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Thesis, Term 1

Specific Aims Outline: DNA Methylation in AML

1. Introduction
   1. Hook
      1. {placeholder}
   2. Known Information
      1. Prevalence of AML
      2. Known epigenetic causes
      3. Effect on prognosis/treatment based on methylation patterns
   3. Gap in Knowledge
      1. Gene level methylation patterns (variability) on AML oncogenes
      2. Promoter/enhancer differences
   4. Critical Need
      1. Gaining this knowledge may aid in diagnosis/treatment decisions/prognosis predictions
      2. Aids in continuing research on methylation effects in cancer
2. Second Paragraph: The Solution
   1. Long-Term Goal
      1. Gain knowledge on how methylation is affected in AML oncogenes and non-related genes
   2. Proposal Objective
      1. Explore the methylation profiles of AML oncogenes and non-AML related genes using:
         1. Illumiuna 450k methylation array data and normalization methods
         2. Known AML oncogene information
         3. Differential Methylation analysis
         4. Statistical methods for model construction
   3. Rationale
      1. Similar analyses have been done, but have not focused on variability between gene types and effects on promoter/enhancer regions
   4. Hypothesis
      1. As with many cancer processes, we would expect to see a dysregulation from the normal methylation patterns, resulting in increased variability of the methylation in genes related to AML
      2. We expect to find some sort of signal around the variability of methylation in related genes
   5. Pay-off
      1. This information will help guide further research into methylation in AML and other cancers. Potentially, this method could be replicated to analyze for effects in other types of cancers as well.
      2. Understanding the change in variability of methylation will inform further studies into methylation and finding differentially methylated regions
3. Specific Aims
   1. Aim 1:
      1. Acquire, clean, normalize, and annotate data
   2. Aim 2:
      1. Analyze the differential methylation patterns of AML oncogenes and non-AML oncogenes for variability
4. Final Summary Paragraph
   1. Innovation
      1. Method for analyzing the change in methylation variability of known pathways/related genes for AML that can be extrapolated to other cancers/conditions with known epigenetic mechanisms
   2. Expected Outcomes
      1. Greater insight into the methylomic changes for related and non-related genes of AML
   3. Impact/Pay-Off
      1. Continuation of recent research into methylation pattern changes and their relation to disease