PATENT WATCH

En banc — all together now

The US Court of Appeals has issued an order on behalf of the Mayo Foundation granting an en banc rehearing — that is, the matter is being referred to all the circuit judges in regular active service. Last year, this column highlighted a case in which two Elan–Athena Neurosciences patents covering mice transgenic for Alzheimer's disease were restored by the Court of Appeals, in a two-to-one decision, having previously been declared invalid in a lower court after challenge by the Mayo Foundation. The case involves the issue of inherent disclosure in prior art. Before Elan filed for their patents, the inventor Michael Mullen had filed one that included a discussion of creating transgenic mice on the basis of the Swedish mutation of amyloid precursor protein, the same mutation used in the transgene of the Elan mice. Judge Dyk, dissenting from the majority opinion, thought that the decision would have serious and unfortunate consequences in the future, as patent rights to existing inventions could be granted if the patent applicant identifies an inherent characteristic of that product that was not identified in the prior art. Now, all the circuit judges of the Court of Appeals will add their opinions to the table.

WEB SITE

US Court of Appeals Order: http://www.ipc.org/2002/IPCcourts/Elan_Order.htm

Erythropoietin gets bloody

In the latest round of battles between Aventis Pharma/Transkaryotic Therapies (TKT) and Amgen over the alleged infringement of five Amgen patents protecting the production of the recombinant erythropoietin Epogen, Aventis/TKT have emerged from the Federal Court of Appeals slightly worse for wear. The US Court of Appeals for the Federal Circuit upheld the Massachusetts District Court's decision that Aventis/TKT product — the fully human erythropoietin Dynepo — infringed two of Amgen's patents relating to Epogen. However, the Appeals Court also confirmed the invalidity of one of Amgen's patents and remanded the case back to the District Court for further consideration over validity issues of another patent in the light of potentially invalidating prior art. Dynepo was developed using TKT's patented gene-activation technology and Aventis Pharma is responsible for the development and commercialization of the product. Although Dynepo received marketing approval from the European Agency for the Evaluation of Medicinal Products in March 2002, Aventis Pharma has not launched the product. In July 2002, the Court of Appeal in the United Kingdom issued a unanimous opinion in favour of TKT and Aventis Pharma in a similar patent infringement suit involving Amgen.

WEB SITE

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

CANCER

Parc keeper

In the complex and crowded environment of the cell, where you are is just as important as what you are. Get caught in the wrong place and there could be dramatic consequences. The tumour suppressor p53 acts as a transcription factor, so it must be in the nucleus to carry out its pivotal role in activating cell-cycle arrest and apoptosis to prevent the growth of abnormal or damaged cells. When p53 is not required in unstressed cells (that is, during normal cell growth) large amounts of inactive p53 accumulate in the cytoplasm. However, tumour cells also have high cytoplasmic levels of p53, so knowing how p53 is normally retained in the cytoplasm and how this becomes altered in cancer is of fundamental importance.

Now, in *Cell*, Gu and colleagues report the purification and characterization of a protein that anchors p53 in the cytoplasm and prevents the tumour suppressor from entering the nucleus. Parc (p53-associated, parkin-like cytoplasmic protein) exists as part of a large complex in the cytoplasm and contains several domains that are associated with ubiquitin-ligase activity, which mediates the degradation of proteins (although the authors found no direct evidence to suggest that Parc regulates p53 stability through this mechanism).

The authors found that overexpression of Parc promoted the cytoplasmic sequestration of p53, and that neuroblastoma cells (which have high levels of cytoplasmic p53) expressed high cytoplasmic levels of Parc. In addition, RNA-interference-mediated downregulation of Parc induced the nuclear localization of p53 and p53-mediated apoptosis in neuroblastoma cells, which shows that agents that lower Parc levels might be of therapeutic importance. Further investigation of the Parc–p53 interaction and whether Parc interacts with a protein called Mdm2, another ubiquitin ligase recently shown to be involved in the reverse process (the nuclear export of p53), will shed light on what seems to be yet another level of control of this remarkable protein.

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References and links

ORIGINAL RESEARCH PAPER Nikolaev, A. Y., Li, M., Puskas, N., Qin, J. & Gu, W. Parc: a cytoplasmic anchor for p53. *Cell* **112**, 29–40 (2003)

FURTHER READING Kastan, M. B. & Zambetti, G. P. Parc-ing p53 in the cytoplasm. *Cell* **112**, 1–5 (2003)