EVOLUTION OF GENE REGULATION IN MAMMALIAN TISSUES

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INTRODUCTION

Variation in genotype does not play a solitary role in the diversity of mammals; instead, it has been hypothesized that differences in gene expression contribute significantly to the diversity of life [1]. Differentially expressed genes can explain the divergence in an organism’s phenotype. Meanwhile, conserved expression profiles among various species may indicate that the precise expression level of a certain gene or module is under purifying selection [2,3], thus indicating the evolutionary importance of these gene regulatory networks.

At present, over 30 mammalian genomes are available, many of them recently sequenced. In order to gain further insight into variation of gene expression throughout evolution, we have chosen to use microarray technology. Microarrays are the method of choice in most large-scale whole-transcriptome studies because they allow analysis of an entire genome in a single experiment through use of high density oligo-nucleotide based arrays.

Currently, a large scale comparative gene expression study is in progress to evaluate conserved and diverged gene regulatory systems within twelve vertebrates: ten eutherian mammals, one marsupial (the opossum) and one non-mammalian vertebrate (the chicken). Numerous tissues are being investigated in order to gain a fuller understanding of evolutionary patterns of gene expression.

My goal is to compare gene expression between human and mouse in eight tissues: spleen, heart, brain, kidney, liver, testes, ovary and thymus.

METHODS

Gene correlation analysis shows conserved expression between human and mouse

Corresponding tissues between species are clustered together, with the exception of spleen and thymus, and cerebellum and brain.

• Many genes exhibit a high correlation in relative expression across all tissues, as is indicated in the general shift to the right compared to the randomized correlation.

• Greater similarity of expression within a species (colored quadrants, upper right and lower left)

• High correlation between thymus and spleen, especially in mouse (arrows)

• Brain and cerebellum highly correlated to each other, but not to other tissues (blue perimeter)

RESULTS

Clustered Expression Heat Map shows conserved and diverged sets of genes

Corresponding tissues between species are clustered together, with the exception of spleen and thymus, and cerebellum and brain.

**Conserved expression: Genes are down regulated in human and mouse kidneys.

**Conserved expression: Genes are down regulated in mouse cerebellum and down regulated in human cerebellum.

Diverged expression: Genes are up-regulated in mouse cerebellum and down regulated in human cerebellum.

Conclusions

• The gene and tissue correlation analyses demonstrate high conservation of expression between corresponding tissues in human and mouse.

• We have identified sets of genes which exhibit high conservation of expression and have shown that they are enriched in developmental genes, ion transport and other important processes.

• We have discovered gene sets which show a consistent difference in expression between human and mouse in certain tissues. These genes will be followed up on using experimental validation.

• Further profiling in other mammalian species will be performed in order to track down the evolutionary changes in these gene expression patterns.

Geneset analysis reveals differences in expression across species

For each tissue and gene set, we tested for changes in expression between human and mouse. Shown are the gene sets with significant change in expression.

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References