IN THIS ISSUE

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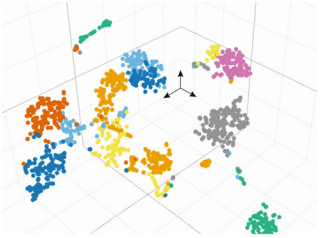
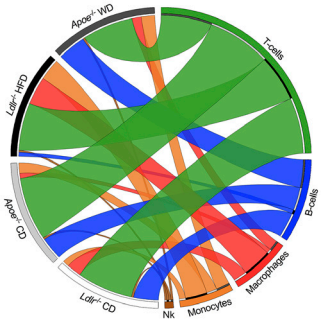


scRNA-Seq of Aortic Macrophages in Atherosclerosis (p 1661)

Using single-cell RNA sequencing, *Cochain* et al uncover the macrophage medley of atherosclerotic plaques.

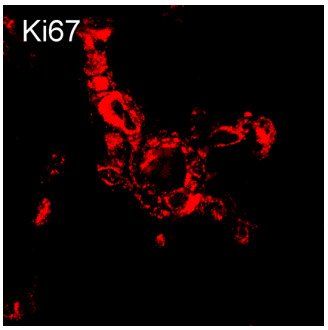
Macrophages accumulate in atherosclerotic plaques through a combination of recruitment and differentiation of circulating monocytes, proliferation of local resident macrophages, and transdifferentiation of vascular smooth muscle cells and progenitors. Because of these assorted origins, it has been proposed that several types of macrophage coexist in plaques. However, an unbiased, systematic investigation of plaque macrophage phenotypes has been lacking—until now. Cochain and colleagues collected and sequenced the RNA of a total of 854 single leukocytes from the aortas of atherosclerotic mice and compared them with 372 leukocytes from healthy aortas. The resulting expression profiles indicated the presence of 13 immune cell types, including 3 different populations of macrophages. Two of these populations—inflammatory macrophages, and a novel population identified by TREM2 receptor expression—were almost exclusively present in the diseased aorta. Furthermore, the team found evidence that these 2 disease-associated types may be present in human plaques. This unbiased census of plaque macrophages and their transcriptomes should serve as a valuable resource for researchers wishing to target or tweak such cell populations.



Leukocyte Heterogeneity in Atherosclerosis (p 1675)

In a companion paper to that of *Cochain* et al, *Winkels* et al examine the immune cell repertoire of atherosclerotic plaques.

Like Cochain and coworkers, Winkels and colleagues used single-cell RNA sequencing to assess the full range of leukocytes present in plaques. In this study, however, the team combined their RNA findings with protein data from mass cytometry. For their RNA analysis, the team collected and sequenced over 900 leukocytes from atherosclerotic mouse arteries. The resulting transcription profiles revealed 11 distinct cell clusters. Mass cytometry of the aortic plaque leukocytes using a panel of 35 immune cell markers identified 23 cell clusters that largely correlated with, or represented subsets of, the 11 RNA-defined clusters. Mass cytometric analysis of leukocytes from patient plaques had comparable cell heterogeneity—19 cell clusters—and the relative frequencies of these cell types predicted clinical outcomes. Specifically, a lack of memory T cells was found to be associated with an increased risk of ischemic events. Together, these results provide a detailed directory of plaque immune cell diversity and highlight the usefulness of such a two-pronged approach for cell identification.



Dominant Treg Effects in Females (p 1689)

In rats, pulmonary hypertension is more severe for T reg-lacking females than males, *Tamosiuniene* et al report.

Pulmonary hypertension (PH) is characterized by inflammation and narrowing of pulmonary arterioles. The resultant increase in blood pressure leads ultimately to right ventricular failure and death. The lungs of PH patients have abnormally low levels of immunosuppressive T regs, and rats lacking T regs are particularly susceptible to PH. Boosting T reg numbers in these animals mitigates their vulnerability. However, these rat studies were performed in males only. Now, Tamosiuniene and colleagues have extended this analysis to females. They found that T reg-lacking females fair worse than their male counterparts when PH is experimentally induced, exhibiting more severe inflammation, periarteriolar fibrosis and right ventricular hypertrophy, and more dramatic reductions in the levels of certain vasoprotective factors and T reg mediators. Nevertheless, T reg reconstitution was equally effective in protecting both sexes from PH. Although it remains unclear how the results obtained with rats relate to humans, in whom PH is more prevalent in women, but more severe in men, the work does highlight the importance of considering sex differences when assessing manifestations of cardiovascular disease.

Written by Ruth Williams

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