Suggested Projects

Mysteries of Yeast metabolism

Almost nothing is known about yeast proteins YMR278W and YMR027W. A researcher at the University of Toronto has preliminary evidence that YMR278W breaks down ribose-1-phosphate and YMR027W breaks down fructose-1-phosphate. She says "We don't know what ribose-1-phosphate and fructose-1-phosphate are doing in metabolism! More information about the evolutionary history and conservation of these proteins could shed some light on the matter." Identifying potential homologs in mammals would help guide the next phase of this research.

TIGAR (TP53-induced glycolysis and apoptosis regulator)

The TIGAR protein in human is thought to modulate apoptosis induction by p53, a protein that protects cells from uncontrolled growth associated with cancer. It is also reported to act as an FBPase (fructose 2,6-bisphosphatase), an enzyme involved in regulating glycolysis allosterically. However, recent laboratory experiments with modern methods of mass spectrometry have failed to substantiate FBPase activity. So what is TIGAR's role in the cell and how does it unite metabolism and apoptosis? Can a phylogenetic analysis identify a clear homolog in yeast (either *S. pombe* or *S. cerevisiae*) would be more experimentally tractable than working with TIGAR in mammalian systems.

GPP130, a golgi protein with a putative role in toxin susceptibility.

Dr. Linstedt would like to learn as much as possible about the evolutionary history of GPP130, a glycoprotein involved in Golgi trafficking. Researchers in the Linstedt lab recently hypothesized that GPP130 is the host cell receptor for Shiga toxin; a report on this work is currently under review at Science. Humans and other primate species are extremely susceptible to Shiga toxin. Sheep and cattle are not. A phylogenetic analysis could relate the history of GPP130 to the species susceptibility to the toxin. Expression of a glycolipid (Gb3) is also required for Shiga susceptibility. An expanded project, involving a larger team, would be to build trees for GPP130, Gb3, and, possibly, Gb3 synthase for a comparative analysis.

Yeast orthologs – or maybe they aren't orthologs?

In 2003, Rokas et al published an analysis of phylogenetic trees from 106 orthologous gene families in Nature (see abstract below). This study was touted as a break-through in genome scale phylogenetic analysis. However, the spatial arrangement of these genes suggests that a

number of the families (e.g., YBL091C, YDL031W) include paralogous genes as well. Obtaining accurate yeast phylogenies is challenging. These species arose through several rapid speciation events in succession, providing little time between divergences for mutations to accrue. As a result, the phylogenetic signal is weak. Can new phylogenetic methods reconstruct a branching pattern that is consistent with the spatial evidence?

Biomineralization proteins in sea urchin

Proteins in the C-type lectin domain superfamily have been co-opted to perform a surprising array of specialized functions: snake toxin and anti-toxins, fish antifreeze and eggshell development in birds. Dr. Ettensohn has discovered novel lectin proteins with involved in biomineralization in sea urchin. Phylogenetic analsyis could reveal how this specialized adaptation was acquired and whether it is related to lectins involved in biominrealization in birds.

Aging in Drosophila

Dr. Lopez is interested in a phylogenetic analysis of the mitochondrial F1 ATPase epsilon subunit (the eukaryotic epsilon, not the prokaryotic). In *Drosophila melanogaster* there are at least three (two are products of one gene by alternative splicing, the third is a product of a separate gene). Interestingly, he has found that they have different tissue expression and age-dependent expression. He has observed two functions: as a structural coupling factor in oxidative phosphorylation and as a ligand for the lifespan-determining GPCR methuselah. How these functions map to the specific proteins is unknown.

Horizontal gene transfer in pathogenic bacteria

Horizontal gene transfer is a fundamental process in bacterial genome evolution. In the context of infections it can provide pathogenic bacteria with ready access to crucial resistance determinants or virulence factors. High-throughput, short read sequencing technologies offer an unprecedented opportunity to study these processes: it is now possible to obtain whole genome sequence for many strains within the same bacterial species and even within the same colony, biofilm or host. This project offers two challenges: inferring accurate trees from very similar DNA sequences and then using those trees to infer horizontal transfers within a population of *Streptococcus pneumoniae*.