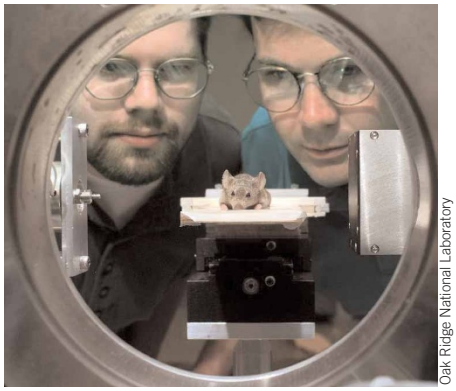
High-flying patents get their wings clipped in Europe

Researchers in Europe are benefiting from the European Patent Office's (EPO) decision to prune several high-profile patents, a result of key differences between US and European policy. The EPO's rulings broaden avenues of research that would otherwise be choked off by licensing fees, but some scientists and citizen groups say the decisions are still not enough.

On 6 July, the EPO restricted a patent on the OncoMouse model for cancer research from including all rodents to just mice. In May, the agency revoked one of three patents Salt Lake City–based Myriad Genetics has on the breast cancer gene *BRCA1*. Months earlier, the EPO had granted a patent similar to Myriad's on another breast cancer gene, *BRCA2*, to Cancer Research UK. The charity announced in August that it would allow free access to academic researchers, undermining Myriad's position.

Unlike the US, Europe forbids patents that threaten "ordre public' or morality.' The EPO invoked this clause against the OncoMouse patent and, in July 2002, the Edinburgh patent on stem cells.

The agency is also less flexible in allowing corrections to patents, says Siobhan Yeats, EPO's director of Examination and Opposition in Biotechnology. Corrections to Myriad's initial *BRCA1* patent, which was found to have gene sequencing errors, would not be allowed in Europe, says Yeats.



Oak Ridge National Laboratory

The OncoMouse patent is one of several whose scope is limited by the European Patent Office.

Those sequencing errors might be enough to overturn the other two *BRCA1* patents in Myriad's portfolio, says Gert Matthijs, a geneticist at the University of Leuven, Belgium. But scientists cannot rely on such technicalities to battle patents, he notes. "What will happen with other major patents that don't have errors?"

Matthijs says he is worried about patents on *BRCA2*, against which he and others filed an opposition earlier this year, and on a gene related to the disease hemochromatosis, for which a European patent is expected next year. Those patents lack an "inventive step," he says. Isolating and sequencing a mapped gene "is a major breakthrough but not a major invention."

Fortunately for Matthijs, the EPO allows 'routine' questioning of patents, and about 80% end up being limited. One reason for this is that the cost for opposition is in the tens of thousands of dollars, compared with hundreds of thousands in the US, giving even citizen and animal rights groups the opportunity to contest patents.

Still, the road ahead for these patents is unclear. Patent opponents argue that the OncoMouse patent, which had already been restricted in 2001 from covering all mammals, should be overturned completely. "It just solves a small controversy on the broad scope of the patent," says Marcos Malumbres, a researcher at the Spanish National Cancer Centre.

The OncoMouse patent can no longer be challenged except at the level of EPO member-states. The *BRCA1* and Edinburgh decisions are awaiting appeals. In the case of *BRCA2*, the existence of two conflicting patents on the same gene has led to confusion among researchers—and at the EPO itself. Asked what a researcher should do in the *BRCA2* case, says EPO's Yeats, "Consult a lawyer."

David Cyranoski, Tokyo

California dreaming about 'ill-conceived' stem cell plan

Come November, California might become the first state to fund stem cell research, in direct opposition to the federal government's policy. If voted in, Proposition 71 would allow the state to issue bonds for up to $3 billion over ten years for the research. But given the state's $10 billion deficit, some groups are questioning whether the proposal is financially sound.

Dismayed by the restrictive federal policy, researchers Irving Weissman and Lawrence Goldstein, Hollywood producer Jerry Zucker and real estate developer Robert Klein conceived the proposal in 2003. Klein and Zucker both have children with diabetes—a leading candidate for stem cell therapies.

By mid-August 2004, the campaign had garnered widespread publicity and about $5.3 million. The goal is to raise $20 million by November. The project could be just what the doctor ordered for the state's ailing high-tech industry, says Jim Cunneen, president of the Silicon Valley Chamber of Commerce. Apart from researchers—and, presumably, patients—the initiative could indirectly benefit venture capitalists, biotechnology companies and real estate developers.

But the project's hefty price tag has provoked some groups—such as Doctors, Patients and Taxpayers for Fiscal Responsibility—to call it "ill-conceived." Although the proposal is structured to postpone draining tax revenue, repaying the bond is expected to cost $6 billion over 30 years.

Opponents argue that much of the money would line the pockets of California's real estate developers. Up to 10% of the $3 billion pie would go to building new research centers. But if the federal government limits stem cell research in buildings funded with federal grants, scientists will need independent labs, says Zena Werb, a researcher at the University of California in San Francisco. "It costs over $100 million to build a single research building," Werb says. "That's one of the reasons that the bond calls for so much money."

Another 3% of the funds would create the California Institute for Regenerative Medicine, which will administer independent audits, public hearings and annual reports. Funds would be monitored by a public committee and a board of directors including scientific experts, patient groups and California businesses. Evaluation of grant applications would be modeled after the NIH's system, says Goldstein.

The bond's size would give researchers a stable framework unaffected by politics or the economy, Goldstein says. "We can't work in this political environment," he says. "Scientists need to know that they can start a long-term research project without having to worry about the next election." The stability would help encourage young investigators to enter the field, he adds. California might also benefit from royalties on research discoveries, and potential cures could cut its healthcare costs, which at $110 billion are the nation's highest.

Asked whether the funds might not instead go to California's struggling school system or other problems, Goldstein says, "Sure, there are lots of other things that the state could do with the money, but it's not as though there are five other proposals put forward with credible plans … We have an actual plan."

Kris Novak, San Francisco