

Plagiarism

Sperm Oddities

Recently, an odd case of scientific plagiarism generated many controversial comments from the scientific community. On 8 July *Stem Cells and Development* published a paper online, ahead of print, on the generation of sperm-like cells from human embryonic stem cells. Corresponding author was Karim Nayernia from the North East England Stem Cell Institute and the University of Newcastle.

In the paper, the authors described how they had succeeded in deriving sperm precursor cells from human embryonic stem cells *in vitro*. These derived cells were able to divide and generate cells with tail-like structures and just one set of chromosomes, as is characteristic of sperm. Given this claim, the paper, of course, immediately caused a major media stir.

At the same time, however, Graham Parker, editor-in-chief of *Stem Cells and Development*, received an email pointing out that two paragraphs from Nayernia's introduction constituted a direct copy from a 2007 review published by Makato Nagano from Montreal in *Biology of Reproduction*. Strangely, these two paragraphs exclusively described previous work from Nayernia's group itself, raising questions about what the motivation was for such a plagiarism. The data in the paper, on the other hand, was not questioned at all.

When confronted by Parker, Nayernia blamed postdoc and initial first author, Jae Ho Lee, who has since left the group, for inserting the offending text without attribu-

tion to its original author. According to Nayernia, however, the copied text was just part of a working version of the paper, which had finally been submitted by mistake instead of the correct version.

Since the paper itself had been published online before copy editing or proof-reading, Nayernia immediately sent Parker the correct version. Strangely, Jae Ho Lee, who had meanwhile apologised to his co-authors, no longer appeared on the paper for his 'mistake'.



Parker, however, wasn't convinced. On 21 July he announced on the journal's homepage that the paper was being retracted, without giving details. "The available evidence does not substantiate the claim of an accidental submission of the wrong manuscript," Parker was quoted by *Science*.

Nayernia now intends to submit the paper to another journal. This, however, might also have further problems. Miodrag Stojkovic, another co-author of the paper, working at the Prince Felipe Research Centre in Valencia, told the German newspaper *Süddeutsche Zeitung* that he had asked Nayernia

to remove him from the paper's author list. "I have never received any final version for inspection. That's not the way it should be," he was quoted. Nayernia claimed that he had sent the manuscript to every single co-author prior to submission. However, Wolfgang Engel, another co-author from Göttingen University, also confirmed that he had never seen a final draft.

In addition, Stojkovic has meanwhile joined the critics stating that Nayernia's claims go too far. According to them, there is no doubt about the data but proof is still lacking that Nayernia's 'sperm-like cells' are indeed sperm precursor cells.

Concerning the plagiarism issue, the comments were split. Allan Pacey, secretary for the British Fertility Society, for example, told *Associated Press*, "This is clearly scientific misconduct. I can understand why people might think, if they were sloppy here, maybe they were sloppy elsewhere."

However, Graham Parker has also become the target of some harsh criticism. A comment on *Nature's* website says, "I cannot understand the journal editor's decision at all. He requested first the correct version of the paper from the authors, but he himself retracted the correct version after submission. [...] It seems that he had made his decision far before and his action appears more like a political mischief rather than a sound and fair decision based upon solid reasoning."

Perhaps another comment on *Science's* blog *ScienceInsider* actually hits the mark, "Both the authors and the publisher deserve this mess, because their primary goal is not good science, but good publicity." -RN-

BY RAFAEL FLORÉS

PAUL THE POSTDOC



Recently Awarded

► **Lars Jansen** from the Gulbenkian Institute for Science in Oeiras, near Lisbon, is the recipient of an **EMBO Installation Grant**. He will receive funding beginning in 2009, similar to the seven further awardees previously announced in December 2008. The 36 year-old moved from California to Portugal last year to head the Epigenetic Mechanisms group. His new team currently consists of five researchers and focuses on chromosome segregation, specifically the formation of the centromere. EMBO Installation Grants support young group leaders relocating to selected European countries committed to developing their research infrastructures. The grants offer €50,000 annually for three to five years, to help the scientists establish their groups and themselves in the European scientific community. According to Jansen, the grant “will give a huge boost to our research. It is a great recognition of the relevance of our current work and the science we propose. Moreover, access to the EMBO Young Investigator Programme allows me to fully integrate our newly established laboratory in the larger European scientific community.” (See p. 38)

► **Axel Ulrich**, director at the Max Planck Institute of Biochemistry in Martinsried, Germany, received the 2009 **Dr. Paul Janssen Award for Biomedical Research**, established by Johnson & Johnson and endowed with US\$100,000. According to the jury, Axel Ulrich “was chosen for his pioneering work in applying molecular biology and molecular cloning to the discovery of protein therapeutics for the treatment of a wide range of diseases, including diabetes and cancer.” One example was his studies that have led to the development of the anti-cancer drug Herceptin® (trastuzumab). Likewise, Ulrich’s team discovered that inhibiting the vascular endothelial growth factor receptor (VEGFR) suppresses the generation of blood vessels in tumours and slows down cancer cell growth. Based on their results, in 2006 a VEGFR inhibitor was approved for the treatment of kidney carcinoma and gastro-intestinal stromal tumours. -RN-

Medical Ghostwriting

A Can of Worms

The level at which the pharma industry tries to indirectly influence medical literature is apparently broader than previously suspected. Only last year, a report in the *Journal of the American Medical Association* criticised Merck & Co. for hiring companies to produce reports about in-house studies on the painkiller Vioxx for medical journals and paying other, presumably ‘independent’, scientists to lend their names to the papers (*JAMA* vol. 299(15): 1800-12).

Of course, nobody thinks that Merck is alone. On the contrary, the *JAMA* article noted that ghostwriting appears to be widespread in the pharma industry as part of their marketing efforts.

Quite frequently, those articles are aimed at downplaying the risks of drugs.



A dubious practice when considering that Vioxx was first a best-seller – but then became a fiasco. Merck had to withdraw the drug because of links to heart attacks and agreed to pay US\$4.85 billion to settle related lawsuits.

“It almost calls into question all legitimate research that’s been conducted by the pharmaceutical industry with the academic physician,” said the report’s lead author, Joseph Ross of the Mount Sinai School of Medicine, New York.

The next dispute has only recently surfaced. Last December *PLoS Medicine* and the *New York Times* asked the court to unseal documents that provide details about a ghostwriting campaign by Wyeth Pharmaceutical. End of July the documents were made public.

According to the *New York Times*, the documents show that Wyeth Pharmaceutical hired the medical communications company DesignWrite to produce 26 review articles that appeared in 18 medical journals between 1998 and 2005. All of them relat-

ed to Wyeth’s hormone replacement drugs Prempro and Premarin, emphasising their benefits and downplaying their risks. (Later studies confirmed that menopausal women taking certain hormones acquire an increased risk for breast cancer, heart disease, stroke and dementia).

In its article, the *New York Times* described one example in more detail. DesignWrite wrote a 14-page outline for an article; the author was listed as “TBD” (to be decided). The outline was sent to Gloria Bachman, a professor of obstetrics and gynaecology at the Robert Wood Johnson Medical School in New Brunswick, New Jersey. After she had made “only one correction”, she received a draft of the article a couple of weeks later. In 2005, the article, an almost word-for-word copy of the DesignWrite draft, finally appeared in *The Journal of Reproductive Medicine*. Gloria Bachman was listed as primary author. The acknowledgments thanked several medical writers for their “editorial assistance” but did not disclose any connection to DesignWrite, who charged Wyeth US\$25,000 to generate the article.

Following the same pattern, all 26 articles written by DesignWrite were signed by ‘independent’ top physicians, although many of them contributed little or no writing. DesignWrite itself did not appear in any of the reviews.

Michael Lampe, a Wyeth spokesman, defended this practice. “Pharmaceutical companies routinely hire medical writing companies to assist authors in drafting manuscripts,” he stated. Furthermore, he added that the authors of the articles in question exercised substantive editorial control over the content of the articles and had the final say, in all respects.

A year ago, however, in the Merck case, Joseph Ross came to a completely different conclusion. “Putting someone as the first author is saying this is the person most responsible for the study, who did the analysis, interpreted the data, and wrote the paper,” he told the *Boston Globe*. “It gives the appearance of sound, more rigorously conducted science. It’s just wrong.”

One thing, however, is becoming increasingly clearer: the can of worms regarding hidden medical ghostwriting still needs to be opened much wider. -RN-

European research Council (ERC)

Reforms Needed

A scathing review of the European Research Council (ERC) has called for urgent changes in the way it treats scientists. Chaired by the former President of Latvia, Vaira Vike-Freiberga, the reviewing panel's report (23rd July) found extensive bureaucratic problems associated with the ERC's functioning and vision of scientific research. It urges a series of immediate reforms and another independent review in two years time, to reassess the need to render the ERC completely independent of the European Commission's counter-productive ethos.

The ERC was launched in 2007, as part of the European Union's Seventh Framework Programme. It was intended to represent a major departure from existing European funding agencies with an exclusive mission to support fundamental research, irrespective of national boundaries (*i.e.* ignoring traditional EU political considerations outlining national quotas). With a budget of €7.5 billion through to 2013, the ERC was created in response to fears that Europe was lagging behind in its capacity to generate truly original scientific research, compared to its international partners/competitors. So far, it has awarded

€900 million to 600 projects. But unfortunately, despite its ambitious mission, the ERC has been hampered from its conception by what the review panel refers to as "original sin".



The ERC's organisation is divided between a Scientific Council that sets its scientific strategy and an Executive Agency that is responsible for all the management and administration. Unfortunately, all real power lies with this Executive Agency, which, although theoretically autonomous, is effectively controlled by the Commission. Fur-

thermore, it has only one representative from the Scientific Council who has no formal power. This, the review panel says, is why the ERC has been operating according to the European Commission's standard commercial practices – the Executive Agency does not understand that scientists and their research should not be treated in the same way as sub-contractors for paper clips, software packages and road repairs. In addition, a culture of mistrust has been enforced at the Commission in the wake of fraud scandals that resulted in 1999's wholesale resignation of the Commission's President, Jacques Santer, and all the commissioners.

Currently, scientists who succeed in obtaining ERC funding for their projects are required to sign legally binding contracts that oblige them to keep time sheets, detailed accounts for all expenses and restrict their capacity to change research direction as their projects evolve. "You want these people to do first-rate frontier research and then you impose contractual obligations on them. The symbolic value of this is obvious!" said a member of the ERC's scientific council. The panel agrees that scientists doing basic research need to be trusted and given flexibility, for example, by awarding "lump sums" of grant money with few ►►



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► obligations other than to ultimately show the “fruits of their labour”.

Strict rules are also threatening the willingness of scientists to review ERC grant applications. They need to prove their identity by mailing a copy of their passport, which the commission must authorise before they can be given any information about the applicant or the grant proposal they are being asked to review. The panel says this is “completely abusive”. The chairman of ERC’s peer-review committee for mathematicians, Jean-Pierre Bourguignon, said he had “never seen anything like this”. Potential peer reviewers “refused to be involved. They were upset”. He felt obliged to write e-mails to outraged reviewers apologising about ERC rules, trying to persuade them personally to change their minds. And if you do agree to review, it takes a long time to be reimbursed for any travel expenses. One scientist told the panel that they “would not agree to review again. I have reviewed for a

large number of international funding bodies and this was the worst experience I have had in 30 years.” The review panel says that reviewers “are not contractors but valuable volunteers and should be treated as such.”



The key recommendations for reform of the ERC all seek to shift the control of the organisation into the hands of scientists. There are calls to adequately pay the

working scientists who are on the Scientific Council, to place the management of reviewers and panellists under scientific control and to “create a fair balance” in the numbers of scientists and non-scientists in the Executive Agency. But to do this, they need to break the Commission’s hold, facilitating “the recruitment of qualified scientists even in positions that are now ‘reserved’ for Commission career personnel.”

However, the biggest change would be if the ERC became completely independent of the European Commission, something that is legally possible under Article 171 of the treaty governing the European Union. In this case, the ERC could operate and govern itself much more freely as a body funding basic scientific research, although it would still have to account for its proper use of EU funds. For the moment, this option was recommended as a “long-term structural change in time for the 8th Framework Programme”, i.e. in another few years. -JG-

Machine in the Brain

A Swedish team creates an artificial nerve cell capable of specifically communicating with mammalian neurons.

In 1638, René Descartes wrote in ‘Discourse on the Method’, a study on proving self existence, that a person would not know if an evil demon had trapped his mind in a black box and was controlling all inputs and outputs. A notion, still up-to-date when it comes to neural implants and machine-to-brain-interfacing.

However, who would care about such ethico-philosophical questions if Descartes’ ‘person’ clearly benefited from the “machine in the head”? That’s probably the main reason why there are hardly any complaints when, for example, trying to help impaired people by inserting retinal or cochlear implants into their eyes or ears, and electrodes used directly in their brains.

One problem with those implants, however, is that the electrodes, based on electrical stimulation only, activate *all* cell types in their vicinity. In order to avoid the resulting undesired effects, Swedish scientists at Karolinska Institutet and Linköping University have now developed a new concept to fine-tune such machine-to-neuron-signalling (*Nature Materials* vol. 8(9): 742-6). They constructed an ion pump out of electrically conducting material to create a new type of “delivery electrode” that instead releases neurotransmitters to communicate with brain cells. The advantage is that only those neighbouring cells with receptors for the specific neurotransmitter will be activated.

To test their idea of selectively transporting neurotransmitters electronically, the researchers used the hearing organ in guinea pigs as a

model system. The tip of the ion pump, of similar design to a small syringe, was inserted in animals near the round window in the inner ear. When the power was switched on, exact doses of glutamate, the most important neurotransmitter in the cochlea, were delivered via an electrically charged plastic film and diffused through the round window to the intended target, the hair cells.

By measuring the auditory response of the brainstem, the researchers were able to study what was happening as the transport of glutamate was taking place. After one hour, the glutamate concentration reached levels where the result was loss of hearing – as was expected, since excessive quantities of glutamate are toxic and lead to cell depletion. The authors, therefore, conclude that their delivery electrode can, indeed, be used to control the hearing function in the brains of guinea pigs. And, “Having demonstrated the ability to translate electronic addressing signals, through neurotransmitter signalling, into brainstem responses, this technology establishes a new paradigm in machine-to-brain interfacing,” they wrote.

Whether new paradigm or not, according to lead author Agneta Richter-Dahlfors, the next step is clear: to develop a small implantable unit that can be wirelessly programmed to allow the flexible and individually adapted release of neurotransmitters for each patient. -RN-



(More research results from European labs on pp. 30-35)