

Single-cell T cell receptor sequencing of paired human atherosclerotic plaques and blood reveals autoimmune-like features of expanded effector T cells

Received: 5 August 2022

Accepted: 20 December 2022

Published online: 30 January 2023

 Check for updates

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Atherosclerosis is a lipid-driven chronic inflammatory disease; however, whether it can be classified as an autoimmune disease remains unclear. In this study, we applied single-cell T cell receptor sequencing (scTCR-seq) on human carotid artery plaques and matched peripheral blood mononuclear cell samples to assess the extent of TCR clonality and antigen-specific activation within the various T cell subsets. We observed the highest degree of plaque-specific clonal expansion in effector CD4⁺ T cells, and these clonally expanded T cells expressed genes such as *CD69*, *FOS* and *FOSB*, indicative of recent TCR engagement, suggesting antigen-specific stimulation. CellChat analysis suggested multiple potential interactions of these effector CD4⁺ T cells with foam cells. Finally, we integrated a published scTCR-seq dataset of the autoimmune disease psoriatic arthritis, and we report various commonalities between the two diseases. In conclusion, our data suggest that atherosclerosis has an autoimmune component driven by autoreactive CD4⁺ T cells.

Atherosclerosis is the major underlying pathology of acute cardiovascular events, such as myocardial infarction and stroke. It is characterized by accumulation of lipids and subsequent inflammation of the medium and large arteries. As low-density lipoprotein (LDL) particles are important instigators of atherosclerosis, cardiovascular disease (CVD) has

primarily been treated as a lipid-driven disorder, with a treatment focus on lowering LDL cholesterol levels. Nonetheless, inflammation plays a critical role in perpetuating the growth and instability of atherosclerotic lesions, highlighted by the success of recent clinical trials with anti-inflammatory agents^{1,2}. Elucidating the dominant inflammatory

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Tcell Receptor Use In Human Autoimmune

Yijin Wang



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