AN OPTIMIZED PIPELINE FOR EXTRACTING TRANSCRIPTOMIC DATA FROM THE HUMAN PROTEIN ATLAS: INSIGHTS FROM NORMALIZED MCAD MRNA EXPRESSION ANALYSIS

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Introduction

Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency is an inborn error of metabolism in the beta-oxidation of fatty acids caused by mutations in the ACADM gene. Individuals with MCAD deficiency have a reduced ability to oxidize medium-chain fatty acids, leading to the accumulation of lipids and their derivatives in the blood and biological tissues.

Methods

Expression data for the ACADM gene in both the central nervous system and peripheral tissues were retrieved from The Human Protein Atlas (HPA), with measurements expressed in normalized transcripts per million (nTPM). The independent variables selected for analysis included species, tissue type or specific brain regions, sex, and developmental stage. To ensure reproducibility and efficient data extraction, a custom Python-based pipeline and a R Shiny application were developed.

Objectives

Develop an optimized pipeline and Shiny app to analyze ACADM mRNA expression across tissues and brain regions, advancing understanding and management of MCAD deficiency.

Results

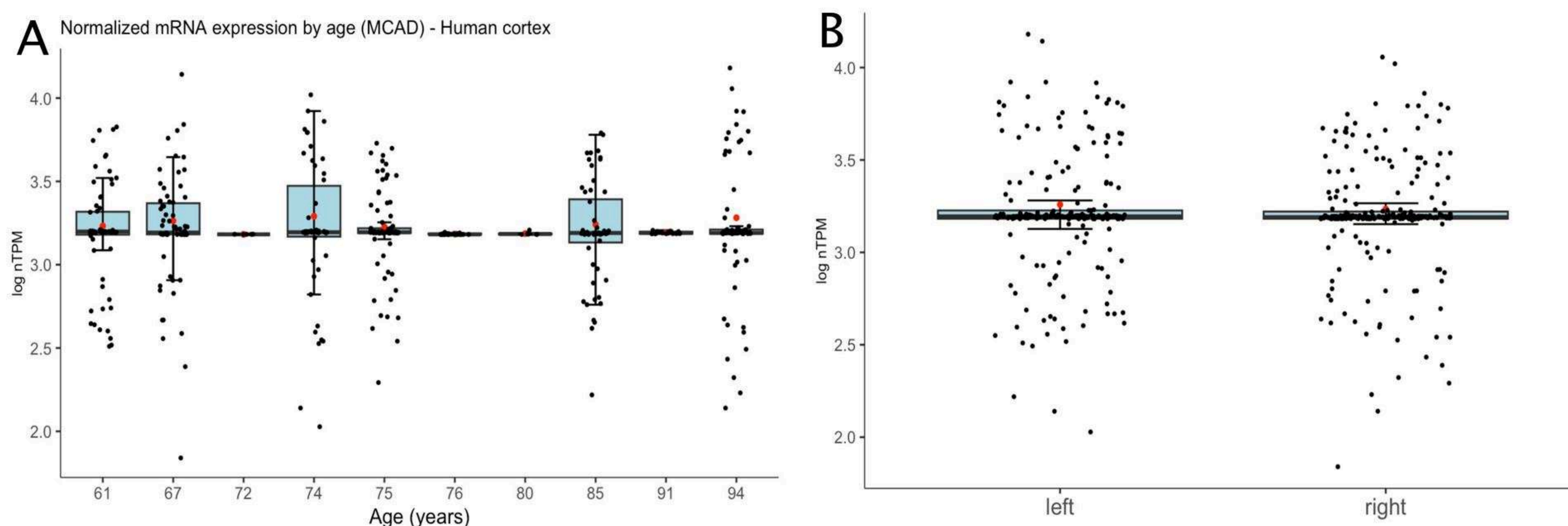### Figure 1. Cortical ACADM mRNA expression by age and hemisphere.

Figure 1 (A): ACADM gene expression in the brain cortex, measured as log nTPM, through several age groups, ranging from 61 to 94 years of age. Boxplots are filled in light blue with a red dot marking the mean log nTPM values.

Figure 1 (B): Overall cortical expression of ACADM by brain hemisphere. Boxplots are filled in light blue with a red dot marking the mean log nTPM values.

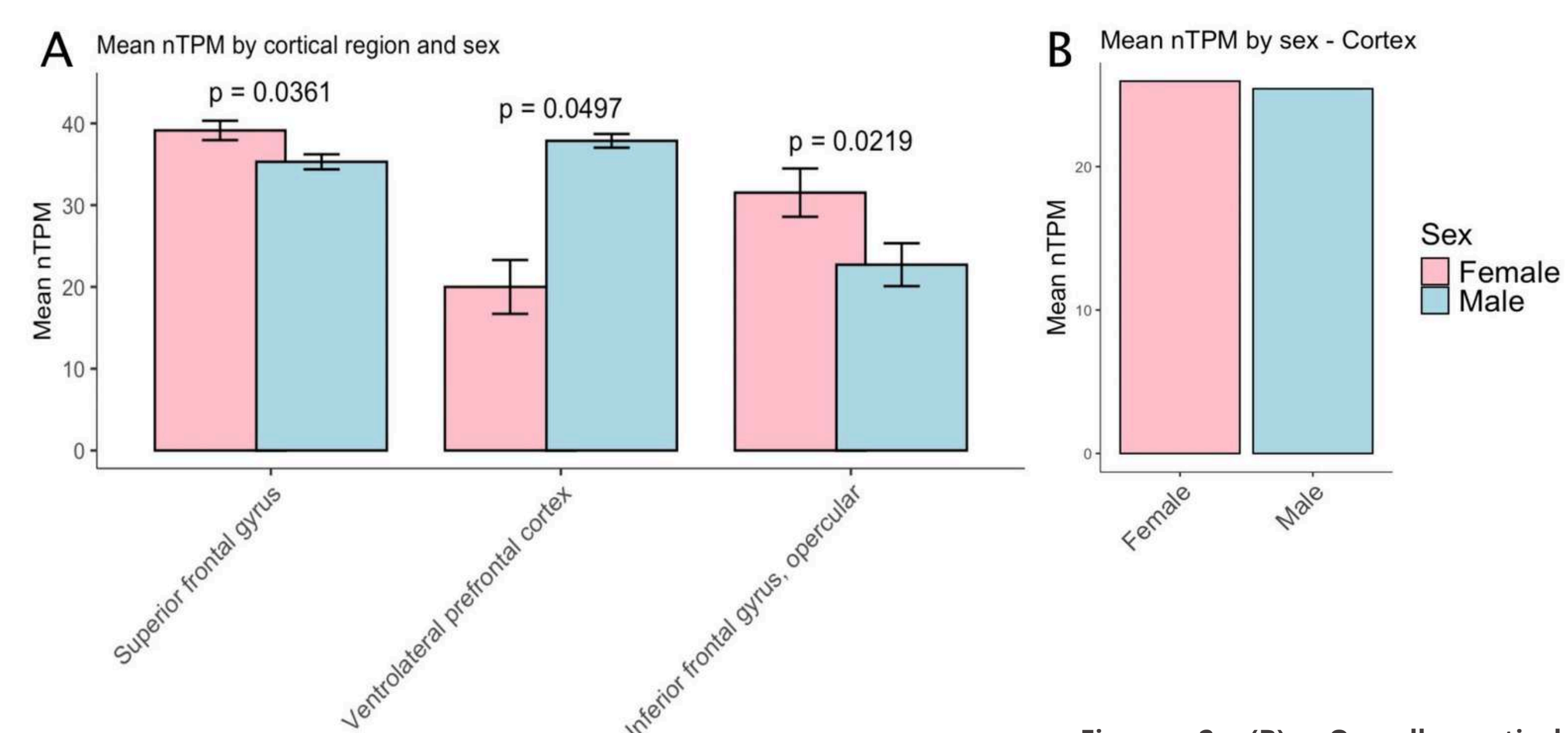### Figure 2: Differential cortical ACADM expression by sex.

Figure 2 (A): Cortical areas with ACADM expression differences between sexes. Data is presented as mean ± standard error.

Figure 2 (B): Overall cortical expression of ACADM by sex. Pink and blue bars indicate female and male samples, respectively.

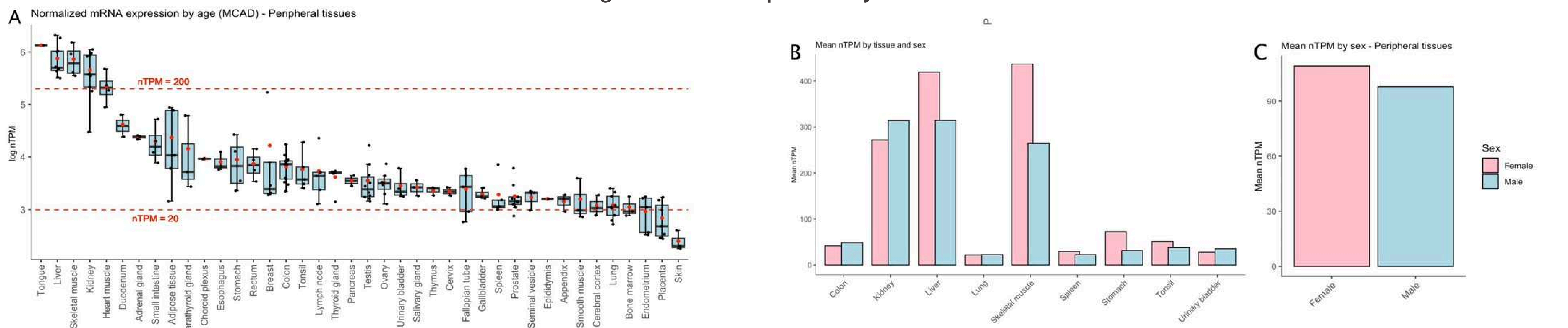### Figure 3. ACADM expression by tissue and sex.

Figure 3 (A): ACADM expression across different peripheral tissues. Boxplots are filled in light blue with a red dot marking the mean log nTPM values.

Figure 3 (B): ACADM expression in tissues where the data was available for both sexes (p> 0.05 for all comparisons).

Figure 3 (C): Overall tissue expression of ACADM by sex. Pink and blue bars indicate female and male samples, respectively.

Conclusion

Our study shows that ACADM expression is stable across age groups and cortical hemispheres. Sex-specific differences were observed, with females showing higher expression in the superior and opercular inferior frontal gyri, and males in the ventrolateral prefrontal cortex. Energy-demanding peripheral tissues exhibited significantly higher ACADM expression levels.

Acknowledgements

References

Pugliese, M. et al., 2020. Outcomes in pediatric studies of medium-chain acyl-coA dehydrogenase (MCAD) deficiency and phenylketonuria (PKU): A review; **Brackett, J. C. et al., 1994.** A novel mutation in medium chain acyl-CoA dehydrogenase causes sudden neonatal death; **Sjöstedt, E. et al., 2020.** An atlas of the protein-coding genes in the human, pig, and mouse brain.