business”

Sweden's rather unique system of technology transfer not only brings a number of benefits to both scientists and their employers but also some constraints – in particular, when it comes to funding.

Klementina Österberg, CEO of the Gothenburg-based technology transfer agency, GU Holding, must cope with a lack of funds.



Photo: J. Uhler

Sweden, known for singing blondes, roaring moose, red wooden houses and flatpack furniture, is a small country with a strong and growing biotech landscape. About 30,000 people work in over 700 life science companies, of which around 50 percent belongs to the biotech sector. Swedish biotech's hidden strengths are its liberalism and its main focus on drug discovery and development, biotech medical technology, tools and bioproduction. The number of new, still micro-sized companies (no more than ten employees) has increased dramatically in the past 15 years.

In the Gothenburg biotech region, which is the Swedish number two in size after the dominant Stockholm/Uppsala area, the technology transfer agency GU Holding helps academic scientists to turn their research findings into companies. GU is entirely owned by the Swedish state. The technology transfer agency is linked to the Uni-

versity of Gothenburg and has contributed to some 120 start-ups since 1995.

Lab Times arranged a meeting with two of GU Holding's key personnel: Klementina Österberg, CEO, and Lorna Fletcher, Project Manager, to learn about the Swedish way of managing and succeeding in biotechnological knowledge transfer.

## Sweden's unique TT system

Getting investment at the early stages of developing a business is extremely difficult in Sweden, as elsewhere, due to the high risk that these companies involve. Sweden's rather unique system of technology transfer (TT) brings a number of benefits, but also some constraints – in particular when it comes to funding.

GU Holding is a company with barely 20 employees that supports University of Gothenburg researchers who want to commercialise their results. The University, based in Sweden's second largest city, is one of Europe's largest, with close to 40,000 students and 6,000 employees. It also encompasses the University hospital. So there should be no shortage of research and ideas, right?

*How strong is the demand for the services offered by GU Holding's services?*

**Klementina Österberg:** We do go out looking for ideas but there are a lot of people knocking on our door. Every year, GU Holding receives 40 to 60 business proposals from people connected in one way or another to the University of Gothen- ▶▶

*“Outside of Sweden [where the employer owns researchers' results], you have to strike a balance with researchers who want to work with you and the ones who come in because they have to. The latter are never good to put forward.”*

burg. We have established 118 projects or companies since 1995, of which 77 are currently in business, though many of these are still in the very early phases and are not yet that mature. Three are listed on a stock exchange.

*What about the importance of life sciences, which make up most of your portfolio at about 65%?*

**Österberg:** It's safe to say that different life science areas have really cutting edge research. Our biggest areas are, for instance, vaccines, treatment of cancer, metabolic diseases as well as orphan indications, diagnostics, biomaterials and orthopaedics, and even dental.

### Different from the rest of Europe

Of the 77 companies in current operation, 47 are owned by GU Holding and 30 have been sold to other owners. The remaining 41 have been closed. Nevertheless, Österberg calls this ratio, "a pretty good success rate." The Swedes look on the bright side, it seems.

Let's take a look at Sweden's peculiarities, particularly regarding the commercialisation of academic research. What happens, for example, to the inventions that a professor makes during his daily work at the bench? Most European universities and other public research organisations have long since adopted a system similar to the US where, since a change in legislation in 1980 (the Bayh-Dole Act), they have the right to own inventions from state-funded research. This spurred the creation of technology transfer offices (TTOs) within many, if not all, universities to help commercialise research.

In Sweden, which has been a member of the European Union since 1995, it's different. As Lorna Fletcher, a business development manager and IP strategist at GU Holding explains, "Swedish researchers own their results, not the university. If a researcher has something that's patentable, he or she owns that, too. So, they are free to work with any actor they want." In Gothenburg, that actor is usually GU Holding. Not always, though, according to Fletcher, "We are an option for researchers. They don't necessarily have to come to us."

In the US and most of the rest of the world, researchers have no choice but to work with the TTO of the University that owns their inventions. Oddly enough, the

only other highly developed country in Europe with a distinctive university system that operates in the same way as Sweden is both geographically and culturally very different: Italy.

*In your opinion, which system is better?*

**Österberg:** That's a tough question to answer. A TTO is an internal university department in some way, while we are an external and more business-orientated office. We choose the ideas we want to develop and invest in. In that case it's always in close collaboration with the researcher. We have to reach some kind of co-understanding. Plus, they have chosen to come here, and that is a really important difference, that might lead to a better and more ambitious commercialisation.

***"The researchers' ownership of their own inventions is a big plus. Because they have more ownership and control, that might keep them more engaged and committed to drive their ideas forward."***

Another difference though is the fact that GU Holding or similar organisations are not nearly as well-financed, like, for instance, my former employer, the University of Manchester and its TTO.

*Lorna, you worked previously in England and are familiar with the TTO system there. What was your experience of the British model?*

**Fletcher:** You have to strike a balance with researchers who want to work with you and the ones who come in because they have to. These projects are never good to put forward when the only reason they come in is because they know they have to come to you first.

*Is Sweden's way more attractive for technology transfer?*



Klementina Österberg (left) and Lorna Fletcher in their Gothenburg office in June this year.



**Fletcher:** The researchers' ownership of their own inventions, and therefore also the freedom to choose whom to work with, is a big plus. It's a choice the researcher makes. Because they have more ownership and control, that might keep them more engaged and committed to drive their ideas forward, whereas if the TTO has 100% ownership and most of the revenue, they may lose interest. Though, it's not the money that really drives people, it's that they want to feel they have control. It's incredible the number of different actors in Sweden and the number and variety of places people can go to for support. It's not like this in Britain at all, where if the university doesn't help you, nobody will.

**Österberg:** I also believe that many researchers are driven by the wish to utilise their research findings to do some good and contribute to our society, as well as make some money of their own out of the value that they have created.



*Sweden is investing a lot in courses and education to train young entrepreneurs.*

**Fletcher:** Some British colleagues on a visit here recently commented to me on how impressed they were with how well-educated, how confident and how mature Swedish students are.

*Some say that there's a huge disadvantage to the Swedish system: the lack of capital.*

**Österberg:** That's right. Here, we may have a lot of sources of advice, but maybe not that much money. Normally, a TTO would actually get funded by the university, and, in the majority of cases, they have a lot more money. In our situation, we don't get any capital injections from the university, even though we do sell some services to them. We need capital continuously, as we have to buy ourselves into the idea by issuing shares or by different agreements. And for that we have to have investment capital, which the universities in Sweden are not allowed to give us according to governmental conditions they are to follow.

*This is surprising given that GU Holding is fully owned by the Swedish state.*

**Österberg:** We are, of course, lobbying so that this can be changed in a better way. We're talking to all the other actors and government about how can we get their help to secure more money for our investments. Otherwise, we are making our own capital by exits [getting out of an investment that has been made in the past], even though they are scarce and cyclical.

### Standing on their own feet

When GU Holding started, they received funds from the Swedish government in the form of start-up capital of €660,000 and, some years later, funding from the Technical Bridge Foundation, which no longer exists. Since then, they have mostly made their own money, Österberg says. According to her, they have invested around €8.3 million from investment return, that is to say from exits. The rest of the funding for GU Holding's companies comes, in

*"In the Swedish system, we don't get any capital injections from the university, even though we do sell some services to them. We need capital continuously, as we have to buy ourselves into the idea by issuing shares or by different agreements. And for that we have to have investment capital."*

most cases, from business angels and venture capitalists and from governmental organisations that contribute with allowances and soft loans.

In addition to funding its companies, GU Holding also has to cover its own operations, running costs and salaries. Half of this is now paid for by revenue from the services it sells to its partners, companies and the university. The other half comes from allowances and contributions from governmental organisations and foundations.

Of the 40 to 60 proposals a year GU Holding receives, about half or more enter the verification stage, and in the end only about 7 are given the GU Holding green light. If Österberg and her colleagues think that a proposal could be transferred into a viable business plan, they have the ability, through Sweden's state funding agency, Vinnova, to procure up to €33,000 of seed capital.

It should be noted that €33,000 isn't much more than a drop in the ocean. A complete biotech seed funding is something around €1 million, and this means that GU must inject additional money later and that additional investors must jump onto the bandwagon to get the new business started. After an idea is verified and has met with a positive response, an invitation to join the GU Holding incubator is made, Österberg says. According to her, GU Holding has currently about 50 companies in their portfolio, of which 26 are in the incubator and 8 in the pre-incubator.

*"I believe that many researchers are driven by the wish to utilise their research findings to do some good and contribute to our society, as well as make some money of their own."*

*How complicated is it to get additional money after the first seed?*

**Fletcher:** They only get investments when they really need them. They don't just get money thrown at them. So we're always checking during the process: Is this something we really want to go forward with?

**Österberg:** We will have invested up to €110,000 to €220,000 per project, carefully released in separate instalments. We never give such a sum at once. Usually it's €30,000 to €50,000 per issue of shares. ▶▶

*If all goes as planned, what's next?*

**Österberg:** Once we have achieved all we aimed to do during the incubator phase, we probably have a company that's on its feet with financing, the team, and customers, but that still can be developed. But in that case they leave our incubator because we are very focused on the earliest phases. And then they are free to develop it further by themselves or join another incubator in later phases. At this point, if they can, GU Holding will want to sell their shares in the company, or parts of. Towards the end of the incubator phase, we are exit-ready.

*To date, GU Holding has generated €5.8 million from exits, which they then re-invested in new projects...*

**Österberg:** With one of our biggest exits, we had invested about €11,000 in 1997 in a clinical research organisation, A+ Science. We gained €2.4 million after gradually selling all our shares by 2009/10.

*What does a typical GU workday look like?*

**Fletcher:** It's very much establishing the network, knowing contacts, knowing what's going on everywhere. Knowing what people want to fund so we can make sure we put the right applications in at the right time. So if we know they're interested in e-health, for example at the moment, we get those applications in quick while it's still a hot topic. We stay on top of all this by attending meetings and networking, so we are building good relationships and are in other people's minds.

**Österberg:** When you have fifty companies in development at various stages, you meet a lot of different people all the time.

*What is the biggest problem that GU Holding faces?*

**Fletcher:** Exactly the same as the researchers – getting money!

*“Some academics have all of the skills to be great business people, as the best researchers are not only experts in their field but also great at identifying problems and solving them.”*

**Österberg:** Finding money in the earliest phases of the starting up process during the first years is quite tough. Before, you have either clinical data in humans or you have a viable product that people are buying, it's difficult.

**Fletcher:** The very first money is sort of easy to get because you only need so much and there's a lot of soft finance – money that the researcher does not have to pay back, nor give up ownership for. And then you have the venture capital phase. But the few years in between are really difficult because no one wants to invest because it's too early, too risky and you might still not have any paying customers.

researchers in their business (or should one say, increasing interest in starting a business?) But another motive is becoming ever more important: Boosting their chances of getting their own research funding. As grant applications require more and more emphasis on impact and commercialisation, researchers are perhaps feeling both an aspiration and a need to think in terms of technology transfer. Obviously, the clearest way of demonstrating this is by showing that you have already started a company that was successful.

*Aren't academics bad at business?*

**Fletcher:** Not at all. Some of them have all of the skills to be great business people, as the best researchers are not only experts in their field but also great at identifying problems and solving them, pre-



**Lorna Fletcher, Project Manager at GU Holding, sees no drawbacks to commercialising research.**

Photo: J. Uhler

*What about the challenge of matching a researcher with the right entrepreneur?*

**Fletcher:** If you can get that right, it's really good.

*And if not?*

**Österberg:** It can be quite difficult. We can change entrepreneur three or four times before we actually find the right one and the right team. Also, there can be some conflict between the researcher, who wants the research to be more open, while the investors are looking for focus. But we can cope with that conflict, it's not that difficult.

Both Österberg and Fletcher agree that they see a trend of increasing interest from

researchers, sending their ideas, selling their expertise, securing funding, managing people and budgets.

*Are there any negatives to commercialising research?*

**Fletcher:** Not if you do it properly. That's why it's really important for researchers to come to the right people with experience and who know how to do it and to do it in good collaboration with a research environment. Our focus isn't purely 'we need to make lots of money'. It is to make sure everything is done in the right way as well.

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INTERVIEW BY JAY UHLER





*A conversation with Geoffrey Burnstock, Royal Free Hospital, London*

# “I’m a Great Fan of Individuality”

Geoffrey Burnstock is famous for discovering purinergic signalling and as the inventor of the antiplatelet drug Clopidogre. Now 85 years of age, Burnstock is still active in research – he has published five papers this year already.

**I**n total, Geoff Burnstock has 1,328 publications listed in Scopus and has been cited 87,547 times. His 1998 paper in *Pharmacological Reviews* alone has been cited 2,943 times.

But it is for his discovery of purinergic signalling that he is best known – the then outrageous idea that ATP, the energy molecule of all cells, is actually used as a neurotransmitter. This was in the days when received wisdom stipulated that there were only two neurotransmitters: acetylcholine and noradrenaline. It is quite appropriate, then, that Burnstock was awarded the 2000 Royal Medal by the Royal Society for “his development of new hypotheses challenging the accepted views on autonomic neurotransmission, leading to new advances in the understanding of purinergic neurotransmission. There is now universal recognition of the importance of purine”. He has been a fellow of the Roy-

*“I think the current way research is funded is not good. I would favour a totally different approach.”*

al Society since 1986. “I don’t believe in clubs,” Burnstock told me, “because you have to toe a party line. I suppose my membership of the Royal Society may be an exception but it is a little different.”

I took advantage of the fact that Burnstock can still be found in his first floor office at the Royal Free Hospital in London and asked for an interview. “Come any time, I’m always in,” was the instant reply.

I was escorted through the Hospital’s labyrinth by Gill Knight, now his secretary and once his PhD student. I stepped into his office and entered a different decade. As I sat with Burnstock at his desk, it took me a few moments to realise what was missing – there was no computer (“Oh, I do everything on paper – my secretary types my messages up and sends them by email”). And the shelves of index cards took me back to my PhD supervisor’s office back in the early 1980s. Mem-

orabilia of a life well-lived were scattered around the office like a personal museum, each item inviting a personal explanation. Knowing I was in for a treat, I posed my favourite questions.

*Biology has become very industrialised over the past few decades – scientists are “trained” rather than educated. Do you think our universities are doing a good job of encouraging real novelty of thought?*

**Geoffrey Burnstock:** The trend in Universities these days seems to be unsympathetic to novelty of thought. They favour research directed to particular topics, especially those with practical importance. And they favour secure, well-established topics, rather than imaginative hypotheses. Examinations test memory, rather than problem-solving and imagination. In some cultures, school children are not encouraged to be different and this idea extends into science, although admittedly some excellent work is still carried out.

Your major disadvantage when you were starting out as a scientist was a rigid class system that discouraged you from pursuing a career in medicine. You made it through – who knows what great minds may have been discouraged by it. Do you think there are different barriers today that might be holding Britain's young talent back?

**Burnstock:** Yes, in the 1940s the class system was strong and I failed to be accepted for medical school, largely because I came from the wrong school, a working class family, wrong accent, wrong clothes. Sadly, class bias still exists today but perhaps not as strongly as in the past.

You have always emphasised the need for a robust individualism to be a good scientist. Is that possible – or even desirable – in our day of big-budget science?

**Burnstock:** I am a great fan of individuality, and believe it should be encouraged for good science. It is not encouraged today but is still possible, if they have the courage.

Grant committees are often accused of being biased against the intellectual status quo. Does the way we decide who gets funded stifle original thinking?

**Burnstock:** Grant committees favour projects at the quantitative edges of established doctrines, rather than imaginative, original hypotheses.

Related issue: do you think the way we fund research could be changed, or is it more or less okay?

**Burnstock:** I think the current way research is funded is not good. I would favour a totally different approach. I would divide funding into two parts:

First, for established groups with very successful track records: award them five-year grants without forcing them to predict their research over five years and waste valuable creative time preparing elaborate detailed project proposals.

Second, for young scientists without track records: award them three-year grants based on interviews with a group of very experienced research group leaders, instead of basing decisions on project proposals often written largely by their PhD supervisors or future bosses of their post-doc position.

Of course, the future support of both established groups and young researchers would be monitored closely for their

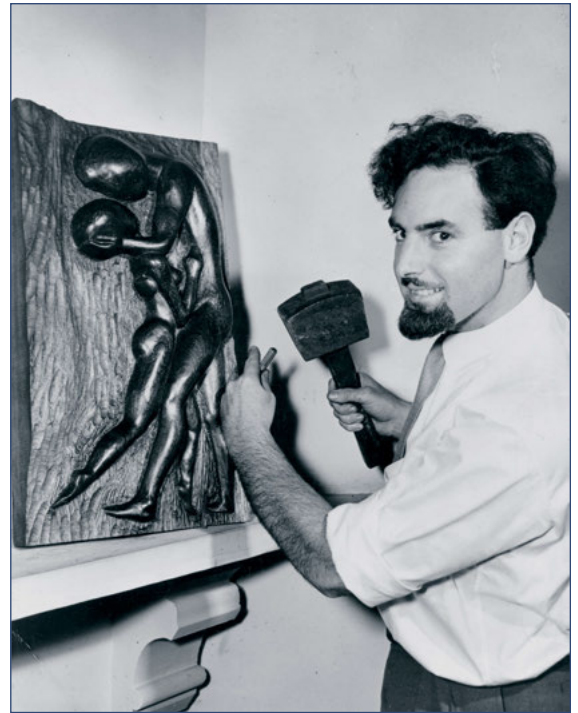
creative success, publication record and citations.

You established your reputation by challenging the established dogma of the time that there were really only two neurotransmitters. Which idol would you like to see dethroned today?

**Burnstock:** Sir Henry Dale was a great man and his evidence for only two neurotransmitters was outstanding in the 1930s. With scientific research, it is cumulative. The truth emerges successively as new techniques are applied. It is important not to be afraid to challenge established dogmas, if new evidence emerges. But there is no justification or pleasure in dethroning top scientists, who made the earlier discoveries. Classical papers often hold up progress in a field because nobody has the courage to challenge them.

You have long-standing hobbies – your wood carving for one. You have been doing them for many years and, if I may say so, the quality of your carvings reflect a serious devotion to the art. Do you think they have helped you do your day-job?

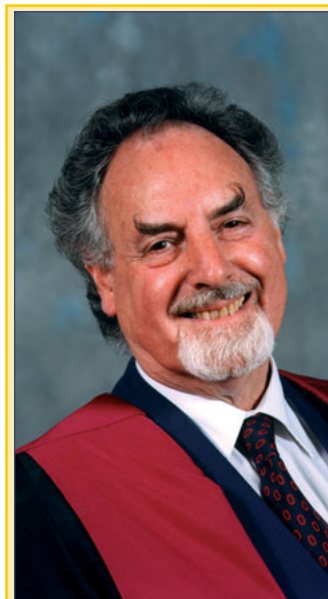
**Burnstock:** When I took my first job in Australia, I foolishly neglected to organ-



Burnstock started wood carving in Australia in the 1960s, while waiting for his research equipment.

*“Grant committees favour projects at the quantitative edges of established doctrines rather than imaginative, original hypotheses.”*

ise funding in advance of taking up my position and had no equipment to carry out experiments for the first six months. I like to think that I am driven by the urge to be creative and that this ambition is true for both science and art. So that is why I took up wood carving to satisfy my creative spirit, while waiting to start creative scientific experiments.



## Geoffrey Burnstock

...was born in London in 1929 into a “happy but frugal” working class family. He went to Greenford County Grammar School in the 1940s and tried unsuccessfully to get into medical school in the early 1950s. Obviously, he was coming from the wrong social background. But that doesn't hold back a young Geoffrey Burnstock from getting into neuroscience research. And what started with a bizarre PhD work – he put a condom on a fish with a “window” to see how the gut works *in vivo* – evolves into one of the most fascinating careers in life science research. Burnstock has earned countless honours and awards for his work on the purinergic signalling pathway and published more than 1,000 papers, reviews and books. He is an emeritus professor since 2004 but still puts forward new ideas and hypotheses of purinergic signalling.





*If you could only keep one of your wood carvings, which would it be and why?*

**Burnstock:** Many of my wood sculptures were of mother and child (a relationship which I think is very important) but then I started doing some abstracts. My favourite carving is an abstract that in retrospect was probably a woman!

*There is a lot of talk about changing the way we publish science, such as the retreat from paper to online publishing, even going as far as open science and abandoning peer review for open discussion (online) of papers. What is your opinion of that?*

**Burnstock:** Personally, being an old man, I still prefer paper publications. But I suspect that the modern generation is probably more comfortable with online publications to read on their computers.

Do I think we should abandon our peer-review system? Well, I think peer review of publications is still the preferable way, although I recognise that it is sometimes problematic.

*“Well, I think peer review of publications is still the preferable way, although I recognise that it is sometimes problematic.”*

*You told me you do all your work on paper – what are your thoughts on the effect computers have had on the way academics work?*

**Burnstock:** Again, probably because I am an old man, I prefer to write my papers by hand rather than using a computer but my guess is that this is not true for most younger scientists.

*“The trend in Universities these days seems to be unsympathetic to novelty of thought.”*

*At what point did you realise that your discovery of purinergic signalling was going to have a big impact?*

**Burnstock:** There were three major times when I felt that purinergic signalling would have a big impact. First, I was very excited and felt intuitively it was going to be very important when I published a review, proposing the purinergic hypothesis as far back as 1972. Secondly, when I recognised that ATP was a cotransmitter with classical neurotransmitters in 1976. Thirdly, when we and others cloned and characterised the receptors in the early 1990s, which allowed us to show extraordinarily wide immunolocalisation of the receptors on many different cell types, in both healthy and diseased tissue.

*You originally came from a boxing family – is boxing good training for a scientist?*

**Burnstock:** I wouldn't think boxing is a great basis for good science. However, I suppose you could argue that fighting hard for your ideas is useful and learning to handle defeats as well as success. And also not to miss opportunities when they arise.

*You finished your PhD under the legendary (John Zachary) JZ Young. What do you remember of him?*

**Burnstock:** JZ Young was a great scientist, controversially a Zoologist becoming the Chairman of an Anatomy Department at UCL. He was always kind and supportive during my PhD training. It was amaz-

ing to me that I was invited to take over his Headship of Anatomy and Developmental Biology in 1975!

*What qualities do you look for in a young scientist?*

**Burnstock:** Six things: intelligence, manual dexterity, resilience (you are going to need a lot of this, science can be incredibly discouraging at times), courage (if you discover something new, you'll have to stand by it against opposition), judgement (knowing when to give up on a line of inquiry) and passion.

*If you hadn't made it in science after all, what would you have spent your life on?*

**Burnstock:** If I hadn't made it in science, there are three things that might have been. For one, there's my wood sculpture – but sadly I'm still very much an amateur.

*What does your wood carving mean to you?*

**Burnstock:** I go to a deserted beach every year in New Zealand and do my carvings. It is important to me. If I couldn't do it, I would try to find some other creative direction.

*What was the second thing?*

**Burnstock:** I used to have the usual academic scepticism about business but I changed my mind when I met my father-in-law, who was a business man. He was not focussed on making money but rather on creative thinking, solving problems and trying to serve the community. I considered leaving science and working with him.

*And the third?*

**Burnstock:** I was once passionate about being a flamenco guitar player. I bought a cheap motor bike and went to Spain. I spent some time learning to play and a local told me there was a place where I should go to play. “If you are good, they will dance,” he told me. I played. No-one danced. So I never became a flamenco guitar player.

*If you could relive one day of your life, which day would that be?*

**Burnstock:** This would be marrying my wife, Nomi. This has lasted, so far, for 55 good years, with three lovely daughters and seven wonderful grandchildren.



*A conversation with Sarah Teichmann, European Bioinformatics Institute, Hinxton*

# “I’d Just Hate to be Ordinary”

Sarah Teichmann gets into Bioinformatics in the late 1990s when it was anything but a “cool” discipline. But what started as a “weird and bizarre” topic put her right into the middle of the current single cell genomics revolution.

Our regular readers will know that we at *Lab Times* have been very excited about developments in single cell genomics. We really believe this is one of the big developments in biology. Why? Because it will change the way we think about living tissues. For centuries, practical constraints have forced us to iron out the individuality of cells with our means and standard errors. Now, we can start looking at, not away from, the things that make individual cells different from each other.

And *Lab Times* isn’t alone in this opinion. Last year, for example, the Sanger Institute – the geometrical centre of the genomics universe – opened their Single Cell Genomics Centre, calling single cell genomics “the next frontier in molecular biology”. So I decided to mark our 50<sup>th</sup> issue by chatting with Sarah Teichmann at the European Bioinformatics Institute, Hinxton, Cambridge, UK.

Now, if you are at all given to professional jealousy, I must warn you to stop reading this feature right now. Sarah got her PhD in 2000 and has been running on all four cylinders ever since. Within a year of getting her PhD she was put on an MRC programme leader career track, got herself

a junior research fellowship at Trinity College Cambridge and became an MRC programme leader in 2005. At the same time, she became a fully-fledged fellow and director of studies at Trinity, and last year was appointed to the status of Group Leader at EBI. Phew!

Earlier this year, Sarah’s team hit the news with the discovery, using single-cell genomics, of a previously unknown self-regulation mechanism in T-cells. She found that once the T-cells had battled off an infection, they then release steroids to turn each other off, thereby re-balancing the immune system.

Fortunately for our readers, Sarah is not too busy to talk to us about her career and where she sees herself going in the next five years.

*You became an MRC programme leader within five years of graduating. What’s the secret?*

**Sarah Teichmann:** I think it all comes down to having a successful time as a PhD student. So, I guess that rolls back to asking what it was about that period that made

it successful? I think it comes down to two things: finding a good environment to do your PhD in and, I have to admit, being in the right field. It is important your PhD is done in a supportive environment – mine was just that. And as for being in the right field, I am the first to admit that I just happened to hit a big wave.

I’m talking about the bioinformatics and genomics wave. Not that I knew it was a wave at the time. But I just happened to be in the right place at the right time – scientifically I mean. I am going back to the late 1990s, and these disciplines were only really

just up and coming. As far as I remember, the word “bioinformatics” didn’t even exist.

I remember that, at the time, what we now call bioinformatics was a bit of a “weird” thing to do. I remember looking around and noting that, sure, there were computational PhDs being done – they were in areas like X-ray crystallography and nuclear magnetic resonance (NMR). But somehow that wasn’t quite what I was looking for. I knew that what I really wanted was a data-mining project but I wanted one that would give me a broad biologi-

*“As far as I remember, the word bioinformatics didn’t even exist.”*



cal perspective. And that's what I really like about genomic biology. You are looking at the big picture of an entire genome and it gives you quite a shift in perspective compared to standard microbiology.

So the best answer I can give to your question is to do what feels interesting to you. Looking back, I can see that I had picked a winning subject but at the time anyone would have told you that what I was into was not a "cool" topic: it definitely was an unusual thing to do – I would go so far as to say it was weird and bizarre. After all, the genome campus was just being built at the time.

*What influence did your PhD years have on you?*

**Teichmann:** The group I did my PhD in was a bit on the unusual side. For one thing, it was really small. It only had the principal investigator and three PhDs. But like I said, it was a great environment to do a PhD in. And what made it so good? It was the interaction with the supervisor. Even though all my bios say I came from a bioinformatics background, in reality, when I started on my PhD I had, in fact, very little programming background. But the students supported each other technically. I guess the best indicator of the quality of the nurturing environment I can give, is to point out that nearly all the PhD students went on to become PIs.

*What brought you into the field of single-cell transcriptomics?*

**Teichmann:** It was through my interest in computational approaches. As far as my biological interest is concerned, that was definitely in the regulation of gene expression. When I started up my group in 2001, I decided I wanted to work on transcription factors – how the expression of genes is regulated. In fact, my very first paper was on the evolution of transcriptional networks and single cell genomics. Before that, we had been using traditional RNA sequencing but we soon went on to using RNA transcriptomics of single cells.

*Why?*

**Teichmann:** If you drill down to the level of single cells, you get a number of pretty major benefits. First of all, you get to learn more about the very basic biochemistry. I am thinking of the kinetics of the transcription process and its stochasticity. What I mean by that is that the noise is important functionally and it can help us to

get new insights into the biochemistry of transcription.

The second big plus you get with single cell transcriptomics is you can start doing things on a high throughput scale. So, you are not just looking at one population but rather hundreds or thousands of individual cells. This is very data-rich and allows you to do some pretty fancy fun bioinformatics, including correlations between transcription factors and target genes, coregulatory modules of coexpressed genes, and so on.

And a third advantage is that, in addition to transcriptional regulation, you can look at the cell state – either individual cells or at least different subpopulations of cells. My favourite example is the steroid story I published this year.

And it is not just biochemistry and molecular biology: doing experiments this way, we will find previously unknown stuff about the physiology as well. I think a lot of people have secretly been thinking that physiology has all been done, that there wasn't anything new to discover at the level of tissues and how they function. I think those people are going to get a lot of surprises: RNA sequencing of single cells is going to show us tons of new things we haven't even guessed at today.

*Which researcher, dead or alive, has influenced you most?*

**Teichmann:** Oh, that has to be my good friend and colleague, Carol Robinson in Oxford. I have done lots of scientific collaborations with her, mostly looking at protein complexes. She is one of the two scientists in the world, who has got non-covalent mass spectrometry working (also known as macromolecular mass spectrometry). It is an amazing technique – it allows you to do mass spec on protein complexes held together without covalent bonds.

I would never have thought that possible. But as well as through our collaborations, she has also influenced me as a person – showing me the value of just going for things. She is a real "go-getter" and I have learned a lot from that.

*Tell us about your current research interests at EBI*

**Teichmann:** Single cell genomics on T cells is where I am going at the moment. I

really think this could be an important development and I want to look further at T cell heterogeneity using single cell genomics technology.

*Do you still get time at the bench?*

**Teichmann:** I'm afraid that went out when my first child arrived! So, I just have to be more efficient now. But I still have my own independent projects. I spend a lot of my time directing the research of students and postdocs. I love that. Am I a hands-on director? Yes, I like to get involved with postdocs' research. But I realise that as I concentrate on directing research and doing my own work at the computer, people I work with have become highly specialised in wet work. Such as dissecting out tissues, or doing the biology on T cells from different tissues.

*Which technologies or technical developments over the past ten years do you think will have the biggest impact on biology? (I think I can answer that one for you . . .)*

**Teichmann:** Yes! Well, it has to be single cell genomics, doesn't it? To be serious for a moment, I honestly can't think of anything that comes near it for impact. I honestly believe it is a game-changer, to use a well-worn phrase. Especially when applied to transcriptional regulation and looking seriously at the "noise" in these pathways.

*But do you think researchers focus too much on techniques rather than on the biology?*

**Teichmann:** This is an age-old question and to be honest I don't think I really know the answer. I suppose people have agonised over this since biology began. Look at the honours given to people at EBI, for instance. We have Nobel Prize winners for the development of green fluorescent protein and for the polymerase chain reaction.

That's all biotechnology. And there is absolutely no question that they have done a wonderful service to biology. Personally, I just love technology – that's one reason I chose to do computational biology. I guess it is a bit like when someone gives you a microscope for the first time – what do you do? If you have an ounce of curiosity, you'll get out into your garden and start looking at things. And a lot of the time what you find depends a lot on having a hunch as to where to look. And coming back closer to home, my choice of T cells was a bit of opportu-

*"I spend a lot of my time directing the research of students and postdocs. I love that."*

*"If you drill down to the level of single cells, you get a number of pretty major benefits."*



Photo: Teichmann lab

Sarah Teichmann and her energetic group at the European Bioinformatics Institute.

ism, if I am perfectly honest. I chose them because they were easy to get hold of and we guessed they might have something interesting to tell us.

*With a lot of “omics” technologies, a big problem is in interpreting the data. Even the basic statistics are far from straightforward. Are the statistics keeping up with single-cell omics?*

**Teichmann:** Yes, the stats issue has been a problem with all the new technologies. But let’s be realistic – there is always low-hanging fruit to go for! The most obvious correlations will always just pop straight out at you. But, of course, to get the most out of your data you will need more sophisticated statistical techniques. And it has to be said that the software has always lagged behind the techniques. As for me, we are really quite lucky – we’ve got the EBI next door so we can always talk to them. The software is catching up quickly, though, and on the good side the awareness amongst scientists and software developers is higher than it used to be. Biolo-

gists are catching on that T-tests aren’t always enough!

*Is single-cell omics for the expert only, or can any lab adopt it? These techniques are high investment. Is there no room then for the small lab?*

**Teichmann:** I have often asked myself this question and it does make me feel a little uncomfortable. Indeed, it is one reason why I left LMB to come to EBI because they have the expertise and the investment. But theory and computation do actually lend themselves to a small group. And if you are smart enough, you can still be a world leader with very little money, just by using the data in public databases. But yes, if you want to get in on single cell sequencing you need the expertise. And the money. For instance, we rely on a little microfluidics robot – and you won’t get much change from €125,000 (£100,000) for one of those.

*If you were to be remembered for only one contribution to science, what would it be?*

**“Biologists are catching on that T-tests aren’t always enough.”**

**Teichmann:** I have to cheat here because I have two loves! Would it be the protein complexes? Predicting canonical assembly pathways – how proteins find each other, how they stick to each other in the right order, perhaps? I am thinking of my paper in *Nature* in 2008 and my work with Carol Robinson in my *Cell* paper last year.

On the other hand, it may be the work on transcriptional regulation. I think my most important contribution will hopefully turn out to be a deeper understanding of cell heterogeneity. Especially what I found about steroid signalling in T cells last year. Another group in Colorado has also found it, so I think this might emerge as an important physiological signalling pathway.

*If you had failed at science, what would you be doing right now?*

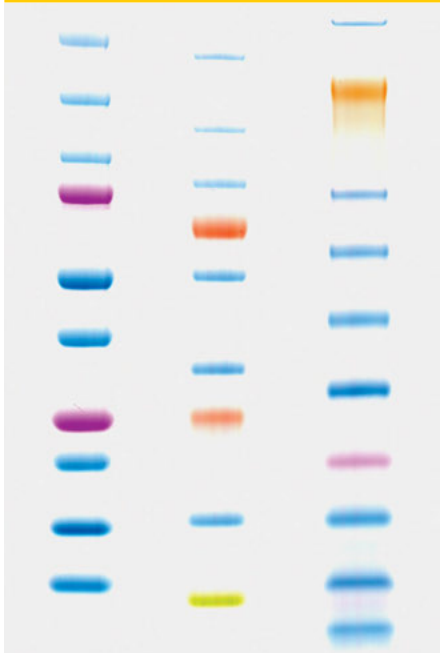
**Teichmann:** A Wimbledon tennis champion. Another Steffi Graf! Well, something like that – so long as it is not a standard career path followed by so many Cambridge graduates. I’d just hate to be ordinary!

INTERVIEW: STEVEN BUCKINGHAM



# New Products

## Protein Identification



**Product:** Protein marker

**Name & Manufacturer:** Precision Plus Protein Dual Color Standards from Bio-Rad

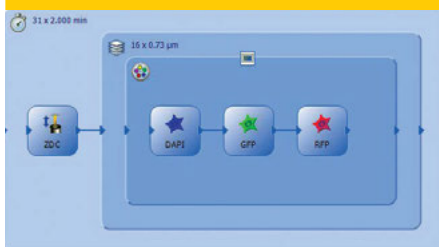
**Technology:** Bands range from 10 to 250 kD with sharp pink reference bands at 25 and 75 kD for simple visualization. The new Dual Color Standards share the same migration pattern as their previous iteration.

**Advantages:** The strong marker persistence throughout electrophoresis and Western blotting, even during rigorous stripping and reprobing protocols, makes the product an effective tool for monitoring separation and estimating protein molecular weights.

**More Information:**

[www.bio-rad.com/pr/DualColor](http://www.bio-rad.com/pr/DualColor).

## Imaging



**Product:** Imaging software

**Name & Manufacturer:** cellSense (version 1.11) from Olympus

**Technology:** Additional models of EMCCD and sCMOS cameras are now supported, such as the

Hamamatsu Imagem X2 and the Andor Zyla 4.2, delivering rapid and sensitive imaging; while 3D applications benefit from the integrated control of piezo-driven devices, for ultra-fast Z-stacking and focussing. Multi-channel imaging of samples with fast dynamics is now supported through the use of an image splitter, with up to four emission channels acquired at the same precise moment.

The exact synchronisation of multiple wavelengths also quickly produces reliable images for advanced applications such as FRET and ratiometric analysis. Moreover, ratiometric analysis can now be achieved "online", enabling the real-time tracking and updating of ratiometric images and graphs during experiments.

**Advantages:** The Graphical Experiment Manager (GEM) interface allows the user to "draw" their experimental schematic on-screen with familiar "drag and drop" actions, enabling complete control and experimental set-up of motorised components and accessories with almost no need for training.

**More Information:**

[www.olympus-europa.com/microscopy](http://www.olympus-europa.com/microscopy)

## RT-qPCR

| No. of controls | Assays (n) |    |      |     |      |     |      |     |      |     |  |  |  |  |  |  |
|-----------------|------------|----|------|-----|------|-----|------|-----|------|-----|--|--|--|--|--|--|
|                 | 1          |    | 10   |     | 24   |     | 48   |     | 96   |     |  |  |  |  |  |  |
| 1               | 2          | 3  | 11   | 12  | 25   | 26  | 49   | 50  | 97   | 98  |  |  |  |  |  |  |
| 10              | 20         | 12 | 110  | 21  | 250  | 35  | 490  | 59  | 970  | 107 |  |  |  |  |  |  |
| 24              | 48         | 26 | 264  | 35  | 600  | 49  | 1176 | 73  | 2328 | 121 |  |  |  |  |  |  |
| 48              | 96         | 50 | 528  | 59  | 1200 | 73  | 2352 | 97  | 4656 | 145 |  |  |  |  |  |  |
| 96              | 192        | 98 | 1056 | 107 | 2400 | 121 | 4704 | 145 | 9312 | 193 |  |  |  |  |  |  |

Traditional RT(-) strategy      ValidPrime™

**Product:** Genomic DNA background subtraction in RT-qPCR

**Name & Manufacturer:** ValidPrime from TATAA Biocenter

**Technology:** Novel, cost-saving and performance-enhancing approach to assess genomic DNA (gDNA) background in expression profiling that replaces no RT (RT-) controls in RT-qPCR. The assay targets a non-transcribed locus that is present in one copy per haploid normal genome and measures the level of gDNA contamination. The kit also contains purified reference gDNA to assess the gDNA sensitivity of the assays.

**Advantages:** The assay reduces the number of control reactions needed in RT-qPCR. When analysing m samples for n genes, the number of control qPCRs is m + n + 1 instead of m x n qPCRs + m RT reactions when performing RT-controls. Precision is enhanced because of the lower C<sub>q</sub>'s measured. This allows for reliable correction for up to 40 % gDNA contamination.

**More Information:**

[www.tataa.com](http://www.tataa.com)

## Single-use Bioprocessing



**Product:** Single-use bags

**Name & Manufacturer:** Flexsafe from Sartorius Stedim Biotech

**Technology:** The bags are based on a multilayer, proprietary polyethylene (PE) film, called S80, and have been developed in close collaboration with resin and film suppliers. A standardised cell growth assay has been used to optimise film formulation, determine the operating ranges for extrusion, welding and gamma-irradiation processes and to establish specifications and process controls.

**Advantages:** The bags enable the implementation of single-use bioprocessing throughout all steps of drug manufacture, from process development to production, in upstream and downstream.

**More Information:** [www.sartorius.com](http://www.sartorius.com)

## Immunoassays

**Product:** Assay development

**Name & Manufacturer:** 2-D DIGE Western Blot service from BioGenes

**Technology:** Host Cell Proteins (HCPs) comprise the majority of protein contaminants derived from the manufacturing of therapeutic proteins and vaccines. HCPs are often immunogenic, can alter the therapeutic efficacy of a therapeutic drug substance and may affect patient safety. 2-D DIGE Western blot is a DIGE based fluorescent two-dimensional gel electrophoresis combined with a Western Blot. It allows the protein spots to be aligned perfectly with immuno-detected spots, thus eliminating any gel-to-membrane variations.

**Advantages:** The assay uses two CyDye fluorescent dyes for labelling of total protein and HCP antibodies, which enable signal detection at different wavelengths. CyDye fluorescence labelling is very sensitive and produces sharp and clear spots allowing an accurate and fully electronic analysis.

**More Information:**

[www.biogenes.de](http://www.biogenes.de)



Levent Yilmaz (third, right), world champion in show-barkeepsing, shows how to shake cocktails.

Photo: Europapark Rust

*Product survey: Bioreactors and cell bags*

## The Art of Mixing

The decision making of potential bioreactor buyers may be boiled down to two simple questions: shaken or stirred and single-use or re-usable?

**B**arkeepsers and cocktail drinkers may get into fierce debates when it comes to the question whether a certain cocktail should be shaken or stirred. As a rule of thumb, cocktails are usually shaken when they include fruit juice, cream liqueurs or other thick mixers and stirred when they contain distilled spirits or light mixers. The question “shaken or stirred” is not only a hot topic amongst cocktail drinkers. Life scientists looking for a new bioreactor may argue about the very same question. Should they go for a traditional stirred-tank bioreactor (STR) or opt for a shaken plastic cell bag?

STRs are essentially cylindrical reaction vessels made of glass or stainless steel and closed with a stainless steel or plastic lid. A motor-driven impeller system installed

through a sealed void in the lid agitates the culture media, while gases such as air, oxygen or carbon dioxide are flushed to the bottom of the vessel via spargers. Additional sensors integrated into the lid may control crucial cell culture parameters, such as temperature, pH or dissolved oxygen. Easy scalability is one of the major advantages of stirred-tank bioreactors. Hence, they are available with working volumes varying from a few dozen millilitres in small research reactors up to 20,000 litres, or even more, in production plant reactors.

### Magnetic paddles

Spinner flasks are basically slimmed-down versions of stirred-tank reactors devoid of impeller motor, spargers and control units. They usually come with simple plas-

tic screw caps and a magnetic paddle system, or a hanging stir bar mounted underneath the cap that is rotated by a magnetic stirrer. Two angled sidearms permit access to the interior of the flasks and allow a firm gas exchange.

### Exploding gas bubbles

Paddles and impellers of spinner flasks and STRs allow an easy mixture of suspension cultures. They may, however, also cause considerable damage, especially to delicate cells such as mammalian cells due to shear stress. Another issue of STRs are “exploding” gas bubbles, stemming from gas sparging, which may also harm sensitive cells.

In their quest for bioreactors, allowing homogeneous liquid mixing and a high



mass-transfer rate without detrimental effects to the cells, researchers came up with the idea for cultivating cells in plastic bags – which are shaken, not stirred – in the 1960s, already. Since the gas exchange through the plastic material was pretty lousy and mixing wasn't very efficient, the culture bags soon fell into oblivion. It took until 1996, before Vijay Singh, then working for the US Pharma company Shering-Plough, solved the mixing and gas exchange issues of plastic bags with two simple modifications and a clever shaking technique.

### Simple and efficient

He connected two short flexible tubes to the disposable gamma-irradiated plastic bags: one serving as the inlet for air (oxygen), the other as an exhaust pipe for carbon dioxide. His brilliant idea, however, was to fill the inflated cell bag only partially with culture media and place it on a rocking shaker platform, to create a media wave running back and forth inside the bag. The media wave ensures a homogeneous, shear-stress-free mixing of the cells and facilitates the transfer of oxygen into the media.

Disposable wave bioreactors, which have been on the market since 1999, have turned into serious competitors of traditional STRs. They are available in different sizes, ranging from 100 millilitre working volume for small scale applications to 1,000 litre monster bags, designed for biopharmaceutical production lines. Upscaling the pillow-shaped wave bags beyond the 1,000 litre frontier, however, is limited – which might play well into the hands of disposable orbital shaken bioreactors (OSRs) developed by Florian Wurm's group at the École Polytechnique Fédérale de Lausanne.

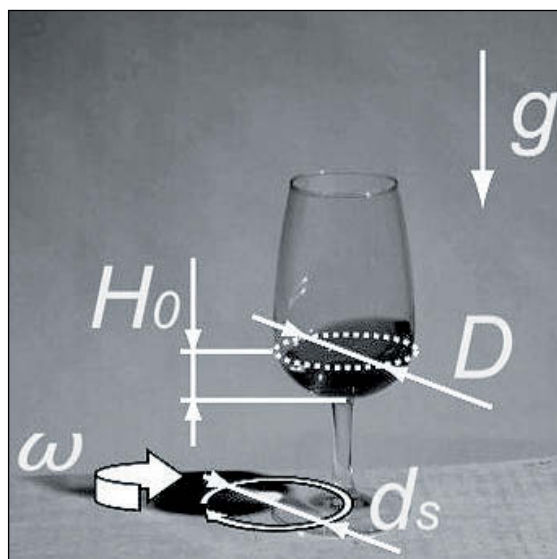
The Swiss group got the idea for OSRs during an extensive screen for cell culture parameters in CHO cells under "bioreactor-equivalent" conditions in 2004. They initially took the simplest approach and filled the suspension cultures into 50 ml centrifuge tubes, with slightly loosened screw caps, to allow gas exchange and ran them at 130 to 250 rpm on an orbital shaker.

To their surprise, the cells grew to similar densities as in stirred-tank bioreactors equipped with sophisticated control units. Obviously, the orbital shaking mode ena-

bles a thorough and fast mixing of the media as well as an efficient aeration. Prototypes of orbital shaking bioreactors have already been upscaled to 1,000 litres, using cylindrical disposable bags fixed into orbital-shaken stainless steel vessels. But that's not the end of the line, Florian Wurm has plans for even bigger OSRs with 2,500 litres.

### Single-use boom

The recent boom in cell bags has sparked a general trend towards disposable bioreactors and single-use systems (SUS). For good reason: they save researchers from cumbersome cleaning and sterilisation processes, and may reduce production costs. However, single-use systems made of plastic not only place an extra burden on the environment. A paper published by a group from Amgen's product development unit in Thousand Oaks, California, early this year, also suggests that leachable compounds found in some disposable cell bags may also harm your cells (Hammond *et al.*, *Biotechnol. Prog.*, 30, 332-37).



The basic parameters of orbitally shaking liquids are rather simple, the physics behind it, however, is devilishly complex.

Matthew Hammond and his co-workers grew CHO cells in six different bag types from five vendors and checked their viability. Cell growth was impaired in three bags, with almost no viable cells in one bag type. Further investigations revealed that the cytotoxic compound bis(2,4-di-tert-butylphenyl) phosphate (bDtBPP), leaching out of the bag films, was responsible for the reduced cell growth. Obviously, bDtBPP is generated by the degradation of tris(2,4-di-

tert-butylphenyl)phosphite (TBPP), which is added to the plastic film as an antioxidant stabiliser.

### Everything is fine now?

The cytotoxic effects of certain bags could be traced back to mistakenly high TBPP concentrations applied during film production, which has led manufacturers of bag films to take action and control the TBPP concentrations more closely. That's certainly not a bad idea but probably not enough, as Hammond points out, "I am not ready yet to say that the only important parameter is the concentration of TBPP in the film – there may be complex interactions with other additives, polymers and the manufacturing processes used."

Asked for some advice to researchers working with disposable cell bags he says he would "call the vendor of any SUS bags and specifically ask if the product I was considering for use is known to have an issue with leaching this compound. The other suggestion I would make is to follow some of the recommendations we made in our *Biotech Progress* paper: if there is a worry that bDtBPP leaching might be problematic, avoid using SUS bags at very low working volume (relative to the capacity of the bag) or very low initial cell density".

### New bag material

The manufacturers of single-use systems and cell bags are also aware of the problem. Sartorius Stedim, for example, announced on June 1 in a notification paper that it has changed the material of the polymer film used for SUS and introduced a new product line that will succeed the CultiBag RM system (which will be discontinued after December 31, 2016). According to Sartorius, the new bag material has been validated by an independent round-robin study conducted by the DECHEMA temporary working group on "single-use technology in biopharmaceutical manufacturing" (Eibl *et al.*, ISBN 978-3-89746-149-9).

However, changes in plastic production processes are still an immanent problem of SUS. Or as Hammond puts it, "SUS vendors will have to work hard with their suppliers to make sure that there are no unannounced changes to the formulations (or other processing parameters) of the plastics they receive."

And researchers should keep their eyes open when deciding to work with disposable bioreactors.

| Bioreactors and Cell Bags  |  |   |   |  |   |
|--|--|---|---|--|---|
| Company/Distributor  | Name of Product  | Volumes   | Applications  | Miscellaneous, Specialities, Generally   | Price [EUR]   |
| <b>Biotehniskais Centrs (BTC)</b><br>Riga, Latvia<br>www.btc-automation.lv<br>Contact: btc@edi.lv<br>Phone +371 6755 35 18 | Laboratory glass bioreactor EDF-5.4_1  | 6 litres (working volume 2-4 litres)                                | Submerged cultivations of microorganisms  | Novel magnetic drive   Metallic bottom   Bottom placed sampling device   Fully automatic control   | 16,240.-  |
|  | Pilot scale bioreactor EDF-(volume)  | 30-5,000 litres   | Submerged cultivations of microorganisms as separate bioreactors or connected in the production line                  | Novel magnetic drive   Fully automatic control including sterilisation   | 60,740.<br>(30 l) to<br>124,180.-<br>(1,000 l)  |
|  | Automatic control unit for single use and other bioreactors  | Different volumes   | Automatic control of different bioreactors  | Fully automatic control with extension and customisation possibilities   | 14,800.-  |
| <b>CellGenix</b><br>Freiburg, Germany<br>www.cellgenix.com<br>Contact: info@cellgenix.com<br>Phone +49 761 888 890         | VueLife 1PF-0002   | 2 ml  | Cell culture  | FEP cell culture bags with 1 FEP female luer port   FEP: lowest permeability for humidity and highest permeability for gases, biologically, chemically and immunologically inert, temperature range: +200°C to -200°C, high flexibility, even in liquid nitrogen   Bags with rounded corners and laser-welded seam | On request  |
|  | VueLife 2PF-0002   | 2 ml  | Cell culture  | FEP cell culture bag with 2 FEP female luer ports  | On request  |
|  | VueLife 32-C<br>VueLife 72-C<br>VueLife 118-C<br>VueLife 197-C   | 32 ml<br>72 ml<br>118 ml<br>197 ml                                  | Cell culture  | FEP cell culture bag with Y-tubing (PVC, 1 sealed end, 1 female luer lock) & 1 female luer valve   | On request  |
|  | VueLife 290-C  | 290 ml  | Cell culture  | FEP cell culture bag with tubing (PVC, 1 female luer lock) & 1 female luer valve   | On request  |
|  | VueLife 750-C1   | 750 ml  | Cell culture  | FEP cell culture bag with Y-tubing (PVC, 1 sealed end, 1 female luer lock) & 1 female luer valve & 1 covered exit spike port   | On request  |
|  | VueLife 32-AC<br>VueLife 72-AC<br>VueLife 118-AC<br>VueLife 197-AC<br>VueLife 290-AC   | 32 ml<br>72 ml<br>118 ml<br>197 ml<br>290 ml                        | Cell culture of adherent cells  | FEP cell culture bag with Y-tubing (PVC, 1 sealed end, 1 female luer lock) & 1 female luer valve   | On request  |
|  | VueLife 750-AC   | 750 ml  | Cell culture of adherent cells  | FEP cell culture bag with Y-tubing (PVC, 1 sealed end, 1 female luer lock) & 1 female luer valve & 1 female luer port  | On request  |
|  | KryoSure 6-F   | 6 ml  | Cell culture of adherent cells  | FEP Kryo bag (1 sealed tube (PVC)   1 needle access septum exit port (Polyisoprene)  | On request  |
|  | KryoSure 20-F  | 20 ml   | Cell culture of adherent cells  | FEP Kryo bag with Y-tubing (1 sealed end, 1 PVDF female luer lock)   1 FEP exit spike port   | On request  |
|  | KryoSure 60-F<br>KryoSure 120-F<br>KryoSure 180-F  | 60 ml<br>120 ml<br>180 ml   | Cell culture of adherent cells  | FEP Kryo bag with tubing (female luer port) & 2 FEP exit spike ports   | On request  |
|  | <b>Dunn Labortechnik</b><br>Asbach, Germany<br>www.dunnlab.de<br>Contact: info@dunnlab.de<br>Phone +49 2683 43094<br>Cellexus (Manufacturer) | CellMaker   | Up to 8 or 50 litres  | Bioreactor for the cultivation of bacteria and yeast   | Convenient single use disposable bioreactor bag   Airlift-technology for efficient mixing   Enclosed heating and cooling device   Temperature range 15°C - 40°C |
| CellMaker Plus   |  | Up to 8 or 50 litres  | Bioreactor for the cultivation of insect and mammalian cells  | Convenient single use disposable bioreactor bag   Airlift-technology for efficient mixing -pH and DO sensor   Enclosed heating and cooling device   Temperature range 15°C - 40°C  | On request  |
| <b>Cesco (Manufacturer)</b>  | BelloCell  | Up to 4 x 500 ml  | System for the cultivation of insect and mammalian cells for highest cell densities                                   | Compressable sterile single-use bottles with "BioNOC" microcarrier for large surface area   Cycles of nutrition and aeration through compression system   Low shear stress and foaming   Compatible to most serum free media   | 5,405.-<br>7,101.-  |
| <b>Fibercell (Manufacturer)</b>  | Fibercell  | Cultivation in hollow fiber cartridges under constant medium supply | System for the production of antibodies and other proteins in mammalian cells (e.g. lymphocytes or endothelial cells) | Hollow fiber bioreactor   Secreted proteins will be concentrated up to 100-fold, no splitting of cells required, cell cultivation and antibody production for up to several months, low consumption of serum   | From 2,499.-  |
| <b>Chemglass Life Sciences (Manufacturer)</b>  | Cell Culture Bags Premium  | 10-50 litres  | Mammalian and plant cell culture  | Fits GE Wave rocking platform   8 ports   Solution contact layer EVA or PE   EVOH gas barrier   Gamma sterilised and 100% leak-free single use bags  | From 272.-  |
|  | Cell Culture Bags Ultra Clear  | 10-50 litres  | Mammalian and plant cell culture  | Fits GE Wave rocking platform   6 ports   Solution ultra clear Flex 600 film   Gamma-sterilised and 100% leak-free single use bags   | From 232.-  |
| <b>Eppendorf</b><br>Hamburg, Germany<br>Contact: see page 56   | BioBLU 0.3c Single-Use Vessel  | 100-250 ml  | Mammalian and human cell lines, stem cells, insect cells  | Proven rigid wall stirred-tank design   Liquid-free Peltier condenser   Magnetic drive with 3-blade pitched-blade impeller   30-600 rpm   Industry standard sensors  | On request  |



Scalable Bioprocess Solutions:  
BioBLU® Rigid Wall Single-Use Vessels



# Highly Scalable

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With renowned expertise in plastics manufacturing, Eppendorf is proud to offer scalable single-use vessels to be operated with the DASbox® parallel mini bioreactors system, DASGIP® Parallel Bioreactor Systems or New Brunswick™ CelliGen® BLU controllers.

- > Proven for animal and human cell lines as well as bacteria and yeast
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- > User-friendly set-up for shorter development times and lower operating costs

[www.eppendorf.com](http://www.eppendorf.com)

| Bioreactors and Cell Bags  |                                   |  |  |   |             |
|--|-----------------------------------|--|--|---|-------------|
| Company/Distributor  | Name of Product                   | Volumes  | Applications   | Miscellaneous, Specialities, Generally  | Price [EUR] |
| <b>Eppendorf</b> (continued)<br>Hamburg, Germany<br><a href="http://www.eppendorf.com">www.eppendorf.com</a><br><b>Contact:</b><br>Phone +49 2232 4180 | BioBLU 1c Single-Use Vessel       | 320 ml - 1.25 litres   | Mammalian and human cell lines, stem cells, insect cells   | Proven rigid wall stirred-tank design   Liquid-free Peltier condensor   Magnetic drive with 3-blade pitched-blade impellers   20-500 rpm   Industry standard sensors  | On request  |
|  | BioBLU 5c Single-Use Vessel       | 1.25-3.75 litres   | Mammalian and human cell lines, stem cells, insect cells   | Proven rigid wall stirred-tank design   Liquid-free Peltier condensor   Magnetic drive with 3-blade pitched-blade impellers   25-200 rpm   Industry standard sensors, optional optical pH measurement   | On request  |
|  | BioBLU 14c Single-Use Vessel      | 3.5-10.5 litres  | See above  | See above   | On request  |
|  | BioBLU 50c Single-Use Vessel      | 18-40 litres   | Mammalian and human cell lines, stem cells, insect cells   | Proven rigid wall stirred-tank design   Magnetic drive with 3-blade pitched-blade impellers   25-150 rpm   Industry standard sensors, optional optical pH measurement   | On request  |
|  | BioBLU 0.3f Single-Use Vessel     | 65-250 ml  | Bacteria, yeast, fungi   | Proven rigid wall stirred-tank design   Liquid-free Peltier condensor   Magnetic drive with two 6-blade Rushton-type impellers   20-2000 rpm   Industry standard sensors  | On request  |
|  | BioBLU 1f Single-Use Vessel       | 250 ml - 1.25 litres   | Bacteria, yeast, fungi   | Proven rigid wall stirred-tank design   Liquid-free Peltier condensor   Magnetic drive with two 6-blade Rushton-type impellers   100-1600 rpm   Industry standard sensors   | On request  |
|  | BioBLU 0.3p Single-Use Vessel     | 250 ml   | Mammalian and human cell lines, stem cells, insect cells   | Proven rigid wall stirred-tank design   Magnetic drive with innovative FibraCel packed-bed impeller   25-150 rpm   Industry standard sensors, optional optical pH measurement   | On request  |
|  | BioBLU 5p Single-Use Vessel       | 3.75 litres  | See above  | See above   | On request  |
|  | DASbox                            | 60-250 ml  | Mammalian and human cell lines, stem cells, insect cells   Bacteria, yeast, fungi   Plant cells  | 4-fold parallel system (parallel operation of 4, 8, 12 or more bioreactors)   Glass and single-use bioreactors   Optimal for Design of Experiments (DoE)   Monitoring and precise control of all critical process parameters as well as mass flow-controlled gassing   Variable speed pumps for operation in batch, fed-batch, continuous and cyclic perfusion mode | On request  |
|  | DASGIP Parallel Bioreactor System | 35 ml - 3.8 litres   | Mammalian and human cell lines, stem cells, insect cells   Bacteria, yeast, fungi   Plant cells, algae, phototrophic bacteria  | 4-fold parallel system (parallel operation of 4, 8 or more bioreactors)   Glass and single-use bioreactors   Monitoring and precise control of all critical process parameters as well as mass flow-controlled gassing   Variable speed pumps for operation in batch, fed-batch, continuous and cyclic perfusion mode   Online calculation of OTR, CTR and RQ       | On request  |
|  | CelliGen BLU                      | 1.3-40 litres  | Mammalian and human cell lines, stem cells, insect cells   | Single-use bioreactors   Eliminates vessel auto-claving and cleaning   Monitoring and precise control of all critical process parameters   Touchscreen interface   Non-invasive DO and pH technology  | On request  |
|  | BioFlo / CelliGen 115             | 400 ml - 10.5 litres   | Mammalian and human cell lines, stem cells, insect cells   Bacteria, yeast, fungi   Plant cells, algae, phototrophic bacteria  | Entry-level system   Preprogrammed fermentation and cell culture modes   Glass and single-use bioreactors   Monitoring and precise control of all critical process parameters   Touchscreen interface for control of up to 3 bioreactor units   | On request  |
|  | BioFlo 310                        | 800 ml - 10.5 litres   | Mammalian and human cell lines, insect cells   Bacteria, yeast, fungi   Plant cells, algae, phototrophic bacteria  | Glass and single-use bioreactors   Broad range of accessories   Monitoring and precise control of all critical process parameters   Touchscreen interface for control of up to 4 bioreactor units   cGMP compatible   | On request  |
|  | CelliGen 310                      | 800 ml - 10.5 litres   | Mammalian and human cell lines, insect cells   Plant cells, algae, phototrophic bacteria   | Glass and single-use bioreactors   Broad range of accessories   Monitoring and precise control of all critical process parameters   Touchscreen interface for control of up to 4 bioreactor units   cGMP compatible   | On request  |
| BioFlo 415   | 2-15.5 litres                     | Bacteria, yeast, fungi   Plant cells, algae, phototrophic bacteria | Unique Sterilisable-In-Place (SIP) technology without external steam supply   Stainless steel bioreactor   Monitoring and precise control of all critical process parameters   Touchscreen interface   | On request  |             |
| BioFlo 510   | 5.2-32 litres                     | Bacteria, yeast, fungi   Plant cells, algae, phototrophic bacteria | Pilot Sterilisable-In-Place (SIP) stainless steel bioreactor   Multiple impeller and gas flow options   Monitoring and precise control of all critical process parameters   Fully automated SIP sequence for sterilisation   Touchscreen interface | On request  |             |



## Bioreactors and Cell Bags

| Company/Distributor  | Name of Product                           | Volumes                        | Applications   | Miscellaneous, Specialities, Generally  | Price [EUR] |
|--|---|--------------------------------|--|---|-------------|
| <b>Eppendorf</b> (continued)<br>Contact: see page 56         | CelliGen 510                              | 5.2-32 litres                  | Mammalian and human cell lines, insect cells   Plant cells, algae, phototrophic bacteria | Pilot Sterilisable-In-Place (SIP) stainless steel bioreactor   Multiple impeller and gas flow options   Monitoring and precise control of all critical process parameters   Fully automated SIP sequence for sterilisation   Touchscreen interface  | On request  |
|  | BioFlo 610                                | 13-100 litres                  | Bacteria, yeast, fungi   Plant cells, algae, phototrophic bacteria   Insect cells        | Pilot Sterilisable-In-Place (SIP) stainless steel bioreactor   Mobile skid for simplified transport   Monitoring and precise control of all critical process parameters   Integrated load cell for online volume monitoring   Touchscreen interface   | On request  |
|  | BioFlo Pro                                | 32-2,400 litres                | Bacteria, yeast, fungi   Plant cells, algae, phototrophic bacteria                       | Large scale Sterilisable-In-Place (SIP) stainless steel bioreactor   Multiple impeller and gas flow options   Open piping skid for easy accessibility   Monitoring and precise control of all critical process parameters   Touchscreen interface   | On request  |
|  | CelliGen Pro                              | 18.8-520 litres                | Mammalian and human cell lines, insect cells   Plant cells, algae, phototrophic bacteria | See above   | On request  |
| <b>GE Healthcare Life Sciences</b><br>www.gelifesciences.com | ReadyToProcess WAVE 25 system             | 300 ml - 25 litres             | Convenient handling and control of cell cultures up to 25 litres                         | Consists of a rocker, a gas mixer/controller and a pump, all operated by Unicorn software installed on a client computer   The system is equipped with integrated temperature sensors and load cells and it supports pH, DO control and perfusion culture   Suitable for use in a regulated environment   CFR Part 11 compliant | On request  |
|  | WAVE Bioreactor System 20/50              | 300 ml - 25 litres             | Basic rocking bioreactor for cell cultures up to 25 litres                               | Basic rocker with integrated temperature sensors and CO <sub>2</sub> mixer  | On request  |
|  | WAVE Bioreactor 200                       | 10-100 litres                  | Rocking bioreactor cell cultures up to 100 litres  | Self-contained system with integral temperature control, aeration pump and rocking controller   | On request  |
|  | WAVE Bioreactor 500/1000                  | 25-500 litres                  | Rocking bioreactor cell cultures up to 500 litres  | See above   | On request  |
|  | Cellbag 2L (BC10, Basic)                  | 1 litre                        | Upstream Bioprocessing   | Single use culture bag for use with ReadyToProcess WAVE 25 or WAVE Bioreactor 20/50   | On request  |
|  | Cellbag 2L (BC10, DO)                     | 1 litre                        | Upstream Bioprocessing   | See above   | On request  |
|  | Cellbag 2L (BC10, Perfusion, DO)          | 1 litre                        | Upstream Bioprocessing   | See above   | On request  |
|  | Cellbag 10L (BC10, Basic)                 | 5 litres                       | Upstream Bioprocessing   | Single use culture bag for use with ReadyToProcess WAVE 25 or WAVE Bioreactor 20/50   | On request  |
|  | Cellbag 10L (BC10, Perfusion, DO)         | 5 litres                       | Upstream Bioprocessing   | See above   | On request  |
|  | Cellbag 20L (BC10, Basic)                 | 5 litres                       | Upstream Bioprocessing   | See above   | On request  |
|  | Cellbag 20L (BC10, DO)                    | 10 litres                      | Upstream Bioprocessing   | See above   | On request  |
|  | Cellbag 20L (BC10, Perfusion, DO)         | 10 litres                      | Upstream Bioprocessing   | See above   | On request  |
|  | Cellbag 50L (BC10, Basic)                 | 2,5-25 litres                  | Upstream Bioprocessing   | Single use culture bag for use with ReadyToProcess WAVE 25 or WAVE Bioreactor 20/50   | On request  |
|  | Cellbag 50L (BC10, Perfusion, DO)         | 2,5-25 litres                  | Upstream Bioprocessing   | See above   | On request  |
|  | Cellbag 50L (BC10, DO)                    | 2,5-25 litres                  | Upstream Bioprocessing   | See above   | On request  |
|  | Cellbag 50L (BC10, Perfusion, DO)         | 2,5-25 litres                  | Upstream Bioprocessing   | See above   | On request  |
|  | Cellbag 100L (Oxywell Version)            | 2,5-50 litres                  | Upstream Bioprocessing   | Single use culture bag for use with WAVE Bioreactor 200   | On request  |
|  | Cellbag 200L (Oxywell Version)            | 10-100 litres                  | Upstream Bioprocessing   | See above   | On request  |
|  | Cellbag 1000L (pH Version)                | 50-500 litres                  | Upstream Bioprocessing   | Single use culture bag for use with WAVE Bioreactor 500/1000  | On request  |
|  | Cellbag 500L (pH Version)                 | 25-250 litres                  | Upstream Bioprocessing   | See above   | On request  |
|  | Xcellerex Single-use Bioreactor XDR-10 SV | 4.5-10 litres (working volume) | Cell culture; batch, fed-batch, perfusion  | MFCs, pumps, touchscreen, PLC control   | On request  |

| Bioreactors and Cell Bags   |   |  |  |  |             |
|---|---|--|--|--|-------------|
| Company/Distributor   | Name of Product                           | Volumes                                      | Applications   | Miscellaneous, Specialities, Generally   | Price [EUR] |
| <b>GE Healthcare Life Sciences</b> (continued)  | Xcellerex Single-use Bioreactor XDR-10 MV | Up to 4 times 4.5-10 litres (working volume) | Cell culture; batch, fed-batch, perfusion  | Multi-vessel controller  | On request  |
|   | Xcellerex Single-use Bioreactor XDR-50    | 22-50 litres                                 | See above  | Jacketed stainless vessel, modular, turn-key   | On request  |
|   | Xcellerex Single-use Bioreactor XDR-200   | 40-200 litres                                | See above  | See above  | On request  |
|   | Xcellerex Single-use Bioreactor XDR-500   | 100-500 litres                               | See above  | See above  | On request  |
|   | Xcellerex Single-use Bioreactor XDR-1000  | 200-1,000 litres                             | See above  | Bottom drive, bag hoist  | On request  |
|   | Xcellerex Single-use Bioreactor XDR-2000  | 400-2,000 litres                             | See above  | See above  | On request  |
|   | Xcellerex Single-use Fermentor XDR-50     | 25-50 litres                                 | Microbial fermentation; batch, fed-batch, chemostat  | Rushton impeller, condenser, large exhaust   | On request  |
|   | Xcellerex Single-use Fermentor XDR-200    | 40-200 litres (working volume)               | See above  | See above  | On request  |
|   | Xcellerex Single-use Dual-Purpose XDR-50  | 25-50 litres (working volume)                | Cell culture and Microbial fermentation; batch, fed-batch, chemostat   | Application-specific bag & accessories   | On request  |
|   | Xcellerex Single-use Dual-Purpose XDR-200 | 40-200 litres (working volume)               | See above  | See above  | On request  |
| <b>Greiner Bio-One</b><br>Kremsmuenster, Austria<br>www.gbo.com<br>Contact: office@at.gbo.com<br>Phone +43 7583 6791-0                          | CELLreactor                               | 15 ml<br>50 ml                               | Culture of cells, bacteria and other microorganisms   Plasmid preparation   Production of antibodies and recombinant proteins in cells | Culture and centrifugation in one tube   Excellent gas exchange through filter screw cap (0.2 µm capillary pore membrane and 6 cap openings)   Easy to use with standard orbital shakers   Ideal for parallelisation e.g. optimisation of culture conditions | On request  |
| <b>Infors HT</b><br>Einsbach, Germany<br>www.infors-ht.de<br>Contact:<br>infors.de@infors-ht.com<br>Phone +49 81 35 83 33                       | Minifors                                  | 0.6-3.5 litres (working volume)              | Fermentation; cell culture   | For entry-level fermentation   | On request  |
|   | Multifors 2                               | 0.1-1.0 litres (working volume)              | Fermentation; cell culture   | Parallel bioreactor with up to 6 vessels   | On request  |
|   | Labfors 5                                 | 0.5-10 litres (working volume)               | Fermentation; cell culture   | First bench-top bioreactor with CIP/SIP  | On request  |
|   | Labfors 5 Lux                             | 1.6-1.8 litres (working volume)              | Photosynthetic culture   | Flat panel vessel with LED lightning   | On request  |
|   | Labfors 5 BioEtOH                         | 1.0-2.5 litres (working volume)              | Bioethanol   | Simultaneous saccharification and fermentation   | On request  |
|   | Techfors-S                                | 3- 30 litres (working volume)                | Fermentation; cell culture   | <i>In situ</i> sterilisable pilot bioreactor   | On request  |
|   | Techfors                                  | 5-670 litres (working volume)                | Fermentation; cell culture   | Flexible and sophisticated pilot bioreactor  | On request  |
|   | Terrafors-IS                              | 3-4 kg solids/semi-solids or 7 litres liquid | Solid state  | Compact & <i>in situ</i> sterilisable  | On request  |
| <b>Integra Biosciences</b><br>Fernwald, Germany<br>www.integra-biosciences.de<br>Contact:<br>info@integra-biosciences.de<br>Phone +49 6404 8090 | Celline CL-1000                           | 1,000 ml                                     | MAK-production, recombinant proteins   | Simple handling, high yields, small footprint   Membrane technology   Homogeneous mixing and gas transfer  | 530.-       |
|   | Celline CL-350                            | 350 ml                                       | See above  | See above  | 730.-       |
|   | Celline AD-1000                           | 1,000 ml                                     | See above  | See above  | 530.-       |
| <b>m2p-labs</b><br>Baesweiler, Germany<br>www.m2p-labs.com<br>Contact:<br>info@m2p-labs.com<br>Phone +49 2401 805330                            | BioLector Microbioreactor                 | 48/96 wells                                  | Synthetic biology, clone screening, media optimisation, bio process development, anaerobic and micro-aerophilic fermentation           | Biomass/ pH / DO/fluorescence measurements   Real time kinetic   Micro fermentation in standard MTP format   Excellent reproducibility   High throughput   | On request  |
|   | RoboLector Automated Microbioreactor      | 48 wells                                     | Triggered processing, growth synchronisation, induction / -pH profiling, process characterisation, DoE (Design of Experiment)          | In combination with BioLector or BioLector Pro   Automated upstream-process   Media preparation   Automated sampling   | On request  |
|   | BioLector Pro Microbioreactor             | 48 (32 wells, 16 reservoir wells)            | See above, fed-batch development, -pH profiling, feeding rate optimisation, induction profiling  | See above   pH control by acid or/and base   Triggered upstream (linear, exponential or continuous mode)   Easy scale up to lab fermenters   | On request  |



## Bioreactors and Cell Bags

| Company/Distributor  | Name of Product  | Volumes  | Applications  | Miscellaneous, Specialities, Generally  | Price [EUR]                           |
|--|--|--|---|---|---------------------------------------|
| <b>Miltenyi Biotec</b><br>Bergisch Gladbach,<br>Germany<br>www.miltenyibiotec.com<br><b>Contact:</b><br>macs@miltenyibiotec.de<br>Phone +49 2204 83060 | MACS GMP Cell Expansion Bags   | Compartmentalised culture chamber with easy-to-open seals. This allows for expandable culture volume from 8-100 ml           | <i>in vitro</i> cultivation and expansion of human cells from heterogeneous hematologic cell populations (e.g. for the expansion of antigen-specific T cells) | 5 units, individually packed; sterile, tested for endotoxins, gas-permeable and transparent for microscopy   Manufactured and tested under a certified ISO 9001 quality system  | On request                            |
|  | MACS GMP Cell Differentiation Bag<br>- 100<br>- 250<br>- 500<br>- 1000<br>- 3000 | Nominal:<br>100 ml (minimal fill volume 20 ml)<br>250 ml (30 ml)<br>500 ml (50 ml)<br>1,000 ml (120 ml)<br>3,000 ml (220 ml) | <i>in vitro</i> cultivation and expansion of cells from heterogeneous hematologic cell populations  | See above   | On request                            |
| <b>MoBiTec</b><br>Goettingen, Germany<br>www.mobitec.com<br><b>Contact:</b> Arne Schulz<br>info@mobitec.com<br>Phone +49 551 707220                    | 2 l Fermenter Complete   | 1-2 litres   | Bench-top handling  | Strong heating element (50 W for 220 V version; 100 W for 110 V version) with precise temperature regulation ( $\pm 0.5$ °C)   Variable control pump delivers air to the bubbler   For special gas mixtures, connections to cylinders are also possible   Delivered with all essential components required for its use  | Please contact your local distributor |
|  | 100 ml Fermenter Complete  | 100 ml   | Bench-top handling  | Heating provided by warmed water flowing through the glass envelope (external water bath needed)   Delivered with the following components: Screw caps, sterile air filters (hydrophobic), bubbler, needles for taking samples, silicone tubing   Replacement parts and suggested improvements are available separately | Please contact your local distributor |
| <b>Pierre Guerin/Biolafitte</b><br>St. Cloud (MN), USA<br>www.dci-bio.com<br><b>Contact:</b> info@dci-bio.com<br>Phone +1 320 257 4378                 | Tryton (Autoclavable fermenters and Bioreactors)                                 | 1-10 litres  | Microbial fermentation and cell cultivation   | Dedicated to start-up, universities, R&D laboratories   | From 25,000.-                         |
|  | BioPro EVO (SIP fermenters)  | 10-30 litres   | Microbial fermentation  | See above   | From 70,000.-                         |
|  | BioPro Lab & Pilot Series (SIP fermenters)                                       | 10-300 litres  | Microbial fermentation  | Dedicated to R&D laboratories, biotech industries   | From 100,000.-                        |
|  | BioPro Industrial (SIP fermenters)   | 350-30,000 litres  | Microbial fermentation  | Dedicated to biotech industries   | From 500,000.-                        |
|  | BioCell Lab & Pilot (SIP Bioreactors)  | 10-300 litres  | Cell cultivation  | Dedicated to start-up, universities, R&D laboratories and biotech industries  | From 150,000.-                        |
|  | BioCell Industrial (SIP Bioreactors)   | 350-30,000 litres  | Cell cultivation  | Dedicated to biotech industries, vaccine, mAb's and recombinant proteins manufacturers  | From 550,000.-                        |
|  | Nucleo (Disposable Bioreactors)  | 25-1,000 litres  | Cell cultivation  | See above   | From 100,000.-                        |
|  | BioVessel (Formulation vessels)  | 10-40,000 litres   | Formulation & filling   | Dedicated to the pharmaceutical industries  | From 50,000.-                         |
| BioClean (CIP Units)   | 450 litres   | Cleaning in place  | Dedicated to bio-pharmaceutical industries for cleaning-in-place  | From 90,000.-   |                                       |
| <b>Pall Corporation</b><br>Port Washington (NY), USA<br>www.pall.com<br><b>Contact:</b><br>Phone +1 516 484 3600                                       | Micro-24 Micro-reactor System  | 24 wells with 10 ml each (5-7 ml working volume)   | Rapid microbial and cell culture development  | 24 simultaneous experiments with independent control of each reactor's DO, temperature and pH   | 90,000.-                              |
|  | Allegro XRS20 Single-Use Bioreactor  | 20 litres  | Therapeutic proteins, viral vaccines, cell therapy  | Rocker style, advanced biaxial agitation  | 55,000.-                              |
|  | Allegro STR200 Single-Use Bioreactor   | 200 litres   | Therapeutic proteins, viral vaccines, cell therapy  | Single-use stirred bioreactor   | 185,000.-                             |
|  | Integrity Pad-Reactor Mini   | 16 litres (5 to 13 litres working volume)  | Therapeutic proteins, viral vaccines, cell therapy  | Small scale single-use paddle agitated square bioreactor  | 14,000.-                              |
|  | Integrity PadReactor   | 25, 50, 125, 250, 600, 1,200 litres in total (8-1,000 litres working volume)   | Therapeutic proteins, viral vaccines, cell therapy  | Single-use paddle agitated square bioreactor  | 65,000.- to 115,000.-                 |
|  | Integrity iCellis nano   | 0.53-4 m <sup>2</sup>  | Therapeutic proteins, viral vaccines  | Small scale, fixed-bed single-use bioreactor  | 14,000.-                              |
|  | Integrity iCellis  | 66-500 m <sup>2</sup>  | Therapeutic proteins, viral vaccines  | Production scale, fixed-bed single-use bioreactor   | 225,000.-                             |
|  | Integrity Xpansion   | 600-122,000 cm <sup>2</sup>  | Cell therapy  | Multiplate bioreactor cell expansion system   | 1,800.- to 9,900.-                    |

| Bioreactors and Cell Bags   |   |  |  |  |   |
|---|---|--|--|--|---|
| Company/Distributor   | Name of Product   | Volumes  | Applications   | Miscellaneous, Specialities, Generally   | Price [EUR]   |
| <b>Sarstedt</b><br>Nuembrecht, Germany<br>www.sarstedt.com<br>Contact: info@sarstedt.com<br>Phone +49 2293 305 0  | miniPerm Bioreactor   | Production module<br>35 ml and 50 ml,<br>nutrient module<br>max. 400 ml              | Cultivation of hybridoma<br>cells   Biomass production  <br>Cultivation of transfected cells<br>for obtaining recombinant<br>proteins or viruses   | High cell densities   High product concentration  <br>Easy handling   Multiple harvesting   The production<br>module is available in various sizes   | On request  |
| <b>Sartorius Stedim<br/>Biotech</b><br>Goettingen, Germany<br>www.sartorius.de<br>Contact:<br>info@sartorius.com<br>Phone +49 551 3080  | Biostat RM  | 20/50/200 litres   | Cell culture – mammalian, in-<br>sect & plant cells   Shear sen-<br>sitive cells such as stem cells<br>  Suspension cells & adherent<br>cells on micro-carriers etc.   | Fully GMP-compliant single-use bioreactor („wave<br>induced mixing”   As seed production for large<br>bioreactors   Easy to use rocker with advanced<br>control capabilities   Space-saving, individual<br>control of two bags on the same platform  | From<br>15,000.-  |
|   | Flexsafe RM   | 0.1-100 litres<br>(working volumes)  | See above  | Same film material across all cell culture steps  <br>Optimised resin with minimised additive package for<br>excellent and consistent cell growth performance  <br>Robust and strong 2D-single use bag with optical sen-<br>sors for pH, DO and biomass measurement   Custom-<br>ised bag designs (configurations) possible   Compat-<br>ible with other wave-induced mixing bioreactors   | From 140.-  |
|   | Biostat STR, CultiBag<br>STR  | 50 / 200 / 500 /<br>1,000 / 2,000 litres /<br>12.5-2,000 litres<br>(working volumes) | Cell culture – mammalian,<br>insect and plant cells   High<br>cell density suspension cell<br>culture   Adherent cell culture<br>on microcarriers   Production<br>of rec. proteins (mAb) and<br>vaccines   Ideal for process<br>development in R&D and<br>for GMP large scale manu-<br>facturing | Stirred single-use bioreactor in classical design  <br>Scalability up to 2,000 litres – geometrical similarity<br>  Consistent and efficient aeration and mixing<br>strategies   Single as well as twin configuration of<br>Biostat STR with fully independent process control<br>for extra small space requirement is available  <br>Reliable optical single-use sensors for pH and DO<br>measurement   Holistic process safety concept | From<br>70,000.-  |
|   | Biostat A   | 1–5 litres   | Cell cultivation and microbial<br>fermentation   | Entry-level bioreactor/fermenter designed for easy<br>control of cell growth and fermentation   Simple and<br>automatic aeration system   Intuitive operation  <br>Integrated recirculating chiller for microbial<br>fermentation   Flexibility between choosing a<br>UniVessel Glass or UniVessel SU  | On request  |
|   | Biostat B   | 1–10 litres  | Cell cultivation and microbial<br>fermentation   | Stirred and rocked, reusable and single-use culture<br>vessels   Single or Twin set-up for control of one or<br>two vessels   Freely configurable   Gassing system<br>comparable to our STR and with up to four mass flow<br>controllers   | On request  |
|   | Biostat B-DCU II  | 0.5–10 litres  | Cell cultivation and microbial<br>fermentation   | Compact design with independent process control<br>for up to six culture vessels   Superior gas mixing  <br>Up to six integrated peristaltic pumps   Glass<br>or single-use culture vessel   Non-invasive optical<br>pH and DO single-use measurement when operated<br>with the UniVessel SU   | On request  |
|   | Biostat Cplus   | 5-30 litres  | Cell cultivation and microbial<br>fermentation   | Sterilisable-In-Place (SIP) stainless steel fermenter  <br>bioreactor   Closed loop temperature control<br>system   Compact and mobile design  <br>Open frame piping skid  | On request  |
|   | Biostat D-DCU   | 10-200 litres  | Cell cultivation and microbial<br>fermentation   | Sterilisable-In-Place (SIP) stainless steel fermenter/<br>bioreactor   Single or twin configuration   Fully<br>configurable   Automatic SIP and Cleaning-In-Place<br>(CIP) sequences   Powerful industrial-rated<br>DCU control system   | On request  |
|   | UniVessel SU  | 2 litres   | Cell culture   | Compatible with your existing bioreactor controller<br>  Completely single-use from vessel to sensor  <br>Proven and scaleable design   Interchangeable with<br>glass vessels   Single-use sensors   | On request  |
|   | <b>Scienova</b><br>Jena, Germany<br>www.scienova.com<br>Contact: info@scienova.com<br>Phone +49 3641 504586 | MD 100<br>MD 300   | 100 µl<br>300 µl   | Protein <i>in vitro</i> synthesis,<br>enzyme reactor, cell culture<br>(Erythrocytes)   | Compatible with microplate format   Easy handling,<br>autoclavable   Different membranes and high<br>surface to volume ratio for fast compound exchange |
| <b>Takara Bio Europe</b><br>St.Germain-en-Laye, France<br>www.clontech.com/takara<br>Contact:<br>orders@takara-clontech.eu<br>Phone +33 1 3904 6880<br><b>Clontech (Manufacturer)</b> | CultiLife Spin  | 60 cm <sup>2</sup> culturing surface   | Retroviral and lentiviral gene<br>delivery, gene therapy   | Can be coated with RetroNectin (incl. GMP-<br>compliant version) for enhanced viral transduction<br>efficiency   Can be centrifuged to intensify binding<br>of virus to the coating and increase transduction<br>efficiency (centrifuge adapter sold separately)  <br>The flat underside of the cell bag facilitates micro-<br>scopic observation  | 872.-<br>(10 cell<br>bags)  |



# Calendar

## 2014

6/7-10/7 Bad Honnef (DE)  
**3rd International Congress of Respiratory Science**,  
 Info: [www.respiratory-science.org](http://www.respiratory-science.org)

6/7-10/7 Gatersleben (DE)  
**17th International Symposium on Iron Nutrition and Interactions in Plants - 12th Gatersleben Research Conference**, Info: <http://isinip2014.ipk-gatersleben.de>

6/7-10/7 Rhodes (GR)  
**16th International Congress on Molecular Plant-Microbe Interactions**, Info: [www.mpmi2014rhodes-hellas.gr](http://www.mpmi2014rhodes-hellas.gr)

6/7-10/7 Sheffield (UK)  
**18th International Meeting on Oxygen-Binding and Sensing Proteins**,  
 Info: [www.sebiology.org/meetings](http://www.sebiology.org/meetings)

6/7-11/7 Lucca/Barga (IT)  
**Gordon Research Conference: Mitochondria and Chloroplasts**,  
 Info: [www.grc.org](http://www.grc.org)

8/7-9/7 Cambridge (UK)  
**Biomarkers in CNS Drug Discovery and Development: From Discovery to Clinical Diagnostics**,  
 Info: [www.selectbiosciences.com](http://www.selectbiosciences.com)

8/7-11/7 Dresden (DE)  
**5th International Congress on Stem Cells and Tissue Formation (SCC)**, Info: [www.stemcellcongress-dresden.org](http://www.stemcellcongress-dresden.org)

10/7-11/7 Lago Maggiore (IT)  
**Multiple Mechanisms of Neurodegeneration and Progression - IBRO Symposium (International Brain Research Organization)**,  
 Info: [www.facebook.com/events/275472752606617](http://www.facebook.com/events/275472752606617)

12/7-15/7 St. Petersburg (RU)  
**9th International Conference on Mass Data Analysis of Images and Signals**, Info: [www.mda-signals.de](http://www.mda-signals.de)

12/7-17/7 Lisbon (PT)  
**18th European Bioenergetics Conference**, Info: [www.ebec2014.org](http://www.ebec2014.org)

12/7-18/7 Lucca/Barga (IT)  
**Gordon Research Seminar and Conference: Single Molecule Approaches to Biology**, Info: [www.grc.org/meetings.aspx?year=2014](http://www.grc.org/meetings.aspx?year=2014)

12/7-24/7 St. Petersburg (RU)  
**World Congress on the Frontiers in Intelligent Data and Signal Analysis**,  
 Info: [www.worldcongressdsa.com](http://www.worldcongressdsa.com)

13/7-16/7 Edinburgh (UK)  
**16th European Congress on Biotechnology**,  
 Info: [www.ecb16.com](http://www.ecb16.com)

14/7-15/7 Cambridge (UK)  
**4th International Cambridge Stem Cell Institute Symposium: Stem Cells in Medicine**,  
 Info: [www.stemcells.cam.ac.uk/news-events/events](http://www.stemcells.cam.ac.uk/news-events/events)

14/7-15/7 London (UK)  
**Immunogenicity Conference**,  
 Info: [www.smi-online.co.uk/pharmaceuticals/uk/conference/Immunogenicity](http://www.smi-online.co.uk/pharmaceuticals/uk/conference/Immunogenicity)

14/7-16/7 Chester (UK)  
**Angiogenesis and Vascular Re-Modelling: New Perspectives**,  
 Info: [www.biochemistry.org/Conferences](http://www.biochemistry.org/Conferences)

14/7-18/7 Zurich (CH)  
**EMBO Conference on Viruses of Microbes: Structure and Function, from Molecules to Communities**, Info: <http://events.embo.org/14-virus-microbe>

15/7 London (UK)  
**Molecular Mechanisms in Signal Transduction - Symposium**,  
 Info: <https://bsi.immunology.org>

16/7-19/7 Zurich (CH)  
**ParaTrop2014: 26th Annual Meeting of the German Society for Parasitology / Meeting of the German Society for Tropical Medicine and International Health / 72nd Meeting of the Swiss Society of Tropical Medicine and Parasitology (Joint Meeting)**,  
 Info: [www.paratrop2014.uzh.ch](http://www.paratrop2014.uzh.ch)

17/7-20/7 Prague (CZ)  
**European Conference on Behavioural Biology (ECBB)**, Info: [www.ecbb2014.agrobiology.eu](http://www.ecbb2014.agrobiology.eu)

19/7-25/7 Girona (ES)  
**Gordon Research Seminar and Conference: Thiol-Based Redox Regulation and Signaling**,  
 Info: [www.grc.org/meetings.aspx?year=2014](http://www.grc.org/meetings.aspx?year=2014)

22/7-25/7 Vienna (AT)  
**Euro EvoDevo 2014: 5th Meeting of the European Society for Evolutionary Developmental Biology (EED)**, Info: <http://evodevo2014.univie.ac.at>

23/7-26/7 Cambridge (UK)  
**3rd Wellcome Trust Conference on Nicotinic Acetylcholine Receptors**, Info: [www.hinxton.wellcome.ac.uk](http://www.hinxton.wellcome.ac.uk)

23/7-26/7 Heidelberg (DE)  
**EMBL Conference: Microfluidics**,  
 Info: [www.embl.de/training/events/2014/MCF14-01](http://www.embl.de/training/events/2014/MCF14-01)

23/7-26/7 Potsdam (DE)  
**Life at the Edge: The Nuclear Envelope in Transport Genome Organisation and the Cell Cycle**, Info: <https://nuclearenvelope2014.com>

26/7-1/8 Girona (ES)  
**Gordon Research Seminar and Conference: Neurobiology of Brain Disorders**, Info: [www.grc.org/meetings.aspx?year=2014](http://www.grc.org/meetings.aspx?year=2014)

29/7-30/7 London (UK)  
**The Biological and Biomedical Consequences of Protein Moonlighting**, Info: [www.biochemistry.org/Conferences](http://www.biochemistry.org/Conferences)

29/7-30/7 Norwich (UK)  
**Meeting of New Phytologist Next Generation Scientists**,  
 Info: [www.newphytologist.org/symposiums](http://www.newphytologist.org/symposiums)

3/8-7/8 Edinburgh (UK)  
**11th International Congress on the Biology of Fish (ICBF2014)**,  
 Info: <http://icbf2014.sls.hw.ac.uk>

3/8-7/8 Mainz (DE)  
**Annual Meeting of the Society of Invertebrate Pathology (SIP 2014)**, Info: [www.sipweb.org](http://www.sipweb.org)

3/8-7/8 Potsdam (DE)  
**Annual International Dictyostelium Conference (Dicty 2014)**, Info: [www.dicty2014.de](http://www.dicty2014.de)

3/8-8/8 Lucca/Barga (IT)  
**Polycystic Kidney Disease: From Molecular Mechanism to Therapy**, Info: <https://secure.faseb.org>

3/8-8/8 York (UK)  
**10th European Congress of Entomology**, Info: [www.royensoc.co.uk/meetings](http://www.royensoc.co.uk/meetings)

10/8-15/8 Potsdam (DE)  
**8th International Congress of Dipterology**, Info: [www.icd8.org](http://www.icd8.org)



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20/8-23/8 Heidelberg (DE)

**EMBO Conference on Chemical Biology,**

Info: [www.embo.org/events](http://www.embo.org/events)

23/8-27/8 Heidelberg (DE)

**11th EMBL Conference: Transcription and Chromatin,**

Info: [www.embo-embl-symposia.org/symposia/2014/EES14-04](http://www.embo-embl-symposia.org/symposia/2014/EES14-04)

24/8-28/8 Poznan (PL)

**21st International Round Table: Nucleosides, Nucleotides and Nucleic Acids – Chemical Biology of Nucleic Acids,** Info: [www.irt2014.pl](http://www.irt2014.pl)

24/8-28/8 Prague (CZ)

**9th World Congress on Alternatives and Animal Use in the Life Sciences,** Info: [www.wc9prague.org](http://www.wc9prague.org)

24/8-28/8 Stockholm (SE)

**22nd International Conference on Pattern Recognition (ICPR 2014),** Info: [www.icpr2014.org](http://www.icpr2014.org)

25/8-28/8 Ascona (CH)

**Early Events in Virus Infection – Conference,** Info:

<http://events.mnf.uzh.ch>

25/8-29/8 Rennes (FR)

**27th Conference of European Comparative Endocrinologists (CECE 2014),**

Info: [www.cece2014.org](http://www.cece2014.org)

27/8-30/8 Heidelberg (DE)

**EMBO-EMBL Symposium on Epithelial Biology: The Building Blocks of Multicellularity,**

Info: [www.embo.org/events](http://www.embo.org/events)

30/8-4/9 S. Feliu de Guixols (ES)

**EMBO Conference on Synthetic Biology of Antibiotic Production II,**

Info: <http://syntheticbio.esf.org>

30/8-4/9 Paris (FR)

**FEBS-EMBO 2014: Joint Conference of the Federation of European Biochemical Societies, the European Molecular Biology Organization & the French Society for Biochemistry & Molecular Biology,**

Info: [www.febs-embo2014.org](http://www.febs-embo2014.org)

31/8-4/9 Egmond aan Zee (NL)

**11th Symposium on Lactic Acid Bacteria – Health, Sustainability, Diversity and Application,**

Info: [www.lab11.org](http://www.lab11.org)

31/8-4/9 Hamburg (DE)

**1st INPPO World Congress on Plant Proteomics: Methodology to Biology,** Info:

[www.inppo2014.uni-hamburg.de](http://www.inppo2014.uni-hamburg.de)

1/9-2/9 Loughborough (UK)

**Emerging Challenges and Opportunities in Soil Microbiology,**

Info: [www.sgm.ac.uk/en/events/conferences](http://www.sgm.ac.uk/en/events/conferences)

1/9-3/9 Hull (UK)

**14th Conference of the Collaborative Computing Project for NMR (CCPN),**

Info: [www.ccpn.ac.uk/meetings](http://www.ccpn.ac.uk/meetings)

1/9-4/9 Nantes (FR)

**Food Micro 2014 – 24th Conference of the International Committee on Food Microbiology and Hygiene (ICFMH),**

Info: [www.foodmicro2014.org](http://www.foodmicro2014.org)

1/9-5/9 Cambridge (UK)

**Harden Conference: Total Transcription,** Info: [www.biochemistry.org/Conferences](http://www.biochemistry.org/Conferences)

1/9-6/9 Hydra (GR)

**Molecular and Cellular Biology of Helminth Parasites VII (2014 Hydra Conference),**

Info: <http://hydra.bio.ed.ac.uk/content/hydra-2012>

2/9-4/9 Edinburgh (UK)

**3rd World Congress of Reproductive Biology (WCRB),**

Info: [www.grc.org/meetings.aspx?year=2014](http://www.grc.org/meetings.aspx?year=2014)

4/9-7/9 Cambridge (UK)

**The Dynamic Cell 2014 – Joint Conference of the British Society of Cell Biology and the Biochemical Society,**

Info: [www.jointbscbbbs.org](http://www.jointbscbbbs.org)

5/9-8/9 La Ciotat (FR)

**EMBO Conference on Brain Development and Disorders,**

Info: [www.embo.org/events](http://www.embo.org/events)

6/9-10/9 Portorož (SI)

**14th International Symposium on Proteinases, Inhibitors & Biological Control,** Info: [http://eventgrids.com/events/2014\\_XIVth\\_International\\_Symposium\\_on\\_Proteinases](http://eventgrids.com/events/2014_XIVth_International_Symposium_on_Proteinases)

6/9-10/9 Roscoff (FR)

**Infectious Diseases as Drivers of Evolution: the Challenge Ahead,** Info: [www.cnrs.fr/insb/cjm/2014/Milinski\\_e.html](http://www.cnrs.fr/insb/cjm/2014/Milinski_e.html)

6-10/9 San Feliu de Guixols (ES)

**EMBO Conference on the Molecular and Cellular Basis of Regeneration & Tissue Repair,** Info: <http://events.embo.org/14-regeneration>

7/9-9/9 Stockholm (SE)

**Nordic Life Science Days 2014,** Info: [www.nlsdays.com/](http://www.nlsdays.com/)

7/9-10/9 Edinburgh (UK)

**50th Congress of the European Societies of Toxicology (Eurotox 2014),** Info: [www.eurotox2014.com](http://www.eurotox2014.com)

7/9-10/9 Tenerife (ES)

**11th European Nitrogen Fixation Conference,** Info: [www.enfc2014.com](http://www.enfc2014.com)

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**International Conference on Gonadotropins & Receptors**, Info: <http://bios.tours.inra.fr/ICGR11>

7/9-11/9 Lisbon (PT)

**23rd International Symposium on Medicinal Chemistry (EFMC-ISMC 2014)**, Info: [www.ismc2014.org](http://www.ismc2014.org)

7/9-11/9 St. Petersburg (RU)

**10th International Congress on Extremophiles**, Info: [www.extremophiles2014.ru](http://www.extremophiles2014.ru)

7/9-12/9 Monte Verità (CH)

**Monte Verità CSF Conference: Hand, Brain and Technology**, Info: [www.relab.ethz.ch/hbt2014](http://www.relab.ethz.ch/hbt2014)

7/9-12/9 Prague (CZ)

**18th International Microscopy Congress**, Info: [www.imc2014.com](http://www.imc2014.com)

9/9-10/9 Goettingen (DE)

**1st International Conference on Post-Translational Modifications in Bacteria**, Info: [www.efb-central.org/FunctionalGenomics/Docs/PTMannouncement.pdf](http://www.efb-central.org/FunctionalGenomics/Docs/PTMannouncement.pdf)

9/9-10/9 Bristol (UK)

**Arabidopsis: The Ongoing Green Revolution (GARNet 2014)**, Info: [www.garnet2014.org](http://www.garnet2014.org)

9/9-11/9 Oxford (UK)

**Influenza 2014 – One Influenza, One World, One Health**, Info: [www.lpmhealthcare.com/influenza-2014](http://www.lpmhealthcare.com/influenza-2014)

9/9-12/9 Trondheim (NO)

**Virtual Physiological Human Conference**, Info: [www.physoc.org/virtual-physiological-human-2014](http://www.physoc.org/virtual-physiological-human-2014)

10/9-12/9 Edinburgh (UK)

**Protein Acylation: From Mechanism to Drug Discovery – A Biochemical Society Meeting**, Info: [www.biochemistry.org/Conferences](http://www.biochemistry.org/Conferences)

10/9-12/9 London (UK)

**Metabomeeting 2014 (Metabolic Profiling Forum)**, Info: [www.selectbiosciences.com/meta2014](http://www.selectbiosciences.com/meta2014)

10/9-13/9 Murnau (DE)

**5th Murnau Conference on Structural Biology – Signal Transduction**, Info: [www.murnauconference.de](http://www.murnauconference.de)

10/9-13/9 Sofia (BG)

**16th Congress of the European Neuroendocrine Association**, Info: [www.eneassoc.org/meetings.htm](http://www.eneassoc.org/meetings.htm)

11/9-12/9 Vilnius (LT)

**Life Sciences Baltics 2014: The Biochemistry, Biology and Pathology of MAP Kinases II**, Info: [www.lsb2014.com](http://www.lsb2014.com)

11/9-12/9 York (UK)

**Global Microbial Identifier – 7th Meeting**, Info: [www.fera.co.uk/events/GMI2014](http://www.fera.co.uk/events/GMI2014)

11/9-13/9 Hertfordshire (UK)

**A Biochemical Society Focused Meeting on Single Biomolecules – in silico, in vitro and in vivo**, Info: [www.biochemistry.org/Conferences](http://www.biochemistry.org/Conferences)

11/9-14/9 Uddevalla (SE)

**18th International Conference on Lymphatic Tissues and Germinal Centres in Immune Reactions (Germinal Centre Conference)**, Info: [www.gcc18.com](http://www.gcc18.com)

13/9-18/9 Pultusk (PL)

**EMBO Conference on Long Regulatory RNAs**, Info: <http://ma.esf.org>

13/9-21/9 Dubrovnik (HR)

**Microbial Specialised Metabolites: Origins and Application (Summer School)**, Info: [www.jic.ac.uk/science/molmicro/Summerschool](http://www.jic.ac.uk/science/molmicro/Summerschool)

14/9-16/9 Ghent (BE)

**25th Joint Glycobiology Meeting**, Info: [www.25thjgm.be](http://www.25thjgm.be)

14/9-17/9 Montpellier (FR)

**12th Euro Fed Lipid Congress: Oils, Fats and Lipids – From Lipidomics to Industrial Innovation**, Info: [www.eurofedlipid.org](http://www.eurofedlipid.org)

14/9-17/9 Riga (LV)

**5th ESWI (European Scientific Working group on Influenza) Influenza Conference**, Info: [www.eswiconference.org](http://www.eswiconference.org)

15/9-16/9 London (UK)

**3rd Annual Cancer Vaccines Conference**, Info: [www.smi-online.co.uk/pharmaceuticals](http://www.smi-online.co.uk/pharmaceuticals)



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16/9-18/9 Oxford (UK)

**Phages 2014 – Bacteriophage in Medicine, Food and Biotechnology**, Info: [www.lpmhealthcare.com/phages-2014](http://www.lpmhealthcare.com/phages-2014)

16/9-20/9 Berlin (DE)

**10th International Conference on Bone Morphogenetic Proteins**, Info: <http://userpage.fu-berlin.de/bmp>

17/9-19/9 Cambridge (UK)

**Wellcome Trust Conference on Cancer Pharmacogenomics and Targeted Therapies**, Info: [www.hinxton.wellcome.ac.uk](http://www.hinxton.wellcome.ac.uk)

17/9-20/9 Primosten (HR)

**Power of Viral Vectors in Gene Therapy and Basic Science, Summer School**, Info: [www.fems-microbiology.org](http://www.fems-microbiology.org)

18/9-19/9 Cambridge (UK)

**James Black Meeting – Inspired Biologics 2014**, Info: [www.bps.ac.uk/meetings/Biologics](http://www.bps.ac.uk/meetings/Biologics)

21/9-24/9 Cambridge (UK)

**14th Wellcome Trust Conference on Genome Informatics**, Info: [www.hinxton.wellcome.ac.uk](http://www.hinxton.wellcome.ac.uk)

21/9-24/9 Cambridge (UK)

**EMBO Conference on Interdisciplinary Plant Development**, Info: [www.embo.org/events](http://www.embo.org/events)

21/9-23/9 Cologne (DE)

**30th Ernst Klenk Symposium in Molecular Medicine: DNA Damage Response and Repair Mechanisms in Aging and Disease**, Info: [www.zmmk.uni-koeln.de](http://www.zmmk.uni-koeln.de)

21/9-26/9 Ascona (CH)

**All Roads Take to the Brain: Neural Control of Human Energy Homeostasis in Health and Disease**, Info: [www.ascona-workshop.ethz.ch](http://www.ascona-workshop.ethz.ch)

23/9-25/9 Basel (CH)

**MipTec 2014: European Conference and Exhibition for Drug Discovery**, Info: [www.miptec.com](http://www.miptec.com)



23/9-25/9 Kiel (DE)  
**Genetic Variation in Plant Breeding (GPZ 2014) – Meeting of the German Society for Plant Breeding**, Info: [www.plantbreeding.uni-kiel.de/de/gpz2014](http://www.plantbreeding.uni-kiel.de/de/gpz2014)

23/9-25/9 Oxford (UK)  
**Drug Design 2014: Fragment- and Ligand-based Drug Design**, Info: [www.lpmhealthcare.com/drug-design-2014](http://www.lpmhealthcare.com/drug-design-2014)

23/9-26/9 Saarbrücken (DE)  
**Cell Physics 2014 – Interdisciplinary Platform for Scientific Exchange Between Participants from Cell Biology and Biophysics**, Info: [www.cell-physics.uni-saarland.de](http://www.cell-physics.uni-saarland.de)

24/9-26/9 Edinburgh (UK)  
**3rd World Congress of Reproductive Biology (WCRB 2014)**, Info: [www.wcrb2014.org](http://www.wcrb2014.org)

24/9-26/9 Valencia (ES)  
**3rd International Conference on Clinical Microbiology & Microbial Genomics**, Info: <http://clinicalmicrobiology2014.conferenceseries.net>

25/9-26/9 Cambridge (UK)  
**Conference: Are There Limits to Evolution?**, Info: <https://wsew4.esc.cam.ac.uk/atle>

25/9-26/9 Nice (FR)  
**Symposium on Metabolism & Cancer**, Info: [www.canceropole-paca.fr](http://www.canceropole-paca.fr)

26/9-28/9 Ascona (CH)  
**8th International Symposia on the CGRP Family; CGRP, Adrenomedullin, Amylin, Intermedin and Calcitonin**, Info: [www.vetphys.uzh.ch/CGRP2014](http://www.vetphys.uzh.ch/CGRP2014)

28/9-3/10 Lucca/Barga (IT)  
**AMPK: Biological Action and Therapeutic Perspectives**, Info: <https://secure.faseb.org>

29/9-1/10 Amsterdam (NL)  
**3rd International Conference on Responsible Use of Antibiotics in Animals**, Info: [www.bastiaanse-communication.com/rua2014](http://www.bastiaanse-communication.com/rua2014)

29/9-1/10 Paris (FR)  
**EMBO Conference on Innate Lymphoid Cells**, Info: [www.ilc1.org](http://www.ilc1.org)

30/9 Cambridge (UK)  
**Cambridge Immunology Forum**, Info: <https://bsi.immunology.org>

30/9-3/10 Lisbon (PT)  
**EMBO Conference on Centrosomes and Spindle Pole Bodies**, Info: <http://events.embo.org/14-centrosome-spb>

1/10-3/10 Luxembourg (LU)  
**Neurogenetics & Related Diseases – Annual Conference of the German Genetics Society**, Info: <http://neuroconference2014.uni.lu/eng>

1/10-3/10 Madrid (ES)  
**International Conference on Antimicrobial Research**, Info: [www.icar-2014.org](http://www.icar-2014.org)

5/10-8/10 Copenhagen (DK)  
**The Social Brain – Conference of the Federation of European Neuroscience Societies**, Info: [www.fens.org/Meetings/Brain-Conferences](http://www.fens.org/Meetings/Brain-Conferences)

5/10-8/10 Heidelberg (DE)  
**EMBO-EMBL Symposium: The Complex Life of mRNA**, Info: [www.embo-embl-symposia.org](http://www.embo-embl-symposia.org)

5/10-8/10 Madrid (ES)  
**13th World Congress of the Human Proteome Organization (HUPO 2014)**, Info: [www.hupo2014.com](http://www.hupo2014.com)

6/10-7/10 Heidelberg (DE)  
**SFB 638 International Symposium: Macromolecular Complexes in Biosynthetic Transport**, Info: [www.sfb638.uni-hd.de](http://www.sfb638.uni-hd.de)

8/10-9/10 Vilnius (LT)  
**Current Issues in Echinococcosis: Conference of the European Scientific Counsel for Companion Animal Parasites**, Info: [www.dgparasitologie.de/images/pdf/escap.pdf](http://www.dgparasitologie.de/images/pdf/escap.pdf)

8/10-12/10 Kusadasi, Aydin (TR)  
**17th International Symposium on the Biology of Actinomycetes**, Info: [www.isba17.com](http://www.isba17.com)

9/10-10/10 Dublin (IE)  
**Biomarker Summit Europe**, Info: [www.gtcbio.com/conference](http://www.gtcbio.com/conference)

9/10-10/10 Leipzig (DE)  
**Medicinal Stem Cell Products – Fraunhofer Life Science Symposium**, Info: [www.fs-leipzig.com/](http://www.fs-leipzig.com/)

9/10-10/10 London (UK)  
**Calcium Signalling: The Next Generation – A Biochemical Society Focused Meeting**, Info: [www.biochemistry.org/Conferences](http://www.biochemistry.org/Conferences)

9/10-10/10 Manchester (UK)  
**Inflammation and its Contribution to Disease**, Info: <https://bsi.immunology.org>

9/10-11/10 Frankfurt/Main (DE)  
**Viral Hepatitis Congress 2014**, Info: [www.viral-hep.org](http://www.viral-hep.org)

9/10-12/10 Bonn (DE)  
**RNA Biochemistry Meeting 2014 & Workshop RNA Modification**, Info: [www.rna-biochemistry.de/wp/meeting-2014](http://www.rna-biochemistry.de/wp/meeting-2014)

9/10-12/10 Glasgow (UK)  
**9th European Mucosal Immunology Group Meeting**, Info: <https://bsi.immunology.org>

9/10-12/10 Heidelberg (DE)  
**EMBO Conference: Stem Cells in Cancer and Regenerative Medicine**, Info: [www.embo.org/events](http://www.embo.org/events)

9/10-12/10 Mainz (DE)  
**The 2014 IMB Conference: Nuclear RNA in Gene Regulation and Chromatin Structure**, Info: [www.imb-mainz.de](http://www.imb-mainz.de)

9-12/10 Mont Sainte Odile (FR)  
**39th European Symposium on Hormones and Cell Regulation**, Info: [www.hormones-cell-regulation.eu](http://www.hormones-cell-regulation.eu)

9/10-12/10 Vipava (SE)  
**Yeast Fermentation: From Genes to Application Aspects (ISSY 31)**, Info: [www.yeast-cornucopia.se](http://www.yeast-cornucopia.se)

10/10 Hannover (DE)  
**3rd Symposium on cCMP and cUMP as New Second Messenger**, Info: [www.mh-hannover.de/ccmp2014.html](http://www.mh-hannover.de/ccmp2014.html)

11/10-15/10 Roscoff (FR)  
**Cell Cycle: Bridging Scales in Cell Division**, Info: [www.cnrs.fr/insb/cjm/2014/Musacchio\\_e.html](http://www.cnrs.fr/insb/cjm/2014/Musacchio_e.html)

12/10-15/10 Heidelberg (DE)  
**EMBO Conference: Experimental Approaches to Evolution and Ecology Using Yeast**, Info: [www.embo.org/events](http://www.embo.org/events)

14/10-15/10 Strasbourg (FR)  
**Abcam Conference on Chromatin and Epigenetics: From Omics to Single Cells**, Info: [www.abcam.com/events](http://www.abcam.com/events)

14/10-17/10 Ghent (BE)  
**4th international Conference on Novel Enzymes**, Info: [www.novelenzymes.ugent.be](http://www.novelenzymes.ugent.be)

14/10-17/10 Uppsala (SE)  
**12th Nordic Photosynthesis Congress (NPC12)**, Info: [www.kemi.uu.se/npc12](http://www.kemi.uu.se/npc12)

18/10-21/10 Berlin (DE)  
**27th Congress of the European College of Neuropsychopharmacology (ECNP2013)**, Info: [www.ecnp.eu/meetings/agenda](http://www.ecnp.eu/meetings/agenda)

20/10-22/10 London (UK)  
**Vaccines 2014: Next Generation Vaccines / Advances in Overcoming Co-Infections / The Use of Pseudotypes to Study Viruses, Virus Sero-Epidemiology and Vaccination**, Info: [www.regonline.co.uk/vaccines2014](http://www.regonline.co.uk/vaccines2014)

21/10-22/10 Leipzig (DE)  
**Translational Regenerative Medicine Congress 2014**, Info: <https://selectbiosciences.com/TRMC2014>

22/10-24/10 Vienna (AT)  
**ESCMID Conference on Reviving Old Antibiotics**, Info: [www.escmid.org/dates\\_events](http://www.escmid.org/dates_events)

24/10 Rennes (FR)  
**Young Life Scientists' Symposium on DNA Damage Response in Physiology and Disease**, Info: <http://yls2014.sciencesconf.org>

26/10-31/10 Girona (ES)  
**EMBO Conference: The Endoplasmic Reticulum (ER) as a Hub for Organelle Communication**, Info: [www.embo.org/events](http://www.embo.org/events)

28/10-31/10 Cambridge (UK)  
**Wellcome Trust Epigenomics of Common Diseases Conference**, Info: [www.hinxton.wellcome.ac.uk](http://www.hinxton.wellcome.ac.uk)

29/10-1/11 Bad Nauheim (DE)  
**14th International Paul-Ehrlich-Seminar on Allergen Products for Diagnosis and Therapy: Regulation and Science**, Info: [www.pei.de/EN](http://www.pei.de/EN)

29/10-1/11 Prague (CZ)  
**16th Biennial Meeting of the European Society for Immunodeficiencies (ESID 2014)**, Info: [www.2.kenes.com/esid2014](http://www.2.kenes.com/esid2014)

1/11-4/11 London (UK)  
**4th International Conference on Regulatory T Cells and Th Subsets and Clinical Application in Human Disease**, Info: <https://bsi.immunology.org>

2/11-6/11 Glasgow (UK)  
**HIV Drug Therapy Glasgow Meeting 2014**, Info: [www.hivglasgow.org](http://www.hivglasgow.org)

5/11 Birmingham (UK)  
**Mechanisms of Immune Regulation**, Info: <https://bsi.immunology.org>

5/11-7/11 London (UK)  
**Antibiotic Alternatives for the New Millennium**, Info: [www.regonline.co.uk/antibiotic2014](http://www.regonline.co.uk/antibiotic2014)

5/11-7/11 Wuerzburg (DE)  
**34th International Symposium on the Separation of Proteins, Peptides and Polynucleotides**, Info: <http://events.dechema.de/Tagungen/ISPPP+2014.html>

7/11-10/11 Cambridge (UK)  
**3rd Wellcome Trust Conference on Epigenomics of Common Diseases**, Info: [www.hinxton.wellcome.ac.uk](http://www.hinxton.wellcome.ac.uk)

8/11-11/11 Heidelberg (DE)  
**EMBL Conference: From Functional Genomics to Systems Biology**, Info: [www.embl.de/training/events](http://www.embl.de/training/events)

8-13/11 San Feliu de Guixols (ES)  
**Flies, Worms and Robots: Combining Perspectives on Minibrains and Behaviour**, Info: <http://minibrains.esf.org>

9/11-11/11 Heidelberg (DE)  
**Molecular Mechanisms of Cellular Surveillance and Damage Responses (SFB 1036 Meeting)**, Info: [www.zmbh.uni-heidelberg.de/sfb1036/congress\\_2014](http://www.zmbh.uni-heidelberg.de/sfb1036/congress_2014)

10/11 London (UK)  
**Advancing Applications of Super Resolution Imaging**, Info: [www.biochemistry.org/Conferences](http://www.biochemistry.org/Conferences)

10/11 Vienna (AT)  
**The World Plant Toxin Forum**, Info: [www.bastiaanse-communication.com/wmf](http://www.bastiaanse-communication.com/wmf)

10/11-12/11 London (UK)  
**The 2014 Innate Immunity Summit: Interactions with Pathogens / Investigating Interactions of the Innate and Adaptive Immune Systems / Therapeutic applications of the Innate Immune System**, Info: [www.innateimmunitysummit2014.com](http://www.innateimmunitysummit2014.com)

10/11-12/11 Vienna (AT)  
**The World Mycotoxin Forum – 8th Conference**, Info: [www.bastiaanse-communication.com/wmf](http://www.bastiaanse-communication.com/wmf)

11/11-13/11 Cambridge (UK)  
**Wellcome Trust Conference on Computational RNA Biology**, Info: [www.hinxton.wellcome.ac.uk](http://www.hinxton.wellcome.ac.uk)

13/11-14/11 Dublin (IE)  
**New Perspectives in Thrombosis, Haemostasis and Vascular Biology**, Info: [www.biochemistry.org/Conferences](http://www.biochemistry.org/Conferences)

14/11-16/11 Thessaloniki (GR)  
**International Conference on New Concepts in B Cell Malignancies: From Molecular Pathogenesis to Personalized Treatment**, Info: [www.esh.org/conferences](http://www.esh.org/conferences)

15/11-19/11 Roscoff (FR)  
**Molecular Basis for Membrane Remodelling and Organization**, Info: [www.cnrs.fr/insb/cjm/2014/Antony\\_e.html](http://www.cnrs.fr/insb/cjm/2014/Antony_e.html)

17/11-18/11 London (UK)  
**Modelling Microbial Infection (Focused Meeting)**, Info: [www.sgm.ac.uk/en/events/conferences](http://www.sgm.ac.uk/en/events/conferences)

17/11-20/11 Heidelberg (DE)  
**EMBO-EMBL Symposium: Frontiers in Metabolism – From Molecular Physiology to Systems Medicine**, Info: [www.embo-embl-symposia.org](http://www.embo-embl-symposia.org)

20/11-21/11 London (UK)  
**6th Annual Next Generation Sequencing Congress**, Info: [www.nextgenerationsequencing-congress.com](http://www.nextgenerationsequencing-congress.com)

20/11-21/11 London (UK)  
**2nd Annual Single Cell Analysis Congress**, Info: [www.singlecell-congress.com](http://www.singlecell-congress.com)

20/11-21/11 Vichy (FR)  
**4th Skin Physiology International Meeting**, Info: [www.skin-meeting.com](http://www.skin-meeting.com)

21/11 Dublin (IE)  
**4th Frontiers in Neurology Meeting**, Info: [www.neurologyireland.com](http://www.neurologyireland.com)

1/12-4/12 Cambridge (UK)  
**Wellcome Trust Conference on Rat Genomics and Models**, Info: [www.hinxton.wellcome.ac.uk](http://www.hinxton.wellcome.ac.uk)

2/12 London (UK)  
**PINK1 – Parkin Signalling in Parkinson's Disease and Beyond**, Info: [www.biochemistry.org/Conferences](http://www.biochemistry.org/Conferences)

2/12-4/12 London (UK)  
**Pathology Congress: Progress in Molecular & Cellular Pathology / Developments in Immunohistochemistry / Histopathology: Advances in Research & Techniques**, Info: [www.pathology2014.com](http://www.pathology2014.com)

4/12-7/12 Nice (FR)  
**10th International Congress on Non-Motor Dysfunctions in Parkinson's Disease and Related Disorders**, Info: [www.2.kenes.com/mdpd2014](http://www.2.kenes.com/mdpd2014)

## Lab Times

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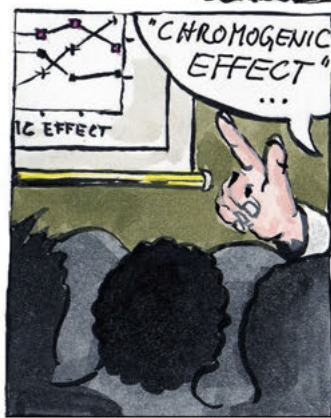
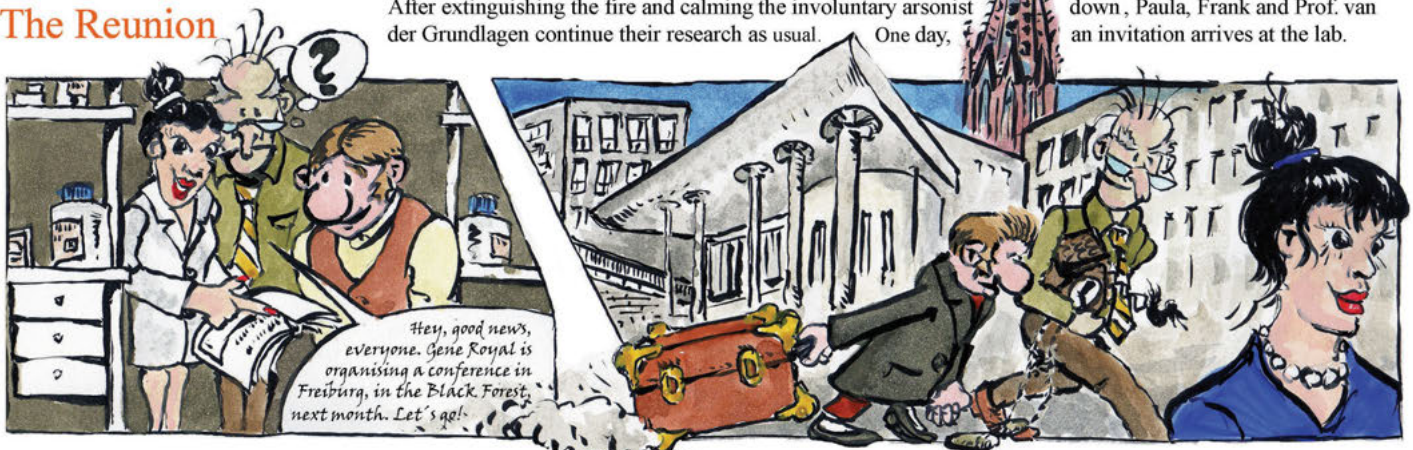


# Lab Tales

## The Reunion

After extinguishing the fire and calming the involuntary arsonist der Grundlagen continue their research as usual. One day,

down, Paula, Frank and Prof. van an invitation arrives at the lab.



... after several more hours of talks and presentations, Paula, the Prof. and Frank, are ready to go home...









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