

NEWS

Mouse patent sparks 'uncivil' spat

Academic institutes lock horns in legal action over mutant mice.

The Jackson Laboratory, a non-profit genetics research centre in Bar Harbor, Maine, is embroiled in its first ever patent dispute — with another non-profit research institute.

"It is almost unheard of for one academic institute to sue another over patent infringement," says the Jackson Lab's corporate lawyer, David Einhorn, who described the dispute on 21 May at a meeting in Rome on sharing data and resources for functional genomics. "The affair is completely uncivil."

The suit was filed by the Central Institute for Experimental Animals (CIEA) in Kawasaki, Japan, which last week reported the world's first transgenic primate able to pass a foreign gene to its offspring (E. Sasaki *et al. Nature* 459, 523–527; 2009). In 2006 the CIEA was granted a US patent on a strain of immunodeficient mice called NOG, which it began to make commercially available in the United States earlier this year. The institute has also trademarked the strain.

The CIEA's lawsuit claims that the Jackson Lab is infringing the patent, a claim the laboratory

denies. Among the more than 4,000 mouse mutant strains that the Jackson Lab maintains and distributes to the worldwide academic community is a mouse similar to NOG, called NSG. The Jackson Lab developed the NSG strain and, since 2006, has made it available to more than 640 research groups worldwide. It does not patent.

The CIEA says it is after recognition, not profits. "We would like scientists around the world to recognize the innovation involved in the creation of the NOG mouse," says Hideo Maeno, general manager in the institute's strategic management department.

The institute distributes NOG mice under quite restrictive terms: purchasers cannot breed or cross-breed from them, and there are extensive 'reach-through' rights that control successive work done with the mice.

Immunodeficient mice are widely used in the study of diseases such as cancer or diabetes because they can be 'humanized' by having human tissue or human transgenes transplanted into them. As their immune system

is suppressed, the mice tend not to reject the foreign tissue.

In the 1980s, an immunodeficient mouse strain called CB17-SCID was generated by a spontaneous mutation. In the 1990s, this SCID mutation was crossed first by scientists at the Jackson Lab, and later at the CIEA, with their respective strains of another, non-obese diabetic (NOD) mouse.

The Jackson Lab and the CIEA then each independently crossed their NOD-SCID strains with mice whose gene for a key immune signalling molecule, IL2R γ , was either partially or completely knocked out. The NOD-SCID IL2R γ -deficient mice — abbreviated as NOG by the CIEA and as NSG by the Jackson Lab — are particularly good at accepting grafted tissue.

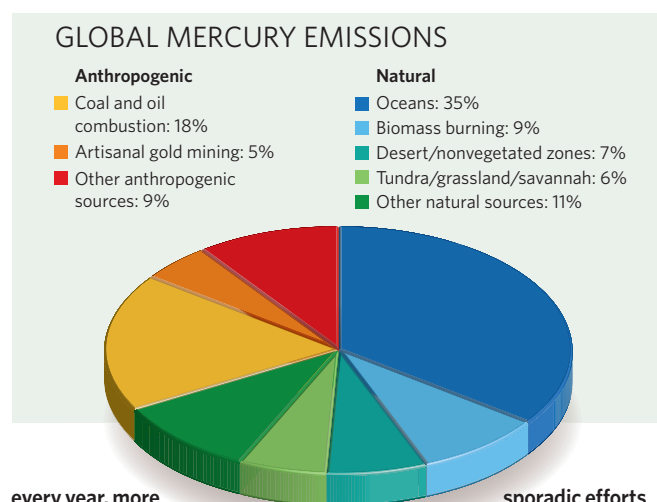
The Jackson Lab denies that it has infringed any patent or trademark rights. Einhorn notes that the long-established NOD and SCID strains used to create the mice were not identical anyway, because of natural genetic drift accumulated over many generations in the separate locations.

Funding struggle for mercury monitoring

Nicola Pirrone may need all the help he can get next week. In the hallways of a conference in Guiyang, China, Pirrone — the director of Italy's CNR-Institute for Atmospheric Pollution Research — will be trying to rustle up support for a global network to monitor mercury pollution.

Such a network would underlie a United Nations Environment Programme (UNEP) treaty to control mercury emissions, which negotiators plan to forge by 2013. So far, countries from Mexico to South Africa to Japan have expressed interest in setting up a monitoring system. But to turn interest into reality, researchers are facing a complex task on what may be shoestring budgets.

Anthropogenic sources emit about 2,500 tonnes of mercury



every year, more than half of which comes from fossil-fuel power plants (see chart). But so far, global monitoring endeavours have been relatively uncoordinated; hundreds of

sporadic efforts can include one-time samplings from a ship cruise or aeroplane flight.

The United States and Canada do have networked and standardized

stations that can monitor mercury deposition at a high enough precision over the long term to be useful in a treaty. These include sophisticated monitors made by Tekran Instruments Corporation in Knoxville, Tennessee, which can collect mercury from both rainfall and dry air and determine its chemical form.

US researchers have been working to combine data from about a dozen Tekran-equipped sites, along with other longer-term studies, into a national monitoring effort called MercNet that could serve as a starting point for a global network. Some initial high-quality worldwide data are starting to become available, for instance from Taiwan's Changbai Mountain (Q. Wan *et al. Environ. Res.* 109, 201–206; 2009).

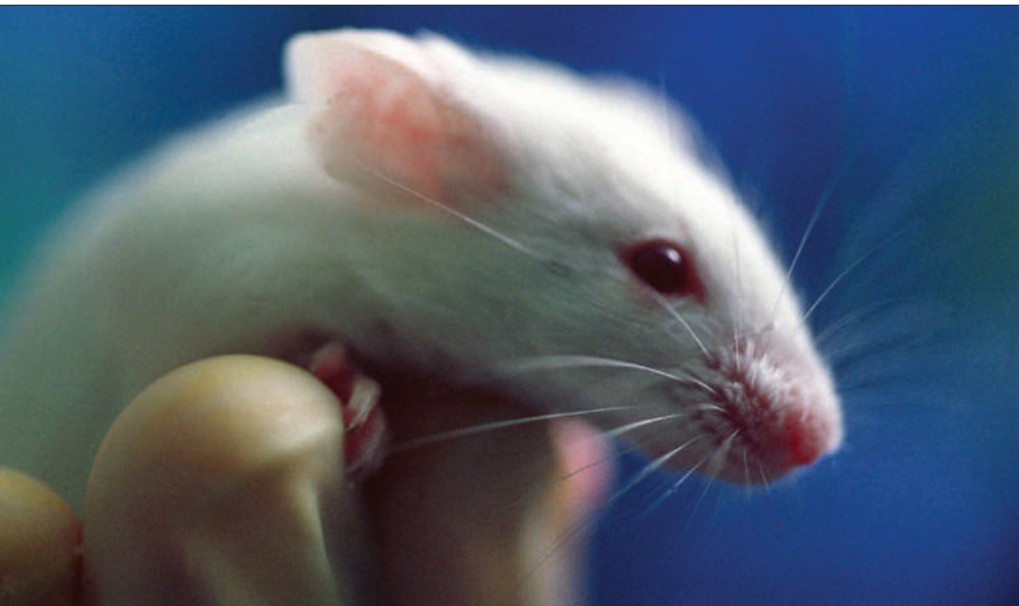
But expanding the number of

SOURCE: MERCURY FATE AND TRANSPORT IN THE GLOBAL ATMOSPHERE (SPRINGER, 2009).



ELECTRODES SPARK NEURON GROWTH

Deep-brain stimulation could help make memories.
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that the CIEA infringed a patent it filed on the knockout mouse used to breed both the NOG and NSG strains. The NIH patents biological inventions to prevent others from patenting and then restricting use.

Jackson Lab scientist Leonard Shultz, who has worked for 35 years on developing humanized mice including the NSG strain, echoes the concerns of many in the community when he says he does not understand the CIEA's motivation. The CIEA says it cannot comment concretely on such matters, because of the ongoing litigation.

On face value, the CIEA does not seem like an aggressively modern, lawyer-wielding institute. It is more old-world, with its rundown buildings tucked into a modest residential area of the working-class city of Kawasaki.

It is still directed by 87-year-old Tatsuji Nomura, the infectious-disease researcher who founded it in 1952 because he was concerned about the variable quality of research animals. It is operated by a foundation funded by some 30 Japanese pharmaceutical and biomedical companies.

"Science is essentially a global enterprise and national profit is not part of our mindset," insists Maeno. "We are absolutely not trying to slow the pace of science."

Alison Abbott

Additional reporting by David Cyranoski

Handle with care: more than 4,000 strains of mice are produced at the Jackson Laboratory.

Einhorn is particularly upset that the CIEA did not contact the lab about its concern before filing the case in December in a US district court in northern California. "The first I heard was three days later when I got a call from a Californian lawyer who had spotted the case and was offering us his services," he says.

Maeno did not respond directly to ques-

tions about why his institute didn't contact the Jackson Lab before filing suit. But, he says, "we have enjoyed a close relationship with the Jackson Lab in the past and we hope to continue that relationship in the future."

The National Institutes of Health, which funds the Jackson Lab repository, has asked the lab to bring a counterclaim on its behalf, saying

sites globally will be expensive. A top-of-the-line Tekran monitor costs about US\$100,000, not including operational costs. On top of that, mercury researchers would like to see a host of other measurements, including regularly scheduled aeroplane monitoring high in the troposphere to see how chemical reactions change airborne mercury; research cruises to measure what is happening in the ocean-air boundary layer; and more data on mercury levels in the oceans themselves.

One money-saving option might be to piggyback mercury measurements on other sites that already collect atmospheric data, says Robert Mason, an environmental chemist at the University of Connecticut in Groton. Mason is advising researchers who are working to set up a network in China, Japan and Korea, including expanding existing stations.

But some researchers worry that the focus on air monitoring may mean that other parts of the

environment get overlooked. "There has to be a biological component to this," says David Evers of the BioDiversity Research Institute in Gorham, Maine. That could mean, for instance, identifying 'hot spots' that receive airborne mercury and turn it into a form that could be taken up by fish and then humans.

Pierrette Blanchard, an atmospheric chemist at Environment Canada, notes that even fish in seemingly pristine lakes in national forests in the United States and Canada can contain high levels of mercury.

In particular, Evers wants to see estuarine and marine sampling in the Amazon basin, where small-scale gold mining releases mercury into environments where fish are caught for food. He and his colleagues have also proposed a marine and estuaries network for monitoring the US Atlantic coast.

And Evers and others have been advising Senator Susan Collins (Republican, Maine) on a bill that

would provide funding from the US Environmental Protection Agency for a national mercury network to include air, water, soils and animals. Collins has tried several times before; in 2007, for instance, she requested that \$18 million be designated, but the effort died at the committee stage. Collins hopes to reintroduce the bill this summer.

The costs of an international monitoring system are unknown, and will depend on how much various countries are willing to put up for equipment and staffing.

That may be a point for discussion when negotiations for the UNEP treaty begin in earnest early next year. The talks have been boosted by the United States, which had long called for voluntary-only mercury monitoring but in February indicated it would support an

international regulatory structure. "What we need to do is to inform the negotiations," says a US state department official who requested anonymity because of the talks.

Bettina Hitzfeld, a UNEP negotiator for the Swiss Federal Office for the Environment, says that treaty discussions need to start moving ahead even in the absence of a complete monitoring system. "We cannot afford to wait," she says, "for a mercury network to be up and running."

Naomi Lubick

H1N1 update

As confirmed by the World Health Organization, as of 1 June:
Cases: 17,410, in 62 countries
Deaths: 115, in 4 countries

UNITED STATES: Cases have now been documented in all 50 states.

For Nature's swine flu coverage, see www.nature.com/swineflu.