PATENT WATCH

Get it down in writing

An Enzo Biochem patent is invalid because of the lack of a written description of the claimed invention, according to a judgment ruling of the US Court of Appeals for the Federal Circuit. The patent covers nucleic-acid probes for the detection of the bacteria that cause gonorrhea. In defining the invention, Enzo had made a deposit of a biological sample and referred to that sample, in combination with defining the function of the invention, in reference to the relative affinity of the probes for different strains of specified bacteria in a hybridization assay. In a two-to-one decision, the Court considered the functional description as inadequate. The decision signals that a functional definition of subject matter is not good enough, and implies that genetic discoveries must refer to specific sequences, which will result in them being more narrowly defined. Enzo intends to seek a rehearing before the full Court of Appeals.

WEB SITES **United States patent database:** http://www.uspto.gov/
Lo, A. US patent 4,900,659

EPO upholds novelty of Roche PCR patents

'Prior art' does not deprive Roche's polymerase chain reaction (PCR) patents of novelty or inventiveness, according to the Technical Board of Appeals of the European Patent Office (EPO). The central issue of the appeal hearing, which was prompted by submissions from several opponents, was whether previous, related publications — otherwise known as prior art — deprived the patents of novelty or inventiveness. Prior art was also the subject of earlier US litigation and re-examination proceedings about the US counterparts to these European patents. One patent covers the exponential amplification of a target nucleic acid, whereas the other governs the detection of the target nucleic acid once it is exponentially amplified. The April 2002 ruling is the final determination of the EPO and cannot be appealed. Roche is now asserting US counterparts to the European PCR patents in a lawsuit against Promega Corporation. Roche claims that Promega has infringed two patents as well as another for Taq DNA polymerase, an enzyme that is used principally for PCR.

WEB SITES **European patent database:** http://gb.espacenet.com/
Mullis, K .B. EP Patent 201,184 | Horn, G. T. *et al.* EP Patent 200,362
United States patent database: http://www.uspto.gov/
Gelfand, D. H. *et al.* US Patent 4,889,818 | Mullis, K. B. US Patent 4,683,195 | Mullis, K. B. US Patent 4,683,202

Caliper tries to block sales of Molecular Devices' IMAP products

Caliper Technologies Corporation has filed a patent infringement lawsuit against Molecular Devices Corporation, in which it alleges that Molecular Devices' IMAP assay products infringe one of Caliper's patents. The suit was filed in the US District Court for the Northern District of California. The Caliper patent covers methods and systems for carrying out a wide variety of high-throughput microfluidic assays. IMAP technology uses the specific binding of trivalent metal ions to phosphate groups and optical detection methods for high-throughput screening of phosphodiesterases, kinases and phosphatases. Caliper is seeking an injunction against future sales of the Molecular Devices IMAP products and damages for past sales.

WEB SITES **European patent database:**
http://gb.espacenet.com/
Lovegren, K. I. EP Patent 247,983
United States patent database: http://www.uspto.gov/
Nikiforov, T. T. US Patent 6,287,774

COMBINATORIAL CHEMISTRY

Survival of the fittest

In dynamic combinatorial chemistry, reversible self-assembly of chemical building blocks is used to generate libraries of compounds. Allowing the library to equilibrate in the presence of a target protein creates a driving force that favours the formation of library members that bind tightly to the target — a self-screening process that could, in theory, greatly accelerate lead discovery. However, although this approach has been successful in simple systems in which the best-binding inhibitor is sufficiently favoured to allow easy identification, the difficulty of distinguishing inhibitors with similar binding constants hinders the application of the technique to large libraries with greater potential for lead discovery. Now, writing in the *Journal of the American Chemical Society*, Cheeseman *et al.* propose a promising strategy for addressing this problem — irreversibly destroying the weak-binding inhibitors to leave the best-binding inhibitor.

The authors tested the potential of their approach by using a small, non-dynamic library of dipeptide inhibitors of carbonic anhydrase. Using two compartments separated by a protein-impermeable membrane — each initially containing a mixture of dipeptides at the same concentration — they showed that the presence of carbonic anhydrase in one compartment could concentrate the dipeptides in that compartment in proportions that reflect their relative binding constants. However, as expected, the concentration differences between dipeptides of similar binding strength were small. But when a protease that could cleave the dipeptides was added to the compartment without the carbonic anhydrase, the ratio of the best binder to weaker binders was significantly enhanced over time, as dipeptides that bind more strongly to carbonic anhydrase were protected to a greater extent from proteolytic hydrolysis.

The results were in line with the theoretical model that was proposed by the authors, providing proof-of-principle for the strategy, and holding promise for its extension to larger dynamic libraries. For the approach to be applicable to large libraries, however, it will be important for the destruction process to be non-specific to avoid biasing the library owing to differences in destruction rate rather than differences in binding to the target. This could be achieved, for example, by physical methods, such as adsorption to a solid phase.

Peter Kirkpatrick

References and links

ORIGINAL RESEARCH PAPER Cheeseman, D. J. *et al.* Amplification of screening sensitivity through selective destruction: theory and screening of a library of carbonic anhydrase inhibitors. *J. Am. Chem. Soc.* 2002 Apr 26 (doi:10.1021/ja017099)
FURTHER READING Ramström, O. & Lehn, J.-M. Drug discovery by dynamic combinatorial libraries. *Nature Rev. Drug Discov.* **1**, 26–36 (2002)