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Dynamics of T cell and B cell receptor repertoires in response to obesity in a murine model of atherosclerosis

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Purpose: Atherosclerosis is caused by a buildup of lipid-rich plaques within arterial walls. While T cells and B cells are both implicated in the immune response associated with atherosclerosis, the specific alterations in their respective receptor repertoires in response to obesity remain poorly understood. Here, we investigate obesity-induced changes in the T cell receptor (TCR) and B cell receptor (BCR) repertoires in a mouse model of atherosclerosis.

Methods: For this study, we used ten Ldlr-/- Apob100/100 mice, of which half received high-fat diet, while the remaining five were fed standard chow diet. From each mouse, we collected four different tissue types: perivascular adipose tissue, aorta, spleen, and epididymal white adipose tissue. The same tissue type from all mice in the same diet group was combined into one pool, resulting in eight sample pools. Afterwards, the tissues were dissociated and aorta samples were enriched for CD45+ cells. Finally, we performed single-cell RNA-sequencing using a 5' gene expression and VDJ immune profiling protocol. By analyzing VDJ repertoires, we aimed to identify clones with shared motifs and inspect them in the context of their gene expression profiles.

Results: The TCR repertoires were markedly distinct between obese and non-obese mice, with a more pronounced overlap between tissues from obese mice, suggesting a potential difference in predominant epitopes between the two diet groups. TCR clones that were more abundant in adipose tissues and/or the aorta were also present in the spleen, albeit in smaller numbers. In contrast, in the BCR repertoires, there was more overlap between the different diet groups, and the largest overlap was again seen between tissues from obese mice. We also observed tissue-specific BCR clones, which, although present in both diet groups, were much more abundant in obese mice.

Conclusion: This study contributes to the broader effort of unravelling the immunological mechanisms underlying cardiovascular diseases. Understanding the effect of diet on the dynamics of TCR and BCR repertoires in various tissues may inform the development of therapeutic strategies aiming to mitigate the progression of atherosclerosis in genetically predisposed individuals.

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