

HIGHLIGHTS

PATENT WATCH

Failing to comply...

Eight European Union (EU) member states are being taken to the European Court of Justice because of their failure to adapt their national patent laws and implement the Biotech Patent Directive. After a ten-year debate, the EU adopted what it called 'strict ethical rules' for patenting biotech inventions in 1998. The directive aims to encourage biotech research by allowing patenting of inventions, yet seeking to allay public concerns about patenting processes using human genes or DNA molecules; the directive also bans patents for cloning human beings or modifying their genetic identity, as well as the use of human embryos for industrial purposes. The EU had given member states until the end of July 2000 to transpose the directive into national law, and earlier this year the European Commission made it clear that it had lost patience with the recalcitrant countries — Germany, Austria, Belgium, France, Italy, Luxembourg, the Netherlands and Sweden — and threatened legal action. The failure to implement the directive across the EU means that although European Patents are granted for gene patents centrally, they could be revoked at any time in one of these member states.

European Commission: http://europa.eu.int/comm/index_en.htm

Paying twice?

The biotechnology companies Biogen Inc, Genzyme Corp and Abbott Laboratories, have filed a lawsuit against Columbia University, claiming that Columbia's 2002 patent for creating protein-manufacturing cells is essentially the same technology as that covered in patents that lapsed two years earlier. The lawsuit, filed in the Boston US District Court, alleges that the school has illegally extended the life of a lucrative patent for gene-splicing technology. In the filing, the companies claim that together they have paid tens of millions of dollars in royalties to Columbia for using the technology in various pharmaceutical treatments, and should not have to pay any more. The companies are seeking a release from obligations to pay Columbia, an injunction prohibiting enforcement of the university's license, and lawyers' fees and expenses. According to the lawsuit, Columbia has received about \$35 million in royalties from Biogen, and about \$25 million from Genzyme. In 1980, the university filed a patent for the process of inserting foreign DNA into a host cell. Columbia received the patent in 1983 (US patent 4,399,216), and two subsequent patents filed in 1983 (US patent 4,634,665) and 1991 (US patent 5,179,017) were also based on the experimental research described in the original 1980 application. The technology was licenced to more than 30 biotech companies, creating many of biotech's best-sellers, and bringing in a revenue of hundreds of millions of dollars for the use of the process.

US patents 4,399,216, 4,634,665 and 5,179,017 are linked online



NEURODEGENERATIVE DISEASE

A puff a day keeps the plaques away?

Can smoking have a neuroprotective effect? The recent observation that exposure to nicotine delays the onset of Alzheimer's disease has researchers racing to identify the mechanism of this surprising phenomenon. Most studies have focused on nicotine itself — few have considered the contribution that metabolites of nicotine, the principal alkaloid component of tobacco, might make to neuroprotection. Now, a study published in the *Proceedings of the National Academy of Sciences* shows that nornicotine — a product of the *N*-demethylation of nicotine — inhibits the formation of the amyloid β -peptide ($A\beta$) fibrils whose aggregation into neuritic plaques is a hallmark of this devastating disease.

As glycation reactions between amines and reducing sugars have recently been implicated in Alzheimer's disease, and nornicotine is known to catalyse aberrant glycation of proteins *in vivo*, Tobin Dickerson and Kim Janda explored the hypothesis that nornicotine might be active against $A\beta$. Following incubation of a 40-amino-acid fragment of $A\beta$ with nornicotine and glucose, mass spectrometry indicated that one glucose and one nornicotine molecule were being added to some of the peptide fragments, resulting in an 18% reduction in fibril formation.

Nuclear magnetic resonance spectroscopic investigations indicated that covalent bonds form between the pyrrolidine ring of nornicotine and a lysine residue of the peptide that the authors suggest is essential to the aggregation of $A\beta$. This assertion is supported by the finding that nornicotine had no effect on preformed fibrils, in which the target lysine residue is 'buried' within a hydrophobic core and is therefore not available for covalent modification.

These new data show that searching for compounds that covalently interact with $A\beta$ might facilitate the development of much-needed treatments for Alzheimer's disease, which is predicted to afflict 22 million people worldwide within the next 20 years. Unfortunately, the considerable toxicity and psychoactivity of nicotine and nornicotine severely limits their therapeutic potential. Sorry to disappoint the smokers among you, but it's unlikely that physicians will be prescribing cigarettes any time soon.

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References and links

ORIGINAL RESEARCH PAPER Dickerson, T. J. & Janda, K. D. Glycation of the amyloid β -protein by a nicotine metabolite: a fortuitous chemical dynamic between smoking and Alzheimer's disease. *Proc. Natl Acad. Sci. USA* **100**, 8182–8187 (2003)

FURTHER READING Wolfe, M. S. Therapeutic strategies for Alzheimer's disease. *Nature Rev. Drug Discov.* **1**, 859–866 (2002).