"My cell has dull colours on the outside because it looks small and boring but it's colourful inside because it's full of life"

Picture taken at the Art of the Body event at the Cheltenham Science Festival 2007.

European stem cell research

Letters to Lawmakers

Scientists of two European-funded stem cell research consortia have complained about the negative impact that differing legislative positions in European countries are having on collaborative research, particularly in Germany and Italy. In a joint statement being sent to Members of the European Parliament, ESTOOLS and EuroStemCell scientists are calling for harmonisation of current laws in the hope that their European counterparts are able to collaborate on international projects without fear of legal reprisal.

Currently, stem cell legislation differs across Europe. Projects that are perfectly legal in Sweden and the UK could result in a three-year prison sentence in Germany. Researchers from countries with very restrictive legislation might also become liable by taking on coordinating positions in other European institutions.

Austin Smith, Director of the Wellcome Trust Centre for Stem Cell Research, added, "EuroStemCell scientists are working together to compare embryonic and tissue stem cells and their potential for medical applications. However, the situations in Germany and Italy present constant difficulties because our colleagues in these countries may be punished for taking part in research activities of the project."

The statement coincided with a position paper by Germany's National Ethics Council that recommended easing legal restrictions intended to limit German scientists' ability to conduct stem cell research. The Council's main concern is that lawmakers should lift a ban placed on German scientists, both in and outside the country, on using cell lines created after Jan. 1, 2002. Instead of using a cut-off date, the Council recommended establishing an independent panel to evaluate scientists' plans on a case-by-case basis.

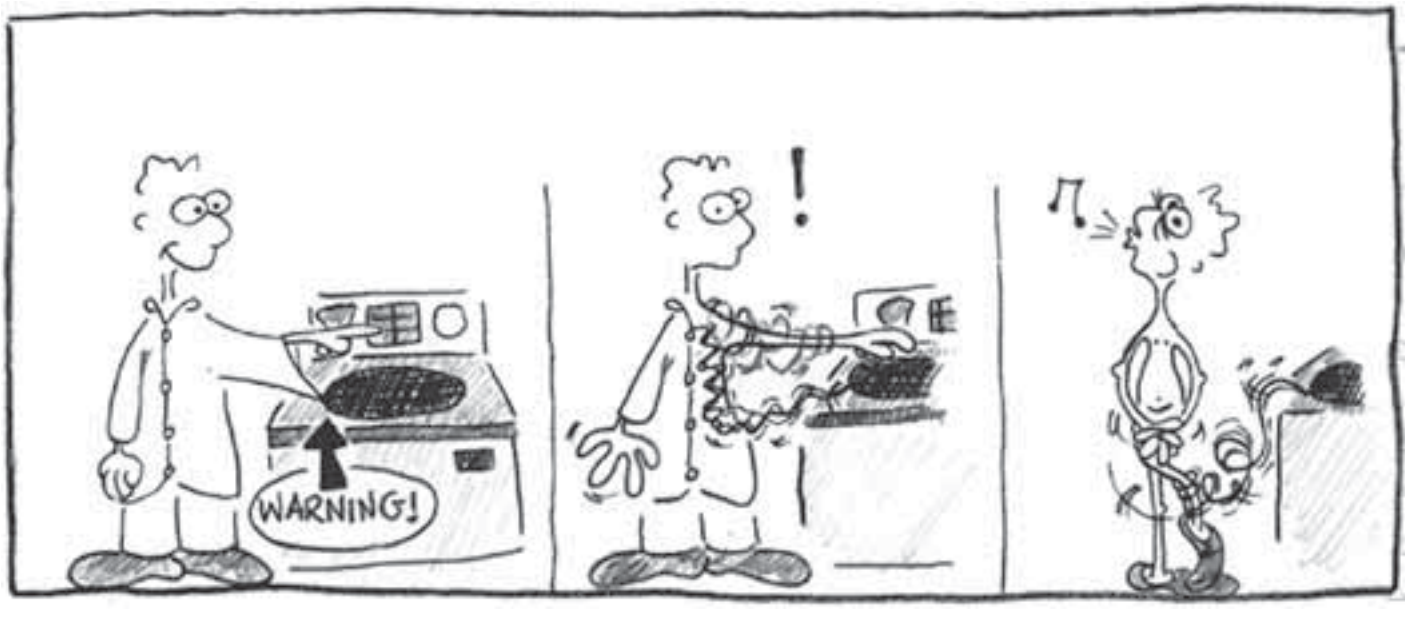
Horst Dreier, professor at the Law School of Würzburg University, said, "If the current rules remain, German science will be hopelessly sidelined." However, the council's vote wasn't unanimous; 14 of the 23 council members favoured changing the law, 9 opposed the recommendation.

In Italy, law permits work on existing cell lines but forbids the creation of new human embryonic stem cell lines. However, in practice the country's public funding bodies only allocate resources to research involving adult human stem cells.

A few weeks ago, Italian scientists, therefore, issued a "manifesto" for scientific research on embryonic stem cells, which asks for funding to be made more easily available for such research. "We seek a re-orientation of the currently imbalanced ▸▸

PAUL THE POSTDOC

BY RAFAEL FLORÉS



Recently Awarded

▶ **Ginés Morata**, CSIC-UAM Centre of Molecular Biology in Madrid, and **Peter Lawrence**, MRC Laboratory of Molecular Biology at Cambridge University, were awarded the **2007 Prince of Asturias Award for Scientific and Technical Research**. Both, alone and in cooperation, have contributed basic insights into the mechanisms of pattern formation in development. They are regarded as principal advocates of the idea that cells in a gradient of a morphogen develop according to their local concentration of the morphogen and that this mechanism is used to generate patterns of cells. Studying Drosophila wing development in particular, Morata and Lawrence have helped establish the compartment theory first proposed by Antonio Garcia-Bellido. In this hypothesis, a set of cells collectively builds a compartment. As development proceeds, a "selector gene" is switched on in a subset of these cells, which become divided into two sets of cells that construct two adjacent compartments.

The **2007 Prince of Asturias Award for Communication and Humanities** went to the two leading scientific journals ***Nature*** and ***Science***.

▶ **Jeffrey Friedman** received the 6th **Danone International Prize for Nutrition** from Danone Institute International, a Paris-based non-profit association supporting research in nutrition. In 1994 Friedman and his team at the Rockefeller University in New York discovered the first obesity gene in mice and humans and subsequently showed that its product, the hormone leptin, acts as a key player in balancing food intake and body fat storage. In the case of increasing body fat, for example, the adipose tissue itself adopts an endocrine function by expressing and releasing increased levels of leptin, which then "tells" the hypothalamus to reduce appetite and food intake. These findings provided the basis for understanding the biological system that controls weight and, if defective, might cause obesity. Friedman received €120,000, which he has to share with his institution to support further research.

▶▶ situation, achievable by the resumption of public funding for research on embryonic stem cells that are already available, which is permitted by Italian law and is a basic feature of the transparent regulation applied in most European countries," the authors state.

A few weeks earlier, the European Group on Ethics (EGE) had delivered its most recent opinion concerning research projects using human embryonic stem cells (hESC) funded by the 7th Research Framework Programme (FP7) of the European Union (EU). The Group suggested that, among others, the following considerations must apply:

▶ FP7 hESC lines have to result from non-implanted IVF embryos;

▶ hESC lines banked in the European Registry should be used where possible;

▶ If alternatives to hESC with the same scientific potential as embryo-derived stem cells will be found in the future, their use should be maximised;

▶ Donors' rights (in terms of health, informed consent, data protection and free donation) have to be protected and safeguarded;

▶ Actions to stimulate public debate on this research area are needed at EU level.

US science

Still So Much Better?

In recent decades many European scientists' have repeatedly lamented that everything is better in the US. At the same time, this perception has frequently served as an argument in favour of implementing certain structural parts of the US research system in European countries. For instance, the tenure track system.

However, recent trends and developments appear to have given way to the notion that not all that glitters is gold in the US science system. Evidence, for example, comes from new data compiled by the Federation of American Societies for Experimental Biology (FASEB). According to this study the number of biomedical PhDs with academic tenure has remained steady since 1981, at just over 20,000. During the same period, however, the number of students in US graduate programmes has steadily increased, as well as the number of post-docs, which has grown from 25,000 to 33,000. The consequence being that the percentage of US biomedical PhDs with tenure track has dropped from 45 to below 30.

This trend is even harder to understand when considering that the US research budget has more than doubled over the same time period. For some reason this money obviously hasn't helped the young US scientists but has, instead, gone into infrastructure.

Almost at the same time the National Science Foundation (NSF) published a study, which according to NSF officials, reveals an "unprecedented and mysterious trend". Since the early 1990s, the absolute number of science and engineering (S&E) articles published by US-based authors in the world's major peer-reviewed journals plateaued. This no-growth is actually seen as quite alarming since over the same period the peer-reviewed literature has steadily expanded and resource inputs that support research and development (R&D), such as funds and personnel, have continuously increased.

In comparison, the absolute number of articles from the so-called EU-15 countries (the 15 members of the European Union prior to 1 May 2004) and from Japan continued to grow throughout most of the 1992–2003 period. During the mid to late 1990s, the number of articles published by EU-15 scientists even surpassed those published by their US counterparts and the difference between Japanese and US article output narrowed.

This trend, however, was least pronounced in biology and biomedicine when compared to other science and technology fields. Nevertheless, the number of US articles in biology and biomedicine "only" went up from 46,272 in 1992 to 48,282 in 2003, whereas the output of the EU-15 countries increased from 36,473 to 49,383 over the same time period.

More dramatic, however, were the numbers indicating the world share of the top 10% cited articles in biology and biomedicine. Whereas between 1992 and 2003 the US performance dropped from 45.9% to 37.6% in biology and from 61.8% to 55.8% in biomedicine, the EU-15 countries increased their shares from 28.0% to 36.6% in biology and from 24.5% to 27.4% in biomedicine. ▶▶

EURYI Awards 2007

The Last Ones

Last month the European Science Foundation (ESF) announced the twenty researchers chosen to receive the **European Young Investigator Award** (EURYI) awards in Helsinki on 27 September. The awards, worth at least €1 million over five years, are designed to attract outstanding young scientists from any country in the world to build their own careers and create research teams in Europe.

These will be the last EURYI awards in its present form. The newly created European Research Council (ERC) of the European Commission will now determine the future for this type of award.

The following eleven awardees are working in biomedicine:

- **Jeroen J.L.M. Cornelissen** (Nijmegen/NL): Virus Capsids as Confined Reaction Spaces;
- **Nynke Hester Dekker** (Delft/NL): Molecular Motors Handling DNA and RNA: Single-Molecule Experiments and Implications for Cellular Function;
- **Andre Fischer** (Göttingen/GER): Epigenetic mechanisms in learning processes, age related cognitive decline and neurodegenerative diseases;
- **Karl A. Gademann** (Lausanne/CH): Directing neurite outgrowth through syntetic natural products;
- **Sonia Garel** (Paris/F): Wiring the forebrain: roles and mechanisms of tangential cell migration in the basal ganglia;
- **Kerstin Lindblad-Toh** (Uppsala/SWE): Disease gene mapping and functional genomics in the domestic dog;
- **Matthias Lutolf** (Lausanne/CH): Bioengineering Microarrayed Stem Cell Niches;
- **Gregor Rainer** (Fribourg/CH): Cholinergic Mechanisms of Learning and Cognition;
- **Natalie Sebanz** (Leipzig /GER): Cognitive and Neural Mechanisms of Joint Action;
- **Terence Strick** (Paris/F): Single-molecule studies of biological nanomachines;
- **Rufin VanRullen** (Toulouse/F): Perceptual and Attentional Dynamics: Periodic Operations of the Brain.

▶▶ Altogether an unexpected development, as the NSF report confesses. However, it concludes, "Although the US share of the world's influential articles dropped substantially, the United States remained dominant in this area."

University rankings

Counts that Count?

There are already a whole lot of criteria by which research qualities of universities can be and actually are ranked. Roughly they can be divided into input indicators (i.e. grants, funding, number of staff...) or output indicators (i.e. papers, citations, awards, production of PhDs...). Recently, Tibor Braun and his colleagues from the

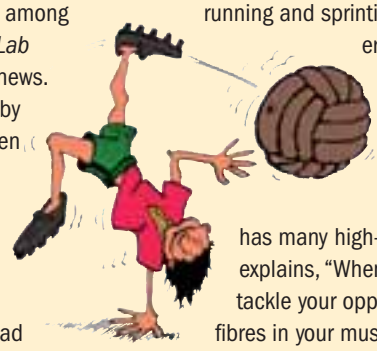
Institute of Research Policy Studies of the Hungarian Academy of Sciences in Budapest introduced yet another output indicator, the "journal gatekeepers".

What does that mean? In a nutshell "journal gatekeepers" is nothing more ▶▶

Healthy Fun

Soccer apparently improves health more effectively than jogging

There are many complaints about the growing bad habit to disseminate research results via press release prior to proper publication in a peer-reviewed research journal. Rightly so! *Lab Times* shares the corresponding concerns of the critics of that practice and therefore don't report on research results, which haven't yet been published. Usually! In this case we shall make an exception - specifically to give the many hobby soccer players among us scientists (in particular *Lab Times* editors) some good news.



A recent press release by the University of Copenhagen states, "Soccer burns more fat than jogging". A Danish team around sports scientist Peter Krustrup followed 14 untrained men aged 20 to 40 years who had a one hour soccer training 2-3 times a week. At regular intervals they were subjected to a number of tests such as fitness ratings, total mass of muscles, percentage of fat, blood pressure, insulin sensitivity and balance. The scientists finally compared the obtained data to data taken in parallel from a group of comparably active joggers as well as from a passive control group.

The press release describes the outcome of the study as "surprising". Krustrup is quoted as saying that "The improvement in fitness rating and the increase in total muscle mass were greater in the soccer players, and during the last 8 weeks of the experiment, only the soccer players showed any improvement." After 12 weeks, the soccer players had lost 3.5 kilos of fat and gained more than 2 kilos of extra muscle mass, whereas the joggers had lost 2 kilos of fat and showed no change in total muscle mass. Both groups showed significant improvements in blood pressure, insulin sensitivity and balance.

According to the press release, Krustrup believes that the shifts between walking, running and sprinting cause the soccer players to experience better health improvements, "Soccer is an all-round form of practise because it both keeps the pulse up and has many high-intensity actions". He explains, "When you sprint, jump and tackle your opponents, you use all the fibres in your muscles. When you jog at a moderate pace, you only use the slow fibres."

Moreover, after being asked how hard the practise was, the soccer players expressed that they did not notice how hard the practise actually was because it was fun and they were caught up by the game. The joggers always said the opposite.

The press release does not mention, however, that besides the positive health effects of soccer, the risk of injury is the highest of all sports disciplines. Hopefully we'll read about this in the discussion of an upcoming original research paper by Krustrup *et al.*

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

than a catchy term for the members of the editorial and advisory boards of science journals. The rationale is that these gatekeepers are selected for the boards because they have proven to have had a high quality research output at their institutes for quite some time (judged by whatever criteria).

Accordingly, Braun *et al.* chose twenty so called "core journals" for 12 different science fields and listed the corresponding board members in a database. Thus, they finally arrived at 240 journals and 13,000 "gatekeepers". The last step in creating a gatekeeper ranking of universities was trivial; one just had to count how many "gatekeepers" each university contributed to the "core journals".

The results of Braun *et al.* were published last May in Scientometrics (where Braun is editor-in-chief and founder). As in most university rankings, US universities occupy almost all top positions. Only 23 European universities made it into the Top 100, the three UK universities Cambridge (10th), University College London (13th) and Oxford (20th) being Europe's Top Three.

However, what might even be more instructive from the paper is its comparison of the gatekeeper ranking with other published rankings achieved by different indicators. For this purpose Braun et al. chose the latest university rankings by the Times Higher Education Supplement, the Shanghai University and the Spanish Webometrics web site (www.webometrics.info).

The correlations were poor. For example, Cambridge University made no's. 2, 6, 10 and 21 in the four rankings; Utrecht University ranked 42, 63, 77 and 95; Heidelberg University came in on 47, 71, 73 and 147.

Accordingly, the paper closes with refreshing openness. "As visible the correlations are quite weak, testifying that the choice of indicators the rankings are based on is significantly influencing the rankings."

R&D expenditures 2005

Small Leaders

The OECD recently published global data on the countries' gross domestic expenditures on research and development (R&D) in 2005. All EU-27 countries together spent 1.84% of their gross domestic products on R&D, exactly equalling their 2004 value. The USA came in at 2.62%, Japan at 3.33%. The highest portion of all nations was achieved by smaller high tech countries, led by Israel (4.5%), Sweden (3.86%) and Finland (3.48%), Switzerland (2.93%) and Iceland (2.81%). Also above the EU-27 average were Germany (2.51%), Denmark (2.44%), Austria (2.36%) and France (2.13%). The United Kingdom performed slightly lower (1.78%), leaving a considerably larger gap to the other two big European nations, Spain (1.12%) and Italy (1.10%).

Time Matters, Too

It's not only concentration but also time of exposure by which developmental signals act

Concentration matters in development. That's not exactly news. Numerous examples have carved that notion in stone over the last decades. And there are still a lot more to come...

Darwin's famous finches on the Galápagos Islands provided one of the more recent ones. It is the classic textbook example for adaptive radiation under natural selection that the 14 finch species have been developing a dramatic variety of beak shapes in order to specialise on the diverse food conditions on the individual islands. But how could all those fancy new beaks evolve from one simple "original" finch beak?

Cliff Tabin and his team at Harvard University found an unexpectedly simple answer to the question of how beak shape is regulated in the developing chicken embryo. The concentration of calmodulin determines how long the beak will grow. At the same time, however, the beak becomes thicker and more robust, the stronger the gene for the bone morphogenic protein 4 (BMP4) is expressed. Apparently, it's the exact level of expression of these two factors by which a beak can be modelled either long and thin for cactus-drilling, or tall and broad for nut-cracking (*Nature* 442: 563-7).

Of course, time also matters in cases like this since the signalling molecules can only exert their concentration-dependent effects within a limited time frame during development. Time alone, however, can play an even more decisive role in regulating crucial developmental decisions, as a Swedish group has just shown. They describe just the opposite mechanism, namely, that differences in the length of exposure but not the concentration of the same signal determine the formation of two fundamentally different organs. Funnily enough, the story is once again about BMP in chick embryos.

BMP signals are generally known to pattern embryonic ectoderm. Ectodermal structures of the vertebrate head, for example, are the olfactory mucous membrane and the eye lens. So it wasn't a big surprise that My Sjödal, Thomas Edlund and Lena Gunhaga from Umeå University also found olfactory and lens placodal cells to be induced from progenitor cells by BMP signals.

However, how does one cell know whether to become an eye or a nose cell when BMP knocks at its membrane? It is not the concentration of the signal, as the Swedish observed in cell culture differentiation experiments. Rather, the time of exposure of the progenitor cells to the BMP signal emerged as the crucial factor. When Sjodal et al. subjected the cells only to a short pulse of BMP they started differentiating into olfactory cells, whilst long periods of exposure gave rise to lens cells (*Dev. Cell* 13: 141-9).

Conclusion: Correct development increasingly proves to be a matter of perfect, finely tuned timing.

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