PATENT WATCH

Pay up for the 21st Century Strategic Plan

Last summer, the head of the US Patent and Trademark Office (USPTO), Jim Rogan, unveiled its aggressive 21st Century Strategic Plan to transform the USPTO from a slow-moving government bureaucracy into a quality-focused, responsive, market-driven intellectual property system. Now, there is much discussion over the cost of the plan, as it calls for substantial fee increases (subject to congressional approval). For large entities seeking patents, the cost would jump from US $8,020 to US $12,110, for small entities, from US $4,010 to US $6,680. A new category of 'micro' patent seekers (an individual, rather than a company) would pay US $6,180. According to the American Bar Association, one of the concerns with the proposed price hikes is that Congress will divert the income produced by the fees away from the patent office budget, leaving the USPTO no better off to implement the goals of the Strategic Plan. Rogan wants to use the extra funding to double the size of the examiner staff (currently 3,500), as it now takes over two years to get a patent, and without significant change in operations, the time will soon grow to three years. Currently, the USPTO have 408,000 older applications on the shelf and expect 340,000 new applications this year.

WEB SITE
United States patent database-21st Century Strategic Plan:
http://www.uspto.gov/web/offices/com/strat2001/21sp_covermemo.htm

No speculation in application

The decision by the UK patent office in 1999 to turn down four patent applications on behalf of Dr Kenneth Prendergast is now looking like quite a significant one. The patents concerned new uses for the potent 5-HT (serotonin) inhibitors ordansetron and granisetron, currently used for treating nausea associated with chemo- and radiotherapy. The patent examiner held that the claimed new therapeutic uses, including combatting stress in civilian and military emergency situations, and treating neurological symptoms and nausea associated with chemical or biological warfare, were not supported by any pharmacological data at the time. The UK patent office declared that it is incumbent on applicants in these cases to illustrate that the compound actually shows the claimed activity, and that the demonstration must be by *in vivo* or *in vitro* test data obtained prior to the patent filing date. Furthermore, the new activity cannot be ascertained by an obvious inference from existing data, or prior art. This case, together with the recent decision by the European Patent Office to revoke an ICOS patent covering DNA sequence information that lacked working examples of function and utility (see Patent Watch, December 2002, Accurate speculation is not enough), seems to be establishing an important precedent: speculation will not get you a patent in Europe, regardless of whether that speculation turns out to be correct.

WEB SITE
The UK Patent Office: http://www.patent.gov.uk/
http://www.patent.gov.uk/patent/legal/decisions/1999/o_015_99.pdf
http://www.patent.gov.uk/patent/legal/decisions/1999/o_016_99.pdf

ADRENOCEPTOR PHARMACOLOGY

Variety is the spice of life

Experimental results sometimes differ despite seemingly identical inputs. Such a situation has sparked a debate in the November issue of *Molecular Pharmacology* over the nature of G-protein partners for β_2-adrenoceptors (β_2ARs). This should be essential reading not just for the dedicated adrenoceptor community, but also for all those using the experimental setup in question: cultured human embryonic kidney 293 (HEK293) cells.

For some years, evidence has been accumulating which indicates that β_2ARs can change their G-protein partner depending on their phosphorylation state. Protein kinase A (PKA) phosphorylation of the receptor was found to lead to an increased activation of G_i and a concommittant reduction in the activation of the β_2AR's usual partner, G_s. This G_i-mediated signalling was proposed to be important in transducing some actions of β_2ARs, such as the activation of extracellular signal-related kinase (ERK) (see further reading). However, other studies have questioned whether β_2ARs are truly able to switch partners upon phosphorylation, and whether such switching would be of functional relevance.

The new papers from the Clark and Lefkowitz groups bring this controversy into the limelight. Clark and colleagues present evidence that β_2AR-mediated activation of ERK in HEK293 cells does not require G_i. In an accompanying Perspective article, Lefkowitz *et al.* review the large body of evidence in the literature that implies that PKA-mediated phosphorylation of β_2ARs regulates their coupling to G_i, and hence their control of various signalling systems, including ERK.

Intriguingly, the key to the observed differences may lie in the non-uniformity of apparently identical experimental systems. Lefkowitz and colleagues present data showing that signalling through endogenous β_2ARs in nine different isolates of HEK293 cells exhibits vastly different sensitivity to pertussis toxin, which inhibits G_i. Clearly, all HEK293 cell lines are far from equal.

Adam Smith

References and links

ORIGINAL RESEARCH PAPERS Friedman, J., Babu, B. & Clark, R. B. β_2-Adrenergic receptor lacking the cyclic AMP-dependent protein kinase consensus sites fully activates extracellular signal-regulated kinase 1/2 in human embryonic kidney 293 cells: lack of evidence for G_s/G_i switching. *Mol. Pharmacol.* **62**, 1094–1102 (2002) | Lefkowitz, R. J., Pierce, K. L. & Luttrell, L. M. Dancing with different partners: protein kinase A phosphorylation of seven membrane-spanning receptors regulates their G protein-coupling specificity. *Mol. Pharmacol.* **62**, 971–974 (2002)
FURTHER READING Daaka, Y., Luttrell, L. M. & Lefkowitz, R. J. Switching of the coupling of the β_2-adrenergic receptor to different G proteins by protein kinase A. *Nature* **390**, 88–91 (1997)