Animals of Invention

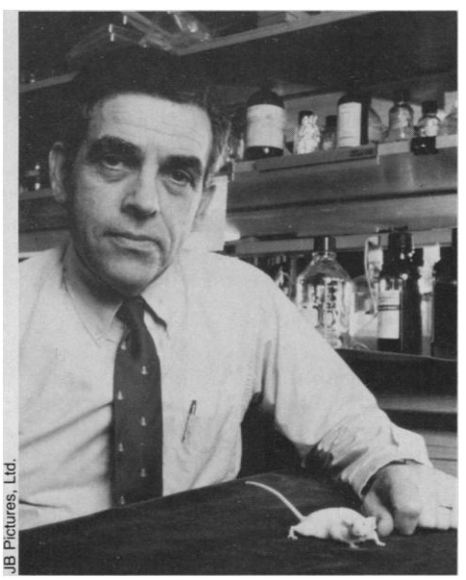
Now that Harvard has been granted the first patent for a tumor-prone mouse, Congress is again considering a moratorium on animal patents

THE award of the first patent for a genetically engineered animal has rekindled debate in Congress over a moratorium on patents for higher life forms. A bill introduced by Representative Charlie Rose (D–NC) would halt animal patents such as the one recently granted to researchers at Harvard Medical School while Congress wrestles with the economic, regulatory, and ethical implications. The bill has gathered 59 cosponsors in the House, including four Democrats on the justice subcommittee which will probably examine the bill this month. Proponents of Rose's 2-year moratorium say that more supporters are quietly waiting in the wings. A similar bill calling for an indefinite moratorium is being pushed on the other side of Congress by Senator Mark Hatfield (R–OR).

Supporters of the moratorium, which include a loose coalition of groups from the religious, environmental, animal welfare, and farming communities, are attacking the animal patent issue on a number of fronts (*Science*, 31 July 1987, p. 480). Religious leaders are concerned with ethics; the environmentalists are worried about the release of genetically engineered animals into the wild; and ranchers are balking at the possibility of having to pay royalties for progeny produced by patented animals. "For ranchers, it's a pretty straightforward concern about economics," says Lynne McAnelly of the Texas Department of Agriculture, which recently polled farmers and ranchers in the Lone Star state and found strong disapproval for patented livestock. In the upcoming debate, the opinions of ranchers and farmers could play a pivotal role, particularly for politicians from states with lots of cows, sheep, pigs, and goats. At present, ranchers pay only for the semen or embryos provided by breeders. They do not pay royalties for offspring.

The biotechnology industry cheered the 12 April decision by the U.S. Patent and Trademark Office to grant Harvard a patent for its mouse carrying an activated cancer-causing gene, calling the move a logical extension of the patenting process and one that follows the landmark 1980 Supreme Court decision which ruled that nonnatural man-made microorganisms were patentable. A decision by the Board of Patent Appeals and Interferences in 1987, which stated that genetically manipulated oysters could be patented, opened the door to higher life forms. Lisa Raines of the Industrial Biotechnology Association warns that a moratorium now would stymie creativity and hobble the industry. A similar moratorium on animal patents was rejected by a House-Senate conference committee last year.

At the center of this flurry of points and counterpoints is "the animal of invention" created by a team of geneticists at Harvard who in the early 1980s successfully introduced a cancer-causing gene into laboratory mice (*Science*, 16 November 1984, p. 823). In the prototype example cited in the patent, Philip Leder of Harvard and Timothy Stewart, now at Genentech in San Francisco, microinjected into fertilized mouse eggs a hybrid gene which contained the naturally occurring mouse oncogene *myc* along with a section of DNA from the mouse mammary tumor virus, or MMTV. The altered embryos were then implanted into foster mothers to develop to term. The mice carrying the hybrid MMTV-*myc* gene showed a strong tendency to develop malignant breast tumors when pregnant. Alone, the normal *myc* gene, which occurs in humans as well as mice, does not appear to produce tumors.



JB Pictures, Ltd.

Leder with patented mouse. *Fortuitously, a benevolent first case.*

Leder says his mice can be used to test with greater sensitivity possible carcinogens. The patent award also states that the tumor-prone mice can be subjected to substances such as vitamin E or beta-carotene which are thought to protect against cancer. "Here is a strain of mice that have taken the first step toward cancer," says Leder. "With them, you can learn some rather powerful and telling lessons about the genesis of cancer in vivo."

The patent is not limited to mice carrying the MMTV-*myc* gene. Rather, the extremely broad patent includes any nonhuman animal into which "any oncogene or effective sequence thereof" has been introduced. The patent goes on to list 33 additional oncogenes and mentions that primates such as the rhesus monkey could also serve as a transgenic animal. All future generations of the animals are covered by the patent.

It has not escaped the attention of cynical Washington types that the first animal patent was awarded to a laboratory mouse from Harvard that could help cure cancer, rather than, say, a "Super Pig" created by an agricultural conglomerate. "I don't think it was the luck of the draw," says Jack Doyle of the Environmental Policy Institute in Washington. Indeed, the patent office took the unusual step of holding a press conference to announce the award, at which Commissioner of Patents Donald J. Quigg said: "I know I'm not supposed to get on a soapbox, but how can anybody say this kind of development is unethical or wrong?" Alvin Tanenholtz, the primary examiner at the patent office who handled the application, says the choice of the Harvard animal was simply "fortuitous." The application was submitted nearly 4 years ago.

Harvard granted an exclusive license to develop the invention to Du Pont, the Delaware-based chemical company, which has donated about $6 million in open-ended grants to Leder's group at Harvard in exchange for the right of first refusal to license. At present, Du Pont has no plans to market the transgenic animals. As for other scientists working with Harvard's mice, or simply making their own, Du Pont is not interested in curtailing their work as long as the scientists are using the animals for research purposes and not commercial exploitation, says Lynn Fisher, a patent attorney for Du Pont.

Officials at the patent office, who keep mum about the exact nature of patents pending, report that 21 genetically altered animals are currently being considered. One widely publicized application involves a female mouse that has been genetically engineered to secrete in its milk the clot-busting human protein called tissue plasminogen activator. ■ WILLIAM BOOTH