Epigenetic Effects of Adverse Lifestyle Choices in Males

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Obesity is an epidemic in the US, with 1 in 3 adults and 1 in 5 children being obese. Additionally, obesity is a major risk factor for metabolic disorders. Hispanic communities in particular have a high prevalence of metabolic disorders and obesity associated with low socioeconomic status and low health literacy. While genomic impacts of offspring health are well-established, there is now increasing evidence that epigenetic determinants, such as genomic patterns of DNA methylation or specific histone modifications, also impact offspring health. Research into paternal origins of health and disease has identified epigenetic changes in sperm that propagate effects of a father's lifestyle and environmental exposures to his offspring, potentially predisposing adverse intergenerational health outcomes. However, the mechanisms responsible for the transmission of information from a male's soma to his germ line, and then from his germ line to his offspring, remain unknown. The primary goal of our study is to understand how obesity and lack of exercise impact epigenetic programming and gene expression profiles in both somatic cells and germ cells in young Hispanic men. Nucleic acids were extracted from peripheral blood mononuclear cells (PBMCs) and sperm from obese, inactive (OI; n=46), and lean, active (LA; n=15) Hispanic men aged 18 to 40 years. Genomic DNA was bisulfite converted and processed for detection of DNA methylation at individual CpG sites using the Infinium MethylationEPIC v2.0 BeadChip. The resulting raw data is being analyzed using the R package, Sesame, to identify genome-wide differences in DNA methylation patterns between samples from OI and LA groups. Results will be presented describing the DNA methylation status at individual CpGs in both somatic and germ cells from each group. In addition, gene expression is being assessed in the PBMCs by RNA-seq and analyzed using the DESeq2 analysis package. Using Sesame's built-in regulatory feature enrichment analysis, KnowYourCG, we will determine the association of differentially methylated DNA sites with PBMC gene expression. We will also determine the association of differentially methylated DNA sites in both sperm and PBMCs in OI group with annotated genomic regions including enhancers, promoters, and transcription factor binding sites. Finally, we will use Gene Set Enrichment Analysis (GSEA) to identify gene

pathways that show significant up- or down-regulation of gene expression data in PBMCs from the OI men compared with LA men.