Poster Number 2

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DNA Methylation Marks in Nuclear and Mitochondrial DNA

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Background:

Epigenetic mechanisms regulate all biological processes from conception to death, including genome reprogramming during early embryogenesis and gametogenesis, cell differentiation, and maintenance of a committed lineage. DNA methylation is the most extensively studied epigenetic modification with 5-methylcytosine (5-mC) and 5-hydroxymethylcytosine (5-hmC) being key epigenetic players. Interestingly, mitochondrial DNA (mt DNA) is believed to be modified by both 5-mC and 5-hmC, however, the presence and function of such epigenetic modifications are still highly debated. In DNA methylation studies, blood is considered an informative study model as CD4+ and CD8+ T cells were reported to be "most distinctly poised for rapid methylome response to physiological stress and disease". Furthermore, mt DNA cellular content differs across tissue types depending on several factors, but the ratio of mitochondrial DNA relative to the nuclear genome in blood cells is not well studied.

Objective:

To investigate the differentially methylated and hydroxymethylated regions in nuclear and mitochondrial genome of CD4+ and CD8+ T cells

Methods:

Whole blood samples were collected from healthy donors and peripheral blood mononuclear cells (PBMCs) were sorted into CD4+ T and CD8+ T cells for analyses of 5-mC and 5-hmC in total cellular DNA. MethylMiner protocol and hydroxylmethylated DNA immunoprecipitation were used to enrich for methylated and hydroxymethylated DNA fragments.

Results:

The samples are being sequenced and bioinformatic analysis for the nuclear and mitochondrial methylome will be done. The diffReps software will be used to analyze the data (500bp window size) and Negative Binomial test will be applied to obtain the differentially methylated regions.

Conclusion:

Variations in the mitochondrial DNA methylation levels between those blood cells are predicted to be found and it might be influenced by their relative nuclear/mitochondrial DNA ratio. This will hopefully broaden our understanding of the epigenetic events in normal physiological state which will impact the future epigenetic analysis of the disease state.