PATENT WATCH

No patent for Harvard oncomouse in Canada

After 17 years in the Canadian court system, the 'Harvard oncomouse' has reached a dead end. The Canadian Supreme Court ruled by a five-to-four decision that the transgenic mouse, genetically engineered with a predisposition to develop cancer, is not an invention and cannot be patented in Canada. Canada is now the only Western nation to deny a patent to the Harvard Mouse. The Canadian Patent Office originally approved Harvard's claim for protection of the process by which the oncomouse was engineered, but denied protection for the mouse itself. This meant that although no one could use Harvard's techniques to produce a new oncomouse without infringing their patent, nothing prevented a third party from obtaining oncomouse offspring by mating an existing oncomouse pair. Harvard's appeal of this decision culminated in the hearing before the Supreme Court. In coming to their decision, the Court focused on two phrases appearing in the Patent Act's definition of invention, namely "manufacture" and "composition of matter". They concluded that "manufacture" should be limited in its interpretation to denote a non-living mechanistic product or process, and thus could not include the oncomouse. In considering the phrase "composition of matter", the Court noted that none of the other words used in the definition of "invention" referred to a higher life form.

WEB SITES

The Supreme Court of Canada: http://www.lexum.umontreal.ca/csc-scc/en/
Harvard College v. Canada
Canadian Patent Act: http://laws.justice.gc.ca/en/P-4/index.html

Markman rules

Following a Markman hearing, the US District Court of Delaware ruled against PolyMASC Pharmaceuticals plc in its patent infringement case against the ALZA Corporation. PolyMASC claims that its patent covering pegylated liposomes for drug delivery is being infringed by ALZA in its manufacture of pegylated-liposome products encapsulating the cancer drug doxorubin. The Markman hearing is a special proceeding required under US patent law in which both sides present to the court their arguments for how they believe certain claims at issue in the lawsuit should be interpreted. The court decides how the patent claim should be interpreted, and this interpretation is used to instruct a jury, should the issue of infringement be reached at trial. Often, the way a court rules on claim construction has a substantial impact on other issues in the case and after the court gives an opinion of the scope of the patent's claims, the outcome of the charge of infringement is inevitable. PolyMASC intends to seek immediate resolution of the current case in the Federal Circuit Court of Appeals, but if the company does not succeed in convincing the appeal court to reverse or modify the Markman ruling, the company's infringement action may not to proceed to trial.

WEB SITE

US Patent and Trademark Office: http://www.uspto.gov/
PolyMASC Pharmaceuticals plc. Liposomes with covalently bound PEG moieties on the external surface which demonstrate improved serum half-life following intravenous administration are provided. US Patent 6,132,763 (2000).

ION CHANNELS

Fluid control

What is the link between the inherited disorder cystic fibrosis and secretory diarrhoea, the biggest killer of children under 5 years of age in developing countries? The answer is the cystic fibrosis transmembrane conductance regulator (CFTR) — a cyclic-AMP-activated chloride channel that is responsible for fluid secretion in the intestines and airways. Mutations in the *CFTR* gene that inactivate the function of the protein lead to cystic fibrosis, and the cholera toxin that causes secretory diarrhoea induces intestinal fluid secretion by affecting CFTR-mediated Cl^- transport. But, so far, the development of treatments that target CFTR has been hampered by the lack of appropriate small-molecule inhibitors to help researchers investigate the relevant pathophysiological mechanisms and potential therapies.

Now, in the *Journal of Clinical Investigation*, Verkman and colleagues report the identification of a class of high-affinity CFTR inhibitors from a screen of 50,000 compounds. They found that six compounds, all thiazolidinones, were potent inhibitors of CFTR-mediated Cl^- transport, and worked in the submicromolar range. The most potent of these inhibitors blocked Cl^- tranport in CFTR, but did not inhibit other Cl^- channels or transporters. This inhibitor was non-toxic in cell-culture and mouse models, and a single dose in mice reduced cholera-toxin-induced fluid secretion by 90% for over 6 hours.

CFTR inhibitors could help advance the development of treatments for secretory diarrhoea and cystic fibrosis in different ways. For secretory diarrhoea, thiazolidinones could provide an alternative line of attack to oral rehydration therapy, which revolutionized the treatment of secretory diarrhoea by single-handedly reducing the mortality of children by more than half. For cystic fibrosis, identifying therapies has been difficult owing to a lack of adequate human-tissue and animal models with impaired CFTR function. But thiazolidinones could at last provide researchers with the much-needed tools to investigate the underlying pathophysiological pathways of this fatal genetic disease.

Simon Frantz

References and links

ORIGINAL RESEARCH PAPER Ma, T. *et al.* Thiazolidinone CFTR inhibitor identified by high-throughput screening blocks cholera toxin-induced intestinal fluid secretion. *J. Clin. Invest.* **110**, 1651–1658 (2002)