PATENT WATCH

All for one, and one for fifteen

After decades of disagreement, the European Union's Competitiveness Council finally agreed an outline for a European Community Patent. According to the proposal, it will be possible to apply for one EU-wide patent as an alternative to 15 patents — one from each of the member states. Under the new system, a patent specification will be drafted in English, French or German, leaving only the claims to be translated into the 11 official European languages following grant of a Community Patent. At present, the process of translating a patent into all of these languages is expensive, and this reform will make the process more affordable. Furthermore, as the number of EU member states will rise to as many as 19 by 2004, the costs of translation will escalate. The proposed transitional jurisdictional arrangements make it clear that courts of individual member states will retain jurisdiction to decide questions of infringement and validity of Community Patents on a Community-wide basis. If the wording of the regulations is agreed on by the end of the year, a diplomatic conference could take place in Spring 2004 to agree the necessary Treaty changes. With ratification of the Treaty changes likely to take two or three years, the European Patent Office could be empowered to accept applications for Community Patents as early as 2006.

EPO Community Patent notice: http://www.european-patent-office.org/news/info/2003_04_30_e.htm

Keep off the pathway

The US District Court for the District of Massachusetts has ruled against Eli Lilly and Company in its bid to dismiss a patent infringement suit filed last year by the small Cambridge-based company Ariad Pharmaceuticals and co-plaintiffs Massachusetts Institute of Technology, the Whitehead Institute for Biomedical Research, and Harvard College. Ariad allege infringement of US patent 6,410,516, which covers methods of treating human disease by regulating nuclear factor-κB (NF-κB) cell-signalling activity. Before the initial discoveries by the research team at plaintiff institutions, Lilly patented two compounds, raloxifene hydrochloride (Evista; US patent 4,418,068) and recombinant human activated Protein C (Xigris; US patent 4,775,624). The company began marketing Evista in 1997 as an osteoporosis therapeutic and has been selling Xigris since 2001 to treat severe sepsis. At the molecular level, these drugs work by inhibiting NF-κB activity, although neither of the two patents mentions NF-κB. Lilly contends that its patents for Evista and Xigris anticipate Ariad's patent, thereby rendering it invalid. However, the court determined that it is unclear at present whether the administration of the drugs was developed in response to the methods claimed in the '516 patent or were derived from methods in the public domain prior to the '516 patent. Ariad intend to proceed to trial and to seek a damage award based on a reasonable royalty on Lilly's sales of Evista and Xigris.

US patent and trademark office: http://www.uspto.gov/

BIOTECHNOLOGY

Virus alert

RNA interference (RNAi) — the process in which double-stranded RNA (dsRNA) binds to specific messenger RNA and silences gene expression — has generated great excitement, as dsRNA could theoretically be created to target any disease-causing gene more quickly, cheaply and effectively than any present method. Preliminary *in vivo* work seems to be maintaining this promise. Earlier this year it was shown that RNAi can silence the expression of the gene encoding the Fas receptor, protecting mice from fulminant hepatitis. Now, Kay and colleagues report for the first time in *Nature Biotechnology* that RNAi can prevent viral replication in live mammals.

The authors used a mouse model of hepatitis B virus (HBV) infection, in which a plasmid carrying the entire HBV genome was transfected into the mouse liver. In these mice, HBV proteins are expressed and most of the stages of viral replication take place. Kay and colleagues co-transfected the mice with a second plasmid that expressed small fragments of dsRNA called short hairpin RNAs (shRNAs), designed to target specific HBV mRNA sequences. This caused a dramatic decrease in viral gene expression at the levels of RNA and protein, and strongly inhibited the replication of the virus.

One of the concerns about testing RNAi in whole animals is that any observed effect could result, fully or in part, from the foreign shRNAs triggering the immune response. But by comparing mice that lack a functional immune system with wild-type animals, the authors showed that the HBV inhibition was a specific effect of targeting viral sequences, rather than being due to a generalized immune-based attack.

At present, there are few effective treatments for hepatitis B once infection is established. The findings not only show the therapeutic promise of RNAi in hepatitis B but also indicate that this strategy could treat other forms of viral infection. But many challenges remain. First, RNAi-based inhibition of infection by intact HBV needs to be proved. Second, new methods of delivery will need to be developed, as the one used in this study is unsuitable for a clinical setting. And finally, successfully silencing the HBV genes of interest without affecting the expression of any host genes must be ensured.

Louisa Flintoft,
Nature Publishing Group

References and links

ORIGINAL RESEARCH PAPER McCaffrey, A.P. *et al.* Inhibition of hepatitis B virus in mice by RNA interference. *Nature Biotechnol.* **21**, 629–630 (2003)