8 Brown, S.P. *et al.* (2003) Brief presynaptic bursts evoke synapse-specific retrograde inhibition mediated by endogenous cannabinoids. *Nat. Neurosci.* 6, 1048–1057

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Microbiology

New places to hide: Salmonella and dendritic cells

Infections with *Salmonella typhimurium* generally occur via oral uptake of contaminated food or water. It is not fully understood how *S. typhimurium* can spread systemically after oral infection, but phagocytic cells have been considered as possible vehicles. *Salmonella* induces two type III secretion systems (TTSS) to invade and survive inside eukaryotic cells. Most of the corresponding genes are located on *Salmonella* pathogenicity islands 1 (SPI-1) and 2 (SPI-2). SPI-2 deficient mutant strains are dramatically attenuated in systemic virulence and reveal reduced proliferation in infected eukaryotic cells.

S. typhimurium is efficiently taken up by dendritic cells (DC) and bacterial antigens are presented by infected DC. A recent study describes the intracellular activities of this bacterial pathogen within DC [9]. Jantsch *et al.* demonstrate that virulence genes of *S. typhimurium* are induced after uptake by DC. Furthermore, a functional TTSS is assembled by intracellular bacteria residing in the parasitophorous vacuole within DC, influencing intracellular trafficking of the bacteria. Both wild-type and an SPI-2-deficient strain persisted to an equal extent in DC over 24 hours but did not proliferate.

These data suggest that the pathogen-containing vacuole in DC is a unique compartment distinct from that in other phagocytic cells. It does not allow proliferation of intracellular *Salmonella* but is permissive for the biosynthesis and secretion of virulence proteins. This specialized vacuole might be a consequence of the function of DC to sample, transport and present antigens. The authors speculate that this compartment is used by intracellular pathogens for distribution in the host organism. Intracellular persistence in DC might be a requirement for the systemic spread of a pathogen.

9 Jantsch, J. *et al.* (2003) Intracellular activities of *Salmonella enterica* in murine dendritic cells. *Cell. Microbiol.* 5, 933–945

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Miscellaneous

Acute regulation of liver metabolism

How the fasted liver responds to refeeding – where the tissue redirects carbohydrate flux from net glucose production to net up-take for storage and utilization – has been the subject of much research for the past 40 years.

Recently, Chu *et al.* [10] addressed this question when they demonstrated that hepatic glucokinase (GK) moves from the nucleus to the cytosol within 10 minutes of an intraduodenal infusion of glucose into rats. Their studies further revealed that insulin could stimulate GK translocation in the same timeframe and that the GK regulatory protein (GKRP) did not translocate to the cytosol.

Their data suggest that disruption of the GK–GKRP complex and translocation of GK to the cytosol are essential components of the acute response of the liver to a meal. These data are complemented by the report of Jin *et al.* that, during the same acute response, the liver also increases the content of fructose-2,6-bisphosphate (F-2,6-P2), a potent activator of 6-phosphofructo-1-kinase (PFK-1), thus up-regulating glycolysis within minutes of an oral gavage in rats [11].

These data suggest that, during the acute response, the liver specifically upregulates the disposal of glucose via glycolysis by concurrent activation of glucose phosphorylation (GK) and the committing step to glycolysis (PFK-1). This is accomplished without inhibition of FBP-1, even when F-2,6-P2 is high, consistent with earlier observations that hepatic glycogen is synthesized primarily by the indirect pathway during the acute response.

These observations are important because it is precisely this response that appears to be compromised in type 2 diabetes mellitus, in which the downregulation of post-prandial hepatic glucose output fails.

10 Chu, C.A. *et al.* (2003) Rapid translocation of hepatic glucokinase in response to intraduodenal glucose infusion and changes in plasma glucose and insulin in conscious rats. *Am. J. Physiol. Gastrointest. Liver Physiol.* (E-pub ahead of print; http://ajpgi.physiology.org)
11 Jin, E.S. *et al.* (2003) Increased hepatic fructose 2,6-bisphosphate after an oral glucose load does not affect gluconeogenesis. *J. Biol. Chem.* 278, 28427–28433

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Business

Collaborations

Aventis and Avalon form oncology collaboration

Aventis (http://www.aventis.com) and Avalon Pharmaceuticals (http://www.avalonrx.com) have entered into a collaboration for the identification, discovery and validation of druggable screening targets. Avalon will provide Aventis with a subset of its library of >200 identified amplicons that have been discovered through cytogenetic analysis.

Thierry Hercend, Head of Aventis Oncology Research, said: 'Through this alliance… Aventis hopes to generate innovative drugs targeting amplified oncogenes, a promising class of caner drug targets.'

Ken Carter, President and Chief Executive Officer of Avalon, said: 'We are excited about this agreement, which allows us to advance our cancer target

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initiative to the next stage of discovery… through smarter use of innovative genomics technologies.'

Aventis is dedicated to treating and preventing disease by discovering and developing innovative prescription drugs and human vaccines; Avalon uses forward chemical genomics-based methods to accelerate the discovery of novel targets and drugs.

Cenix Bioscience and Bayer Healthcare AG

Cenix Bioscience (http://www.cenix-bioscience.com) have announced a research collaboration with Bayer Healthcare (http://www.bayer.com) to screen all known human druggable genes using RNA interference (RNAi) techniques, to identify and validate new therapeutic drug targets for several disease indications.

Using cell-based assays co-developed with Bayer research teams, Cenix will apply its proprietary genome-based HTS RNAi platform to >6000 genes in less than 9 months.

Christophe Echeverri, CEO and Chief Scientific Officer of Cenix, said: 'Having launched these HT-RNAi research offerings… after years of careful R&D, we have been particularly gratified by the overwhelming market interest, of which this agreement represents a first, important milestone.'

The project will make use of the genome-wide library of siRNA molecules designed by Cenix using its industry-leading algorithms. Cenix is a leader in genome-based HT applications of RNAi for the discovery and validation of new therapeutic drug targets. Bayer Healthcare is an innovator in the healthcare and medical products industry with products aiming to enhance quality of life by diagnosing, preventing and treating disease.

Business was written by *Joanne Clough*

People

Appointments

Adenosine Therapeutics announces two appointments

The appointment of two senior executives and officers has been announced by Adenosine Therapeutics (http://www.adenosinetherapeutics.com). William S. Gray joins the company as Vice President of Licensing and Secretary and Shannon Williams joins as VP of Regulatory Affairs and Clinical Development.

Robert S. Capon, CEO and co-founder of Adenosine Therapeutics, said: 'We are very pleased to add such seasoned executives to our company. Gray in his role as outside counsel and Secretary has been a major contributor to our success in negotiating favourable licensing agreements to date. Williams' significant experience in pharmaceutical product development will help us effectively and efficiently navigate the drug development and regulatory approval process.'

NaPro appoint new VP

NaPro Therapeutics (http://www.naprobio.com/therapeutics/) has appointed Anne Bailey as Vice President of Diagnostics and Reagents and General Manager of its Genomics Division. NaPro Therapeutics is a life science company focused on the development of targeted therapies for the treatment of cancer and hereditary disease.

Before joining NaPro, Ms Bailey served as Vice President of Diagnostics at Variagenics and in a managerial career spanning 25 years, has also held positions at Avitech Diagnostics, Photest Diagnostics and Metpath. On her appointment, Ms Bailey said: 'I believe there is a wealth of untapped commercial value for both therapeutic and diagnostic applications for NaPro's gene editing technology. I look forward to participating in the commercialization of this unique platform technology.'

Leonard P. Shaykin, Chairman and CEO of NaPro, commented that: 'We are delighted to have a manager of Anne Bailey's strong background and experience joining us at this time in our Genomics Division.'

New CSO for Entelos

Entelos, a company that specializes in systems biology to identify and validate targets (http://www.entelos.com), has announced the appointment of Mikhail Gishizky as Chief Scientific Officer.

Before joining Entelos, Gishizky was Vice President of Target Discovery at SUGEN/Pharmacia, where he was responsible for establishing their human cancer genetics program. Gishizky did his postdoctoral training at the University of California at Los Angeles (UCLA) working on cancer biology and haematopoetic cell development, during which time he was part of the team that demonstrated the causative role of bcr–abl in chronic myeloid leukaemia.

'This is an exciting time for Entelos and the pharmaceutical industry', said Gishizky, 'I look forward to leading the outstanding team at Entelos and delvering exceptional research to our partners and internal programs.'

Georgia Cancer Coalition announce new President

William J. Todd has been approved as President of the Georgia Cancer Coalition (GCC; http:// www.georgiacancer.org/), effective immediately. The GCC's mission is to build on Georgia's assets in cancer research, treatment and early detection and prevention to eventually eradicate the disease.

Under Todd's direction, the GCC will implement a strategic plan to further establish itself as a leader in the fight against cancer. The GCC Board of Directors also appointed several new members and representatives from medical schools in Georgia. Todd said that he was 'honoured to serve Georgia and the Georgia Cancer Coalition as President. The GCC has done so much for Georgia', he continued, 'In addition to saving lives, it has garnered national attention as a model for other state cancer efforts.'

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