Sex-biased Expression of Neuroimmune Guidance Cues in Cardiovascular Diseases

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Abstract:

Atherosclerotic vascular disease continues to be a leader of morbidity and mortality. Although sex hormones are known to play a role in this lipid- and inflammatory-driven disease, the underlying mechanisms are largely unclear. Neuroimmune guidance cues (NGCs) are key regulators of cell movement and positioning, and have emerged as significant players in inflammation. Here, we analyze several gene expression datasets from human atherosclerotic plaques as well as normal, IFNγ-exposed human induced pluripotent stem cell-derived macrophages (IPSDMs), and acetylated LDL-stimulated IPSDMs. From these, we identify the NGCs that are differentially expressed between females and males in disease. In addition, we detect clusters of NGCs that have similar co-expression patterns with other genes. Furthermore, we identify the differences in co-expression patterns of NGCs between females and males (Figure 1). Using WGCNA's module preservation statistics [1], we determine the co-expression modules that are preserved between males and females. Utilizing single-cell RNA-seq data from 46 patients (unpublished), we assess the cell type specific expression of NGCs. Interestingly we observe that the NGCs from co-expression derived clusters are enriched in macrophages. Taken together, we observe sex differences in expression profiles of NGCs in cardiovascular disease, and these findings enhances our understanding of atherosclerosis development.

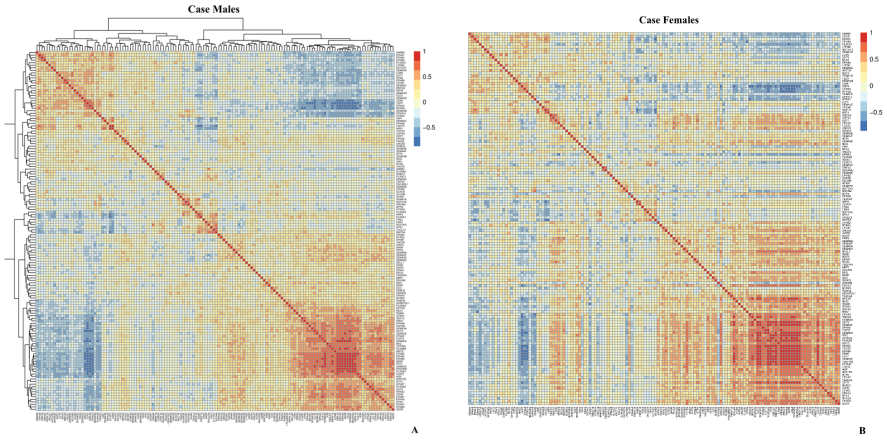

Figure 1: A) Hierarchical clustering of co-expression profiles of NGCs in IFNγ-exposed human induced pluripotent stem cell-derived macrophages (IPSDMs) from 40 male donors, B) same as A except that samples are derived from 44 female donors, gene ordering is the same as A. Data taken from [2].

[1] Langdelfer et al. (2011). Is my network module preserved and reproducible? PLoS Comput Biol. 7(1): e1001057.

[2] Alasoo et al. (2018). Shared genetic effects on chromatin and gene expression indicate a role for enhancer priming in immune response. Nature Genetics. 50. 10.1038/s41588-018-0046-7.