00465 Network Transcriptomics in Adipose Tissue From Metabolically Abnormal Obese Asians

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Aims: Despite similarities in body mass index (BMI), obese patients differ in their degree of metabolic dysfunction and can be classified as metabolically abnormal obese (MAO) or metabolically healthy obese (MHO). However, the molecular mechanisms of MAO are poorly understood, especially in obese subjects of Asian origin. We carried out network transcriptomics in adipose tissue from MAO and normal weight Chinese subjects to unravel the molecular mechanisms underlying the MAO phenotype.

Methodology: Adipose tissue gene expression from 26 MAO and 12 normal weight subjects was obtained via RNA sequencing. Differentially expressed genes were obtained after adjustments for age, sex and muscle contamination. Differentially expressed genes were analyzed via GeneNet package to construct gene coexpression networks. Network sub-clusters were examined for functional enrichment. Candidate network regulators were identified via the weighted Key Driver Analysis (wKDA) tool.

Result: A total of 461 genes were used for construction of the gene coexpression network. Network clustering via EAGLE identified 5 sub-clusters. Pathway overrepresentation analysis showed the enrichment of the sub-clusters for pathways related to immune and inflammatory response (FDR < 0.2%). Weighted key driver analysis on an adipose tissue functional interaction network identified 13 transcription factors (FDR < 0.05 and Fold enrichment > 5), including RGS16, NFKB1, MS4A6A and FGFL2 as potential regulators of network interactions.

Conclusion: These findings provide insights into transcriptomic changes associated with etabolically abnormal obesity in Asian subjects. Specifically, we have identified biological pathways that are enriched in the network sub-clusters generated from differentially expressed genes. Also, our analysis reveals the existence of key driver genes in the adipose network that are associated with the metabolically abnormal obese phenotype. These findings help generate testable hypothesis on the roles of novel genes in MAO and could pave the path for new therapeutic interventions to improve metabolic health of obese subjects.