

## Poster L-4

### A Large Scale Gene Expression Analysis of the Mouse Brain



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**Short Abstract:** A first step towards a complete understanding of the nervous system is the knowledge about genes expressed in each sub region of the brain. In this work, using bioinformatics approaches, we searched and analyzed genes specifically or preferentially expressed in 10 sub regions of the mouse brain.

#### Long Abstract:

The mammalian brain contains several regions that have distinct anatomical and functional characteristics. The proper functioning of the nervous system is dependent on each of these sub regions and on their mutual communication. A first step towards a complete understanding of the functions of each brain sub region is to identify and study the genes expressed in each one. In this work, using bioinformatics approaches, we searched and analyzed genes specifically or preferentially expressed in 10 sub regions of the mouse brain. First, for the identification of the brain genes, we used data from Massively Parallel Signature Sequencing (MPSS), an experimental technique that quantitatively measures gene expression and allows the analysis of rare messages in the transcriptome (potentially, MPSS may identify transcripts expressed once in a cell). Using MPSSs libraries, prepared from more than 25 different tissues and 10 different regions of brain (amygdala, nucleus caudate-putamen-accumbens, cerebellum, cortical mantle, hippocampus, hypothalamus, mid brain, olfactory bulb, olfactory tubercle and thalamus, where each region contains one library for male and another for female), we selected MPSSs tags found exclusively or preferentially in brain tissues. This selection is based on a robust statistical simulation that produces a comparison among all MPSSs libraries and all tags from each library. In the data set of brain tags only sequences presenting a p-value < 0.005 inferred from simulation results have been included. Second, using several data sources (all known full length cDNAs, a reliable dataset of ESTs (Expressed Sequences Tags) and the genome sequence from mouse), we developed a protocol to map the set of tags to the transcriptome data and produces a reliable tag to gene assignment. Finally, we explored several characteristics of candidates genes preferentially or specifically expressed in the brain. For example, we analyzed the expression level of all brain genes, the Gene Ontology classification for each one, the genes expression in male and in female brain, details of genes expression in olfactory bulb, the breadth of gene expression (the number of tissue that a gene is expressed) and we analyzed data from in situ hybridization that are publicly available.

Our results shown that ~3000 candidates genes are specifically or preferentially expressed in the brain (brain genes) and other ~2200 candidates genes present a specific or preferential expression in only one of 10 brain regions (brain region genes). The region that contains the greatest number of specific/preferential genes is the cortical mantle (283 genes)

and the region that contains the lowest one is the olfactory tubercle (182 genes). Analyzing the expression of brain genes we found that each one is expressed on average in ~3 distinct regions and that their expression level is around 33 copies by cell. However, for the brain region genes (that present a more restrict expression pattern) the level of expression is lower, ~15 copy by cell. Gene ontology studies show that our set of candidates contains a significant number of transcripts coding for genes to transport and cell surface receptor (GO molecular function) and a significant number of genes originally located at cellular membrane (GO cellular component). A preliminary comparison of gene expression in male and female showed a significantly number of sex-specific genes, 988 for male and 987 for female. About gene expressed in the olfactory bulb, we identified 270 genes specifically or preferentially expressed in this region (olfactory bulb genes), ~3300 genes with a 'restrict' breadth (expressed in the olfactory bulb and at most 10 other tissues), ~2000 genes with a 'wide' breadth (expressed at olfactory bulb and at least other 41 tissues - putative house keeping genes) and ~6800 genes with an 'middle' breadth (expressed at olfactory bulb and at most in 40 other tissues or at least in other 11 tissues). Gene ontology results show that the olfactory bulb contains a significant number of transcripts coding for genes of binding (mainly regulation of transcription) located at nucleus or cytoplasm. Finally, for a restrict set of olfactory bulb genes we confirm the expression by the analysis of in situ hybridization data. Based on these results, we believe that a consistent large scale study of gene expression at specific brain regions may contribute significantly to the understanding of the function of each one of these regions and may contribute to unveil the complexity of the nervous system in mammals.