(GPX3) peaked by day 1 then declined gradually. Expression of genes coding for key transport proteins (TF, ALB, IGFBP3) or with roles in immune (CD59, CD5L, CCL5) and oxidative stress responses (MSRA, AOX1, ACAD8, CAT) was lowest on day 1 then increased by day 14 to 28. Genes with peak expression on day 14 included some of lipid (ACOX1, SLC27A2, SC4MOL, ACAT2) and carbohydrate (PDK4, DLD, SUCLG2) metabolism, stress responses (SOD1, SEPP1), and apoptosis (CASP6). Results, discovered with a highly replicated design involving 68 microarrays, demonstrate genomic plasticity of bovine liver in response to physiological state. Supported by award 2001-35206-10946, NRI Competitive Grants Program/CSREES/USDA.

822.5

Arsenic-induced changes of gene expression in lung cells

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Arsenic induces cell transformation and tumor formation. However, the molecular mechanisms of how arsenic causes cancer are still unclear. We hypothesized that arsenic alters gene expressions and leads to carcinogenesis. In this study, we examined global gene expression of lung epithelial L2 cells treated with arsenic using an in-house made10K rat DNA microarray. The cells were treated for 1 h with 7.5 μM sodium arsenite (acute exposure) or for 1, 3, 5 and 7 days with 0.75 μM sodium arsenite (subacute exposure). A loop design was used for subacute exposure and a link was added to compare acute and subacute exposures. By K-mean cluster analysis, we identified 10 gene clusters. 4 clusters showed changes during the early phase of subacute exposure, but not in acute exposure and the late phase of subacute exposure. Two clusters changed only at the late phase of subacute exposure. Two clusters had opposite changes between acute and subacute exposure. One cluster was acute exposure-specific while another cluster showed a similar change between acute and subacute exposures. These results suggest that acute and subacute arsenic exposure cause changes in gene expression of lung cells, occurring at the different phases (supported by SWCOEH, NIH HL-52146, HL-071628, AHA 0255992Z, 0315260Z, 0255992Z, OCAST).

822.6

Microarray analysis of gene expression in diabetic versus normal rat bladder

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Patients with diabetes mellitus develop a spectrum of urogenital problems. We have used micro-array gene chip analysis to analyze global changes in gene expression of the bladder that occur in an animal model of diabetes (streptozotocin-induced diabetes in rats). We looked at changes in gene expression in the bladder of male and female animals occurring after one week or 2 months after onset of diabetes. For each time point and gender approximately 2% of the genes out of 8800 genes on the chip had significantly altered expression. The analysis indicates that although there are gender specific genes that are up- or down-regulated, though there is considerable overlap between genders. For example, calgranulins, annexin 1, and lectin galactose binding protein are upregulated in diabetic bladders from both male and female rats, at all time points. Previous reports have shown that these genes play roles in the pathology of diabetes, though there have been no studies prior to these looking at the changes occurring in bladder. There are also genes whose expression is changed over the time course of diabetes. For example, two proteins (high mobility group box 2 and topoisomerase II) involved in transcriptional regulation and cell division are detected at elevated levels in both male and female animals at the one week time point, but not 2 month. Overall our studies highlight that the onset of diabetes is accompanied by marked changes in the transcriptional status of bladder tissue.

822.7

Proteomic pattern analysis using a neural network application

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To determine if exposure to diesel exhaust fumes causes a change in the serum proteomic patterns, serum samples were collected from 80 subjects (46 controls, 34 exposed). Serum proteomic profiles were performed on the Ciphergen Protein Chip® System using WCX2 chips. Proteomic patterns were analyzed by neural network techniques (classification and clustering algorithms) using "Predict" software obtained from Neuralware Inc. The Backpropagation algorithm was used as the classification algorithm and Self-Organizing Maps (SOM) was used as the clustering algorithm. Two methods were used for the identification of the most discriminating peaks. The first method used manual analysis of raw data using Euclidean distance as the criterion and the second method used a p-value statistic obtained from the Ciphergen software. The classification and clustering algorithms were applied to the two data sets. These procedures yielded a sensitivity of 82.5% and specificity of 81% using the peaks selected by the manual data analysis and a sensitivity of 90% and specificity of 92% using the peaks selected by the p-value analysis. These data indicate that a given serum profile pattern can be assigned to diesel exposure group at about 90% confidence limits using a neural network application. (Supported in part by U.S. Army Medical Research Institute of Chemical Diseases).

822.8

Identifying protein markers for resistance to cold storage injury using functional proteomics in hibernators

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Cold storage of livers for 72h followed by warm reperfusion ex vivo causes significant damage in rats and summer (S) ground squirrels but has minimal effects in hibernating (H) squirrels. To identify protein markers associated with cold ischemia/reperfusion (I/R) damage or protection, we harvested livers from rats, S and H squirrels for proteomic analysis. Proteins were extracted then fractionated by 2D gel electrophoresis; those exhibiting quantitative differences were identified using LC-MS/MS and Sequest. No significant changes were detected in the total liver proteome after 72h cold I/R, therefore enriched cell populations (endothelial, Kupffer, hepatocytes) have been isolated to facilitate detection and identification of protein differences. The liver proteome was detectably altered in H vs. S livers, regardless of activity state or storage time. Differences were significant for the antioxidants glutathione-S-transferase and peroxiredoxin 6; lactate dehydrogenase A; and two ER proteins associated with stress responses. Proteomic screens of serum revealed higher expression of peroxiredoxin 2 and apolipoprotein A-1 in H vs. S. This functional proteomic approach to liver I/R injury using hibernation as a model for cold ischemic tolerance should provide new insights into naturally-induced defense mechanisms that increase organ tolerance to stress. Supported by DARPA contract DAAD190110455.

GENE TRANSFER AND THERAPY (823.1-823.8)

823.1

Intracoronary adenylyl cyclase type VI gene transfer increases contractile function in pacing-induced heart failure

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We tested the hypothesis that intracoronary delivery of an adenovirus encoding adenylyl cyclase Type VI (Ad.AC_{VI}) would be associated with increased LV function in pigs with congestive heart failure (CHF). Pigs