Master Research Proposal

Topic: **Investigating the Role of MicroRNAs and IsomiRs as Biomarkers in Psychiatric Disorders**

Psychiatric disorders like depression and anxiety have a significant genetic component and are becoming more prevalent. To improve early diagnosis and personalized treatment, reliable biomarkers are needed. MicroRNAs (miRNAs) and their variants, isomiRs, are emerging as promising biomarkers for these conditions. These small RNA molecules regulate gene expression offering a valuable non-invasive approach to studying psychiatric disorders.

This thesis aims to investigate miRNAs and isomiRs as potential biomarkers in psychiatric disorders. Using data science and bioinformatics techniques such as data normalization, batch correction, ARACNE for network inference, and statistical analysis of gene regulatory networks, we will analyze differences between affected and unaffected individuals (n=70 per group). The study will examine differential patterns in miRNA and isomiR expression, as well as network differences at both node and structural levels. By exploring how these molecules impact gene regulatory networks, we aim to deepen our understanding of the molecular mechanisms underlying psychiatric disorders.

Research Objectives:

The primary objectives of this thesis are:

- **Analyze** the miRNA and isomiR profiles in blood samples from affected and unaffected individuals.
- **Apply** data normalization and batch correction techniques to ensure the accuracy of miRNA and isomiR data.
- **Implement** ARACNE, an information-theoretic network inference algorithm, to construct gene regulatory networks based on miRNA and isomiR data.
- **Investigate** the impact of miRNAs and isomiRs on gene regulatory networks.
- **Conduct** differential network analysis on the affected and unaffected individuals' networks.

The proposed work consists of the following parts:

Step 1: Calculate isomiR ratios and total counts to quantify the relative abundance of isomiRs and miRNAs in the samples.

Timeline: November 2024

Step 2: Standardize miRNA and isomiR-level data to ensure consistency across samples, considering variations in sequencing depth and other technical factors.

Timeline: December 2024

Step 3: Utilize ARACNE to infer gene regulatory networks, focusing on the relationships between miRNAs, isomiRs, and their mRNA targets. Conduct a statistical analysis of the inferred networks, examining metrics such as the number of edges, nodes, and the distribution of mutual information values.

Timeline: January 2024

Step 4: Filter network edges to remove connections linking features of the same gene, and apply thresholding on mutual information values to refine the network and highlight significant regulatory interactions.

Timeline: February 2025

Step 5: Integrate miRNA and isomiR data with other RNA datasets, such as total RNA, to explore overlapping differentially expressed genes and their potential role in psychiatric disorders.

Timeline: March 2025

Step 6: Thesis writing and final presentation preparation.

Timeline: April 2025

By focusing on these tasks and leveraging existing gene expression data, this research aims to provide insights into the role of miRNAs and isomiRs in psychiatric disorders, potentially identifying novel biomarkers and contributing to the development of more effective diagnostic and treatment strategies.

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References:

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2. Kopf-Beck, J., Zimmermann, P., Egli, S. et al. (2020). "Schema therapy versus cognitive behavioral therapy versus individual supportive therapy for depression in an inpatient and day clinic setting: study protocol of the OPTIMA-RCT." BMC Psychiatry, 20: 506. https://doi.org/10.1186/s12888-020-02880-x
3. Margolin, A.A., Nemenman, I., Basso, K. et al. (2006). "ARACNE: An Algorithm for the Reconstruction of Gene Regulatory Networks in a Mammalian Cellular Context." BMC Bioinformatics, 7(Suppl 1): S7. https://doi.org/10.1186/1471-2105-7-S1-S7