PATENT WATCH

Diligent pursuit of invention is necessary

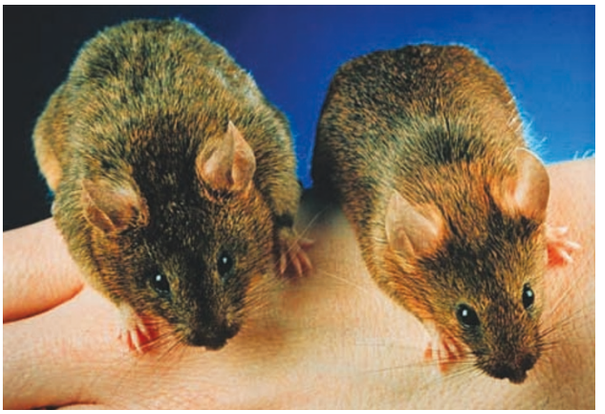
The settling of a dispute over the priority of claims between existing patent holders in favour of Mariano Barbacid and Veeraswamy Manne reinforces the notion that no benefit will come of sitting on a good idea. The patent in question describes an assay for identifying new anticancer compounds that inhibit farnesyl transferase — an enzyme that is involved in the control of cell growth. The Barbacid patent application was filed on 8 May 1990, and the patent was issued on 9 February 1993. Michael Brown, Joseph Goldstein and Yuval Reiss also made a patent application — on 22 December 1992 — but were accorded the benefit of an earlier related application that was filed on 18 April 1990, which made Brown and colleagues the senior party. However, in the US Federal Circuit Court of Appeals, Barbacid was able to prove that they had actively pursued their invention by 6 March 1990, which was not the case with Brown. Intriguingly, the Court discounted a 25 September 1989 experiment (which might have been considered satisfactory evidence in favour of Brown), because Reiss could not authenticate his lab notebooks and autoradiographs. Because the Court did not consider evidence that Brown conceived the invention before Barbacid put it to use, priority of invention was granted to Barbacid as the first to conceive the invention and then exercise reasonable diligence in later "reducing that invention to practice". Use it or lose it, to put it another way.

WEB SITES
United States patent database: http://www.uspto.gov/
Barbacid and Manne US patent 5,185,248 | Brown, Goldstein and Reiss US patent application 07/937,893

Europe upholds oncomouse

The European Patent Office (EPO) has upheld the patent on the Harvard University oncomouse, a mouse strain genetically engineered to be susceptible to cancer. Before its adoption of the European Union's 1998 Directive on Biopatents, which allows such patents to be awarded if the benefit to society is deemed greater than the suffering to the animals, the EPO did not issue patents that covered animals. Since 1998, the EPO has awarded 20 further patents on animals, but this decision is the first to be made by the EPO on an appeal against an animal patent. Although they have upheld the oncomouse patent, the EPO has restricted the breadth of the Harvard University patent — which originally covered all animals that are genetically engineered using the oncomouse technology — to cover only rodents. The EPO limited the patent to rodents because it felt that it was impossible to assume that the balance between benefit to society and suffering to the mouse could be automatically extended to all types of animal. Many organizations and individuals had registered their opposition to the oncomouse patent, which sparked intense controversy when it came into force in 1992.

WEB SITES
European patent database:
http://gb.espacenet.com/
Stewart and Leder, Harvard College European patent EP0169672
United States patent database:
http://www.uspto.gov/
Stewart and Leder, Harvard College US patent 4,736,866



OBESITY

Mighty Mouse: forever fat-free?

According to recent research, Mighty Mouse is unlikely to become obese, and probably has a reduced risk for developing diabetes. In the *Journal of Clinical Investigation*, McPherron and Lee report that mice with increased muscle mass due to loss of the negative regulator of muscle growth, myostatin (MSTN), also show a reduction in both fat accumulation and abnormal glucose metabolism.

MSTN is a member of the transforming growth factor-β (TGF-β) superfamily of secreted growth and differentiation factors, which have essential roles in regulating tissue development and build-up. *MSTN* is expressed predominantly in skeletal muscle and at lower levels in adipose tissue, and individual muscles from *Mstn*-null mice can weigh twice as much as their wild-type counterparts.

Skeletal-muscle function is important for the maintenance of normal glucose function. This, together with the lack of fat in *Mstn*-null mice, raised the question of whether Mstn might be an effective target for suppressing the development of obesity and diabetes in mouse models of this disease. *Mstn*-null mice were crossed with two genetic models of obesity — Agouti lethal yellow (A^y) and obese ($Lep^{ob/ob}$) mice. Agouti mice become obese because of a dominant mutation that results in antagonism of melanocortin receptors in the hypothalamus, and causes increased food intake. Obese mice have a loss of leptin signalling, which results in severe obesity and abnormalities in glucose metabolism, in part related to the melanocortin-receptor pathways. In both mouse models, loss of *Mstn* prevents an age-related increase in adipose-tissue mass. The diabetic profiles of the crossed *Mstn*-null mice were also greatly improved. Agouti mice respond poorly to glucose-tolerance tests; however, glucose and insulin levels after such a test were markedly lower in *Mstn*-null Agouti mice. In addition, the usual development of hyperglycaemia in obese mice was significantly delayed in the *Mstn*-null obese mice. Pharmacological agents that block MSTN function could be useful for slowing or preventing the development of obesity and type 2 diabetes.

Clearly, deletion of *Mstn* affects adipose-tissue mass as well as skeletal mass, although it is unclear whether the effect on adipose tissue is direct or indirect. If MSTN has the same role in humans as in mice, in addition to its potential utility as a drug target in obesity and diabetes, it could also be a target for increasing skeletal-muscle mass in patients with muscle-wasting diseases.

Melanie Brazil

References and links
ORIGINAL RESEARCH PAPER McPherron A. C. & Lee, S.-J. Suppression of body fat accumulation in myostatin-deficient mice. *J. Clin. Invest.* **109**, 595–601 (2002)

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