Understanding the Role of CCR2 during Inflammation Associated with Metabolic Syndrome using Next-Generation Sequence Analysis

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Metabolic syndrome (MetS) refers to a group of factors that increase the risk to various health problems; these risk factors include abdominal obesity that is associated with low-grade inflammation that leads to increased recruitment of macrophages to the fat tissue. Previously, it was reported by the lab in which this study was conducted that the knock-out of the chemokine receptor CCR2 in a mouse model of obesity protected against development of MetS. To understand the molecular mechanisms by which CCR2 knock-out leads to protection against MetS, the hypothesis tested was that the obese mice with CCR2 knock-out (CCR2 -/-) show a distinct genetic signature when compared to obese mice. Whole genome transcriptome sequencing (RNA-Seq) was performed by the laboratory on three groups of mice models (Wild Type, Obese, Obese with CCR2 -/-) in both muscle and visceral fat. Tools were implemented by the student researcher in the Bioconductor package in R statistical program to identify significant differentially expressed genes (FDR<0.05) and analyzed relationships between various genes using pathway analysis. There were highly significant differences in gene expression between CCR2 -/- and CCR2 +/+. Most of these differentially expressed genes between the two groups belonged to an inflammatory pathway. However, these differences were evident in visceral fat and not in muscle tissue. TREM signaling pathway was one of the pathways identified in analysis and has potential implications in inflammation. Thus, CCR2 knock-out reversed the disease phenotype from obese to normal as inflammatory signals that contribute to MetS were reduced in visceral fat.

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