

pro-apoptotic caspases-3 and -9. But in contrast to persistent caspase-3 activity in 'single ischemic' neurons, preconditioning elicited marked, but only transient, activation of caspase-3.

The inhibitors of apoptosis (IAPs) are endogenous caspase inhibitors. The protein expression level of a member of the IAP family, cIAP-2, was upregulated following global ischemia, regardless of preconditioning. However, an IAP antagonist, Smac/DIABLO, was no longer released from the mitochondria in preconditioned neurons. Together, these

results suggest that preconditioning enable CA1 neurons to survive by maintaining mitochondrial membrane integrity, thereby preventing Smac-mediated inhibition of IAPs and allowing IAPs to inhibit caspase-dependent apoptosis.

By identifying the players involved in ischemic tolerance, these findings provided valuable insight into the molecular mechanisms for the prevention of neuronal death associated with stroke and other neurodegenerative diseases. Interestingly, in addition to their anti-caspase activity, previous studies demonstrated that IAPs

also function as negative regulators of Smac via their ubiquitin ligase activity. Therefore, a therapeutic strategy utilizing IAPs to block intrinsic apoptotic pathways might be suitable in ameliorating the outcome of neuronal injuries.

- 5 Tanaka, H. *et al.* (2004) Ischemic preconditioning: neuronal survival in the face of caspase-3 activation. *J. Neurosci.* 24, 2750–2759

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Business

Collaborations

Inpharmatica announces ADME technology agreement with GSK

Inpharmatica (<http://www.inpharmatica.co.uk/>), the selective drug discovery company, has announced that it has entered into an agreement with pharmaceutical company, GlaxoSmithKline (GSK; <http://www.gsk.com/>) to access its ADME technologies. Under the agreement, Inpharmatica will apply its proprietary *in silico* ADME technology to an undisclosed number of GSK's drug discovery programmes in the UK and Europe.

This is the fourth ADME deal to be announced by Inpharmatica in the past six months, providing further validation of the company's expertise and industry-leading technology in this important area in drug discovery. Mike Tarbit, Senior VP of pre-clinical R & D, at Inpharmatica, said; 'we are delighted with the ongoing success of our ADME business and the calibre of partners we are attracting.' Inpharmatica's lead discovery programme is focused on 16 novel nuclear receptors, representing a druggable protein family of high therapeutic interest. The company's chemogenomics technology platform uses one of the largest computer farms in the world.

NIH and FDA launch new human gene transfer research data system

The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) announced today that they have launched

a new genetic modification clinical research information system, GeMCRIS (<http://www.gemcris.od.nih.gov/>) – a web-accessible database on human gene transfer (gene therapy). GeMCRIS, developed collaboratively by the two agencies, is a unique public information resource, as well as an important new electronic tool to facilitate the reporting and analysis of adverse events on these trials. The new system will provide information to the public directly and will improve the government's ability to monitor adverse events in gene therapy.

NIH Director Elias A. Zerhouni, said, 'GeMCRIS is an important achievement and a unique resource for scientists, patients, and the public. GeMCRIS will help advance gene therapy, while allowing NIH, FDA, and the research community to maintain appropriate oversight.'

Acting FDA Commissioner Lester M. Crawford, emphasized that 'the development of GeMCRIS illustrates the government's commitment to addressing public and patient concerns about safety while advancing gene therapy. Providing accurate and complete information about ongoing gene therapy studies is the best way to achieve this goal.'

Protein Mechanics and Aventis

Protein Mechanics (<http://www.proteinmechanics.com/>) and Aventis (<http://www.aventis.com/>) have entered into an agreement to advance the identification, discovery and validation of

highly selective, orally available matrix metalloprotease (MMP) inhibitors, a promising new class of drugs for treatment of a broad array of pathologies involving the extracellular matrix.

This protein family presents significant selectivity challenges when approached with conventional methods. Protein Mechanics will utilize its ImagiRo® predictive simulation technology to provide Aventis with insights into important aspects of specific target-ligand interaction.

Ken Haas, President and CEO of Protein Mechanics, Inc. said 'Aventis has a strong record of commitment and accomplishment in the development of novel therapeutics for important disease areas, so we are extremely gratified that it has chosen Protein Mechanics as a partner in this effort.'

Business was written by
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People

Retirement

USP announces retirement of Joseph G. Valentino

The United States Pharmacopeia (USP; <http://www.usp.org/>) have announced that Joseph Valentino, Senior Vice President and General Legal Counsel at USP, will be retiring after more than 35 years.

Valentino currently directs USP's legal activities. He is also secretary to the USP Board of Trustees and the USP Convention.