represented in the regions upstream to the genes with similar expression profiles as compared to all other upstreams. We rated the patterns based on their overrepresentation. Among the highest rating patterns most have matches to substrings in known yeast transcription factor binding sites. Moreover, several of them are known to be relevant for the expression of the genes from the respective clusters. Experiments on simulated data show that the majority of the discovered patterns are not expected to occur by chance. The information from the expression profiles allowed to discover patterns (such as transcription factor binding sites) that are likely to play a role in transcription regulation by an in silico experiment, completely formally and automatically with very little human intervention.

Vinson, Charles

A-ZIPs: potent dominant negatives that abolish the DNA binding of B-ZIP transcription factors in a leucine zipper-dependent manner

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We have developed potent dominant negatives (DNs), termed A-ZIPs, that abolish the DNA binding of B-ZIP transcription factors in a leucine zipper-dependent manner. These DNs (including those that interact with CREB, CEBP, AP1, ATF2 and TFE) are ideal reagents for exploring the transcriptional targets of B-ZIPs involved in, among other things, chemotheraputic resistance of human cancer cells. To identify B-ZIP gene targets, we are expressing dominant negatives using E1-deleted adenovirus that infect 100% of the cells in culture. Using DNA microarray chips, we have started to identify transcriptional targets in A549 human lung cells infected with the DNs at a multiplicity of infection (MOI) of 10. Under these conditions, cisplatin sensitivity is increased threefold due to the interaction of A-FOS. We have additional data on three pairs of samples: E1-deleted virus versus uninfected cells; A-CEBP–infected cells versus empty virus-infected cells; and A-CREB–infected cells versus empty virus-infected cells. We used two probes: Cy5 labelled dominant negative-infected cells, and Cy3 labelled empty adenoviral-infected cells. Differences in hybridization intensity of the two probes to the microarray reveal the activity of the dominant negatives. We used a microarray chip containing 1,342 genes on a polylysine-coated glass slide. Empty virus infection after one day caused 1.5% of the genes to be misregulated, of which approximately half were overexpressed. A-CEBP or A-CREB, when compared with empty virus infection, changed the expression patterns of about 3% of the genes at least threefold with 25% of these genes being upregulated. We plan on presenting data showing changes in gene expression resulting from addition of cisplatin. Identifying A-ZIP alterations of gene expression of cisplatin-treated cells will suggest potential transcriptional targets of the B-ZIP family in cancer-resistant cells.

Wallace, Don M.

Identification of helicobacter pylori epithelial cell response genes by screening high-density cDNA arrays

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Helicobacter pylori is a Gram-negative spiral shaped bacterium that can colonize the mucous layer of human gastric epithelium. The organism, one of the most common chronic bacterial infections of humans, is associated with chronic active gastritis and is implicated in peptic ulceration and gastric cancer. Disease outcome depends on many factors, including bacterial genotype and host physiology, genotype and dietary habits. Relatively little is known about the response of the human host to *H. pylori* infection. The aim of our study was to identify changes in gene expression in human gastric epithelial cells *in-vitro* upon infection with *H. pylori* using high-density cDNA array hybridization.

KATO III gastric epithelial cells were cultured with *H. pylori* or no bacterium as control. mRNA, isolated at 0 minutes, 45 minutes, 3 hours and 24 hours post-infection, was used as a template for the synthesis of radioactively labelled 1st strand cDNA for hybridization to high-density gridded arrays of PCR-amplified cDNA clone inserts immobilized on nylon membranes. The arrays included a non-redundant version of the human IMAGE Consortium cDNA array (46,302 clones), a redundant spleen cDNA library (12,288 clones), a custom "inflammatory gene set" and Clontech Atlas grids. Hybridization signals were captured by phosphorimaging and image analysis performed using a GW proprietary PC-based software (DGENT). Differentially expressed sequences were confirmed by a second hybridization.

Analysis of the hybridized cDNA arrays identified many genes to be differentially expressed. Sequence analysis revealed more than 200 genes of known function and 60 novel genes/ESTs being differentially expressed. This included sequences encoding growth factors/receptors, cytokines/receptors, apoptosis proteins, oncoproteins and transcription factors. Subsequent RT-PCR of human gastric biopsy samples showed that several of these genes are also differentially expressed *in vivo* (for example p23/histamine releasing factor, amphiregulin and a novel gene hprg1).

The identification of a large number of *H. pylori* host response genes by cDNA array hybridization demonstrates the usefulness of this technology. Also, the cell culture *in vitro* model has shown correlations with human *in vivo* infection. Further *in vivo* gene expression studies and characterization of the genes/pathways involved will improve our understanding of the host response to infection and may aid vaccine development for this important pathogen.

Waring, Jeffrey

Gene induction/repression response profiling of hepatotoxic agents using cDNA microarrays

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DNA microarray technology is a powerful technique that allows for the simultaneous expression analysis of thousands of genes. In the field of toxicology, microarray analysis can be used to identify individual genes or families of genes