STUDYING THE ROLE OF RETINOL TRANSPORTER STRA6L IN REGULATION OF IMMUNE GENE EXPRESSION: RELEVANCE IN DEVELOPMENT OF METABOLIC DISEASE

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Background
Metabolic disease is one of the leading health problems in a modern human society. Functional CD11c+ immune cells, also known as dendritic cells, are required to drive inflammatory changes that disrupt metabolic homeostasis in tissues such as fat. Retinoic acid synthesis by dendritic cells is a critical step in immune cell differentiation during immune response, and is required to maintain the immune program initiated by dendritic cells. Preliminary studies showed that deletion of retinol transporter STRA6L in CD11c+ cells protects mice from obesity induced insulin resistance. This project focuses on studying retinoic acid-dependent immune-gene expression in tissues and immune organs. We will determine which immune response pathways are affected when STRA6L is deleted from CD11c+ cells in order to understand development of pathogenic inflammation in metabolic tissues.

Methods
To study the role of retinol transport in dendritic cells, we used a mouse model with retinol transporter STRA6L deleted using Cre-Lox technology targeting CD11c expressing immune cells. Metabolic and lymphoid tissues were harvested from an aged (15 months old) cohort of KO and littermate WT mice – liver, muscle, mesenteric fat, epididymal fat, and inguinal lymph nodes. RNA was isolated from fresh and frozen tissues, and cDNA was synthesized. RT-PCR was performed using specific target primers on the University Genomics Core equipment. Paraffin embedded liver sections were stained with H&E. Immune cell recruitment foci were analyzed from randomly acquired images.

Results
STRA6L expression was not affected in non-target tissues of KO animals – liver and fat. STRA6L was significantly down-regulated in inguinal lymph nodes, correlating with high CD11c expression in this lymphoid organ. PPARγ and IL-6 were also up-regulated in inguinal lymph nodes. CD11c was up-regulated in both liver and mesenteric fat samples of KO animals. Microscopic imaging supported the above findings, showing abundant immune cell recruitment in liver samples of KO animals.

Conclusion
CD11c-Cre-induced deletion of STRA6L targets CD11c cell lineage specifically. Our results suggest that deletion of retinol transporter STRA6L in dendritic cells affects immune gene expression and immunogenic potential, but does not disrupt basal immune homeostasis in mice.