PATENT WATCH

Accurate speculation is not enough

The European Patent Office (EPO) has revoked an ICOS patent after opposition from SmithKline Beecham and Duphar International Research. The patent described the DNA sequence of a purified and isolated seven-transmembrane protein, V28, which has at least one specific ligand-binding activity. The patent included speculation as to the specific function of the molecule, but lacked working examples of function and utility. The speculation turned out to be correct, retrospectively. The Opposition Division of the EPO, which decides the fate of opposed patents, agreed with the opponents that a list of speculative functions for a DNA sequence that encodes a protein is not a reliable basis for establishing industrial applications for that molecule. Furthermore, the absence of a disclosed ligand for the receptor protein renders the patent not sufficiently disclosed. This decision could have a tremendous impact on patents and applications, many of which describe genes for which no function is shown at the filing date. The patent owner has not filed an appeal — perhaps to avoid the decision becoming enshrined as a good one by an Appeal Board decision at the EPO?

WEB SITE

European Patent Office: http://www.epo.co.at/

Godiska, R., Gray, P. W. & Schweickart, V. L. Novel V28 seven transmembrane receptor. EP Patent WO9412635 (1994).

Madey and the Duke

A case concerning a microwave gun and a free electronic laser could have important implications for all academic research universities. In the 1980s, the laser researcher John Madey moved from Stanford to Duke University, along with substantial equipment. After leaving Duke in 1997, Madey sued the university for patent infringement, because Duke had continued to use his former laser equipment in its facility, violating Madey's laser patents. The university argued that it had no liability for infringement, because its use was 'experimental' and based broadly on Duke's academic missions. The District Court then put the burden on Madey, the patent holder, to prove that Duke's use of the equipment was non-experimental. However, at appeal, the Federal Circuit rejected the District Court's approach of putting the burden of proof on the plaintiff, and also rejected the overly broad interpretation of the experimental use defence to infringement. The circuit judges held that the experimental use defence is intended for uses that are solely for amusement, to satisfy idle curiosity or strictly for philosophical enquiry. Duke's research did not qualify for the experimental use defence because it was in keeping with the alleged infringer's legitimate business.

WEB SITE

US Patent and Trademark Office: http://www.uspto.gov/

Madey, J. M. J. & Westenskow, G. A. Microwave electron gun. US Patent 4,641,103 (1987) | Madey, J. M. J. & Szarmes, E. B. Free-electron laser oscillator for simultaneous narrow spectral resolution and fast time resolution spectroscopy. US Patent 5,130,994 (1992)

BONE DISEASES

Having the cake and eating it

Hormone-replacement therapy (HRT) with oestrogens has been the treatment of choice for counteracting the bone loss that leads to osteoporosis in postmenopausal women, but recent clinical trials have shown increased risks of breast cancer in women taking HRT, challenging previous beliefs that the benefits of HRT outweigh the risks. Writing in *Science*, Manolagas and colleagues now describe a synthetic sex hormone that can increase bone mass and strength in mice without the effects on reproductive organs that could increase the risks of cancer.

Classically, the effects of sex hormones are mediated through nuclear receptors — largely distributed in a sex-specific pattern — that modulate gene transcription when activated by bound hormone. However, recent research has shown that sex hormones can also have effects through a distinct 'non-genotropic' pathway, which is independent of sex, and which can be dissociated from the transcriptional activity of the receptor with synthetic ligands.

Prompted by their previous work showing that one such synthetic ligand, called estren, could reduce apoptosis of bone-synthesizing cells, the authors investigated the effects of estren on bone in male and female mice with their ovaries or testes removed, respectively, to stop the production of natural sex hormones. The resultant loss in bone mass could be reversed by treatment with the appropriate sex hormone — the oestrogen 17β-oestradiol (E_2) in female mice, and dihydrotestosterone (DHT) in male mice — but this also led to above-normal increases in the sizes of the reproductive organs in both cases. By contrast, estren was more effective than E_2 in females, and as effective as DHT in males, at increasing bone mass and strength, but did not significantly affect reproductive organs. It thus seems that such mechanism-specific ligands could offer advantages over oestrogens and selective oestrogen-receptor modulators that are used at present to treat osteoporosis in postmenopausal women, and could also be of therapeutic benefit in men.

Peter Kirkpatrick

References and links

ORIGINAL RESEARCH PAPER Kousteni, S. *et al.* Reversal of bone loss in mice by nongenotropic signaling of sex steroids. *Science* **298**, 843–846 (2002)

FURTHER READING Kousteni, S. *et al.* Nongenotropic, sex-nonspecific signaling through the estrogen or androgen receptors: dissociation from transcriptional activity. *Cell* **9**, 719–730 (2001) | Goltzman, D. Discoveries, drugs and skeletal disorders. *Nature Rev. Drug Discov.* **1**, 784–798 (2002)