NEUROTECHNIQUES

The few, the proud, the miRNA

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An miRNA expression atlas identifies few miRNA genes in mammalian genomes.

Although people love to root for the underdog David in a battle against Goliath, it is surprising that some victorious armies have few soldiers. Researchers estimate that there are thousands of microRNAs (miRNAs) that suppress gene expression in mammals. However, Landgraf *et al.* report that humans and rodents have only approximately 400 miRNA genes, with little tissue-specific variation in expression, in a recent article in *Cell*.

miRNAs are 19-24 nucleotide non-coding RNAs that suppress gene expression by mRNA degradation or translational blockade. miRNAs regulate gene expression during development and other physiological processes.

The authors generated a [freely available](#) atlas of mammalian miRNA expression. They cloned approximately 330,000 sequences from 256 small RNA libraries derived from 26 mammalian tissues and cell types. Approximately 65% of small RNA sequences were miRNA, and each library contained approximately 70 mature miRNAs. Many of the miRNA sequences mapped to miRNA gene clusters that generated indistinguishable mature miRNA. In human, mouse and rat, respectively, the authors identified 340, 303 and 205 mature miRNAs encoded by 395, 363 and 231 miRNA genes. With the addition of miRNA genes identified by orthologs in other species, they report a total of 416, 386 and 325 miRNA genes in human, mouse and rat.

Most miRNAs were expressed at low levels in most tissues. For example, the authors found high expression of miR-16 and low expression of miR-21 in every library. Few miRNAs localized to only one tissue, and only a third were enriched in one tissue relative to all others. miR-9, miR-124, miR-128a and miR-128b were enriched in all brain regions and neuronal cell lines relative to other tissues.

Did miRNA expression in the brain differ across regions or species? In tumor cell lines, miR-124 was neuron-specific, and miR-21 was upregulated in glia. In general, miRNA expression in human and rat brain differed. However, hippocampal miRNA expression was similar in human and rat, suggesting that hippocampal miRNA expression is conserved.

Neuronal miRNA expression is regulated by development and differentiation. Differences in miRNA expression in the adult and embryonic striatum and cortex were carried by the mir-29a(4) cluster, which is absent in embryonic tissues but highly expressed in the adult. To model neuronal differentiation, the authors treated cell lines with differentiating agents. Dibutyl cAMP reduced expression of the mir-16 cluster in neuroblastoma cells.

Retinoic acid induced the expression of mir-21, mir-141(2) and mir-37(46) clusters in the human Ntera2 embryonic carcinoma cell line. In contrast, thyroid stimulating hormone increased miR-21 in thyroid cell lines, suggesting that miR-21 may be important in cell differentiation.

Why are there so few miRNAs genes? Perhaps a limited number of miRNAs mediate gene regulation in many tissues and processes, or additional miRNA genes are expressed only in rare cell types underrepresented in the authors' samples. The latter may be a particular problem for neural tissue, which is highly heterogeneous.

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1. Landgraf, P. *et al.* A mammalian microRNA expression atlas based on small RNA library sequencing. *Cell* **129**, 1401–1414 (2007). | [Article](#) | [PubMed](#) |