

decreased nuclear export. These results are in line with some of the findings of Vousden's group, but leave the question open as to whether NF- $\kappa$ B activation via this pathway indeed increases p53-stimulated apoptosis or decreases it, as suggested by the results of Verma and colleagues.

In the second article [6], Fujioka *et al.* describe p53 stabilization as a novel mechanism for a proapoptotic function of NF- $\kappa$ B. However, this mechanism was found not for DNA-damaging agent but protein synthesis inhibitor doxycycline-induced p53 activation. This compound is believed to inhibit the expression of mitochondrial electron transport chain proteins resulting in the release of superoxide which activates NF- $\kappa$ B. Doxycycline-induced p53 activation and apoptosis was found to depend on the canonical NF- $\kappa$ B pathway, but activation of the transcription factor by this drug does not require p53. Instead, p53 is stabilized to exert its proapoptotic effect, apparently by NF- $\kappa$ B-dependent downregulation of the E3 ubiquitin ligase HDM2 level.

These findings have serious implications for the use of NF- $\kappa$ B inhibitors as adjuncts in anticancer chemotherapy. Although the majority of human tumours lack functional p53, for those that have retained it, the combination of NF- $\kappa$ B inhibitors currently in development with some standard chemotherapeutic drugs might result in increased tumour cell survival rather than death. Further investigation of this important issue will be required before a clear rationale for the inhibition of NF- $\kappa$ B as strategy in anticancer combination chemotherapy can be developed.

- 3 Ryan, K.M. *et al.* (2000) Cancer: pinning a change on p53. *Nature* 404, 892-897
- 4 Tergaonkar, V. *et al.* (2002) p53 stabilization is decreased upon NF $\kappa$ B activation: a role for NF $\kappa$ B in acquisition of resistance to chemotherapy. *Cancer Cell* 1, 493-503
- 5 Bohuslav, J. *et al.* (2004) p53 Induces NF-kappa B activation by an Ikappa B kinase-independent mechanism involving RSK1 phosphorylation of p65. *J. Biol. Chem.* DOI: 10.1074/jbc.M313509200 (E-publication ahead of print; <http://www.jbc.org>)
- 6 Fujioka, S. *et al.* (2004) Stabilization of p53: a novel mechanism for proapoptotic function of NF-kappa B. *J. Biol. Chem.* DOI: 10.1074/jbc.M313435200 (E-publication ahead of print; <http://www.jbc.org>)

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## Business

### Collaborations

#### Inpharmatica and Procter & Gamble

Inpharmatica (<http://www.inpharmatica.com>) have announced a discovery collaboration with Procter & Gamble Pharmaceuticals (P&GP; <http://www.pgpharm.com>). Under the terms of the agreement, P&GP will fund a research program at Inpharmatica and pay additional license fees to use discoveries arising from the collaboration.

The goal of the collaboration will be to develop robust computational structure models and identify chemotypes for families of human G-protein coupled receptors (GPCRs). Inpharmatica will apply proprietary elements of its drug discovery platform PharmaCarta™. Specifically, the Chematica™ component will provide 3D homology modelling, drug binding-site identification and mapping techniques, and proprietary databases will help to identify tractable chemical hits and GPCR family chemotypes.

Malcolm Weir, Chief Executive Officer at Inpharmatica commented, '...this agreement constitutes a very exciting program for Inpharmatica. It will allow the company to use its cutting edge technologies to address the problem of identifying new drugs targeted to members of one of the most important families of drug targets.'

P&GP's Director of Chemistry and Discovery Technologies, Joseph Gardner, said: 'We are always looking for ways to increase productivity in drug discovery, and collaboration with Inpharmatica will move us towards this goal... We expect our joint efforts will bring benefits to both sides.'

#### ParAllele BioScience announce two collaborations

ParAllele BioScience (<http://www.parallelebio.com>) has announced two collaborations; an SNP research agreement with Merck (<http://www.merck.com>), and the early access deal for the company's commercial SNP genotyping solution with the National Cancer Institute (NCI; <http://www.nci.nih.gov>).

In the Merck collaboration, ParAllele will use both its SNP discovery and SNP genotyping technologies to discover genetic variations that could impact the disease susceptibility, prognosis or response to therapy of an individual, in

order to pursue improved drug targets.

ParAllele is also launching an 'out-of-the-box' solution for highly multiplexed SNP genotyping, thus enabling researchers to obtain valuable results at the bench top. The NCI has signed as an early access customer for the company's MegAllele™ SNP genotyping kits.

### Funding

#### UCLA Lab2Market Investment Fund

University California, Los Angeles (UCLA; <http://www.ucla.edu>), has established an investment fund aimed at accelerating the conversion of laboratory discoveries into commercial uses. The UCLA Lab2Market Investment Fund provides up to USD\$25,000 to individual faculty whose research shows promise in the marketplace but who lack funding for additional experiments required to demonstrate commercial viability.

Associate Vice Chancellor for Research Andrew Neighbour, who directs UCLA's Office of Intellectual Property Administration, said: 'By providing funding to faculty for research to aid in product development, the UCLA Lab2Market Investment Fund facilitates the transfer of technology to the marketplace and eliminates a significant barrier in the development of marketable ideas and products.'

The first recipient of a grant from the Investment Fund is Farhad Parhami, an Associate Professor of Medicine at the David Geffen School of Medicine, whose research has shown that certain oxysterols stimulate bone-forming cells that could help in the future treatment of osteoporosis. Parhami hopes to form a company to develop medications based on his research but investors first want to see positive results in animal models, rather than bone cells. Grants for this further research might become available but could take more than a year for application and approval, a timeframe that is not conducive to entrepreneurial product development, which is where the Lab2Market Investment Fund comes in.

The USD\$300,000 Fund was established with equal contributions from three Californian venture capital firms: Cycad Group of Santa Barbara, Draper Fisher Jurvetson of Menlo Park and Zone ventures of Los Angeles.

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