EU biosafety research

Risky Regulations

Some of the EC's proposals for biosafety might turn out to be counterproductive.

iStockphoto/Oliver Sun Kim

European biologists are increasingly raising doubts about the proposals on biopreparedness and biosafety floated by a "green paper" of the European Commission (EC) in July. While there is common agreement on a majority of the ideas proposed in the document, criticism has recently centred around two particular issues: accreditation of biological research facilities and researchers as well as a two-tier publication system for results on biosafety issues.

In order to prevent potential misuse of scientific results, the green paper proposed a "specific procedure [...] where sensitive dual-use research results could be published in two different versions: (1) a public version with no publishing restrictions (without sensitive content), and (2) a restricted version containing the sensitive parts published in a manner allowing access only for relevant and secure bio-stakeholders."

Although the paper furthermore states that "the aim of the proposed actions is not censorship of biological science", several groups fear exactly this. The European Biosafety Association (EBSA), which represents people working in biosafety and associated activities, for example, was quoted by *Nature News* as regarding the two-tier approach as "unworkable and contrary to scientific freedom". Rudi Balling, president of the newly formed German Life Science Association VBIO questioned the practicability of this approach by asking, "How can we be sure that the first round of reviewing, which doubtlessly would have to evaluate the potential biorisks of a publication, won't be accomplished by politicians rather than by scientists only? How shall we avoid that profound scientific results could be filtered and blocked out under the pretences that they might be fraught with too much risk?"

At the same time, Balling criticises the idea of putting forward a Europe-wide system for the accreditation and certification of laboratories suitable for work on potentially dangerous pathogens. He warns that the corresponding bureaucratic efforts might strangle European bioresearch. Neither governmental nor private research institutions would be able to finance the required procedures.

Even more criticism was raised against the paper's proposal of accrediting the individual researcher. According to *Nature News*, the EBSA and the bioindustry body EuropaBio agreed in their statements that it would be very difficult to accredit individual researchers without running into problems regarding discrimination or personal privacy.

Taken together, many people from the science side are afraid that adopting the proposals of the green paper finally might be counterproductive. On the one hand, the EC does want efficient biosafety research; with some of its green paper proposals, however, the EC risks that in the end nobody will want to take it up because the regulative obstacles are regarded as too high.

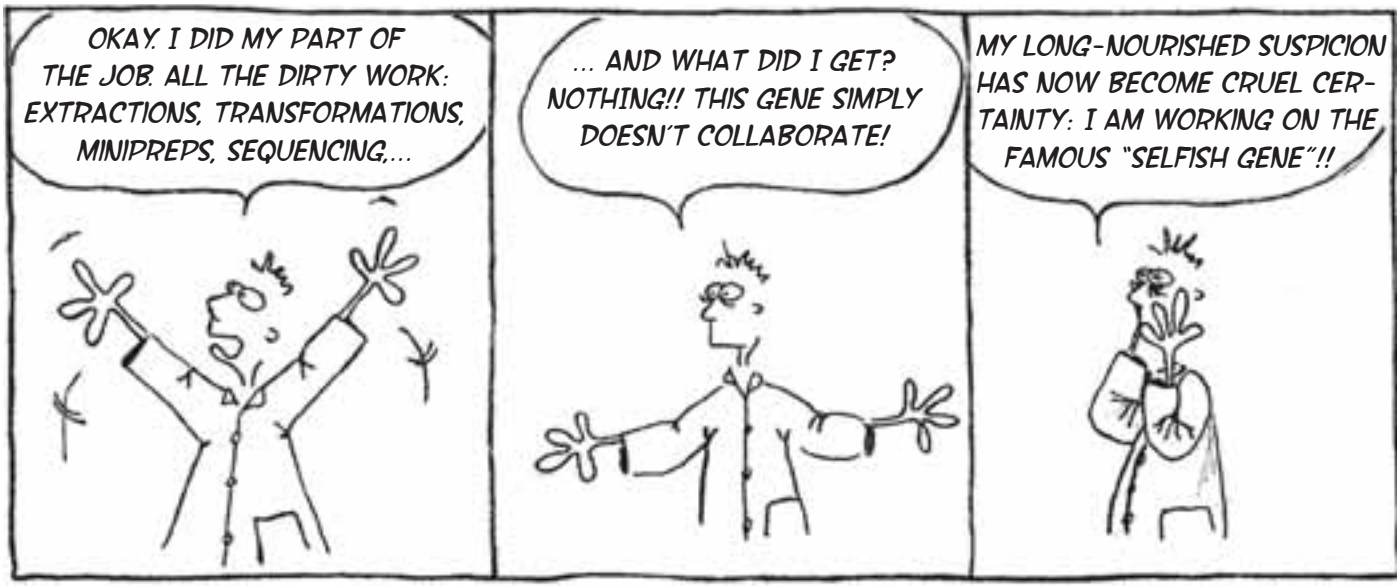
European Reseach Council

The Truth about Young Talent

This year, for the first time, the European Research Council (ERC) was offering grants to talented young scientists, who snapped them up "like hot cakes". According to statistical information based on the first round of applications for the ERC Starting Independent Researcher Grants, ▸▸

PAUL THE POSTDOC

BY RAFAEL FLORÉS



▶▶ 9,167 proposals were submitted to win part of the ERC's 289.5 million euros. Sure enough, one can interpret this as a complete success. On the other hand, however, the keen participation is also a crystal clear documentation of the distress experienced by young European talent.

According to the ERC's numbers, the most desperate country for scientists 2-9 years after having done their PhD is Italy. Italians filed some 1,700 from 8,794 evaluated applications, followed by the Germans who submitted some 1,000 proposals. This may reflect the bad and often criticised situation for research in (not so) "Bella Italia" where working conditions and salaries are poor, especially for junior scientists. No wonder, therefore, that many want to leave the country.

Perhaps they are heading for Great Britain? In any case, the island attracts an above average number of scientists. Notably, only 550 scientists of all principal investigators (PIs) are actually British citizens, on the other hand 1,100 PIs that applied for ERC money are resident in Great Britain.

Switzerland also appears to enjoy a comfortable brain gain, with the ERC statistics listing only around 100 Swiss PIs; however, twice as many people who applied for money are registered as only living in the Alpine Republic.

The ERC's figures also document the notoriously deplorable situation for fe- ▶▶

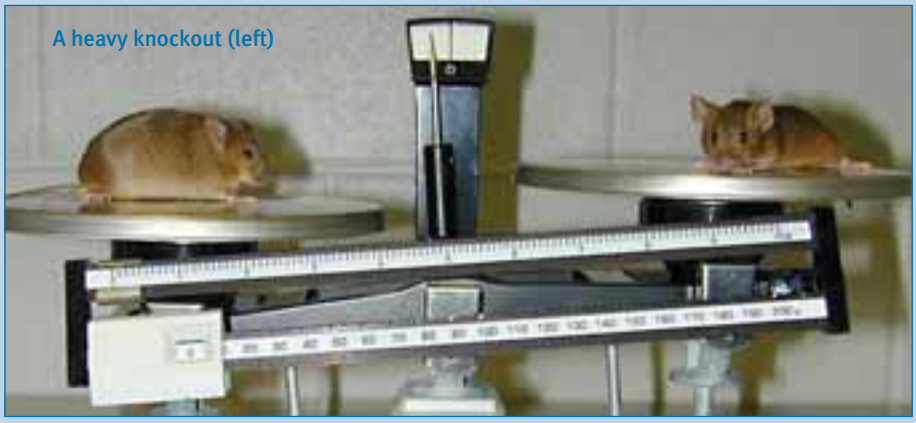
More than Simply Gene Targeting

Nobel Prize also honours first impressive benefit of embryonic stem cell research.

Twenty years ago when Susumu Tonegawa was announced the Nobel Prize winner in Physiology or Medicine for "his discovery of the genetic principle for generation of antibody diversity", the immediate reaction of Georges Köhler was, "We've got it again!" Three years earlier Köhler, together with Cesar Milstein and Niels Kaj Jerne, had also received the Nobel Prize for another discovery in immunology: The production of monoclonal antibodies. This was the reason why he instantly added, "Now it will probably take more than twenty years until another Nobel will go to immunology."

Köhler was wrong. In 1996, only nine years later, Rolf Zinkernagel and Peter Doherty were awarded the next "immunological" Nobel. Nevertheless, this little anecdote demonstrates the common notion that if a Nobel Prize is awarded to a certain research field, there clearly won't be another Prize for this field for quite some time.

From this perspective, this year's Nobel Prize in Physiology or Medicine came as a surprise. Only last year the Nobel committee had honoured Craig Mello and Andrew Fire for their discovery of the mechanism of RNA interference, which today is mainly used as a simple and powerful tool to specifically suppress the expression of designated genes. Next month three researchers will receive this year's Nobel for the development of a technique that basically allows for the same thing: To specifically switch off genes.



A heavy knockout (left)

Strange decision, therefore? First of all, there is no doubt that the two US mouse geneticists Mario Capecchi and Oliver Smithies together with Martin Evans from the University in Cardiff actually deserve the Prize. In the late 1980ies, Capecchi and Smithies independently developed the principles for what is today known as specific gene targeting in mice and widely used to study gene function. In the same breath, however, they thereby became the "fathers" of innumerous lines of so-called knockout mice. Many of these mutant mice, which stably inherit their modified or disrupted genes to their offspring, have since become the "top models" for studying the genetic basis of a whole variety of human diseases as well as potential treatments. This at least constitutes a notable difference to the simpler gene knockdown technology via RNA interference.

Initially, however, Capecchi and Smithies had only demonstrated that genes could be specifically targeted by homologous recombination in cultured cells. What was still missing at this time was a vehicle to transfer the modified genes to the mouse germ line. It was Martin Evans who provided it. He had succeeded in establishing cultures of embryonic stem (ES) cells directly from early mouse embryos. More than this, however, Evans had also developed the methodology to integrate foreign DNA into the chromosomes of ES cells and to transfer the new genetic material from ES cells, through mosaic mice, into the mouse germ line. In 1989, the combination of both – gene targeting by homologous recombination in ES cells – gave birth to the first knockout mouse.

Hence, this year's Nobel Prize in Physiology or Medicine does not only celebrate a method to switch off genes. It also honours the impressive benefit of using embryonic stem cells. This might well be taken as a clear signal in the ongoing debate on using human embryonic stem cells for research.

RALF NEUMANN

Recently Awarded

▶ **Jules Hoffmann**, Académie des Sciences, Paris, and **Bruce Beutler**, The Scripps Research Institute, La Jolla, California, will receive one of the four International **Balzan Prizes** 2007. Both have been honoured "for their discovery of the genetic mechanisms responsible for innate immunity", thereby revealing its broad impact as molecular defence strategy against infectious agents deployed by animals across a wide evolutionary spectrum. Hoffmann and Beutler will share one million Swiss Francs; both must allocate half of their prize for research work, preferably involving young scholars and researchers.

▶ **Peter Seeberger**, professor of organic chemistry at the ETH Zurich, received this year's **Körber European Science Award** worth €750,000. In its statement the Körber Foundation wrote, "Using the automated oligosaccharide synthesizer that he developed, Peter Seeberger and his colleagues succeeded in artificially producing glycans of pathogens known to cause diseases. They were furthermore successful in transforming the glycans into vaccine candidates for illnesses such as leishmaniasis, malaria, AIDS, anthrax and tuberculosis. The vaccine candidates have already demonstrated their effectiveness in animal experiments and the malaria vaccine is to be tested on humans for the first time next year."

▶ **Friedrich Luft**, director of the Experimental and Clinical Research Centre at the Max Delbrück Center for Molecular Medicine in Berlin, received the **Novartis Award for Hypertension Research** from the American Heart Association, endowed with $20.000. He was honoured for discoveries in three areas of hypertension research: 1) sodium intake, kidney function and arterial pressure in humans; 2) immune mechanisms in hypertension (one example being the activation of T lymphocytes in the kidneys of hypertensive rats); and 3) genetics of hypertension, e.g. the identification of a salt-insensitive genetic hypertension syndrome involving shortening of the fingers or toes.

▶▶ male scientists. In many of the "old" EC countries the proportion of female PIs was around 20 to 30 per cent. All these countries should aspire to Finland's example, where only half of all Finnish applicants were male. Wow! Italian women left a marked impression as 40% of the young scientist applicants were female and roughly 30% of the Italian finalists were also women. Wow again!

That leads us to the success rates. From 8,794 peer-reviewed applicants, 559 have been invited to make a second-stage submission. Although the majority of finalists came from Germany, overall the Germans were not too successful with only 7% of them making it to the final round. Belgian and Icelandic applicants, however, faired much better. Approximately 20% of Belgian and 13% of Icelandic grant-seeking scientists can look forward to the second evaluation. By January 2008, the ERC will have selected about 250 scientists for funding. Each of them will be awarded roughly €1 million.

Finally, one of the most amusing and salient statistics was recorded for Cyprus, submitting 5 proposals per million inhabitants. The small country is also the front-runner in "proposals per thousand researchers". It seems that life as a scientist is an appealing profession in Cyprus.

(More details are available at: *http://erc.europa.eu/pdf/erc-stg-statistics-stage1-20071001_en.pdf)* -KHo-

Resolution against Creationism

Spreading Threat

"If we are not careful, creationism could become a threat to human rights." This is a warning issued in a resolution recently passed by the parliament of the Council of Europe, an inter-governmental body that is responsible for, among other things, the European Convention on Human Rights. With the report the 47-nation Council urged its member governments to "firmly oppose" the teaching of creationism – which denies the evolution of species through natural selection – as a scientific discipline on an equal footing with the theory of evolution.

"Creationism ... was for a long time an almost exclusively American phenomenon," the parliamentarians pointed out. ▶▶

Editor's Corner

Genome *Frequencing?*

What? Our editor rubbed his tired eyes. No, the letters didn't turn into "*sequencing*". The headline still read, "Tilapia, a model fish for research and genome *frequencing*".

The text in question was a press release by the French agricultural research centre CIRAD announcing that a project by the so-called Cichlid Genome Consortium had been accepted for funding by the US-National Institutes of Health and had just begun at the Washington University Genome Sequencing Centre.

Sequencing Centre! So was it in fact a Tilapia genome *sequencing* project? After all, it was constantly called referrred to as a "*sequencing* project" later in the text. *Frequencing* must have been just a mistake. However, the editor still wasn't one hundred percent sure. He googled "genome frequencing" and received about 60 results exclusively representing websites, which had just copied this particular Tilapia press release. Absolute certainty finally came from a telephone conversation with one of the researchers involved in the Cichlid Genome Consortium. He was really amused and provided the following surmising scenario, "You know, probably this press office guy suddenly thought, 'Oh, I nearly forgot, I still have to put out this press release from the *fish genome freaks*'. And when hastily writing the headline, *genome sequencing* inadvertently mutated to *genome frequencing*!"

"Today creationist ideas are tending to find their way into Europe and their spread is affecting quite a few Council of Europe member states." The report cites examples from Belgium, France, Germany, Greece, Italy, the Netherlands, Poland, Russia, Serbia, Spain, Sweden, Switzerland, Turkey and the United Kingdom.

"The prime target of present-day creationists, most of whom are Christian or Muslim, is education," the parliamentarians said in the resolution. "Creationists are bent on ensuring that their ideas are included in the school science syllabus. Creationism cannot, however, lay claim to being a scientific discipline."

"Intelligent design, presented in a more subtle way, seeks to portray its approach as scientific and therein lies the danger," they added.

Scientists, however, haven't given the Council of Europe document too warm a reception. "It is strong on generalisations but very weak on evidence", they criticise. Therefore, it lacks "the spirit of science, which they claim to be supporting."

European Science Foundation (ESF)

A Female First

This year the European Science Foundation (ESF) celebrates its 33rd birthday. Based in Strasbourg as an association of 75 member organisations from 30 European countries, it has, since its foundation, coordinated a wide range of pan-European scientific initiatives.

It has taken the same amount of time, however, before the first woman has reached the top post in the organisation. The ESF recently announced that Marja Makarow, Professor of Biochemistry and Molecular Biology at the University of Helsinki, will succeed John Marks as Chief Executive. As one of her foremost aims she proclaimed, "To transform the fragmented nature of European science".

New EMBL partnership

Reaching North

The European Molecular Biology Laboratory (EMBL) has entered a Partnership for Molecular Medicine with the three Scandinavian universities in Helsinki/Finland, Oslo/Norway, and Umeå/Sweden. The aim of the partnership is to complement EMBL's traditional strengths in molecular and cellular biology by Norway's expertise in molecular mechanisms of disease, Sweden's focus on microbial pathogenicity and molecular infection medicine and Finland's strength in genetic epidemiology. The agreement will encourage scientific exchange and collaborations between the partners and will facilitate access to respective scientific infrastructure, facilities and services for an initial period of five years.

Why We Bite As We Bite

A simple mathematical model explains the evolution and variety of mammalian cheek tooth phenotypes.

Show me your teeth and I'll tell you what you eat! Scientists, however, would better turn this around and state: The great variety of features among mammalian teeth closely reflects what each species eats.

Take for example the cheek teeth, or molars. Placental mammals have three molars - M1, M2 and M3 from front-to-back. With only a few exceptions, in plant-eating species M3 is the biggest molar, whereas in animal-eating species M1 is bigger than its two companions. They all have in common, however, that the molars develop from front-to-back so that the first molar appears first and the posterior molars bud sequentially along the jaw.

For a long time the question has been, how were the pronounced species-specific differences in molar morphology among mammals shaped during evolution? Only by ecological interactions? Or did genetic and developmental interactions also influence the species-specific properties?

Kathryn Kavanagh, Alistair Evans and Jukka Jernvall from the University of Helsinki recently provided part of the answer. Their experiments on cultured mouse molars revealed that the size of posterior molars depend on previously initiated molars (*Nature* 449:427-32). Signalling molecules produced by developing mouse molars actually inhibit the development of subsequent buds. However, that was only one part of the story. At the same time, the surrounding tissue secreted another set of signalling molecules, which *activated* molar bud formation.

A simple model emerged. Apparently, the balance between these inhibitor and activator molecules determines when and if an additional molar will form. The higher the ratio of activator to inhibitor (a/i), the more rapidly molar buds will be added to the tooth row. And the more rapidly buds are added, the bigger they get, meaning that a/i is a predictor of the relative sizes of the molar teeth.

Two things remained for the Helsinki researchers to do. Firstly, they succeeded in varying the size pattern of mouse molars in culture by manipulating the relation between activator and inhibitor. And, secondly, by quantifying the experiments, Kavanagh *et al.* constructed a simple mathematical model with which they were able to predict relative sizes of molars across many other mammalian species.

Seen from a broader perspective, these results show how selection can target the molecular regulation of developmental processes, in order to produce ecological adaptations of given structures. Or, as P. Z. Myers wrote in his weblog *Pharyngula*, "Pattern becomes a consequence of clean mathematical rules of form [...] and at the same time, we can see exactly where genetic variation and selection can step in to generate and stabilise particular patterns, with the regulation of just a few developmentally significant processes."

(More research results from European labs on p. 28-33)