

Analysis of Differential mRNA and miRNA Expression in an Alzheimer's Disease Mouse Model

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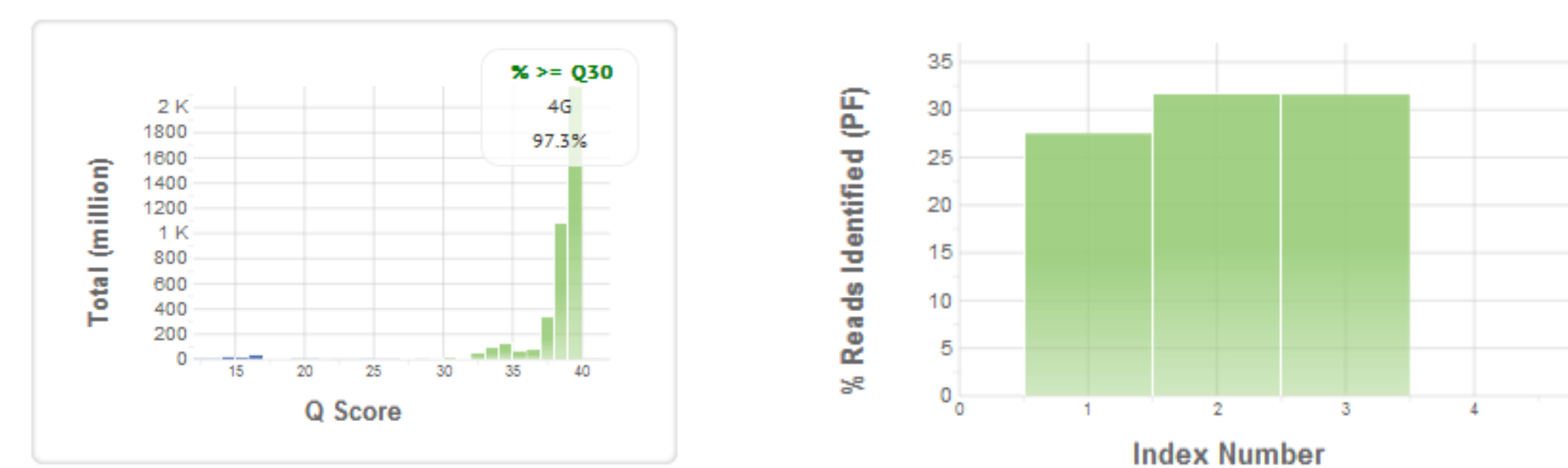


Gene Expression and AD

- The AD brain displays altered gene expression patterns compared to a normal brain
- Other tissues including blood may also exhibit these expression changes
- Research suggests that post-transcriptional regulation by miRNA also plays a role in AD pathology.

Data Analysis

- Sequencing quality was assessed by Qscore ≥ 30 on BaseSpace
- Differential expression was determined using TopHat, CuffLinks, and CuffDiff
- Gene-by-gene confirmations using qPCR



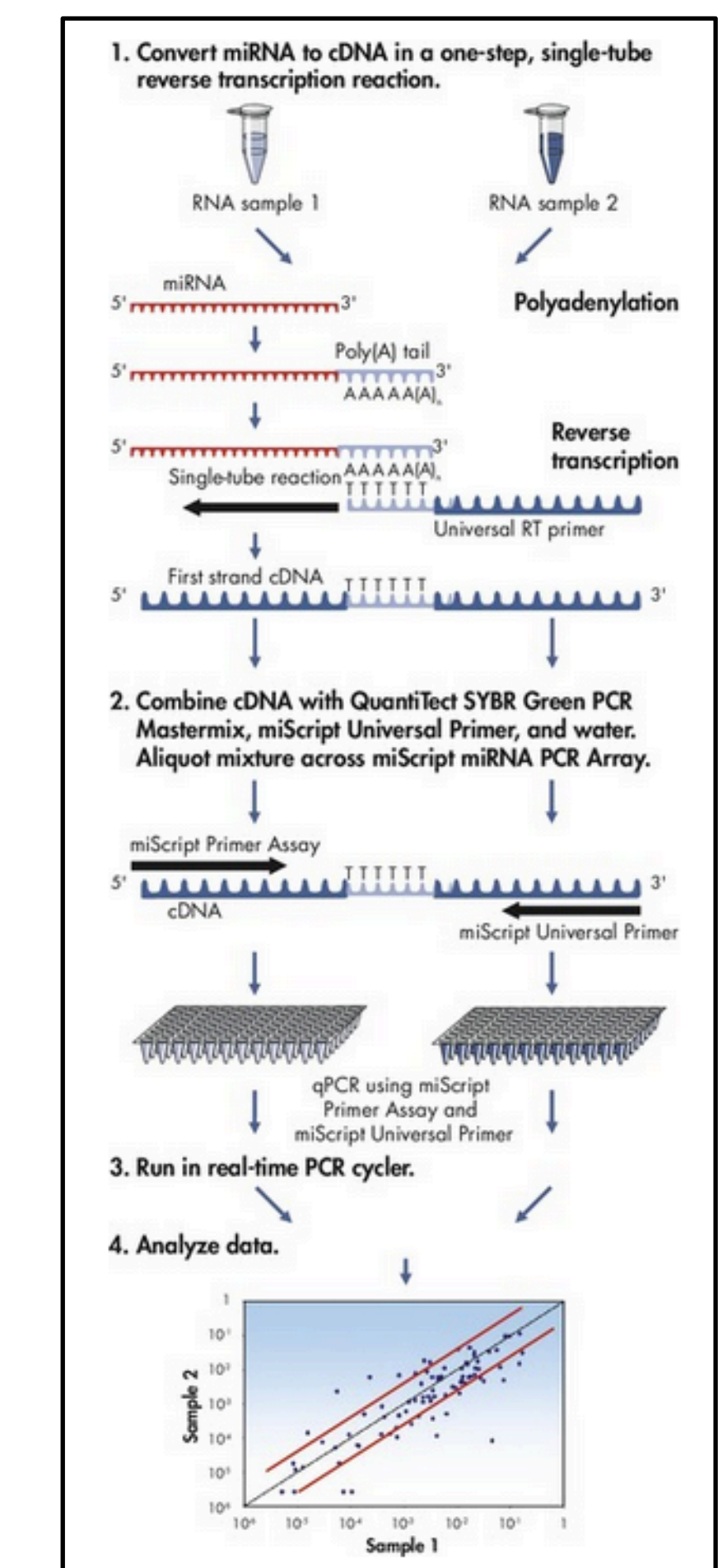
miRNA Expression Analysis

RNA isolated from the hippocampus of AD and control mice

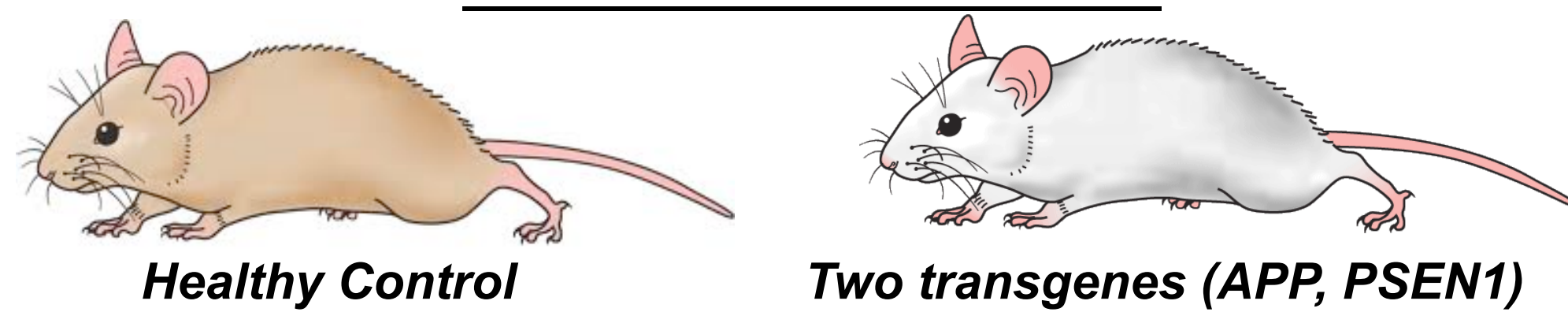
Converted to cDNA using miScript assay (Qiagen) to polyadenylate and add universal tag

miScript assay was used to determine expression of specific miRNA

Differential expression analyzed via differences in fold change



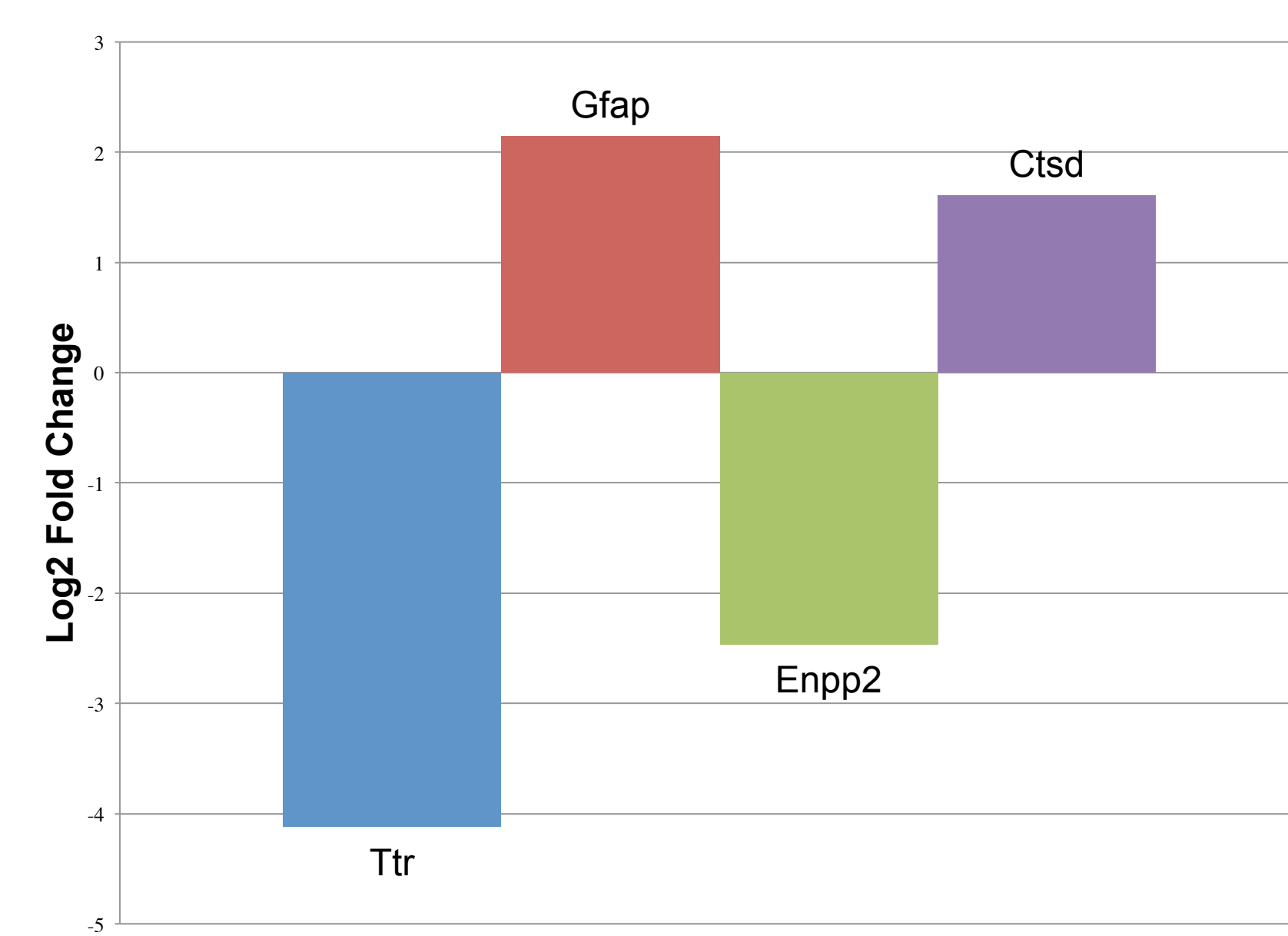
In Vivo AD Model



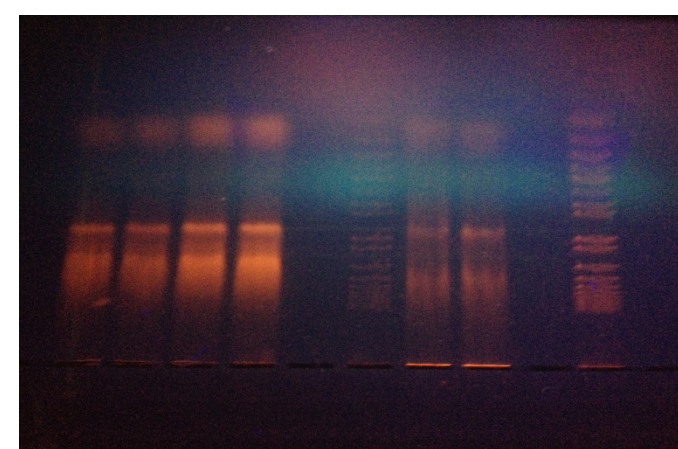
- APP and PSEN1 transgenic mice
- Isolate RNA from mouse brain and blood samples (n=3)
- Determine differential expression levels from mRNA and miRNA

Differential Expression in AD vs. Normal Brain

- 5053 transcripts differentially expressed in the brain
- Known AD-related genes differentially expressed in our model
- Analysis of changing genes not previously linked to AD



RNA Sequencing to Determine Differential Expression



RNA isolated from a laboratory mouse



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RNA was isolated from the hippocampus and blood of AD and control mice.

mRNA was purified and converted to cDNA using an Illumina gene sequencing preparation kit.

Prepared cDNA samples were sequenced using an Illumina MiSeq gene sequencer.

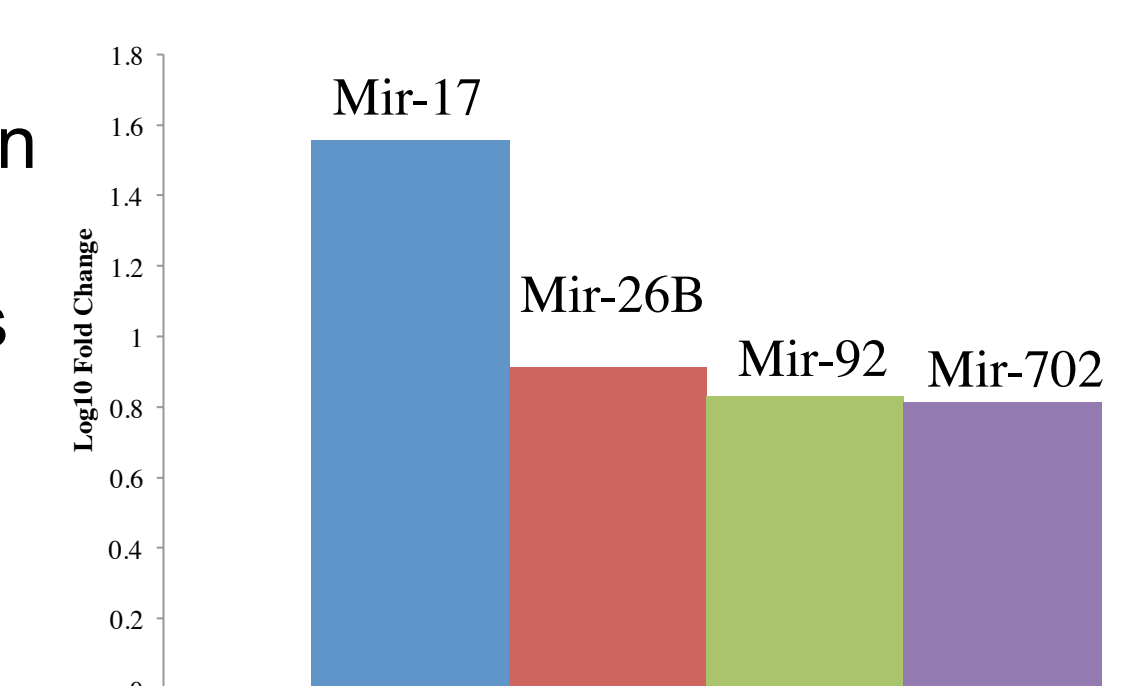
Differential expression was evaluated via the Galaxy data analysis platform.

Significance of miRNA Expression

- Previous research by our group revealed epigenetic modification of genes that code for miRNA.
- Gene products associated with AD are targeted by these miRNA.
- Differences in miRNA expression could shed light on understanding the role of epigenetics in AD pathology.

Preliminary miRNA Data

- Expression changes analyzed in: Mir-17, Mir-26b, Mir-92, Mir-702
- Consistent upregulation of Mir-17 in AD brain
- Genome-wide analysis could prove significant



Application of Expression Data

- Expression patterns in blood will be compared to those in brain
- If changes in brain and blood correspond for an AD model, altered expression in blood could be used as a diagnostic marker for AD
- Expression of miRNA may provide insight into mechanisms of AD development
- Better understanding of AD proves itself valuable in development of AD treatments