

Short Reads

The **Wellcome Trust** announced the establishment of UK PubMed Central, a free online archive of peer-reviewed medical and life science research papers. The database, which is set to launch in January 2007, will be operated by the **British Library**, the **University of Manchester**, and the **European Bioinformatics Institute** under a contract from the Wellcome Trust and eight other UK-based research funders.

A jury decided that **Stratagene** should pay **Invitrogen** nearly \$8 million in damages for infringing its patents. The jury determined that Invitrogen's patent involving a process for developing competent cell products is valid and that Stratagene infringed that patent by making and selling its competent *E. coli* cell products. The judge has yet to make a final judgment, and Stratagene may appeal the verdict.

The **US Department of Energy** will spend \$250 million in the next few years to help create two bioenergy research centers that will use systems biology and other methods to accelerate research on cellulosic ethanol and other biofuels. Universities, national labs, nonprofit organizations, and private firms are expected to compete for the funding.

Shanghai Genomics and **Centocor** have set up a drug discovery collaboration, initially for a period of a year and a half, to investigate inflammatory signaling pathways.

PROTEOMICS

ORGANIZING ORGANELLES: MANN TACKLES PROTEIN PROFILING

Cell biologists view the terrain of organelles using dyes and microscopy, while biochemists try to unlock functional clues by smashing up organelle compartments via density gradient centrifugation. Proteomic scientists have further refined the recipe: take organelle-enriched fractions, then sequence peptides with mass spec. It's been a successful tactic — databases are brimming with cytoplasmic and nuclear organelle data — but it's not perfect.

"The trouble is that mass spectrometry is very sensitive. Even if your fraction is 99 percent pure, that remaining one percent will give you 200 proteins that have nothing to do with the organelle," says **Matthias Mann** of the Max-Planck Institute for Biochemistry.

Incorrectly assigning contaminating proteins picked up by mass spec is a significant worry when generating proteome-wide catalogs.

Mann and his colleagues decided to take on this problem with a technique they pioneered a few years ago when studying human centrosomes. In that study, Mann's team used mass spec data from centrosomal marker proteins to define a consensus profile through a density centrifugation gradient — a technique they termed protein correlation profiling.

What worked for centrosomes seems to work for the entire cell. Using PCP with mouse liver cell extracts, Mann's latest investigation builds on the centrosome study by looking at mass spec data obtained from gradient-fractionated cells and compared with proteins known to localize to specific organelles. The result? A complete map of 1,404 proteins localized to 10 different cellular compartments.

Several proteins found by PCP appeared to home in on more than one compartment, so the MPI investigators opened up their



Matthias Mann at the Max-Planck Institute

cell biology toolkit to take a closer look. Using confocal microscopy and immunofluorescence to visualize overlapping PCPs, the researchers were able to distinguish subtle differences in localization patterns.

Mann readily acknowledges that highly specialized tools are needed to do protein correlation profiling. He says that high-resolution mass spec is integral to a study of this scope, considering the immense number of peptides to keep track of. Analysis time was also significant: it took a year of PC time to analyze the data generated from a single mouse liver cell, he says.

Yet the real strength in Mann's method lies in the promise of integrating quantitative proteomics with classical biochemistry techniques and imaging tools. Applying this methodological über-mix to study the temporal aspects of organellar proteomics is next on Mann's agenda. Let's just hope the computers in Martinsreid can handle it.

— Jennifer Crebs