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# *The arsenic in mice as experimental model for risk modifiers.*

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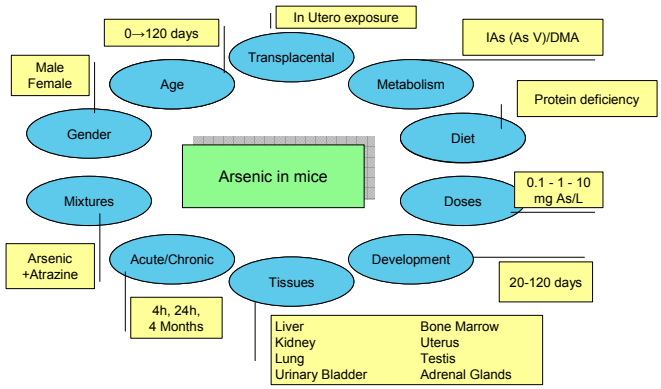
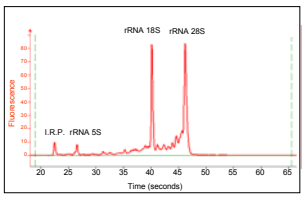
## Arsenic Model

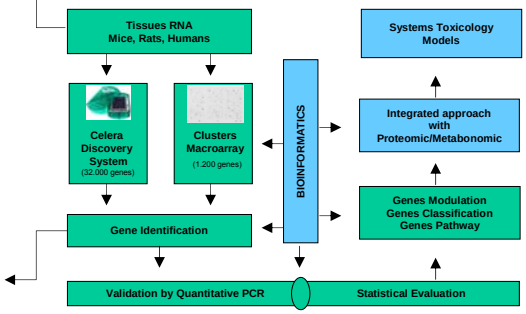



## Experimental Design

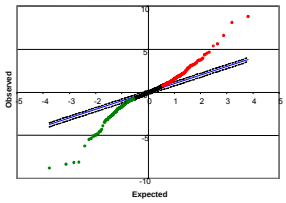
- Exposure:
  - From "in utero" to adult age (up to 4 months)
  - Arsenate/other chemicals in drinking water
  - Doses: 0.1 - 1 - 10 mg As/L
  - Diet: variable proteins content
- Tissues
  - RNA extraction and characterization
- Hybridization
  - Macroarray: Mouse Cancer 1.2 and Toxicology 1.2 clusters (Atlas™, Clontech, U.S.A) using [$^{33}$P]-αdATP (1.185 genes)
  - Microarray: Mouse Applied Biosystems Expression Array System using a chemiluminescence chemistry (32.000 genes).
- Quantitative Real-Time PCR
  - TaqMan Gene Expression Assays (Applied Biosystems) for validating microarray results.
- Data analyses

**RNA Agilent Electropherogram**

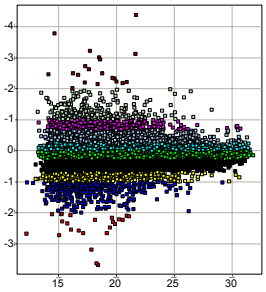



**SAM Plot**



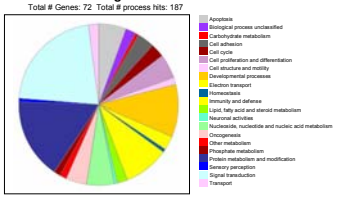

**Differential Expression on 32.000 genes**
**Fold Change vs Signal**



•Flags < 5000 in all arrays
•S/N > 3 in both arrays

**16452 detectable probes**


**PANTHER Biological Process**
Total # Genes: 72 Total # process hits: 187



| | |
|---|---|
| Metabolism | IAs/DMA: specific tissues response for chemical species (i.g. gene modulation in lungs by DMA) |
| Diet | The modulation of gene expression in different tissues was not only depending on the exposure to arsenate but mainly regulated by the level of proteins in the diet. |
| Doses | Apparently low doses are more efficient than higher doses in modulating gene expression in tissues of mice chronically exposed to arsenate. |
| Tissues | Only few genes commonly modulated in different tissues. |
| Acute/Chronic | 4-24 hours/4 months: in the liver, at 4 months only up modulated genes, few in common with 24 hours. |
| Mixtures | The co-exposure to atrazine and arsenate significantly modulates the transcriptional activation of genes in bone marrow cells differently than arsenate or atrazine administered alone. |
| Gender | The molecular mechanisms triggered by arsenic in tissues are totally different in males and females. |

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