

# Current Patents Gazette

## Patenting in Context

News & Highlights from week 0815

National news headlines this week have featured two prominent drug discovery stories that have interesting intellectual property aspects. On April 10 coverage was given to a paper published in the current issue of the journal *Science*, based on research carried out in Cleveland, Ohio, by **Dr Andrei Gudkov** of the **Lerner Research Institute**. In the course of finding out how some cancer cells are able to resist radiotherapy, researchers noted that a compound known as **CBLB-502**, or **Protectan**, was able to assist healthy cells in resisting radiation, without diminishing its antitumor effect. More than a dozen patent applications filed during the 1990s by the **University of Illinois** serve to confirm Dr Gudkov's long-term interest in the genetics aspect of resistance to cancer therapy; an early case, **WO9207071**, was reportedly licensed at one stage to **Rhone-Poulenc Rorer**, now **sanofi-aventis**. **Cleveland BioLabs** is receiving **US Department of Defense** funding for development work on CBLB-502, which is said to act as a TLR5 agonist. Elsewhere CBLB-502 is described as a "mini-flagellin", roughly one-third the size of the original bacterial protein, as described by the **Cleveland Clinic Foundation** team in **WO2006069198**. The basic claims to use of flagellin itself as a radioprotectant appeared a year earlier in **WO2005056042**,

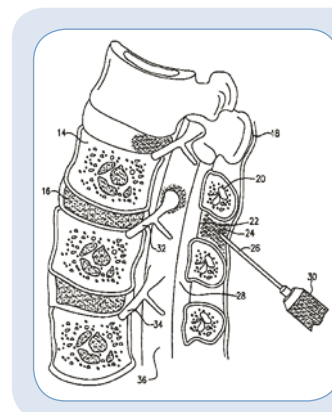
which was published a few days after the filing of **WO2006138238** with claims to protection against apoptosis. This pattern of filing seems to indicate that a sound IP base is being generated to support the development of CBLB-502.

Breaking news on Friday 11 April included early reports of a promising trial of the use of etanercept to improve brain function in Alzheimer's disease (AD). This is based on the work of **Professor Edward Tobinick** at a private clinic in California. The method consists of injecting **etanercept** into the neck, then tilting the patient's body to encourage the drug to flow into the brain; over three years a rapid and only partially reversible effect has been observed in about 90% of patients. Launched originally by **Wyeth** and **Immunex** in the US as **Enbrel** for rheumatoid arthritis late in 1998, this TNF-binding fusion protein has a complex patent position that gave rise to litigation, now resolved, with **Teva** and others, based on fundamental patents filed during the 1980s. However, looking specifically at Prof Tobinick's contribution, we see him as the single most prolific inventor in the set of more than 50 patents now protecting etanercept in various ways. Key to the use in AD is a case filed at the beginning of 1999, **WO0050079**, covering use of TNF agonists in neurological

disorders. Tobinick seems not to have pursued that international patent application, or **WO0149321** filed later the same year, but in the US has instituted a vigorous filing program that has already yielded nine issued patents, with several more pending applications in the pipeline. The granted cases include, for example, **US7214658**, with claims explicitly referring to what is known as "perispinal" delivery of the drug, meaning that direct intrathecal injection is excluded. This patent is now reassigned by the inventor to **TACT IP LLC**, a company seemingly established specifically to take ownership of the patent rights to perispinal etanercept. The next step seems to be placebo-controlled trials, and if a product of this nature should then receive marketing authorization, Prof Tobinick's patents could provide protection through to 2024 or beyond.

The latest issue of the UK Patents Journal (No. 6203)

records the entry into force on **Allergan's EP284288** of the SPC protecting **tazarotene**. The Certificate entered into force March 17, 2008 and will remain in force until December 2, 2011. SPCs were also granted on **EP284288** in most European states, with the notable exception of Belgium, Switzerland and the Netherlands and entered into force at the same time. Allergan has developed **Tazorac**, a topical formulation of tazarotene, a nonirritating retinoic acid receptor agonist indicated for the treatment of patients with plaque psoriasis or acne vulgaris and mild-to-moderate psoriasis. Sales have been declining, however, especially in the main US market, and were around \$100 million in 2007. Consequently, in November 2007, **Stiefel Labs** entered into an agreement with Allergan to develop dermatological products containing tazarotene in Europe and to copromote Tazorac to dermatologists in the US.



**Given "perispinally", etanercept may be useful in treating Alzheimer's disease**

# UK Initial Applications

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A0 applications filed March 3rd – March 9th 2008 – expected to see publication in early September 2009

• **CellCentric** has filed an application (GB0803845) for **cellular programming**. The company was established in 2004 with funding from **Avlar BioVentures** and **Providence Investment Trust**, initially based upon the work of Professor Azim Surani at the Gurdon Institute, **University of Cambridge**. CellCentric specialises in epigenetics particularly in the treatment of cancer. The company's only published application to date appears to be **WO2007128982**, claiming the modification of nucleic acid sequences in vivo to facilitate somatic cell nuclear transfer, but their IP portfolio is complemented by agreements with the **Babraham Institute** and more recently **Massachusetts General Hospital**. CellCentric has also entered into collaborations with Cancer Research Technology and **UCL's Wolfson Institute**.

• **Chroma Therapeutics** has filed a cluster of applications relating primarily to **enzyme inhibitors** (GB0803747, GB0803748, GB0803891 and GB0803895). The first of these refers generally to enzyme and receptor modulators, but the second specifies inhibitors of p38 MAP kinase, and the last pair are glyoxalase inhibitors. Although p38 and similar kinases feature in several of Chroma's published applications (**WO2007129040**, etc), and HDAC and DHFR are recurring targets, glyoxalase appears only in **WO2004101506**, filed initially in May 2003. Lead optimization was under way by

October 2005 across all of these targets, and it is possible that the current batch of applications signals the identification of clear leads.

• **Ghent University** has filed (GB0803668) for a **treatment for mucositis**. This is possibly related to work by Karolien Van Huynegem, a PhD student of Ghent University's Professor Erik Remaut, who has been investigating genetically modified *Lactococcus lactis* as a tool in the prevention and healing of chemotherapy-induced mucositis. The project was completed in November 2007. Elsewhere, **ActoGeniX, Flanders Interuniversity Institute for Biotechnology (VIB)** and University of Ghent spin-off, is investigating **AG-013**. This is a trefoil factor (TFF) delivered by their proprietary **TopAct™** oral administration platform of genetically engineered microorganisms for potential in mucositis. TopAct™ is based upon the work of Lothar Steidler, conducted first at Ghent then later at Flanders. ActoGeniX's first published application appears to be **WO2007063075**, claiming the use of an immunomodulating compound to induce tolerance to antigens by mucosal delivery of an antigen in combination with an immunomodulating compound-producing microorganism.

• **John Payin Okyere** has filed an application (GB0803872) to protect **microarrays**. The applicant, based at the **University of Nottingham**,

previously claimed cross-species microarrays for the identification of one or more oligonucleotides from a first species which could be used to analyse the corresponding nucleotide sequence from a second species (**WO2005093630**). This is probably a continuation of the research into microarrays which may be based on **Affymetrix GeneChip arrays** being investigated in order to develop new genomic methods for drug and chemical evaluations which will decrease the reliance on animal testing. **The University of Nottingham's Institute of Genetics** entered a licensing agreement with **PamGene** in 2004 to use its array technology.

• **Serentis** has filed GB0804122 with claims to **treatment of Raynaud's phenomenon**. On its website, Cambridge-based Serentis refers a "virtual model" for its activities, and the corresponding patent portfolio seems equally elusive. The company was founded in 2006, and neither of the published patent applications traceable to it was originally filed in the name of Serentis. Filed originally in mid-2005, **WO2007025999** is concerned with use of an aureolysin inhibitor in inflammatory skin conditions, naming **Surface Therapeutics** as the applicant; the latter was acquired in October 2007 by Serentis, now formally named as the patent owner. Similarly **Sosei's** beta-blocker repurposing case **WO2006027579** originated pre-Serentis, in October 2004,

but is linked with the company through its R&D Director, Dr Andy Baxter, who is named as an inventor and was formerly Sosei's Discovery Director. Interestingly, Raynaud's phenomenon does not currently feature in the development pipeline shown on the Serentis website, so this new application may mark the inception of a new project.

• **Summit Corporation** has filed GB0803906 covering **compounds for treating Duchenne muscular dystrophy (DMD)**. The application was filed just ten days before publication of a pair of PCT applications relating to treatment of the same condition, **WO2008029152** and **WO2008029168**. Those documents in turn seem to follow on from **WO2007091106** and **WO2007091107**, which appeared in August 2007 naming an extended team of eleven inventors. Summit, formerly **VASTox**, has used its zebrafish chemical genomics platform to test its lead compound in this field, designated **SMT-C1100**. That project, now benefitting from EMEA Orphan Drug status, seems to have its origins in patenting undertaken in the mid-1990s by Isis Innovation, prior to the spin-off of VASTox from **Oxford University**. That early patent property includes **WO0125461** for example, which is licensed to Summit, along with patents from the MRC relating to the original utrophin gene promoter target (**WO9634101**, etc).