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**CARDIOPULMONARY BYPASS INDUCES DIFFERENTIAL GENE EXPRESSION IN THE KIDNEY**

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**Introduction:** Acute renal dysfunction is common after cardiac surgery and is associated with increased morbidity and mortality. The lack of any effective strategy against this complication is partly due to incomplete understanding of renal disease pathophysiology and limited therapeutic options to prevent disease progression. To begin dissecting the molecular mechanisms underlying this process, we utilized cDNA microarrays to identify cardiopulmonary bypass (CPB) induced renal gene expression profiles. Using an established animal model, we tested the hypothesis that exposure to CPB induces differential expression of genes in the kidney.

**Methods:** We performed two sham (control) and two cardiopulmonary bypass rat experiments using an established model (Figure). (1) Fasted rats were randomized to 60 minutes of normothermic non-pulsatile cardiopulmonary bypass using a roller pump and a membrane oxygenator, or to serve as sham-operated controls after undergoing the same surgical preparation. Whole kidneys were snap-frozen in liquid nitrogen and stored at -70°C until further use. Kidney tissue was processed and microarray experiments were performed and analyzed using an established protocol. We used Atlas™ Clontech nylon expression microarrays (Rat 1.2 and 1.2 II) to assess the expression of 2,352 genes. Genes with more than a two-fold change in normalized intensities between the CPB and sham-controls were considered differentially expressed. (2)

**Results:** We observed a distinct pattern of CPB-induced gene expression in the rat kidney. There were 33 genes that were differentially expressed between CPB and sham animals. These genes were clustered into six functional groups: cytokines, intracellular calcium regulation, transcription factors, signal transduction, mitochondrial transport and metabolic function. Findings are summarized in the Table.

**Discussion:** We confirmed the hypothesis that CPB induces differential expression of genes in the kidney. This study represents the first report on the use of microarray technology to elucidate differential renal transcriptional profiles in response to CPB-induced injury in vivo. Because kidney disease pathophysiology is complex, expression analysis can identify candidate genes and gene networks involved in renal disease pathogenesis, which eventually could become targets for therapeutic intervention.

**References**

1. Mackensen GB, et al. Anesthesiology. Dec 2001;95(6):1485-1491
2. Meltzer PS. In: Bioinformatics: A Practical Guide to the Analysis of Genes and Proteins. 2nd ed. New York: Wiley-Interscience; 2001:393-412

**Table:** Differentially expressed rat renal genes after cardiopulmonary bypass. Downregulated genes indicated by italics and (♭). Upregulated genes are underlined and indicated by (♯). Fold-changes in parentheses. ND= below the threshold of detection in either sham (♭) or bypass (♯) animals.

Transcription Factors	Calcium Regulatory Genes	Signal Transduction
<i>RB a-chain</i> ♭ (2.3) <i>e-myc</i> ♭ (ND) <i>NF-E2</i> ♭ (ND) <i>CTD BP AS</i> ♭ (ND) <i>NM23/NDK-B</i> ♭ (2.2) <i>Neural zinc transcription factor 1</i> ♭ (ND) <i>RNA Polymerase I</i> ♭ (ND) <i>Mef2D</i> ♭ (ND)	<i>Phosphatase 2A</i> ♭ (5.5) <i>CaBP 2</i> ♭ (2.6) <i>Annexin I</i> ♭ (3.1) <i>Phosphatase 2C, Mg<sup>++</sup>/Ca<sup>++</sup></i> ♯ (ND)	<i>Rab 6</i> (6.0) <i>Rab 12</i> ♭ (2.2) <i>Ras-related Rab1 A</i> ♭ (2.0) <i>STAT3</i> ♭ (2.0) <u><i>Transient receptor potential channel 1b</i></u> ♯ (3.9) <u><i>Ost oncogene</i></u> ♯ (4.5) <u><i>Potassium channel 2 (ELK2)</i></u> ♯ (2.4)
Mitochondrial/Electron Transport	Metabolic Enzymes	Cytokines
<i>Cytochrome P450 4F3</i> ♭ (ND) <i>ATP synthase lipid binding protein PL</i> ♯ (2.4) <i>Cytochrome c oxidase VIIa</i> ♯ (2.0) <i>Cytochrome B5</i> ♯ (2.1) <i>ATP synthase D</i> ♯ (2.1)	<i>Cathepsin D</i> ♭ (ND) <i>Aryl sulfatase B</i> ♭ (12.0) <i>Ornithine decarboxylase</i> ♭ (2.0) <i>Lysophospholipase</i> ♯ (2.5) <u><i>Renal Na<sup>+</sup> dependent phosphate transporter</i></u> ♯ (2.3) <u><i>Hydroxysteroid 17b dehydrogenase</i></u> ♯ (2.0)	<i>IL-6</i> (3.6) <i>Interferon Regulatory Factor β</i> ♭ (8.0) <i>Insulin-like growth factor</i> ♯ (3.0)