Scientists behaving badly

Peter Aldhous

@paldhous

(With special thanks to Eugenie Samuel Reich)

Perky cheerleaders?

"Science writers believe in science. They believe science can put men on Mars, can cure cancer and baldness, can feed those African babies. When Professor Schmidtlapp says he's discovered something big, the science writers…don't draw their guns and make him put his cards on the table. They don't flyspeck his raw data, don't check his funding sources, don't scrutinize his previous articles for mistakes. They don't interview his enemies or call his lab technicians at home for an off-the-record assessment of the great man's work.

"They like science, they probably admire Schmidtlapp and they're excited by the prospect that he's right. So they just ask him how to spell whatever it is and write it down."

John Crewdson of the *Chicago Tribune*, in *Nieman Reports*, Winter 1993

The Cloning King

Woo Suk Hwang

First ethics lapses…

Robodocs
NASA looks to automation to keep Hubble out of trouble
p4

Rock show
Fossil exhibition earns mixed response from museums
p5

Up in the air
Microwaves offer clues to Earth's slow cooking time
p7

Isaac who?
Web fame test brings physicists down to Earth with a bump
p8

Korea's stem-cell stars dogged by suspicion of ethical breach

David Cyranoski, Seoul

When, in February, a South Korean team announced that it had derived stem cells from a cloned human embryo, its achievement was heralded as an important step on the road to 'therapeutic cloning'. But the research is now clouded by nagging questions about the source of the key resource for the experiment: human egg cells.

Korean citizens'-rights activists and bioethicists are pressing the team, led by Woo Suk Hwang and Shin Yong Moon of Seoul National University, to prove that the recruitment of women volunteers followed ethical guidelines. *Nature*'s enquiries have also revealed troubling inconsistencies — in particular over whether the donors included junior members of the research team.

The brewing controversy could undermine the domestic public and political support on which Hwang and Moon's progress has depended (see News Feature, page 12). Any suggestion of ethical irregularities in therapeutic-cloning research could also have international repercussions, providing ammunition for activists who are opposed to the technology on moral grounds.

Therapeutic cloning involves creating an embryo by transferring the nucleus from a patient's cell into a human egg cell stripped of its own nucleus. After being grown in culture for a few days, this clone can yield embryonic stem cells, which can develop into any of

Woo Suk Hwang faces increasing scrutiny over how he recruited egg donors for his research.

T.S. WOO/REUTERS

the veins or stroke. "It's a painful procedure and there is risk involved," says Jose Cibelli, a co-author on the paper who studies cloning at Michigan State University in East Lansing. "It would never fly in the United States."

Hwang says that the donors were motivated by a desire to push forward a promising field of medicine. "Many women are sympathetic with our research," he says. Supplementary material published online with the paper says that the volunteers were not paid, and explains that they filled in informed-consent

included students or junior employees on the research team because "it could certainly look like coercion was involved".

The information posted with the paper also states: "Neither donors nor their family, relatives or associates may benefit from this research." Koo, who was a co-author on the paper, arguably did stand to gain professionally from its publication.

Hwang denies that Koo was among the donors. But he declined *Nature*'s requests for further documentary evidence of the procedures for recruiting the egg donors and obtaining their consent. Attempts to get more information from the Institutional Review Board at Hanyang University Hospital in Seoul, which provided ethical approval, were similarly rebuffed. Its chair, university obstetrician Moon-il Park, cancelled an arranged phone interview.

Within Korea, concern is growing about the lack of transparency surrounding the procedures for obtaining the donated eggs. "I'm doubtful women would give their eggs so easily," wrote Pil Pyul Lee, a science historian at the Korea National Open University in Seoul, in the 23 February issue of the *Professors Times*, a nationwide newspaper in which academics express their views on topical issues.

Lee's article also questioned the inclusion as a co-author on the paper of Ky Young Park, a plant molecular biologist formerly at Sunchon National University who is now a science and

…then scientific fraud

nature Vol 439|12 January 2006

NEWS

Verdict: Hwang's human stem cells were all fakes

SEOUL

The results are in. The university committee looking into scientific misconduct in the laboratory of South Korean cloner Woo Suk Hwang announced on 10 January that his 2004 claim to have cloned a human embryo was fake. But his Afghan hound Snuppy is a real clone.

The announcement finally confirms the gravest suspicions of Hwang's work with humans. There are two papers in which Hwang's group claimed to clone human cells — a 2004 article that describes the first cloned embryo and derivation of a stem-cell line from it (W. S. Hwang *et al. Science* 303, 1669–1674; 2004), and a 2005 article that claims the establishment of eleven 'patient-specific' stem-cell lines (W. S. Hwang *et al. Science* 308, 1777–1783; 2005). Both have turned out to be complete and deliberate fakes.

At least Snuppy has been confirmed as a clone.

"Such an act is nothing other than deception of the scientific community and the public at large," concludes Myung Hee Chung of Seoul National University (SNU), who headed the committee.

With the 2005 paper already discredited in have used only 242 eggs for the 2004 study and 185 for the 2005 study.

The findings are a huge setback for therapeutic cloning — the idea that cloned embryos could be used as a source of patient-matched stem cells to replace damaged tissues in a range of diseases. Even using numbers of human eggs of which other researchers can only dream, Hwang's team was unable to derive such stem cells, and the field is now left with no evidence that it is possible in humans at all (see *Nature*, 438, 1056–1059; 2005).

The committee did find that Hwang succeeded in cloning human embryos to the blastocyst stage, from which stem cells can be derived. But the success rate was just 10%, and they were "in poor condition". The only other group to have some success, Alison Murdoch's team at the University of Newcastle upon Tyne, UK, has cloned just a single blastocyst (M. Stojkovic *et al. Reprod. BioMed. Online* 11, 226–231; 2005).

It is possible to create embryonic stem-cell

lines, insists Kevin Eggan, a researcher in the field at Harvard University, Massachusetts. But no one will venture a guess as to when it might be accomplished. "There are many unknowns," says Eggan. "We don't know how many eggs will be needed and we don't know how many women will step forward to contribute."

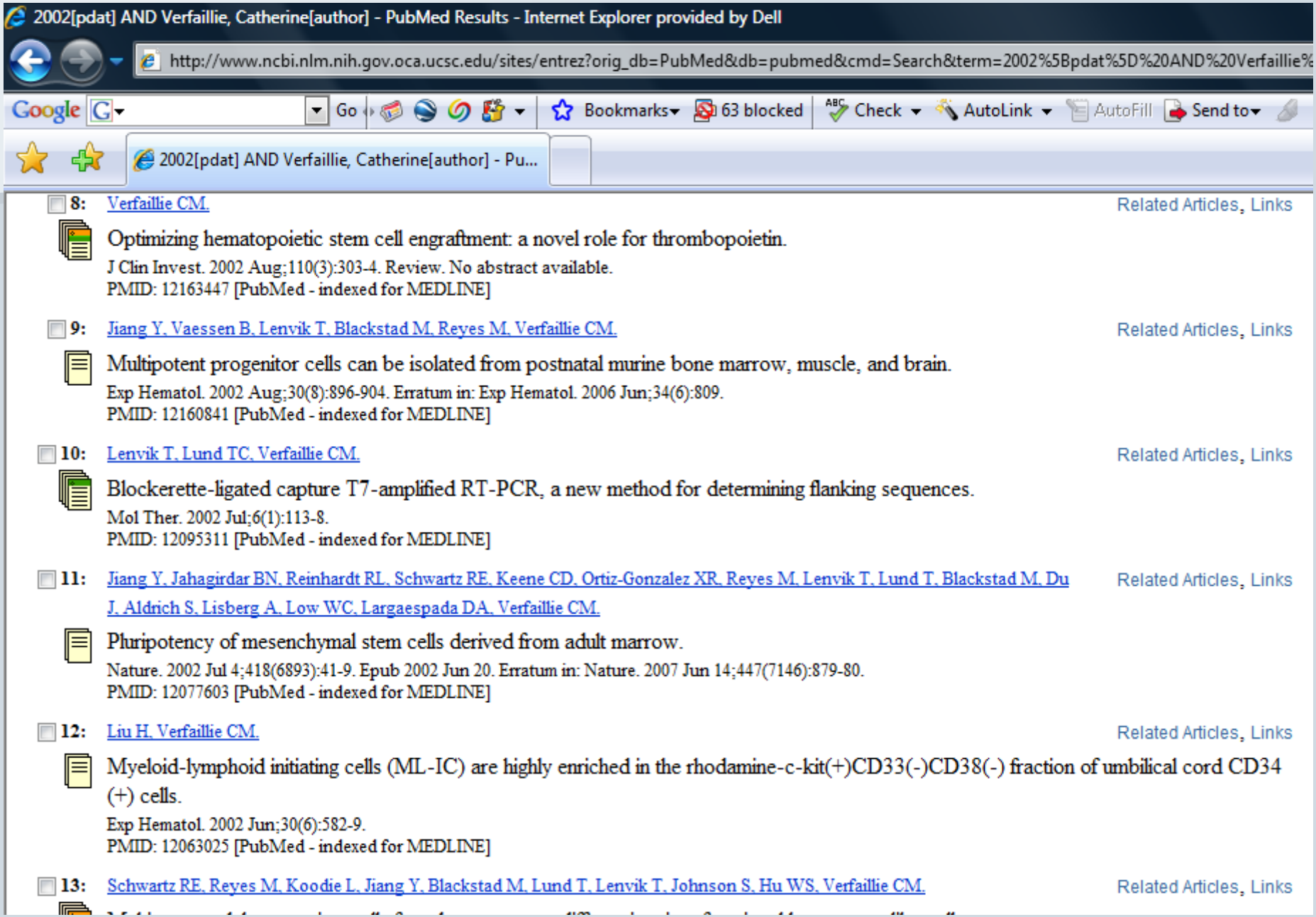
Ethical transgressions in the way Hwang got his eggs — he seems to have coerced junior researchers into donating — have stim-

Minnesota Mystery

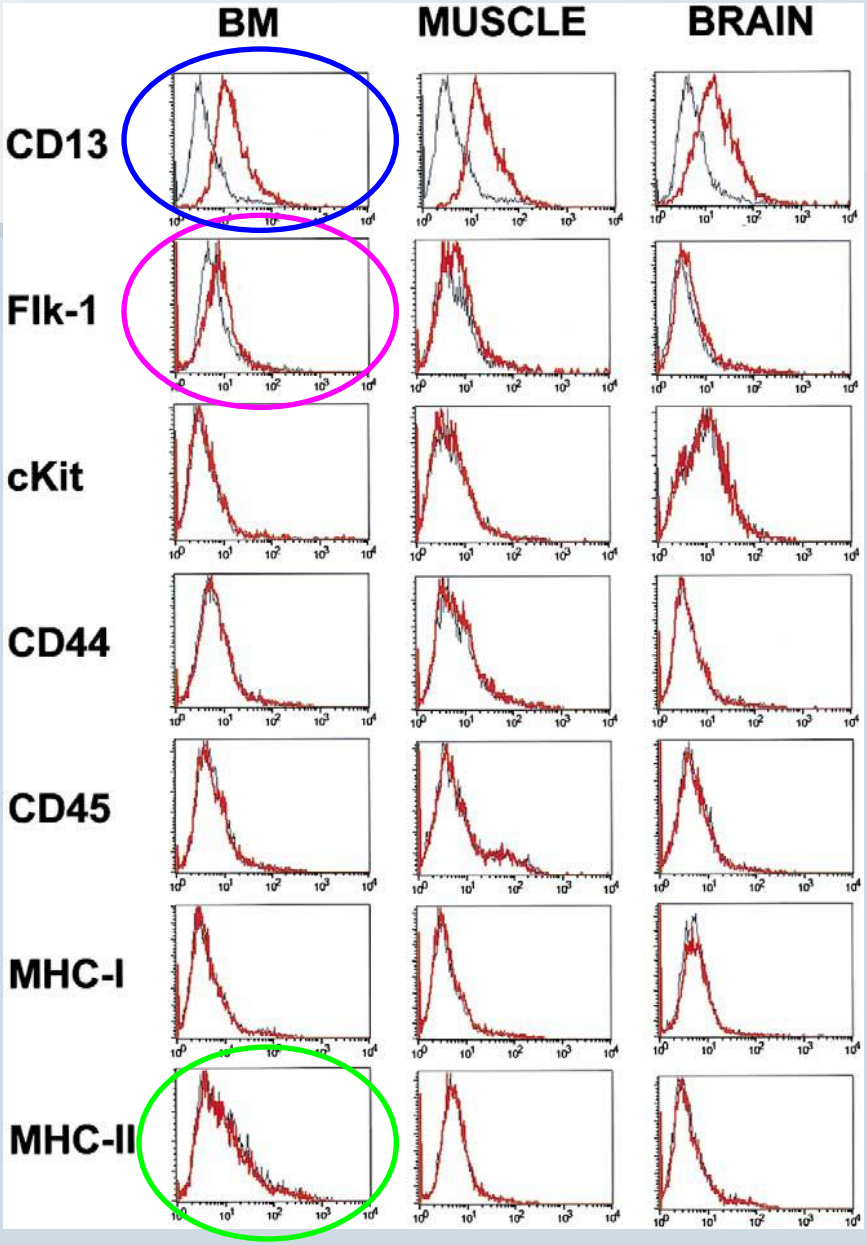
Catherine Verfaillie

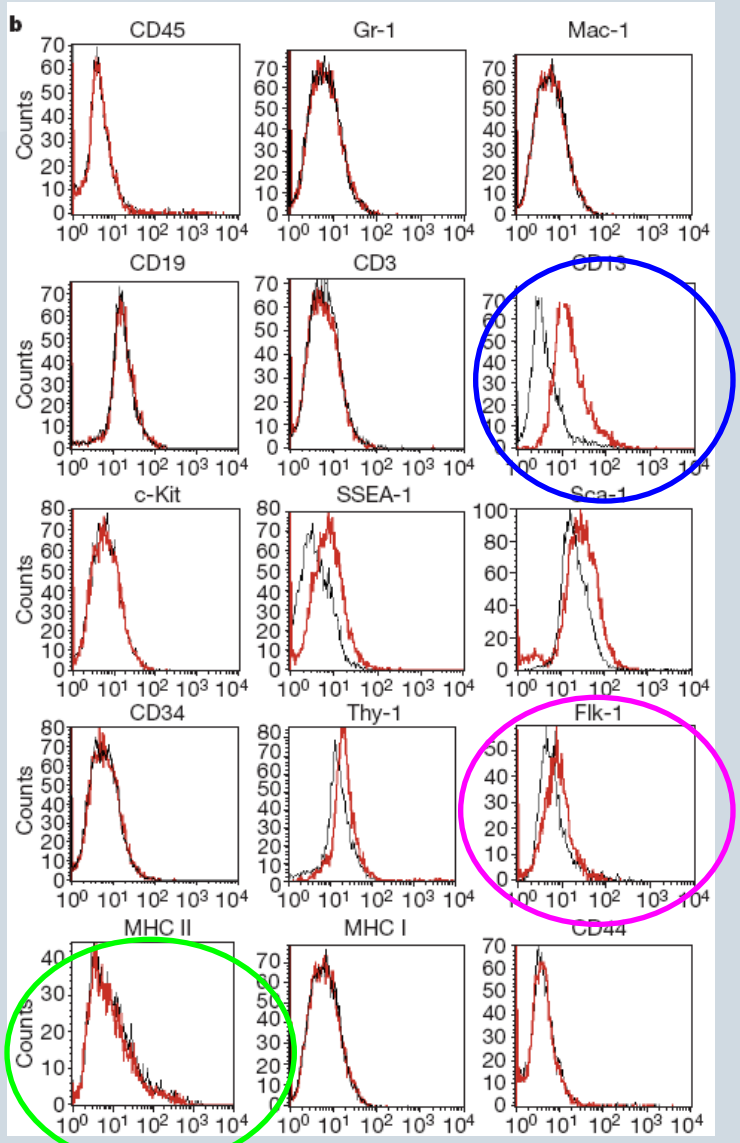
NewScientist

Where did we go? Pubmed



What did we find?





This week

'Flawed' stem cell data withdrawn

PETER ALDHOUS
AND EUGENIE SAMUEL REICH

IT IS one of the best-known stem cell papers in the past five years, describing adult cells that seemed to hold the same promise as embryonic stem cells. Now, following inquiries by *New Scientist*, some of the data contained within the papers is being questioned.

In 2002, a team led by Catherine Verfaillie of the University of Minnesota, Minneapolis, described "multipotent adult progenitor cells" or MAPCs, isolated from the bone marrow of rodents (*Nature*, vol 418, p 41). These cells seemed able to develop into most of the body's tissues. Previously, only embryonic stem cells (ESCs) had proved so versatile, and the work was seized upon by opponents of ESC research, who claimed it showed similarly versatile cells could be harvested without destroying human embryos.

The results proved hard to repeat, and for more than six months from late 2003 even Verfaillie's own group was unable to isolate the cells. When *New Scientist* looked more closely, we found that six plots from the *Nature* paper and its supplementary information were duplicated in a second paper, published at about the same time in *Experimental Hematology* (vol 30, p 896), even though they were supposed to refer to different cells, taken from different mice. The plots described "marker" molecules on the surface of the cells, supposedly characteristic of MAPCs.

After *New Scientist* questioned the results, a panel of experts reviewed the data. Verfaillie, now at the Catholic University of Leuven (KUL) in Belgium, has since written to the two journals informing them of problems with data within the two papers, stating: "It was [the experts'] consensus opinion that the data were flawed and should not be relied upon as accurate representation of MAPC marker profiles."

The flaws she refers to do not relate to the duplications in the papers, and Verfaillie stands by the claim that MAPCs can develop into most of the body's tissues, arguing that later papers have described reliable methods for identifying them. In her most recent paper, Verfaillie and Irving Weissman, a stem cell biologist at Stanford University in California, showed that MAPCs can give rise to all the cell types found in blood (*New Scientist*, 27 January, p 17), but it is still unclear whether MAPCs are as versatile as she claimed in the original *Nature* paper.

Many researchers are unable even to isolate them. "They're very testy cells," observes Amy Wagers of Harvard University, who spent a week in Verfaillie's lab trying in vain to learn the technique.

"The paper describes 'multipotent' cells that seemed able to develop into most of the body's tissues"

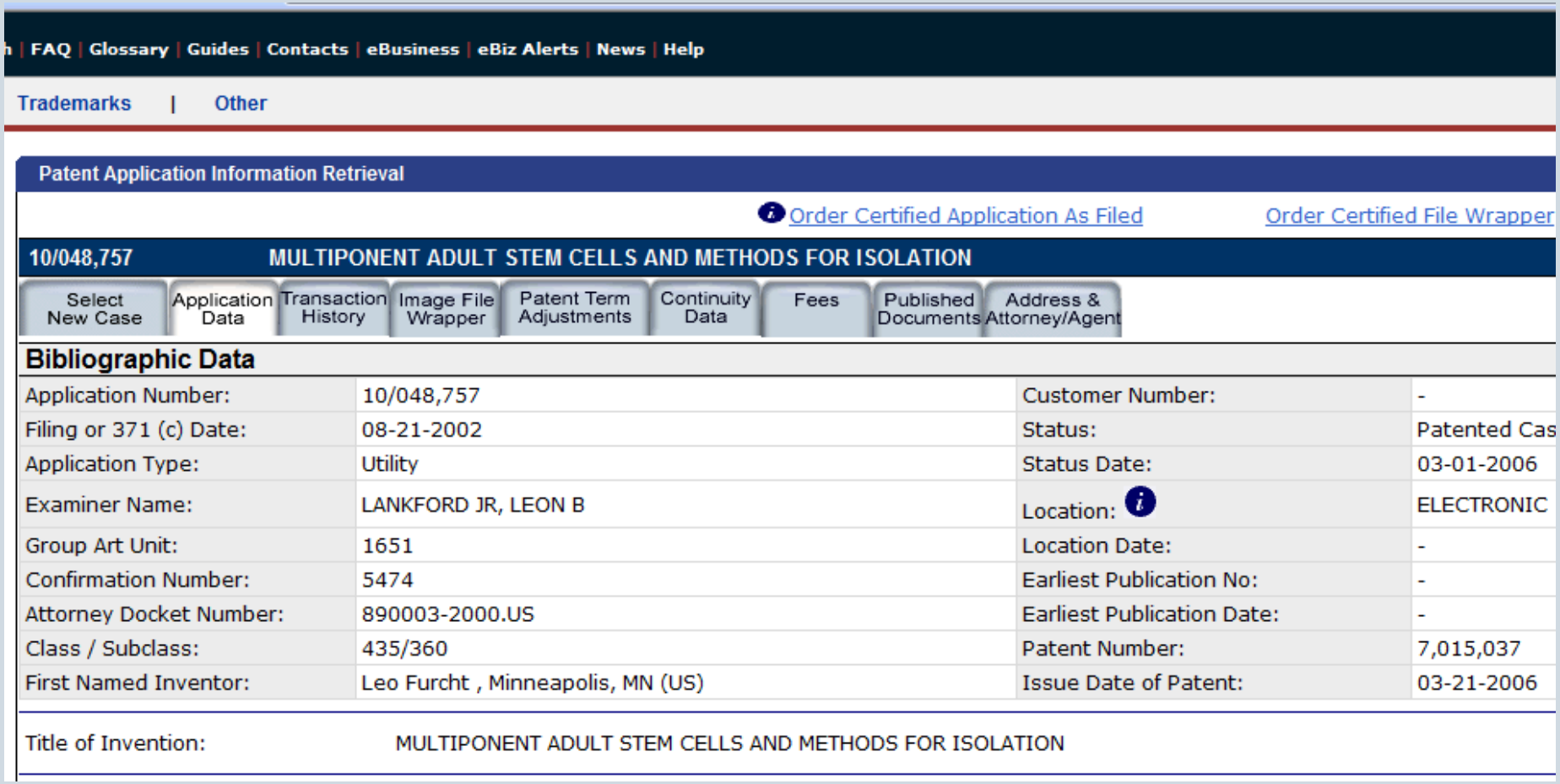
The problems with the marker profiles may help explain these difficulties. "If I had been following this recipe since 2002, I'd be extremely angry," says Jeanne Loring, a stem cell biologist at the Burnham Institute for Medical Research in La Jolla, California.

NewScientist

What next? Let's look at the patents

http://patft.uspto.gov/ **Search issued patents and applications**

http://portal.uspto.gov/external/portal/pair **'Image file wrapper' tab has 'drawings'**



h | FAQ | Glossary | Guides | Contacts | eBusiness | eBiz Alerts | News | Help

Trademarks | Other

Patent Application Information Retrieval

Order Certified Application As Filed Order Certified File Wrapper

10/048,757 MULTIPONENT ADULT STEM CELLS AND METHODS FOR ISOLATION

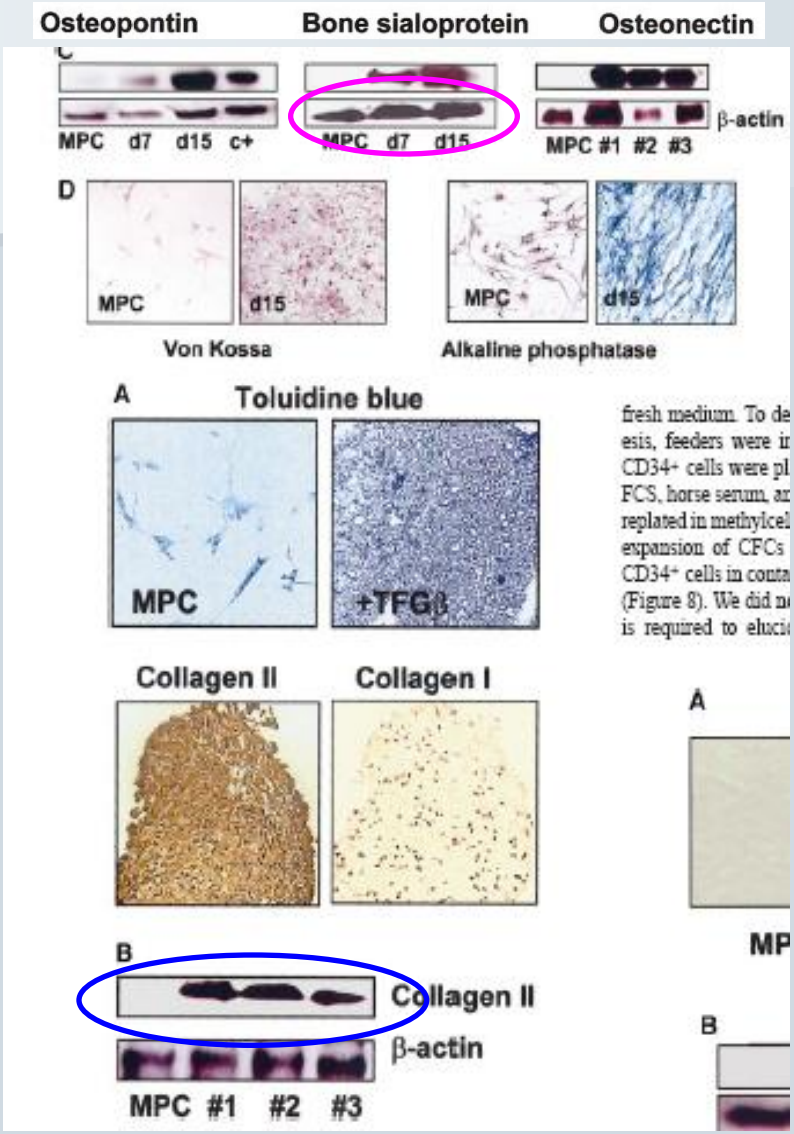
Select New Case | Application Data | Transaction History | Image File Wrapper | Patent Term Adjustments | Continuity Data | Fees | Published Documents | Address & Attorney/Agent

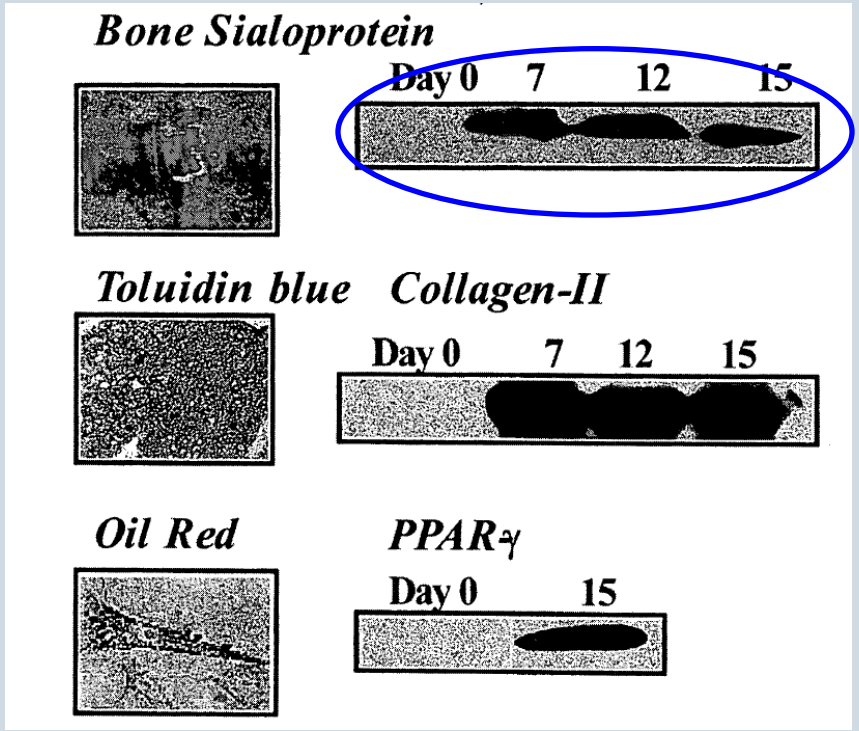
Bibliographic Data

Application Number:	10/048,757	Customer Number:	-
Filing or 371 (c) Date:	08-21-2002	Status:	Patented Cas
Application Type:	Utility	Status Date:	03-01-2006
Examiner Name:	LANKFORD JR, LEON B	Location:	ELECTRONIC
Group Art Unit:	1651	Location Date:	-
Confirmation Number:	5474	Earliest Publication No:	-
Attorney Docket Number:	890003-2000.US	Earliest Publication Date:	-
Class / Subclass:	435/360	Patent Number:	7,015,037
First Named Inventor:	Leo Furcht , Minneapolis, MN (US)	Issue Date of Patent:	03-21-2006

Title of Invention: MULTIPONENT ADULT STEM CELLS AND METHODS FOR ISOLATION

Lightning strikes twice





SPOT THE DIFFERENCE

These apparently duplicated images have been used as evidence for the presence of different proteins produced in different experiments

- First, an image of three bands on a gel is used to represent a control for an experiment in which stem cells are made to differentiate into bone cells (*Blood*, vol 98, p 2620)

- On the same page of the *Blood* paper, a reversed version of the same image, with some small modifications, is used to show the production of collagen II in stem cells made to differentiate into cartilage cells

- The same reversed image is used in US patent 7015037 to show the production of a bone-specific protein in stem cells made to differentiate into bone cells

SOURCE: BLOOD (VOL 98, P 2620) AND US PATENT 7015037

We publish…and wait

This week

Fresh questions on stem cell findings

The discovery of more duplicated data is again casting a shadow over "versatile" adult stem cells

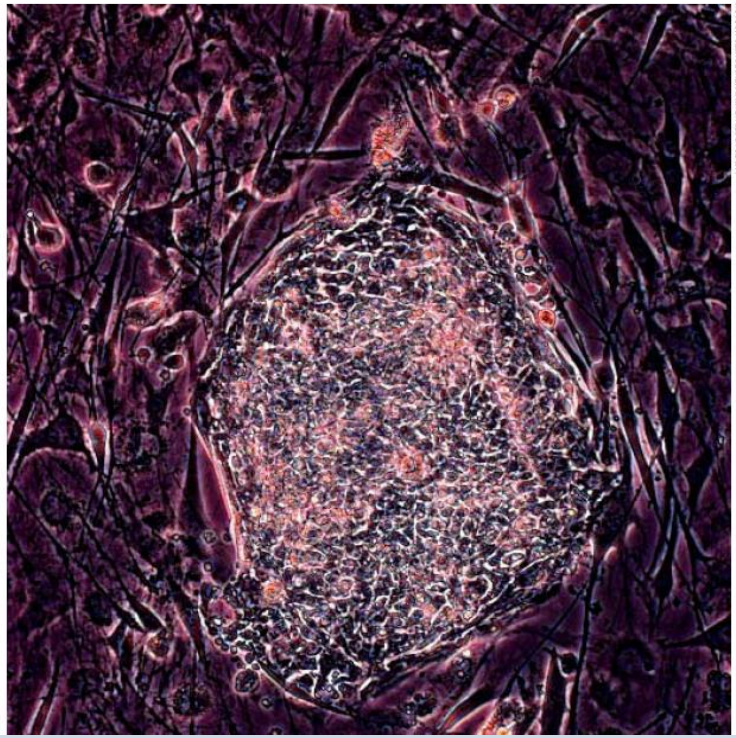
PETER ALDHOUS
AND EUGENIE SAMUEL REICH

FRESH questions surround some of the highest-profile research on adult stem cells. For the second time, *New Scientist* has discovered apparently duplicated data being used to describe results from different experiments in work published by a group of scientists at the University of Minnesota, Minneapolis.

The research relates to a particular type of adult stem cell

Given these difficulties, *New Scientist* decided more than a year ago to take a close look at the *Nature* paper. We found that some of the images within it also appeared in a second paper that was published at about the same time, where they were supposed to relate to a different experiment (see "Flaws and duplications").

Now *New Scientist* has examined a US patent (number 7015037) granted in 2006 that covers the isolation and use of MAPCs. The patent is exclusively



MEDIAGSTOJOVE/SCIENCEPHOTOLIBRARY

NewScientist

Verdict: falsification

Morayma Reyes

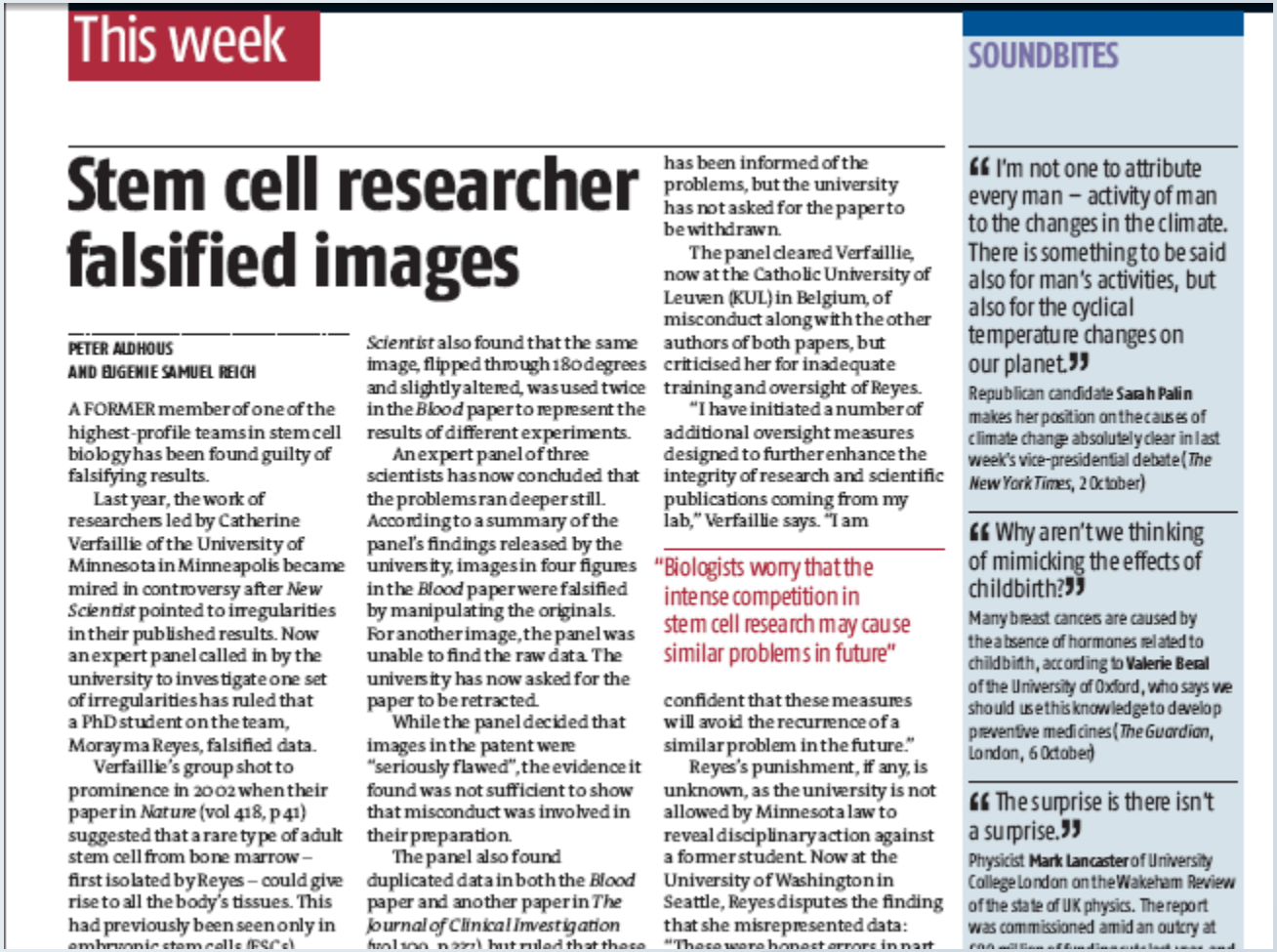
In four figures in the *Blood* paper, the panel concluded that aspects of the figures were altered in such a way that the manipulation misrepresented experimental data and sufficiently altered the original research record to constitute falsification under federal regulations and University policy.

Manipulations identified by the panel included: elimination of bands on blots, altered orientation of bands, introduction of lanes not included in the original figure, and covering objects or image density in certain lanes.

University of Minnesota statement, October 2008

NewScientist

Which we report



This week

Stem cell researcher falsified images

PETER ALDHOUS
AND EUGENIE SAMUEL REICH

A FORMER member of one of the highest-profile teams in stem cell biology has been found guilty of falsifying results.

Last year, the work of researchers led by Catherine Verfaillie of the University of Minnesota in Minneapolis became mired in controversy after *New Scientist* pointed to irregularities in their published results. Now an expert panel called in by the university to investigate one set of irregularities has ruled that a PhD student on the team, Morayma Reyes, falsified data.

Verfaillie's group shot to prominence in 2002 when their paper in *Nature* (vol 418, p 41) suggested that a rare type of adult stem cell from bone marrow – first isolated by Reyes – could give rise to all the body's tissues. This had previously been seen only in embryonic stem cells (ESCs).

Scientist also found that the same image, flipped through 180 degrees and slightly altered, was used twice in the *Blood* paper to represent the results of different experiments.

An expert panel of three scientists has now concluded that the problems ran deeper still. According to a summary of the panel's findings released by the university, images in four figures in the *Blood* paper were falsified by manipulating the originals. For another image, the panel was unable to find the raw data. The university has now asked for the paper to be retracted.

While the panel decided that images in the patent were "seriously flawed", the evidence it found was not sufficient to show that misconduct was involved in their preparation.

The panel also found duplicated data in both the *Blood* paper and another paper in *The Journal of Clinical Investigation* [vol 109, p 327], but ruled that these has been informed of the problems, but the university has not asked for the paper to be withdrawn.

The panel cleared Verfaillie, now at the Catholic University of Leuven (KUL) in Belgium, of misconduct along with the other authors of both papers, but criticised her for inadequate training and oversight of Reyes.

"I have initiated a number of additional oversight measures designed to further enhance the integrity of research and scientific publications coming from my lab," Verfaillie says. "I am confident that these measures will avoid the recurrence of a similar problem in the future."

"Biologists worry that the intense competition in stem cell research may cause similar problems in future"

Reyes's punishment, if any, is unknown, as the university is not allowed by Minnesota law to reveal disciplinary action against a former student. Now at the University of Washington in Seattle, Reyes disputes the finding that she misrepresented data: "These were honest errors in part

SOUNDBITES

"I'm not one to attribute every man – activity of man to the changes in the climate. There is something to be said also for man's activities, but also for the cyclical temperature changes on our planet."

Republican candidate **Sarah Palin** makes her position on the causes of climate change absolutely clear in last week's vice-presidential debate (*The New York Times*, 2 October)

"Why aren't we thinking of mimicking the effects of childbirth?"

Many breast cancers are caused by the absence of hormones related to childbirth, according to **Valerie Beral** of the University of Oxford, who says we should use this knowledge to develop preventive medicines (*The Guardian*, London, 6 October)

"The surprise is there isn't a surprise."

Physicist **Mark Lancaster** of University College London on the Wakeham Review of the state of UK physics. The report was commissioned amid an outcry at

NewScientist

The story continues

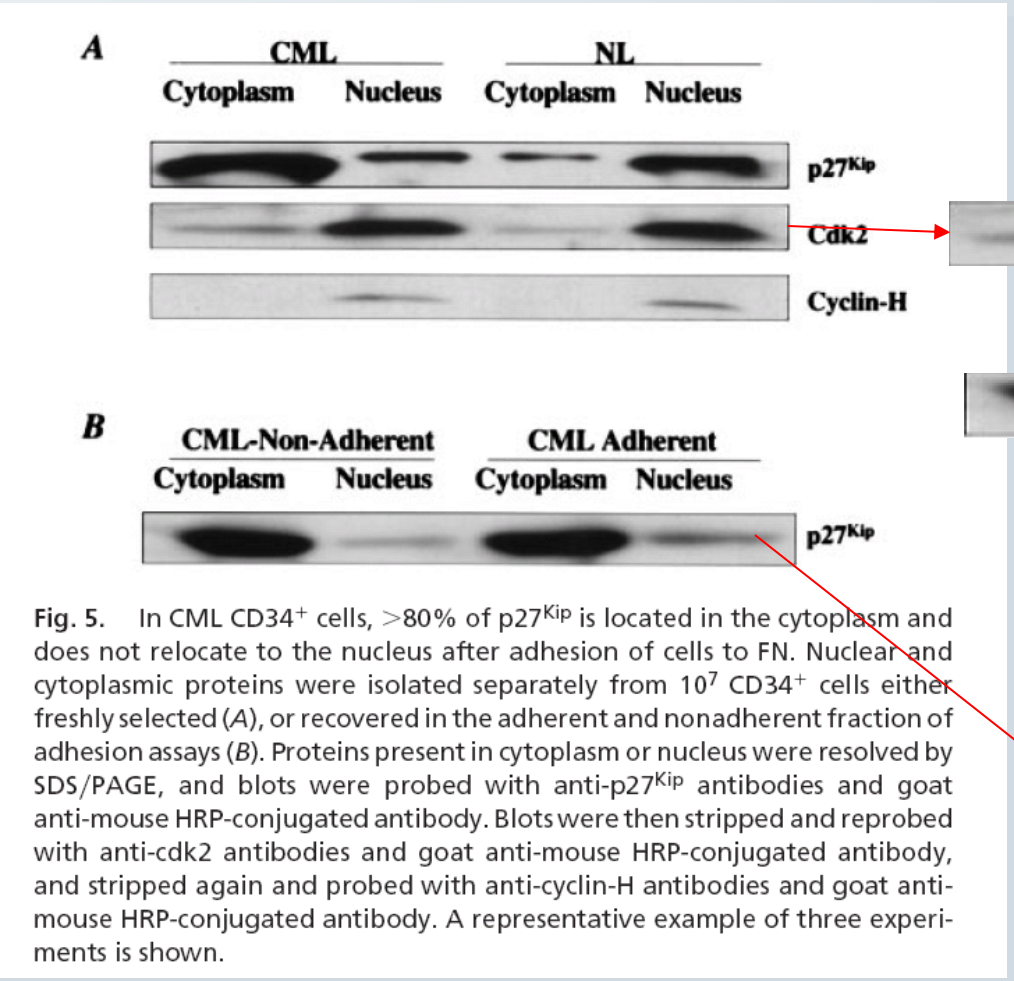
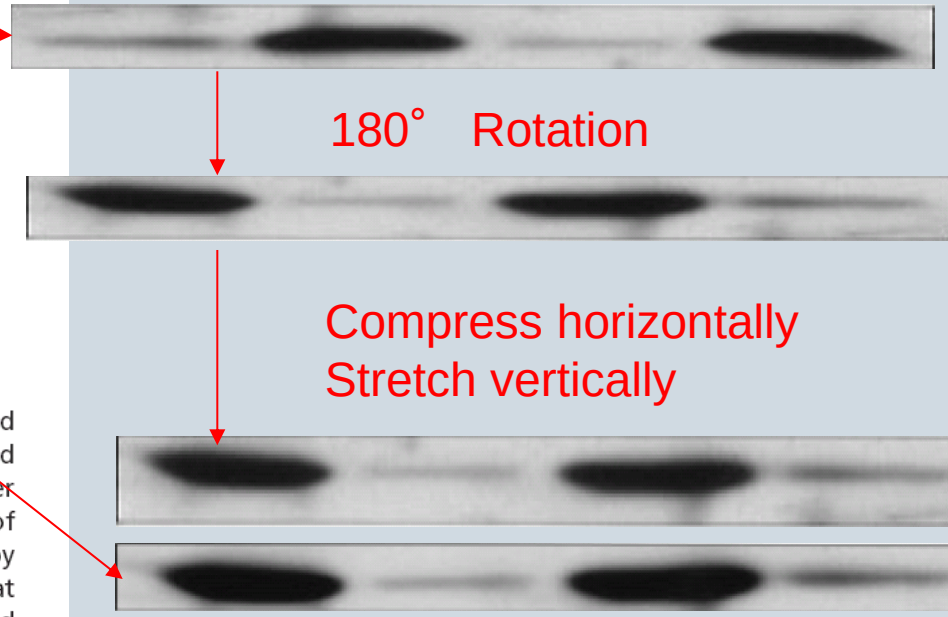


Fig. 5. In CML CD34$^+$ cells, >80% of p27^{Kip} is located in the cytoplasm and does not relocate to the nucleus after adhesion of cells to FN. Nuclear and cytoplasmic proteins were isolated separately from 10^7 CD34$^+$ cells either freshly selected (*A*), or recovered in the adherent and nonadherent fraction of adhesion assays (*B*). Proteins present in cytoplasm or nucleus were resolved by SDS/PAGE, and blots were probed with anti-p27^{Kip} antibodies and goat anti-mouse HRP-conjugated antibody. Blots were then stripped and reprobed with anti-cdk2 antibodies and goat anti-mouse HRP-conjugated antibody, and stripped again and probed with anti-cyclin-H antibodies and goat anti-mouse HRP-conjugated antibody. A representative example of three experiments is shown.

NewScientist



The data in figure 5B appears to be a rotated, distorted, cleaned-up version of data in the middle row of 5A

Digital image forensics

http://ori.hhs.gov/forensic-tools

THE OFFICE OF RESEARCH INTEGRITY

Contact Us | Search this site | ORI 2.0

Home | About ORI | News & Events | Research Misconduct | RCR Resources | Programs | Policies & Regulations | Assurance Program

Home >> Research Misconduct >> Forensic Tools

Printer Friendly

Forensic Tools

Upgraded Forensic Tools from ORI - Tools for Examination of Plagiarism, and ORI's Forensic Tools for Quick Examination of Scientific Images

These Forensic tools illustrate several principles in examining questioned text and images in biomedical science.

Plagiarism Tools:

These are various tools that have been developed by others that may help detect possible problems with improper reuse of text.

ORI's Forensic Image Analysis Tools may be available in two forms (depending in some cases on the specific task):

Forensic Droplets:

A "Droplet" is small desktop application in Adobe Photoshop®, (v.7 and later) that automatically processes image files that are dragged onto its icon. A Droplet can be a nearly "seamless" interface for quickly examining certain features of a scientific image in Photoshop while reading the publication in the FULL TEXT (html) form or in some forms in an Internet Browser. Droplets can be used to automate the batch processing by dragging and dropping a group of image files.

First, Download and Save the Droplet to the desktop and assign it's use to your Photoshop®, program. To use, simply select and drag the highest resolution image from the browser's window to the desk top, where the image will be automatically saved. At this point, dragging the icon of the new desktop file onto the Droplet will 1) then open Photoshop (if it is not already open), and 2) trigger an automatic sequence for the specific Droplet selected.

Forensic Actions (Photoshop® v. CS2-CS3)
Advanced Forensic Actions (Photoshop® v. CS4-CS5):

Misconduct Case Summaries

Newsletter

Follow Us on Twitter

Annual Report System

PHS Administrative Action Bulletin Board

Social Media

ORI Blog | Twitter

May-23 FAQs for the ORI grant application

May-17 Update on Philippe Bois Research Misconduct Case

May-15 Case Study: "My Lab Boss Puts His Name on My Papers and Proposals"

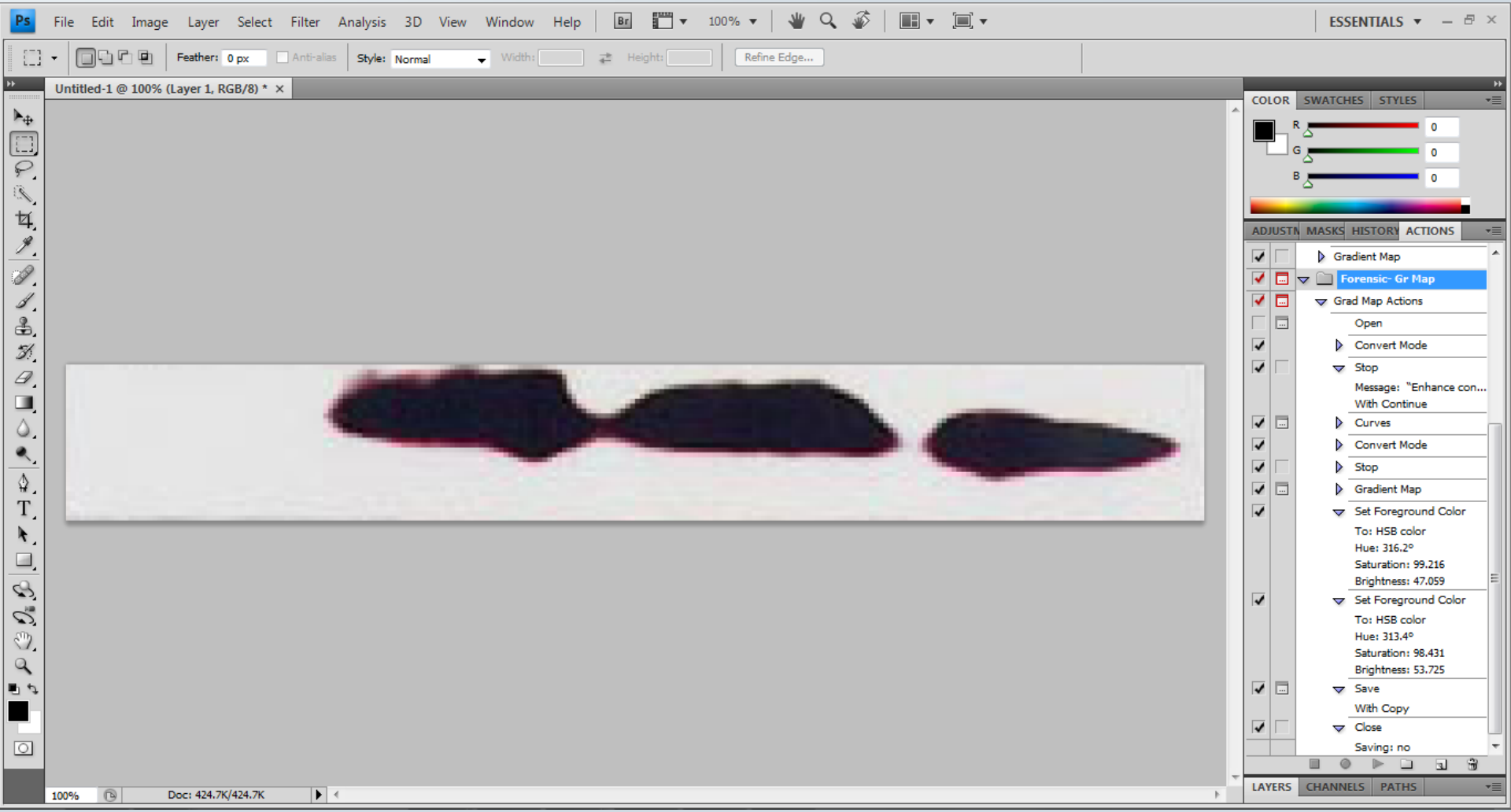
May-08 John Dahlberg Speaks about Plagiarism

ORI forensic tools in action

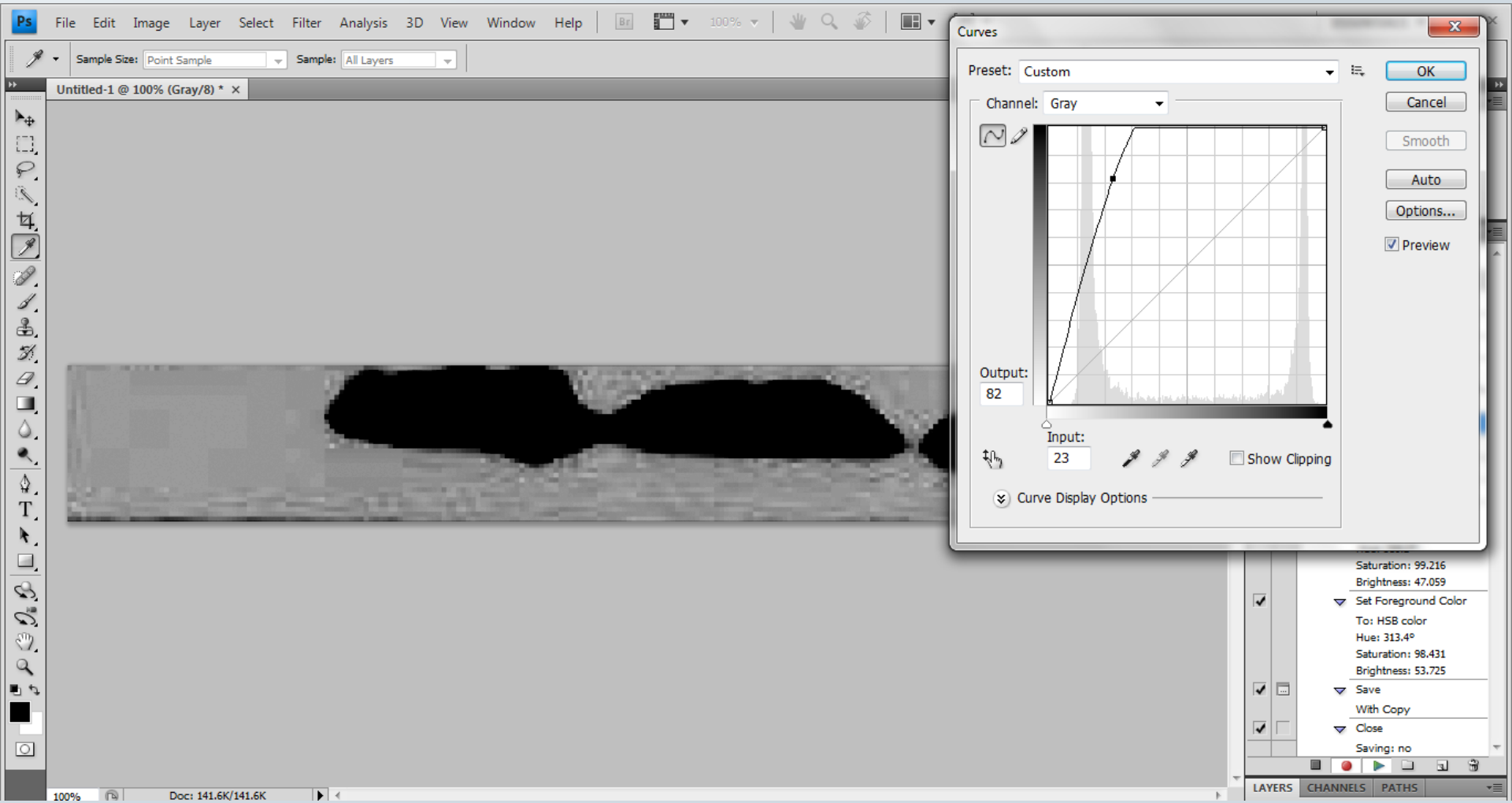
http://ori.hhs.gov/droplets
http://ori.hhs.gov/actions
http://ori.hhs.gov/advanced-forensic-actions

(**Demonstration by Rachel Tompa, UC Santa Cruz, science communication class of 2007-08)**

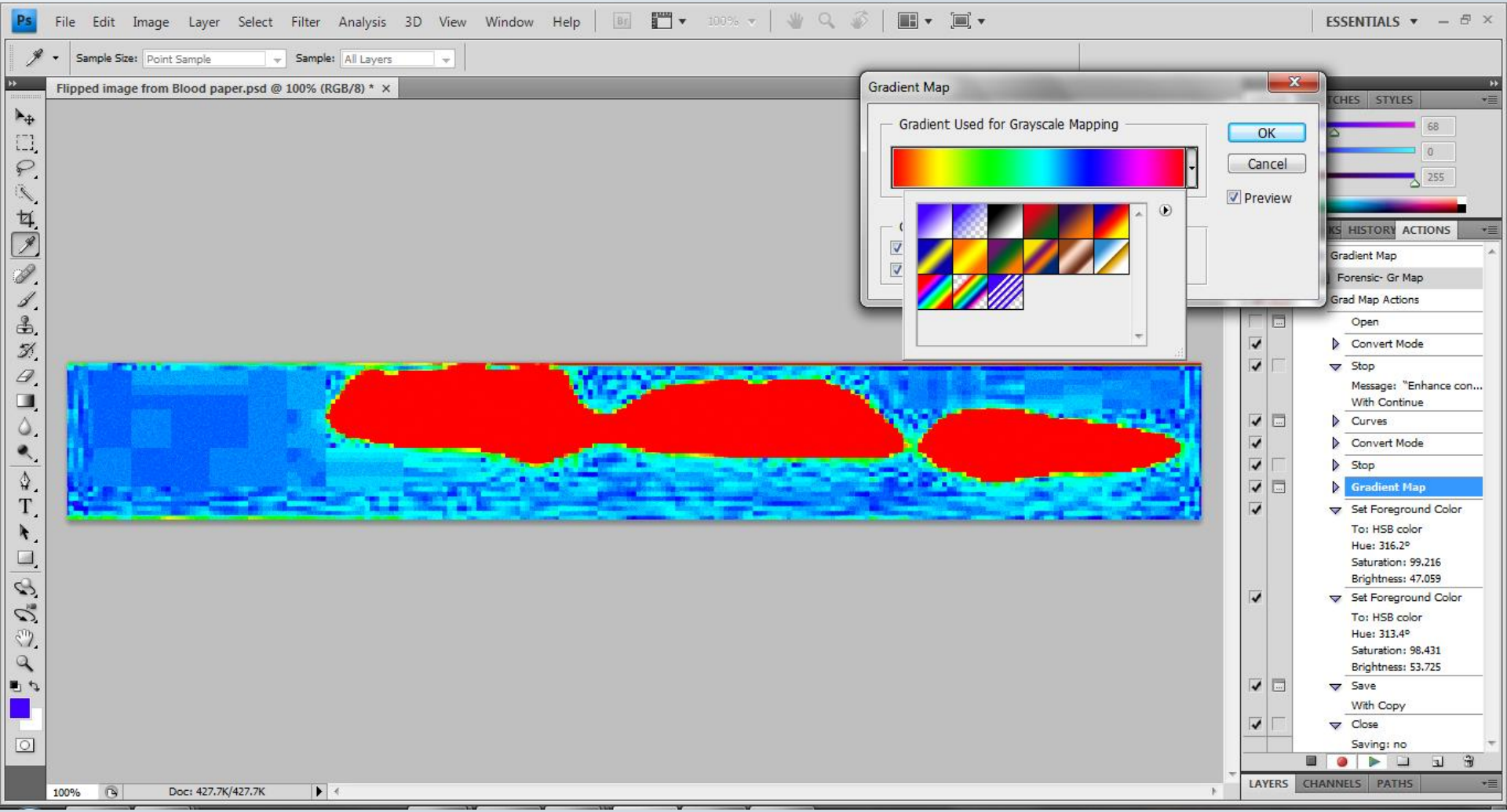
Forensic gradient map:
first, paste the image into Photoshop



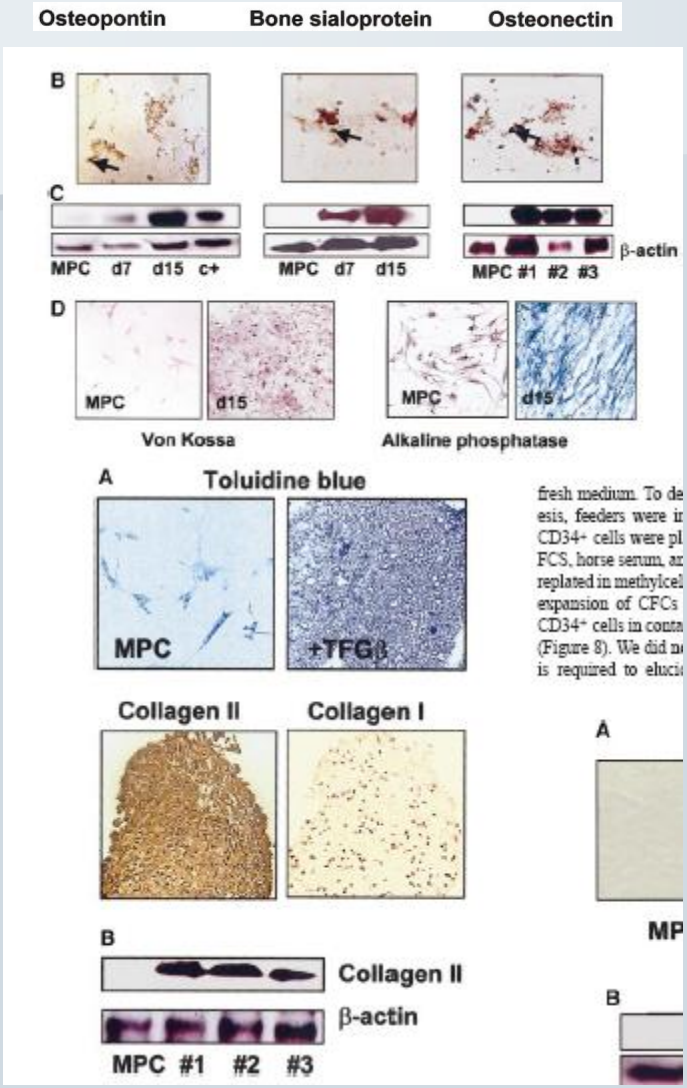
Convert to grayscale, then alter curves to enhance details



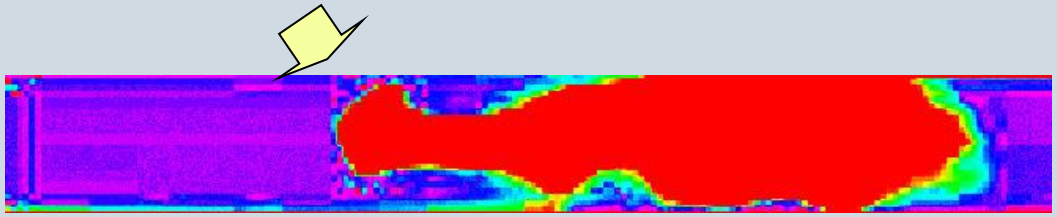
Convert to RGB mode, then map a new color gradient

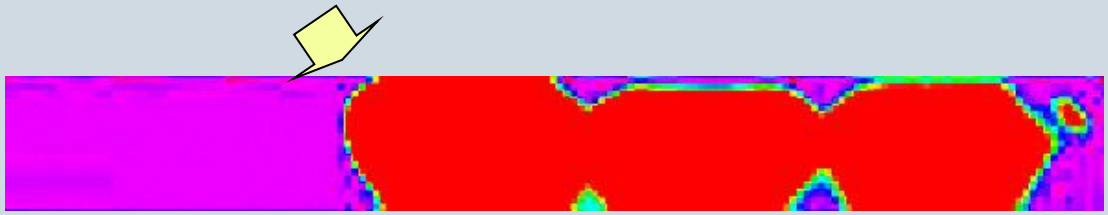


Back to the *Blood* paper

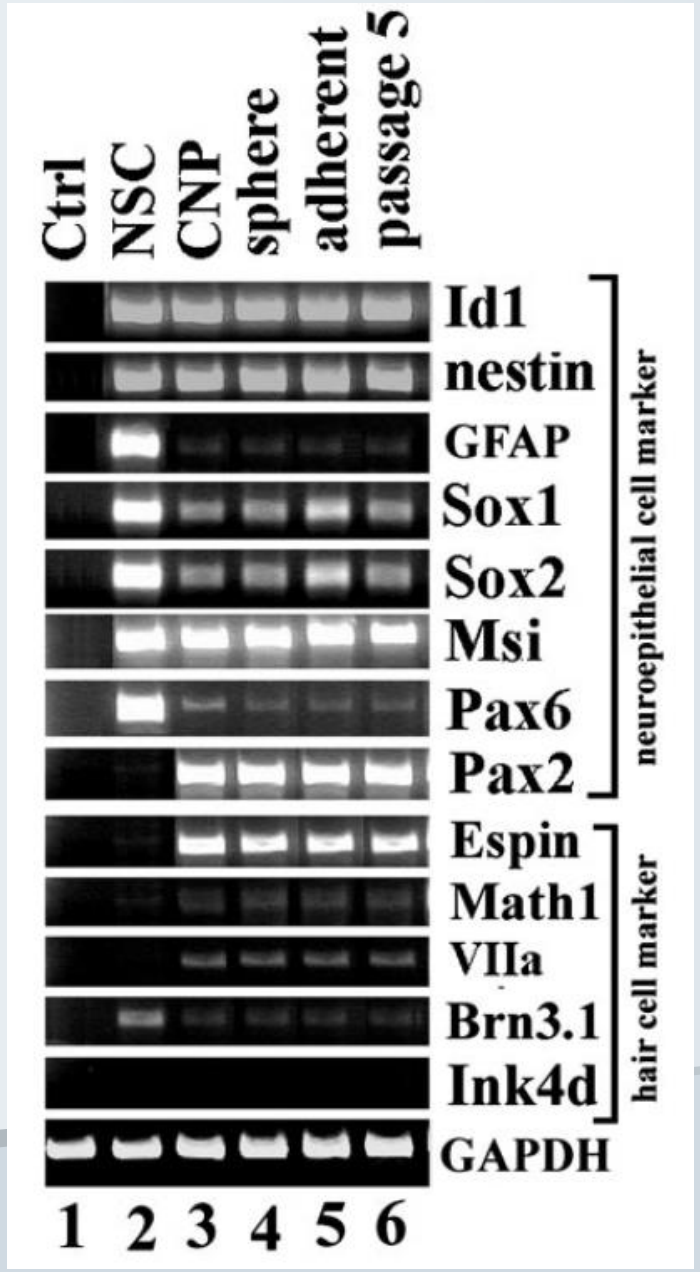


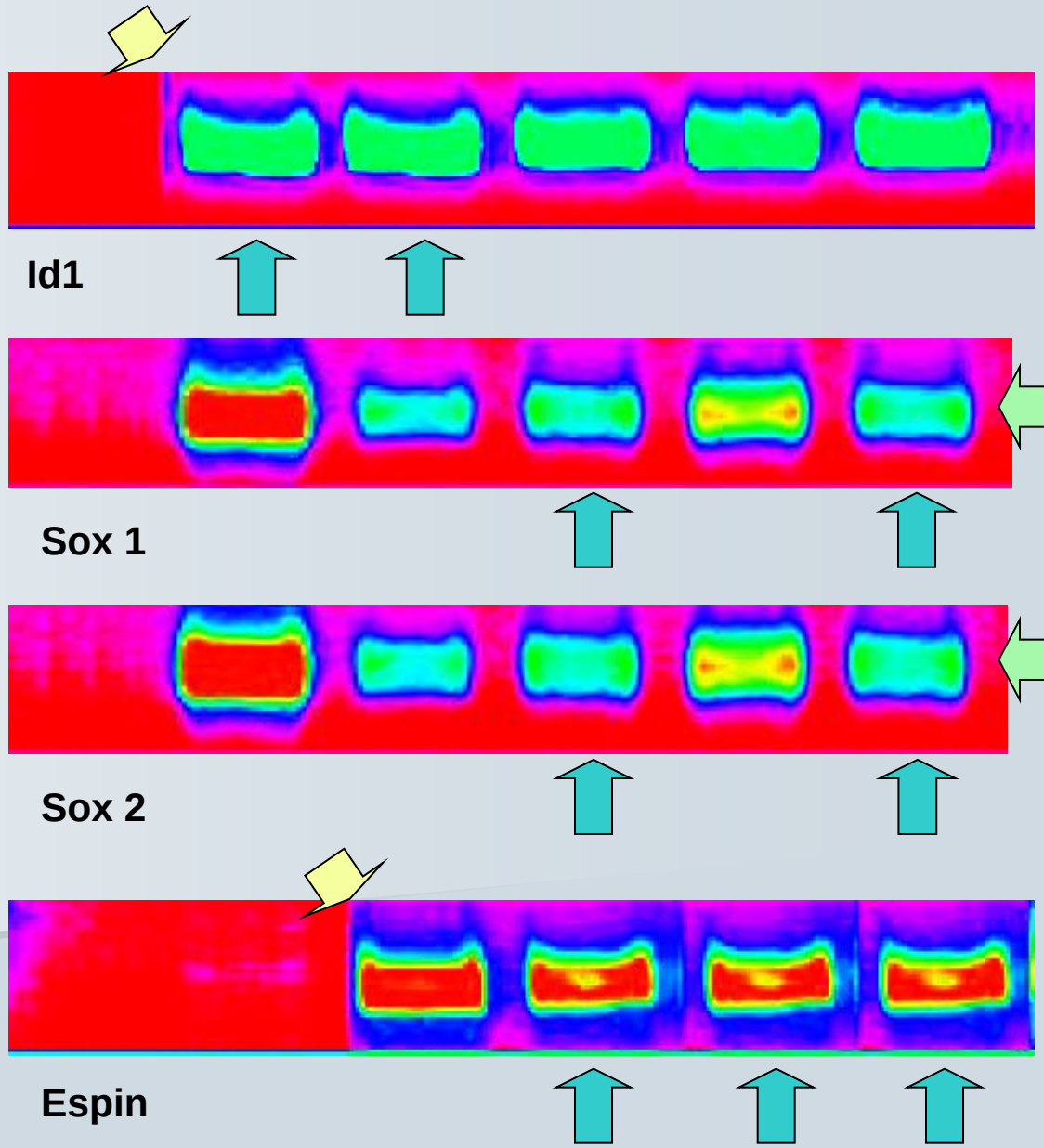
NewScientist





Yet another miscreant?





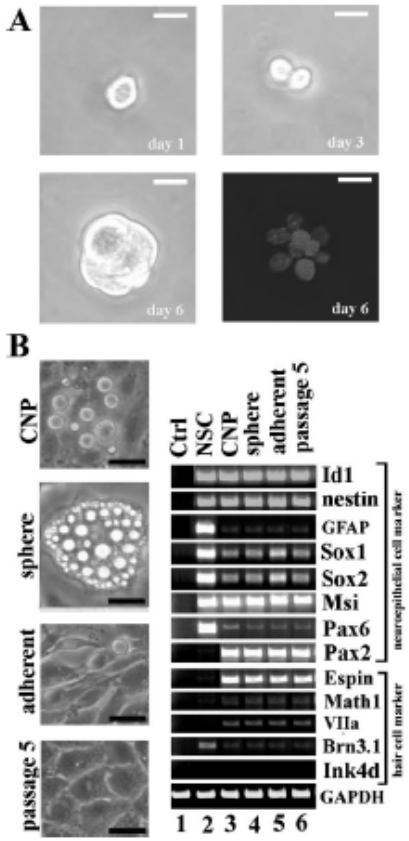
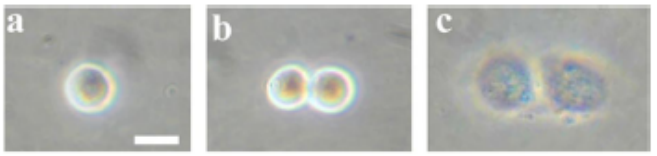
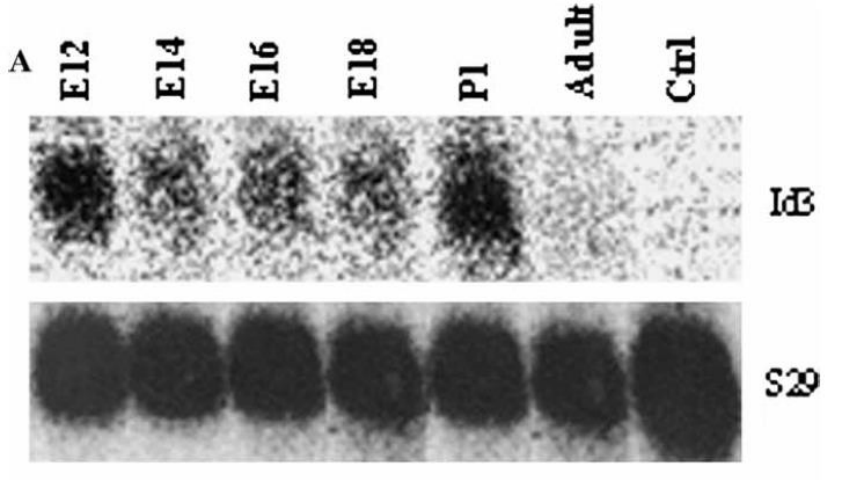


Fig. 3. Expression profile of cellular markers during the maintenance culture of CNPs. CNPs were cultured in SERB. *A*: growing process of CNPs from a single cell to a cellular sphere [bromodeoxyuridine ($BrdU^+$), overlapped with DAPI]. *B*: process was associated with the typical morphology of CNPs, cellular spheres, adherent CNPs, and multiple-passaged CNPs. Accordingly, the gene expression profile of enriched primary CNPs (*lane 3*), cellular spheres (*lane 4*), adherent CNPs (*lane 5*), and passage 5 CNPs (*lane 6*) remained

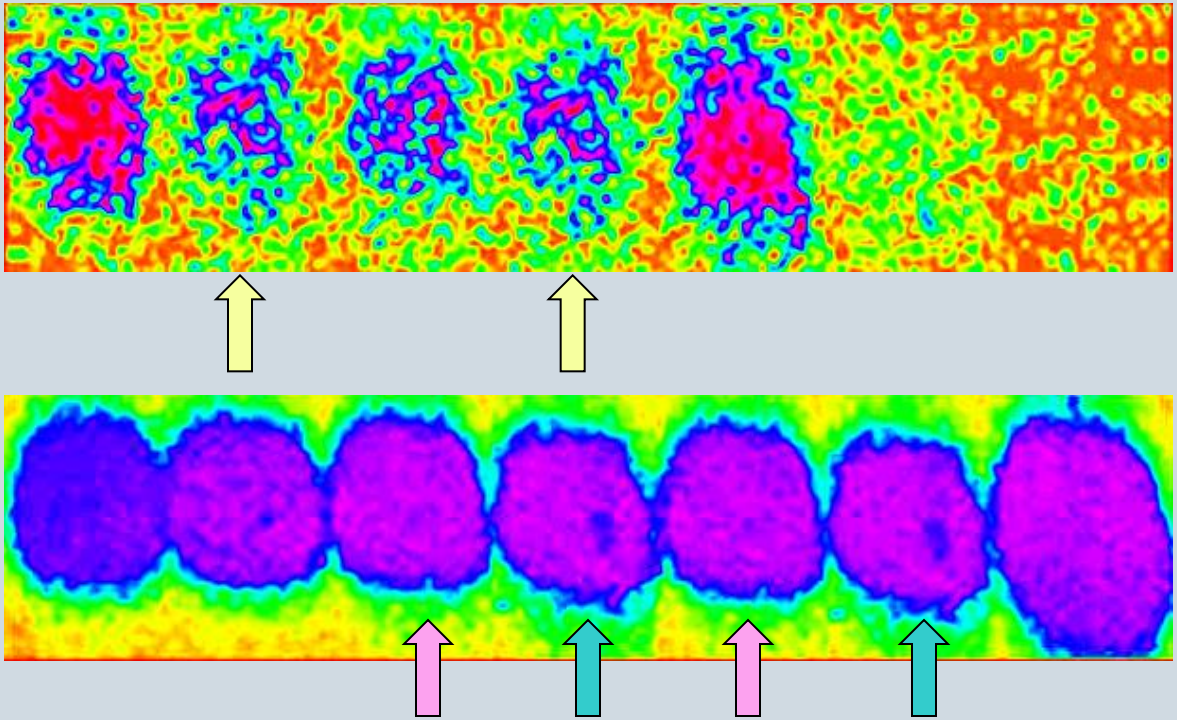
Characterization of clonally derived CNPs

If multiple-passaged adherent CNPs are stem cells, they should be able to both self-renew and generate multiple differentiated cell types. In this experiment, we used clonal cultures that were cloned from the passage 5 of CNPs as described above for examination of their capability to differentiate into distinct hair cell progenitors and neuron progenitors. As noted above, clonal cultures could only be obtained in serum-containing MEM media, as isolated single cells failed to self-renew in serum-free growth media. We used this fact to investigate the generation of differentiated progeny from multiple individual CNPs. CNPs from clone #5 were plated at clonal density (10–100 cells) in eight-well chamber slides, cultured in growth media with addition of 5 μM BrdU, and harvested on *days 1*, *3*, and *6* for immunohistochemistry. Espin was used as a CNP marker (37) because it is expressed in the developing cochlear tissues but not in NSCs. Myosin VIIa was used as hair cell progenitor marker (29), and β3-tubulin was used as a newly generated neuron marker. It was found that division of adherent CNPs in growth media generates daughter cells in either an asymmetric manner (8.2 ± 3.5%; $n = 12$; Fig. 4, *d–f*) or in a symmetric division manner (91.3 ± 8.4%; $n = 12$; Fig. 4, *a–c*). In cells that underwent asymmetric division, cultures began on *day 1* with a single CNP positive for espin (Fig. 4*g*). On *day 3*, one daughter cell was positive for espin,





NewScientist



Id3

S29

Strike three: another inquiry

Further doubts over stem-cell images

Peter Aldhous and
Eugenie Samuel Reich

LIGHTNING never strikes again in the same place? Tell that to the University of Minnesota in Minneapolis, which has launched yet another inquiry into research at its Stem Cell Institute after *New Scientist* raised further concerns about papers that seem to contain duplicated and manipulated images.

Two previous inquiries have led to three papers being corrected, one being retracted, and a finding of misconduct against Morayma Reyes, formerly a PhD student at Minnesota. In October 2008, an expert panel ruled that Reyes falsified images in a 2001 paper in *Blood* (vol 98, p 2615), describing a versatile type of stem cell from human bone marrow (*New Scientist*, 11 October 2008, p 8).

Reyes, who is now at the University of Washington in Seattle, protested her innocence, blaming "inexperience, poor training and lack of clear standards about digital image handling". She also argued that she followed standards for image processing that were common at Minnesota at the time. So *New Scientist* decided to look more closely at other papers co-authored by the Stem Cell Institute's former director, Catherine Verfaillie, in whose lab Reyes worked.

In doing so, we stumbled across problems in the lab of another researcher affiliated with the Stem Cell Institute, Jizhen Lin, who published a paper including Verfaillie among the authors in December 2008 (*American Journal of Physiology – Cell Physiology*, DOI: 10.1152/ajpcell.00324.2008).

This paper explores how stem cells from the inner ears of lab mice can give rise to neurons and specialised "hair cells" that detect sound waves. The question is whether images of gels documenting the activity of various genes have been spliced together, and whether some bands on the gels have been duplicated. In one case, an entire gel appears to have been used twice to describe results for different genes (see images, above).

After combing through more of Lin's research, we found possible duplications within images in six further papers, published between 2001 and 2007. None involved Verfaillie.

In April, *New Scientist* told the university of our concerns about Lin's work. The university took the decision to begin an inquiry in mid-July, but it has not clarified which papers will be covered. Lin declined to comment on the concerns about his work while the inquiry is under way.

Other stem cell biologists are disturbed that so many problems have been found in papers from a single institution. "It's pretty discouraging," says Arnold Kriegstein of the University of California, San Francisco. Given the pressure on scientists in such competitive fields, he wonders what might emerge at other research centres if their publications were subjected to similarly close scrutiny. "It raises serious issues about how widespread this could be," he says. ■

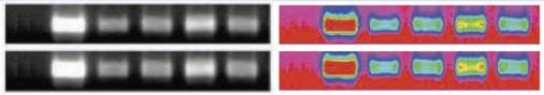
"What might emerge at other research centres if their publications were given similar scrutiny?"

Spot the similarities

Each of these images shows a gel recording the activity of an individual gene in cells from the inner ears of mice

Individual bands on a gel should have subtly different shapes, yet in this gel the first three bands from the right appear identical

These two gels are described as recording the activity of different genes, yet they appear identical. Within each gel, the first and third bands from the right also appear identical



On the right, images are coloured to accentuate variation in their grey-scale using a software tool supplied by the US Office of Research Integrity

SOURCE: AJP - CELL PHYSIOLOGY, DOI: 10.1152/AJPCELL.00324.2008

AN UNEXPLAINED RESEMBLANCE

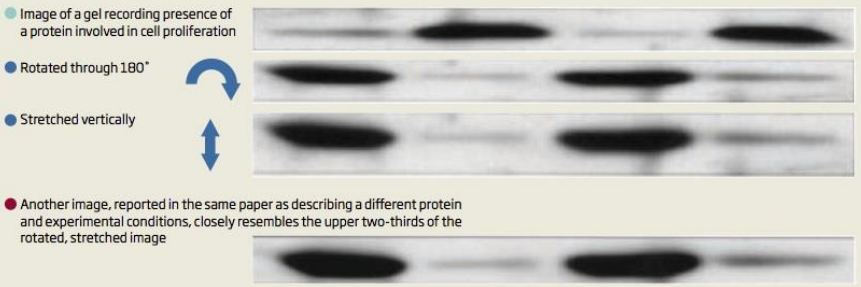
The University of Minnesota's decision to launch an inquiry into the research of Jizhen Lin (see main story) still leaves an earlier concern in limbo.

In November 2008, *New Scientist* raised concerns with the university about a 2000 paper in *Proceedings of the National Academy of Sciences* (vol 97, p 10538) about chronic myeloid leukaemia, a disease in which rogue stem cells cause white blood cells to proliferate uncontrollably. The paper, from researchers led by Catherine Verfaillie, investigates the mechanisms involved in the proliferation.

The concern is that an image recording the presence of one of the proteins involved seems to have been reused in the same paper, rotated through 180 degrees and slightly altered, to describe results for a different protein and experimental conditions (see images, below).

The first author of this paper is Yuehua Jiang, who was also responsible for duplicated and erroneous data in Verfaillie's best-known publication, which claimed that certain cells from bone marrow can mimic the properties of embryonic stem cells (*Nature*, vol 418, p 41).

Verfaillie denies that the images in the leukaemia paper are duplicated. Jiang could not be reached for comment. It is unknown whether the university will launch an inquiry; it says the matter is "in process".



SOURCE: PNAS, VOL. 97, P. 10538

Verdict: not proven

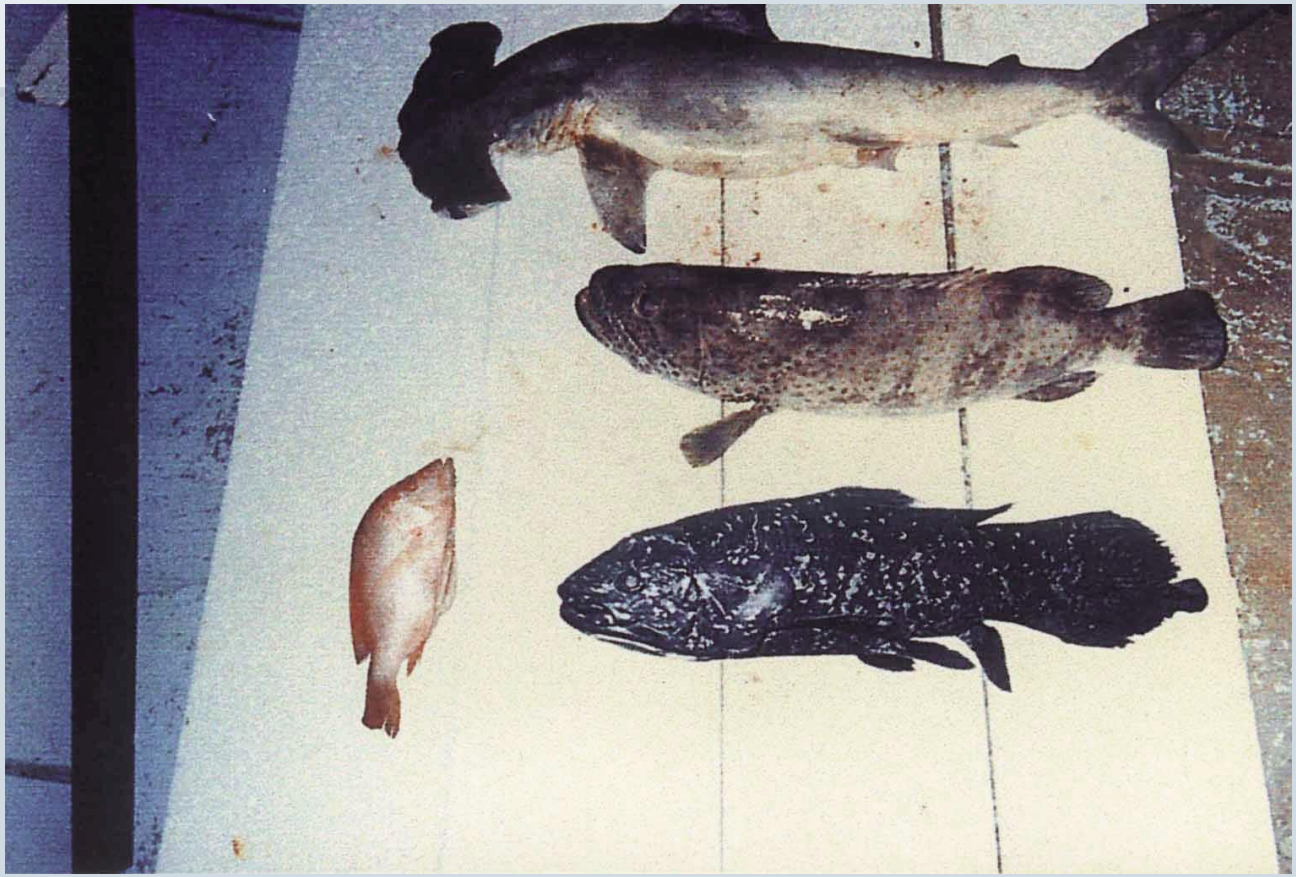
"The investigation panel found that multiple images published in [six] papers were improperly manipulated and invalid.

"The panel determined the evidence was inconclusive as to who prepared the manipulated images, and there was insufficient evidence to find intent to misrepresent results or to find that the images had been submitted for publication with knowledge of the manipulations."

University of Minnesota statement,
February 2011

- Before verdict: one paper retracted; one corrected
- After verdict:
  Nothing more by June 2012

Anything unusual here?



The value of a sharp-eyed copy editor …

nature

scientific correspondence

Indonesian 'king of the sea' discovered

On 30 July 1998, an Indonesian population of coelacanth was discovered. It is apparently the same species as the well-known coelacanth from the Comoran archipelago in the Indian Ocean, *Latimeria chalumnae* Smith.

At sunrise on 30 July, Om Lameh his crew of ten fishermen ng coelacanth from their gill-net off the young vol- Manado Tua, north Sula- . This is almost 10,000 km n population of *L. chalum-* moros[1,2]. The Indonesian n is 124 cm long and weighs bserved live by one of us ore than 3 hours before the -frozen and tissue samples r molecular analysis.

y examination of the speci- morphology suggests that it ith *L. chalumnae*, although firmed by further investiga- mmediately observable dif- published accounts of *L.* he colour. Previous speci- e western Indian Ocean, st one observed by Marjorie ner, are usually described as though there are reports of s appearing brown[2]. The specimen was distinctly es the same characteristic pattern as Indian Ocean has numerous striking gold entire dorsal surface of the These are apparently a pris- f light reflecting off the cles on the scales.

caught in a shark gill-net of , approximately 150 m in n in height, set 3.5 m off the pth of 100–150 m for a 12- rnight. The capture site was steep volcanic slope known cave and crevice topogra- pny, and appears similar to the habitat reported for the Comoran coelacanths[7].

This is only the fourth coelacanth reported to be caught in a net, as the Comoran specimens were captured by fishermen hand-lining for the

The Indonesian coelacanth shortly after capture.

oilfish, *Ruvettus pretiosus*[4]. Of the three previous specimens caught outside the Comoros, two were captured in trawl nets, off South Africa[5] and Mozambique[7], and a specimen from Madagascar was caught in a gill-net[8]. Interviews with fishermen throughout north Sulawesi reveal that, although the oilfish is often caught by hand-line in this area, coelacanth (known locally as *raja laut*, or 'king of the sea') are only ever caught using deep gill-nets.

The new specimen is actually the second coelacanth to be reported from north Sulawesi. On 18 September 1997, the wife of M.V.E. saw a strange-looking fish being wheeled in a cart across the fish market in Manado. The fish was immediately recognized as a coelacanth, but we only managed to take some photographs of the fish and briefly interview the fisherman before it was sold. M.V.E. has since been interviewing fishermen in villages throughout the area, as part of a US National Science Foundation international postdoctoral fellowship with the Indonesian Institute of Sciences and with the support of the National Geographic Society. These surveys have identified several fishermen from north Sulawesi who claim to have captured coelacanths. These interviews, combined with the vast distance from the Comoran archipelago, strongly support the idea that the Indonesian coelacanths are part of an established north Sulawesi population, and not simply 'strays', as has been suggested for the other specimens captured outside the Comoros[9].

The discovery of an Indonesian coelacanth population has biogeographical and conservation implications. It is unlikely that living coelacanth exist only in two small, highly disjunct populations. Comparison of DNA sequences from tissues of the Indonesian and the western Indian Ocean specimens will reveal the depth of divergence between these two populations.

Further expeditions in Indonesia and to the islands in the vast stretch of Indian Ocean between the Comoros and Indonesia may discover additional populations. This would be welcome news for coelacanth conservation, as the fish is considered highly endangered, in part because of its extremely limited distribution and small population size[10]. Nonetheless, the Indonesian government is already considering measures to prevent a repeat of the conservation problems caused by fishing and scientific collection in the Comoros[11].

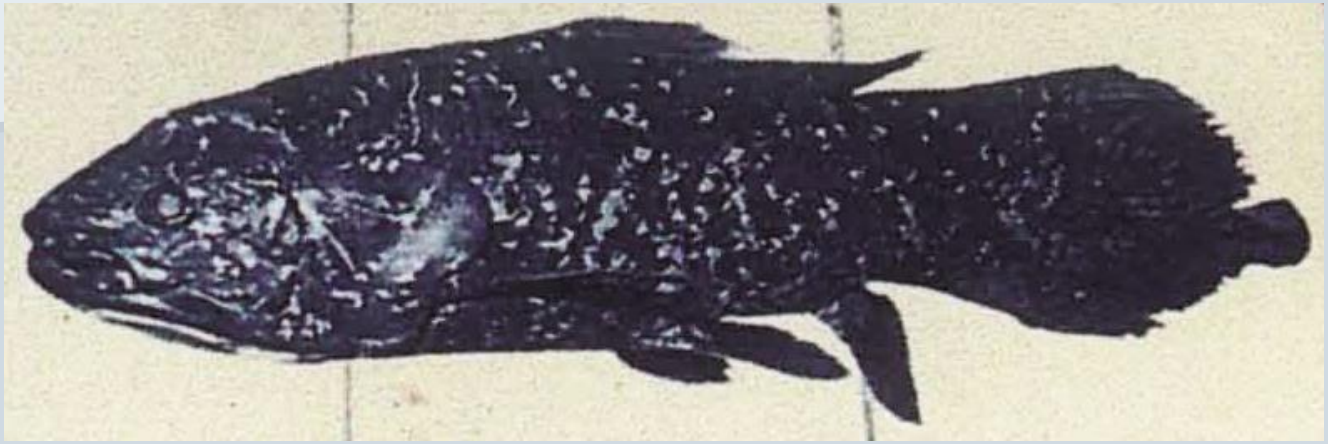
Mark V. Erdmann*†, Roy L. Caldwell*, M. Kasim Moosa†

* *Department of Integrative Biology, University of California, Berkeley, Berkeley, California 94720, USA*

† *Indonesian Institute of Sciences, Jakarta, Indonesia*

1. Smith, J. L. B. *Nature* **171,** 99–101 (1953).
2. Fricke, H. & Plante, R. *Naturwissenschaften* **75,** 149–151 (1988).
3. Smith, J. L. B. *Nature* **143,** 455–456 (1939).
4. Balon, E. K., Bruton, M. N. & Fricke, H. *Env. Biol. Fishes* **23,** 241–280 (1988).
5. Millot, J. *Naturaliste Malgache* (suppl.) **1,** 1–26 (1954).
6. Fricke, H. *et al. Env. Biol. Fishes* **32,** 287–300 (1991).
7. Bruton, M. N., Cabral, A. J. P. & Fricke, H. *S. Afr. J. Sci.* **88,** 225–227 (1992).
8. Heemstra, P. C., Freeman, A. L., Wong, H. Y., Hensley, D. A. & Rabesandratana, H. D. *S. Afr. J. Sci.* **92,** 150–151 (1996).
9. Schliewen, U., Fricke, H., Schartl, M., Epplen, J. T. & Pääbo, S. *Nature* **363,** 405 (1993).
10. Fricke, H., Hissmann, K., Schauer, J. & Plante, R. *Nature* **374,** 314 (1995).
11. Forey, P. L. *History of the Coelacanth Fishes* (Chapman and Hall, London, 1998).

One and the same



nature

Nature **news covers the story**

Brown: plans to increase funding, but some fear a cut in the number of studentships.

in many areas, including the biological and physical sciences.

The government has not yet said how much extra money will be available to cover the increases, leading some to fear that student numbers could fall. Earlier this year the life-science community called for a pay increase, even if it meant cutting back on numbers (see *Nature* 403, 347; 2000). But the Treasury has denied that this is their intention. A spokesperson said the aim was to have more and better research students, and that "this does not mean fewer studentships".

Bob Price, the head of human and corporate resources at the Biotechnology and Biological Sciences Research Council (BBSRC), welcomed the announcement with "open arms" and expects it to raise the quality and quantity of research students.

But earlier this year John Taylor, the director-general of the research councils, decided that stipends did not have to be harmonized, and that individual councils could choose whatever level they thought appropriate. Accordingly, the BBSRC's minimum went up to £7,380 and is under review. Price says it could increase beyond the amount announced by the Treasury, but that this would "need a reduction in the number of places".

But although welcoming the money in principle, many scientists are reserving judgement until the small print is revealed later this month — particularly as the announcements appeared as a leak to two newspapers of a speech by Gordon Brown, the Chancellor of the Exchequer, and as selective details released by the Treasury.

Indeed, science may not be a net beneficiary. Money could be redistributed from other budgets, as was the case with government departmental spending (see *Nature* 404, 909; 2000), or clawed back elsewhere. The full results will be known when the government releases details of the Comprehensive Spending Review in a few weeks. ■

Tangled tale of a lost, stolen and disputed coelacanth

Heather McCabe, Paris & Janet Wright, London

Strange stories have long circulated around the coelacanth, the 'living fossil' fish discovered off the coast of South Africa in the 1930s.

The latest are claims by French researchers who say they were the first scientists to find the Indonesian variety, in 1995. But the photograph they sent to *Nature* to support their claims has been denounced by another researcher as a fake.

Until recently, coelacanths had only been found on the west side of the Indian Ocean. The first recorded Indonesian sample was discovered by a US biologist, Mark Erdmann of the University of California at Berkeley, who published news of his find in *Nature* (see *Nature* **395,** 335; 1998).

In a recent submission to *Nature*, the French team — Bernard Séret, Laurent Pouyaud and Georges Serre — say they were unable to register their specimen in 1995 because it failed to reach the museum to which it had been sent. They say Serre photographed the fish at the time, then lost the picture (their only other evidence) while moving house, and only found it again this year.

But *Nature* staff noticed that the fish in the new photograph appears virtually identical to the one caught by Erdmann. When contacted, Roy Caldwell, a co-author of the 1998 paper, scrutinized the photograph via a picture-editing computer program and said, "I am 100% certain the image is a fake".

When Erdmann spotted a coelacanth off the northeast coast of Sulawesi in 1998, his find expanded the geographical distribution of the fish by roughly 10,000 km. But Georges Serre, a consultant for what is now the French Institut de Recherche pour le Développement (IRD), has long claimed that a 10-kg specimen was caught in 1995 in the Bay of Pangandaran, in Southwest Java.

Serre says he gave the specimen to a fisherman to hand over to the Indonesian fishery service. But the man gave it to a museum, from which it was stolen. Only recently, according to Serre, did Pouyaud, an IRD geneticist in Jakarta, track down the coelacanth to a private collection, whose owner refuses access to the fish.

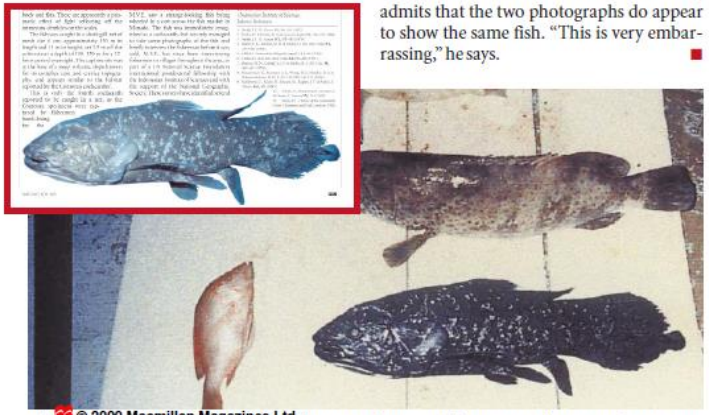
The French team's finding, if confirmed, would further extend the distribution of this elusive creature, as it was caught more than 2,000 km from the spot where Erdmann found his 1998 specimen, suggesting a large distribution in the Indo-West Pacific region.

The whole issue is already shrouded in controversy. After analysing the specimen that Erdmann had given to the Indonesian authorities, Pouyaud and his colleagues at the Indonesian Institute of Science named it as a distinct species, *Latimeria menadoensis* — to the chagrin of Erdmann, who had been analysing tissue samples independently.

Caldwell says that coelacanths have highly individual spot patterns; the pattern in the two photographs is virtually identical. The bulky fish in the 1998 photo was swimming in the sea, yet is seen in the identical position, in the new photo, while lying on a slab. Shadows and other details seen when the image is magnified add to Caldwell's impression that the new photograph has been manipulated.

Serre still claims that the photograph is authentic, though he now says it was taken by a friend who later died and whose widow gave it to Serre before moving abroad.

Séret, who is an ichthyologist at the Muséum National d'Histoire Naturelle de Paris, admits that the two photographs do appear to show the same fish. "This is very embarrassing," he says. ■



Vive la différence! The French fish (right) bears a striking resemblance to one that appeared in *Nature*.

Other forensic tools: plagiarism detection

http://ori.hhs.gov/plagiarism-tools

Plagiarism detection tools

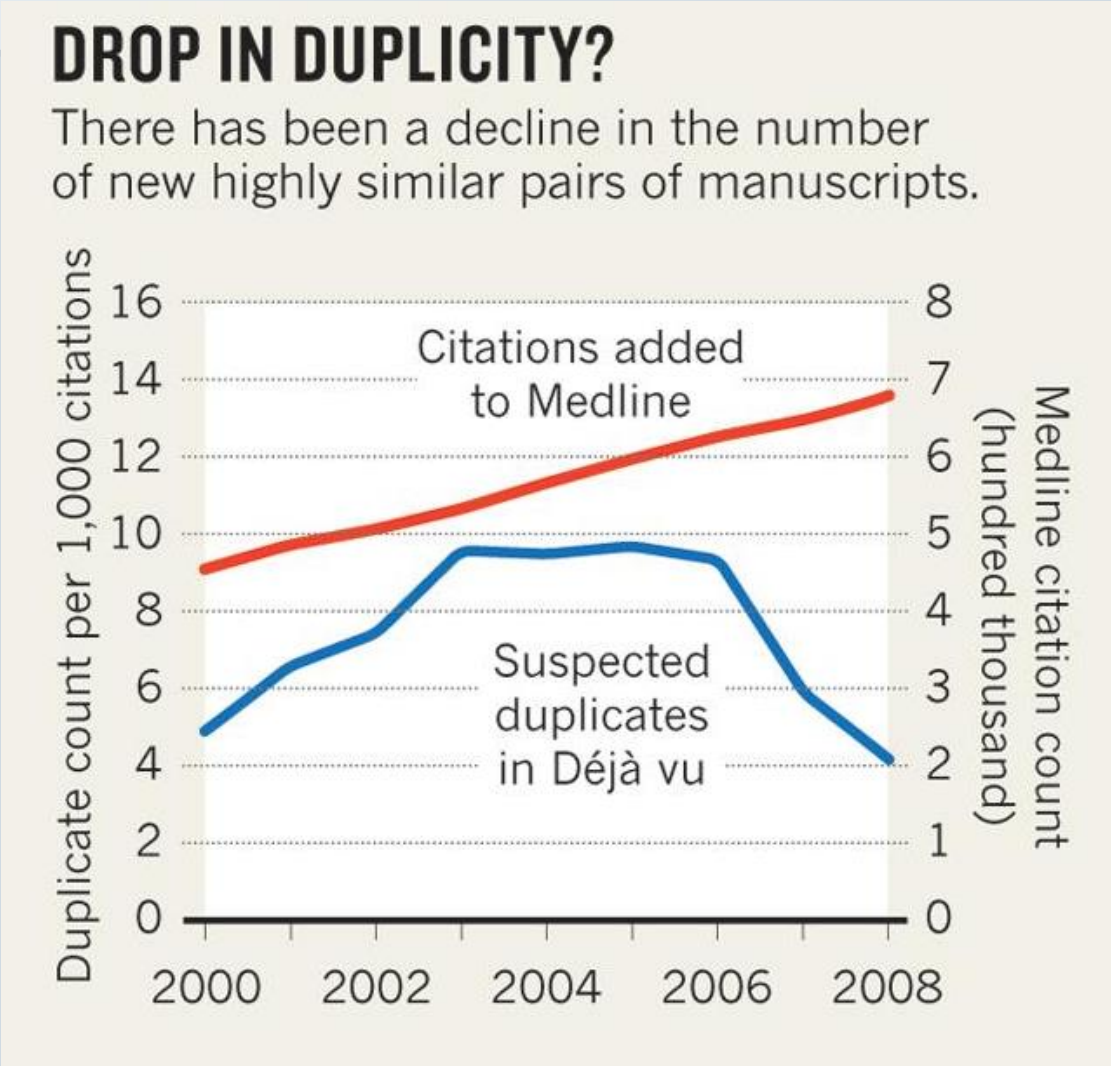
eTBLAST
Text-similarity search engine for PubMed, ClinicalTrials.gov etc
http://etest.vbi.vt.edu/etblast3/

Déjà vu
Database of highly similar papers
http://dejavu.vbi.vt.edu/dejavu/

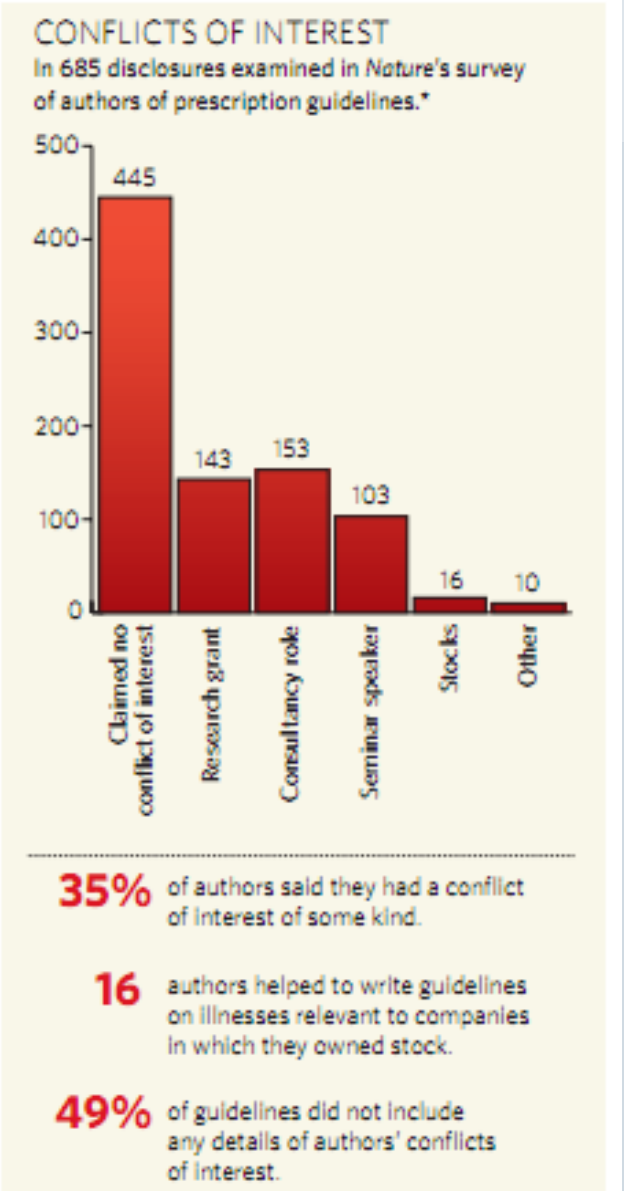
Plagiarism Resource Site
http://plagiarism.bloomfieldmedia.com/
Includes download of free software, WCopyfind

Such tools may be serving as a deterrent

From a study by Harold “Skip” Garner, developer of eTBLAST and Déjà vu, quoted in *Nature*, December 2010



Don’t forget to follow the money!



Cash interests taint drug advice

Rosie Taylor & Jim Giles

***Nature* exposes close ties between scientists and manufacturers.** ▲ Top

Researchers and physicians who write the rules on prescribing drugs have extensive financial connections with the pharmaceutical industry, an investigation by *Nature* has revealed. Public-health experts say that the results of the survey, which is the largest of its kind, suggest that drug companies are distorting decisions about how their products are being prescribed.

In the investigation of the panels that write clinical guidelines — documents that govern the diagnosis and treatment of patients — *Nature* found that more than one-third of authors declared financial links to relevant drug companies, with around 70% of panels being affected. In one case, every member of the panel had been paid by the company responsible for the drug that was ultimately recommended.

These links with pharmaceutical companies are more worrying than the financial conflicts known to plague clinical trials and reviews, say public-health experts, because the guidelines have such a direct effect on the drugs that doctors prescribe. "The guidelines are specifically written to influence the practice of many physicians," says Niteesh Choudhry, a specialist in health policy at Harvard Medical School. "The effects of conflicts may be translated many times over to patients."

nature

Which is sometimes hidden from plain view …

Study says authors are averse to declaring conflicts of interest

Jonathan Knight, San Francisco

Authors are ignoring journal policies that require them to state any conflict of interest over their papers, a new study suggests. But editors of leading journals disagree about whether this poses a real problem and, if it does, what to do about it.

The study, from Tufts University in Massachusetts, examined 61,134 articles that appeared in 1997 in 181 leading journals that had disclosure policies. The journals examined included *Science*, *The Journal of the American Medical Association* and *Proceedings of the National Academy of Sciences*. But *Nature* and *Cell*, for example, did not have disclosure policies, and so were excluded.

The researchers counted every occurrence of a positive disclosure, including honoraria, patents pending, stock holdings or other forms of personal or financial interest. The research appears in *Science and Engineering Ethics* (7, 205–218; 2001). Only a third of the journals surveyed contained papers carrying any disclosure. Of those, fewer than 1% of papers contained a disclosure.

A possible explanation is that few researchers had anything to disclose. But the study's lead author, Sheldon Krimsky of Tufts' Department of Urban and Environmental Policy, says this is unlikely. "What is the chance that in two-thirds of the journals there was no one with a patent, equity interest or honorarium?" he asks.

But some journal editors say that such information is of little value to readers. Kevin Davies, editor-in-chief of Cell Press, says editors usually consider that good science stands on its own merits. "It's the quality of the research that counts," he says.

Science's editor-in-chief Donald Kennedy agrees. But the journal's authors must provide information on potential conflicts of interest. These disclosures are reviewed by editors, but not given to external reviewers. "The peer reviewers' job is to evaluate the science and not to be our ethicists," he says.

But Krimsky argues that complete

Limited disclosure: conflicts are rarely declared.

nature

Scientists' financial interests and funding are worth exploring …

Pharmaceutical industry sponsorship and research outcome and quality: systematic review

Joel Lexchin, Lisa A Bero, Benjamin Djulbegovic, Otavio Clark

Abstract

Objective To investigate whether funding of drug studies by the pharmaceutical industry is associated with outcomes that are favourable to the funder and whether the methods of trials funded by pharmaceutical companies differ from the methods in trials with other sources of support.

Methods Medline (January 1966 to December 2002) and Embase (January 1980 to December 2002) searches were supplemented with material identified in the references and in the authors' personal files. Data were independently abstracted by three of the authors and disagreements were resolved by consensus.

Results 30 studies were included. Research funded by drug companies was less likely to be published than research funded by other sources. Studies sponsored by pharmaceutical companies were more likely to have outcomes favouring the sponsor than were studies with other sponsors (odds ratio 4.05; 95% confidence interval 2.98 to 5.51; 18 comparisons). None of the 13 studies that analysed methods reported that studies funded by industry was of poorer quality.

Conclusion Systematic bias favours products which are made by the company funding the research. Explanations include the selection of an inappropriate comparator to the product being investigated and publication bias.

Introduction

favourable outcome may result in biases in come, and reporting of industry sponsored

A recent systematic review of the financial conflicts on biomedical research studies financed by industry, although as other studies, always found outcomes favou sponsoring company.[5] However, this review papers published only in English, excluded letters and abstracts, and looked at studies other industries. We reviewed the relation b source of funding of the research and th outcomes and investigated whether qua methods in studies funded by pharmaceuti nies differs from that in other studies.

Methods

Study selection

We included only studies that specifically stat analysed research sponsored by a pharmace pany, compared methodological quality o with studies with other sources of funding, a the results in quantitative terms. Outcomes were conclusions about differences in drug e adverse effects, cost outcomes, or publica between industry funded trials and other published in any language was eligible for in

Some studies analysed both pharmaco non-pharmacological trials and combine funded by drug companies and other ind one group. In these cases, if most pharmaceutical trials and were funded industries they were excluded.

Financial ties and concordance between results and conclusions in meta-analyses: retrospective cohort study

Veronica Yank, clinical instructor,[1] Drummond Rennie, professor,[2] Lisa A Bero, professor[3]

ABSTRACT

Objective To determine whether financial ties to one drug company are associated with favourable results or conclusions in meta-analyses on antihypertensive drugs.

Design Retrospective cohort study.

Setting Meta-analyses published up to December 2004 that were not duplicates and evaluated the effects of antihypertensive drugs compared with any comparator on clinical end points in adults. Financial ties were categorised as one drug company compared with all others.

Main outcome measures The main outcomes were the results and conclusions of meta-analyses, with both outcomes separately categorised as being favourable or not favourable towards the study drug. We also collected data on characteristics of meta-analyses that the literature suggested might be associated with favourable results or conclusions.

Results 124 meta-analyses were included in the study, 49 (40%) of which had financial ties to one drug company. On univariate logistic regression analyses, meta-analyses of better methodological quality were more likely to have favourable results (odds ratio 1.16, 95% confidence interval 1.07 to 1.27). Although financial ties to one drug company were not associated with favourable results, such ties constituted the only characteristic significantly associated with favourable conclusions (4.09, 1.30 to 12.83). When controlling for other characteristics of meta-analyses in multiple logistic regression analyses, meta-analyses that had financial ties to one drug company remained more likely to report favourable conclusions (5.11, 1.54 to 16.92).

Conclusion Meta-analyses on antihypertensive drugs and with financial ties to one drug company are not associated with favourable results but are associated with favourable conclusions.

Meta-analyses pool data from multiple studies identified through a systematic review of the literature to provide summary statistics on the efficacy of a given treatment. Such meta-analyses represent the highest level of research evidence in the hierarchy of study types.[14] They also may equal, if not surpass, randomised controlled trials in their cost effectiveness[15] and in their influence on patient care and healthcare policy.[16,17] Drug companies have started to reference meta-analyses in their advertisements.[18]

In the 1990s and early 2000s concerns were expressed about the influence of the pharmaceutical industry on meta-analyses.[19,20] Between 2003 and 2005 the Cochrane Collaboration debated whether its systematic reviews should be funded by drug companies; its current policy statement states that "The sponsorship of a Cochrane review by any commercial source or sources. . . is prohibited."[21] More recently a study compared matched pairs of Cochrane meta-analyses and industry sponsored meta-analyses published in print journals and found evidence that the industry sponsored meta-analyses were more likely to recommend the experimental drug.[22] The study was, however, unable to control for the possible confounding effects of the Cochrane methodology. In addition, the study examined only eight pairs of meta-analyses and so was unable to comment on the characteristics of meta-analyses not represented in its sample.

Some antihypertensive drugs have been shown to dramatically improve mortality and morbidity. The market for these and other antihypertensive drugs is highly competitive and lucrative. According to market research, both angiotensin receptor blockers and calcium channel blockers were in the top 10 list of global therapeutic drug classes by sales in 2005, equating to earnings of over $26b (£13b; €18b).[23] Concern exists about the effect of such profits on doctors. The

… but are often ignored

OPEN ACCESS Freely available online

PLoS one

Reporting Science and Conflicts of Interest in the Lay Press

Daniel M. Cook[1]*, Elizabeth A. Boyd[2], Claudia Grossmann[3], Lisa A. Bero[2]

1 School of Public Health, University of Nevada, Reno, Nevada, United States of America, 2 Department of Clinical Pharmacy, University of California at San Francisco, San Francisco, California, United States of America, 3 Biomedical Sciences, University of California at San Francisco, San Francisco, California, United States of America

Background. Forthright reporting of financial ties and conflicts of interest of researchers is associated with public trust in and esteem for the scientific enterprise. *Methods/Principal Findings*. We searched Lexis/Nexis Academic News for the top news stories in science published in 2004 and 2005. We conducted a content analysis of 1152 newspaper stories. Funders of the research were identified in 38% of stories, financial ties of the researchers were reported in 11% of stories, and 5% reported financial ties of sources quoted. Of 73 stories not reporting on financial ties, 27% had financial ties publicly disclosed in scholarly journals. *Conclusions/Significance*. Because science journalists often did not report conflict of interest information, adherence to gold-standard recommendations for science journalism was low. Journalists work under many different constraints, but nonetheless news reports of scientific research were incomplete, potentially eroding public trust in science.

Citation: Cook DM, Boyd EA, Grossmann C, Bero LA (2007) Reporting Science and Conflicts of Interest in the Lay Press. PLoS ONE 2(12): e1266. doi:10.1371/journal.pone.0001266

Tips on searching for scientists' financial interests

- Competing interest statements on their scientific papers

- Some employers require financial disclosure statements under certain conditions; those for state university and federal employees may be public documents. This is the case for UC, see here.

- Run their names through SEC's full-text search.

- Patent searches

- Google searches on their names with phrases like "financial disclosure," "competing interests" and "speakers bureau"

- For MDs, try ProPublica's "Dollars for Docs" or CMS Open Payments databases

And don't forget to hold scientists to account on other ethical issues!

Forgotten wrongs of cloning 'pioneer'

› 04 February 2006 by Peter Aldhous
› Magazine issue 2537. **Subscribe and save**

A FRAUD, a liar and a charlatan: that is the general verdict on Woo Suk Hwang, South Korea's disgraced "king of cloning". But the reactions to Hwang's transgressions, which have focused on the fraud, are themselves deeply unsettling. His team didn't just fabricate data. It also breached ethical guidelines designed to protect women from exploitation and medical harm. Yet these lapses have attracted less attention and outrage.

Hwang claimed to have created cloned stem cells matched to individual patients. For this he needed human eggs. In May 2004, after *Science* published the first of two landmark papers, *Nature*, where I worked at the time, queried the source of the eggs. A junior researcher in Hwang's lab told one of our reporters that she and a colleague were among the egg donors. If so, that would have breached international guidelines designed to prevent people being coerced into participating in medical research. But the woman soon changed her story, and Hwang denied the accusation.

Then things went quiet, and there was little ethical fuss when Hwang published a second paper in May 2005, describing the creation of 11 lines of patient-specific stem cells. But in November, the Korean TV broadcaster MBC confirmed *Nature*'s allegation and revealed that other women had been paid to donate eggs, contrary to earlier assurances. Hwang apologised, claiming he had only found out about donations from lab members when *Nature* began its enquiries and had lied to protect their identities.

A take-home message

nature

www.nature.com/nature Vol 439 | Issue no. 7073 | 12 January 2006

Ethics and fraud

The trajectory of the Hwang scandal highlights the shortness of the path between unethical behaviour and outright misconduct.

"In view of the pattern of behaviour that led up to Hwang's disgrace, … no one should argue ever again that despotism, abuse of junior colleagues, promiscuous authorship on scientific papers or undisclosed payment of research subjects can be tolerated on the grounds of eccentricity or genius. Research ethics matter immensely to the health of the scientific enterprise. Anyone who thinks differently should seek employment in another sphere."

Nature editorial, January 2006

Scientists behaving badly

Peter Aldhous

@paldhous

(With special thanks to Eugenie Samuel Reich)