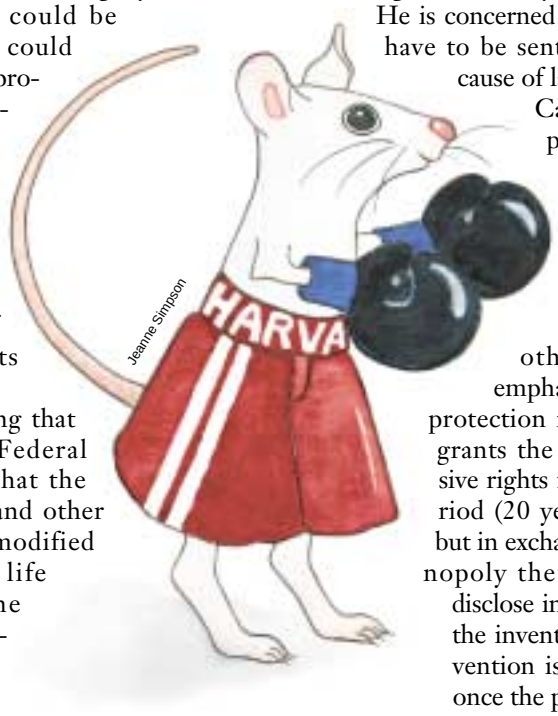
Patenting life: genetically altered mice an invention, court declares

Researchers are hailing a Federal Court of Appeal decision that nonhuman life forms can be patented in Canada, although some doubt that the ruling will have a major effect on their work.

The decision concerns the "oncomouse" developed at Harvard University — a genetically altered mouse that gets cancer very easily, making it an ideal test platform for new therapies. The mouse has been patented for many years in the US. In fact, "transgenic" animals such as the oncomouse can be patented in the US, Japan and many European countries. Until Aug. 3, 2000, however, they could not be patented in Canada. Lower organisms such as bacteria, fungi, yeast and moulds could be patented, as could processes to produce transgenic animals, but an earlier court decision had rejected the patenting of actual plants and animals.

In reversing that ruling, the Federal Court said that the oncomouse and other genetically modified nonhuman life forms fit the Patent Act definition of an invention as a "composition of matter."[1] This opens the door to patenting other transgenic animals used in medical research. Canadian labs have developed dozens of such animals. In basic molecular biology, they are used to study the function of a particular gene by "knocking out" the gene, usually in a mouse. The resulting "knock-out" mouse strain shows what happens when the gene is absent, suggesting the gene's actual function. As well, researchers genetically engineer animals to be susceptible to a particular disease in order to study the disease.



Knock-out mice: researchers remove or "knock out" a gene to see what happens

"If you develop a useful strain, you should be able to protect your interest in it," says Dr. Jim Russell, a University of Alberta professor who has created a transgenic rat model of type 2 diabetes. He finds that keeping a new animal strain going is expensive. "The rats must be bred continuously or the strain will be lost. Once lost it is irrecoverable. The court decision may, in the long run, actually help with this." He is concerned that his rat may have to be sent to the US because of lack of support in Canada. This was precisely the fate of a previous rat model of type 1 diabetes created in Ottawa.

Russell and other researchers emphasize that patent protection is a trade-off: it grants the inventor exclusive rights for a defined period (20 years in Canada), but in exchange for this monopoly the inventor must disclose information about the invention. And the invention is freely available once the protection period expires. Before the oncomouse decision, Russell was advised to treat his rat strain as a trade secret, like the formula for Coca-Cola, because he couldn't patent it.

"These days protection is very important," agrees Dr. Rashmi Kothary, a senior scientist at the Ottawa Hospital Research Institute who develops transgenic mouse models of neuromuscular diseases. "Without protection, other laboratories could quickly reproduce the work that you did at great expense and effort without having to compensate you. With the possibility of protecting your work that won't happen."

But for researchers who use transgenic mice developed elsewhere, won't patent protection increase costs and hamper access to lab animals? Most researchers are not concerned. Dr. Barbara Vanderhyden, who runs the transgenic mouse program at the University of Ottawa, says patents are usually related to restrictions on commercial use, and research use of animals in both academic and industrial contexts remains mainly unaffected. Kothary agrees. His lab sometimes uses transgenic animals developed by colleagues elsewhere, which are freely provided in return for an agreement to share research results and to provide recognition for the animal creators in published papers. Even patented, commercially available animals from the US carry only a nominal cost.

On the other hand, a commercially useful animal can net its creators $35 000 to $100 000, estimates Dr. Michel Tremblay, a McGill University researcher who has created 4 transgenic mouse strains, including a knock-out mouse that is resistant to obesity and diabetes. He has patented his mouse model in the US, which is often more important than patenting in Canada. He says the court decision "is just in fact filling a little gap present in Canada."

Tremblay worked in collaboration with the pharmaceutical company Merck Frosst, but most of the work with transgenic animals is being done in academic settings. "There's not a ton of companies that are working with transgenic animals," says Joyce Groote, president of BIOTECanada, an association representing the biotechnology industry that counts many Canadian drug companies among its members. "I don't

think the impact [of the decision] is as high in medical research as it is in other areas." She cites agriculture technology and biomanufacturing as 2 examples.

Although researchers are generally bullish, there are some concerns. Kothary is worried that very broad patents, covering large areas of technology, will limit further research. He cites a technology patented by a large US chemical company that allows researchers to activate a gene in any animal model. Since this applies to more than one animal, or one strain of animal, it means that no other researcher can use the technology freely to create a new animal model.

The Canadian Environmental Law Association is also concerned about the broad nature of such patents. "What a lot of people don't realize is that Harvard got a patent on all nonhuman mammals" that it can modify in the same way that it has modified the mouse, says Michelle Swenarchuk, a spokesperson for the association. "It applies to all mammals, from a shrew to a whale."

In Canada, the ruling was very clear: patenting does not apply to humans because it is a property-based concept, and humans cannot be considered property. The Environmental Law Association is concerned about considering any form of life as property that can be owned. "This is the commodification of life," says Swenarchuk.

Russell points out that patent protection only goes part way in solving the key problem with developing transgenic animal models — the lack of financial support. Granting agencies support only the associated research projects, and reviewers often say that industry should support the animal models, a suggestion that Russell finds naïve. He is left wondering whether to feed and breed his expensive rats, or send them to the US, where the rats would be maintained, but would be harder to acquire for Canadian research. — *Carolyn Brown*, CMAJ

Reference

1. *Harvard College* v. *Commissioner of Patents* (2000), Linden J.A., Isaac J.A., Rothstein J.A. Available: www.fja.gc.ca/en/cf/2000/orig/html/2000fca27094.o.en.html#ftn4

Dr. Henry Haddad, a professor of medicine from the University of Sherbrooke, will head the CMA in 2001/02. A former vice-dean at the university, he was named president-elect during the CMA's annual meeting in Saskatoon in August. A 1963 graduate of the University of Ottawa, he is a past president of the Quebec Medical Association and former chief of gastroenterology at the University of Sherbrooke. Haddad's main interests within the CMA have involved physician resources, postgraduate training and issues such as the privacy of health information.

World water crisis in the offing?

The world is facing a critical shortage of fresh water in the next 2 decades, according to a report from the World Commission on Water (**www.worldwatercommission.org**). The report, *A water-secure world: vision for water, life and the environment*, predicts that the use of water will increase by 40% in the next 20 years due to growing demands from agriculture, industry and urban areas. Today, 1 billion people don't have access to safe water and another 2 billion don't have adequate sanitation.The commission, whose sponsors include the World Bank and UN, was created to recommend ways to achieve "global water security." Many countries will be looking to Canada for help, since it is to fresh water what Saudi Arabia is to oil.

About 70% of the world's available water is now used in agriculture and the remaining 30% is used for households and industry. With population growth, the amount used in agriculture alone is expected to increase by 17%. Industry and cities will also require more. This "gloomy arithmetic" adds up to a burgeoning crisis for all humans, the commission states. Compounding this are existing, and worsening, environmental-degradation problems. For example, 10% of the world's agricultural food production now depends on mined groundwater that is causing a resulting drop in water tables by as much as a metre a year in parts of China, India, Mexico and elsewhere. "Our attitudes on managing water must change," says Ismail Serageldin, the World Bank's vice-president for special programs. — *Barbara Sibbald*, CMAJ