POSTER - SYSTEMS BIOLOGY AND MODELING

STUDY OF CO-EXPRESSED GENES IN MACROPHAGES FROM DIET-INDUCED OBESE MICE.

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Studies have provided insights into the obesity associations with chronic inflammatory responses, due to accumulation of fat in tissues. The white adipose tissue has an extremely important correlation with immune system on the cytokine, chemokine and adipokine secretion, all controlled by gene expression on immune cells like macrophages. We still do not have studies that elucidate which gene networks are co-expressed in immune macrophages on obesity state, that can trigger this inflammatory profile. Therefore,it would be interesting to verify the gene networks co-expressed in macrophages presented in white adipose tissue during obesity to identify possible key genes that play an important and central role in the inflammatory profile of these cells in disease. In this work, we provide an in silico methodology to create a co-expressed gene network and identify macrophage obesity hub genes.

We search for public RNAseq data from white adipose immune cells from obese mice, and we obtained the data from GEO database, deposited in GEO (GSE126407). A co-expression network identifies which genes tend to show a coordinated expression pattern in a group of samples.This co-expression network can be represented as a gene-gene similarity matrix, which can be obtained using the WGCNA, an R package. In the first step, the individual relationships between genes are defined based on correlation measures or

information between each pair of genes.These relationships describe the similarity between the expression patterns of the gene pair in all samples, for data visualization of co-expressed gene network we used Cytoscape. Our results showed that the most prominent module of gene co-expression network based on the gene expression of macrophages associated with obesity, implies a presence of central genes with high connectivity like Fam129b, Tmcc1, Sema4a, Notch2 and Igf2r that shows a high connectivity on the network. After locating the most connected genes, we used a simulated annealing algorithm from an R package called RNetcarto to identify hub connectors in gene modules, with this approach we were able to discover different hub connector genes such as Ctsd, Ctsk and Hist1h1c.

Co-expression methodology applied to RNAseq data results in a very high amount of data and a high number of clustering modules. However, it shows that on the most prominent module associated with obesity are many genes that are likely to act as central control genes on the important immune systems cells, the macrophages in obesity. Thus, new methodologies are being used in order to unravel some key genes that can elucidate the gene activation pathways involved in the inflammation process during obesity.