Journal Highlights

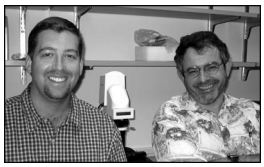
New Angiogenesis Gene

(l-r) Moolenaar, Jonkers, and van Meeteren

Autotaxin (ATX) has long been an enigmatic exo-phosphodiesterase that promotes tumor cell motility and metastasis. Four years ago, researchers discovered that ATX is in fact a phospholipase D that generates a lipid growth factor, "lysophosphatidic acid" (LPA). However, the roles of ATX and LPA in vivo remained unknown. Using ATX-knockout mice, Laurens van Meeteren, Jos Jonkers, and Wouter Moolenaar of the Netherlands Cancer Institute, Amsterdam, show that ATX is essential for blood vessel formation. "ATX-deficient embryos die at midgestation, apparently due to lack of a functional vascular network," says Moolenaar. "The simplest explanation for the observed vascular defects is loss of LPA production and downstream receptor signaling in endothelial cells. . . Given the relevance of new blood vessel formation to tumor progression, ATX may be an attractive target for anticancer drugs. Yet, the physiological role of ATX in adult life is likely to extend beyond angiogenesis, as ATX is found highly expressed in brain and spinal cord where its function is still unknown."

(L. A. van Meeteren, P. Ruurs, C. Stortelers, P. Bouwman, M. A. van Rooijen, J. P. Pradère, T. R. Pettit, M. J. O. Wakelam, J. Sébastien Saulnier-Blache, C. L. Mummery, W. H. Moolenaar, and J. Jonkers. 2006. Autotaxin, a secreted lysophospholipase D, is essential for blood vessel formation during development. Mol. Cell. Biol. **26:**5015–5022.)

How Coxsackievirus Hides from the Immune System

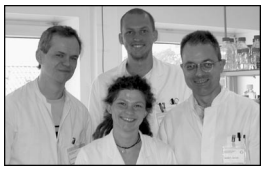


Cornell (l) and Whitton

Coxsackieviruses cause substantial human disease. But the immune system attacks them only weakly. J. Lindsay Whitton et al. of the Scripps Research Institute, La Jolla, Calif., hypothesized this happens because antigen presentation is inhibited because the virus disrupts host protein trafficking. Now they show that one viral protein, 3A, can destroy the Golgi apparatus, which serves as Grand Central Station in the cell, sending lipids, proteins, etc., hither and yon. Among other things, this destruction prevents MHC class 1 molecules, the vehicles that present antigens to the immune system, from reaching their targets, says Whitton, "thus allowing virus-infected cells to be essentially invisible to the immune response. Coxsackieviruses also act as a model for several viruses, including poliovirus. Thus, knowledge gleaned from this virus may apply to other diseases. Our work may help in the development of vaccines against this family of viruses."

(C. T. Cornell, W. B. Kiosses, S. Harkins, and J. L. Whitton. 2006. Inhibition of protein trafficking by coxsackievirus B3: multiple viral proteins target a single organelle. J. Virol. 80:6637–6647.)

Experimental Vaccine Protects Against Multiple Serotypes

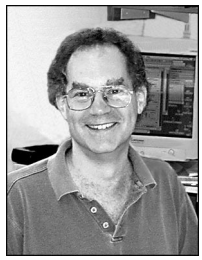


Jacobson (front) and Meens, Maas, and Gerlach (l-r)

Vaccines to prevent bacterial disease are hobbled by the inability to prevent infections on top of preventing disease, the inability to produce immunity against multiple serotypes, and the inability to distinguish immunized from naturally infected animals using serological tests. Also troubling: natural infections, ostensibly caused by a single serogroup of bacteria, are consistently more broadly and strongly protective than anything achieved with simple vaccines. Gerald F. Gerlach and colleagues of the University of Veterinary Medicine, Hannover, Germany, constructed a multiple mutant of *Actinobacillus pleuropneumoniae*. This is one of the most costly porcine respiratory tract infections, with 15 different serotypes, for which conventional vaccines are not cross-protective. "Applying this strain as live vaccine, we were able to induce cross-serotype protection upon a single aerosol application, and differentiate infected from vaccinated animals based on routine serology," says Gerlach. "Using this strain for delivery, we might be able to protect pigs at acceptable costs from various respiratory diseases using a single intranasal application at weaning."

(A. Maas, I. D. Jacobsen, J. Meens, and G.-F. Gerlach. 2006. Use of an *Actinobacillus pleuropneumoniae* multiple mutant as a vaccine that allows differentiation of vaccinated and infected animals. Infect. Immun. 74:4124–4132.)

Housekeeping a Major Chore


Grossman

Genome maintenance—faithful replication, monitoring of integrity, and repair—is a major task for every organism. Alan D. Grossman and colleagues of the Massachusetts Institute of Technology in Cambridge show that mRNA levels of more than 10% of the genes of *Bacillus subtilis* change in response to DNA damage or replication arrest. "We found that the transcriptional responses to different types of damaging conditions were not completely overlapping, indicating that cells respond differently to different types of alterations of replication and DNA damage," says Grossman. "The conserved recombination protein RecA, the transcriptional regulator LexA, and the replication initiation protein and transcription factor DnaA are involved, either directly or indirectly, in much of the response. In addition, many of the genes affected belong to resident mobile genetic elements, including phage and conjugative transposons. Our analyses indicate that many of the regulatory circuits are intertwined, and future work will focus on defining the connections between the various regulators, and how replication status is sensed."

(A. I. Goranov, E. Kuester-Schoeck, J. D. Wang, and A. D. Grossman. 2006. Characterization of the global transcriptional responses to different types of DNA damage and disruption of replication in *Bacillus subtilis*. J. Bacteriol. 188:5595–5605)

Two Pathways Appear Important in Anaerobic Biodegradation of Alkanes

In bioremediation of petroleum spills, while the action of aerobic organisms on alkane-type hydrocarbons is well known, and often involves terminal oxidation of the alkane to fatty acid products, it has been less clear to what extent anaerobes contribute to biodegradation of alkanes and related aliphatic hydrocarbons. Recently, it has been established that fumarate addition to the subterminal carbon of the alkane and carboxylation of the alkane are two distinct mechanisms for anaerobic alkane breakdown. Lily Y. Young and graduate student Amy Callaghan of Rutgers University, New Brunswick, N.J., and their collaborators describe a comparison of these routes for the metabolism of hexadecane in two sulfate-reducing isolates and in a mixed sulfate-reducing consortium. Through GC-MS analysis of isotopically labeled fragments, the investigators proved that one strain carried out fumarate addition while the second used a carboxylation mechanism. Moreover, both pathways appear to function simultaneously within mixed anaerobe populations, suggesting each is an important contributor to alkane degradation by anaerobic microorganisms.

(A. V. Callaghan, L. M. Gieg, K. G. Kropp, J. M. Sulflita, and L. Y. Young. 2006. Comparison of mechanisms of alkane metabolism under sulfate-reducing conditions among two bacterial isolates and a bacterial consortium. Appl. Environ. Microbiol. 72:4274–4282.)

Novel, Hard-To-Detect β-Lactamase Described

Among *Enterobacteriaceae*, β-lactamases such as TEM-1 and SHV-1 are the most prevalent mechanism of acquired resistance to β-lactams. These β-lactamases hydrolyze penicillins and narrow-spectrum cephalosporins. To thwart them, β-lactam antibiotics resistant to the hydrolysis, such as expanded-spectrum cephalosporins, and inhibitors of the TEM and SHV penicillinases were developed. However, resistance quickly evolved. Yet the culprit strain, *E. coli* TO799, was not reproducibly detected as an extended spectrum β-lactamase (ESBL). Now Frédéric Robin of the Centre Hospitalier Universitaire de Clermont-Ferrand, France, and collaborators describe a novel β-lactamase, TEM-125, that is responsible for this phenotype. "TEM-125 is the first complex mutant TEM to present hydrolytic activity against ceftazidime together with a high level of resistance to clavulanate," the researchers write. "The discovery of such an ESBL. . . confirms the emergence of a complex mutant TEM subgroup and highlights the need to evaluate detection methods so as to avoid possible therapeutic failures."

(F. Robin, J. Delmas, M. Archambaud, C. Schweitzer, C. Chanal, and R. Bonnet. 2006. CMT-type β-lactamase TEM-125, an emerging problem for extended-spectrum β-lactamase detection. Antimicrob. Agents Chemother. 50:2403–2408)