Top Ten Things To Know
Effector Memory T cells Are Associated With Atherosclerosis in Humans and Animal Models

1. Adaptive immunity is causally involved in the initiation and progression of atherosclerosis.

2. While the clinical relevance in humans is limited, epitopes are recognized by CD4+ T cells in experimental models and protection against atherosclerosis has been demonstrated by blocking the recognition by these T cells.

3. Simultaneous evaluation of 8 surface markers with polychromatic flow cytometry allowed researchers to identify and measure more than 50 circulating CD4+ T-cell subsets with specialized profiles that may reflect antigen-exposure, even in the absence of an overall alteration in total T cell number, in patients with subclinical atherosclerosis and with coronary artery disease.

4. Central memory T cells (T_{CM}) and effector memory T cells (T_{EM}), which develop from naïve T cells (T_{N}) following the presentation of the antigen by cells in lymphoid organs, constitute relevant T-cell subsets to control infective and autoimmune processes.

5. Levels of T_{EM} subset (identified by CD3+CD4+CD45RA-CD45RO+CCR7-) and related T_{EM} subpopulations best correlated with the extent of atherosclerosis in carotid and coronary districts in 313 subjects.

6. The involvement of an adaptive immune response in cardiovascular disorders is supported by the finding that the typical risk factors for cardiovascular disease and the association of T_{EM} and carotid atherosclerosis are independent.

7. T_{EM} expansion represents a general feature of the immune response associated with atherosclerotic disease. In agreement, in animal models with genetic defects resulting in massive hypercholesterolemia and extensive atherosclerosis (LDL-R knock-out and ApoE knock-out mice), both increased levels of T_{EM} and decreased levels of T_{N} cells were observed.

8. A sustained response to an endogenous antigen, such as low-density lipoprotein cholesterol–associated protein epitopes, could support the expansion of T_{EM}, and T_{EM} could have a role in further maintaining vascular inflammation, thus establishing a vicious circle, leading to cytokine secretion at atherosclerotic sites and possibly to plaque destabilization.

9. The association of atherosclerosis with antigen-experienced T_{EM} and long survival cells that lose CCR7 and express HLA-DR, CXCR3 and CCR5 extends observations in the field. Furthermore, this result strengthens the concept that careful cellular sub-phenotyping will be needed to understand the inflammatory pathogenesis of atherosclerosis.

10. As an addition to controlling for cardiovascular risk factors, the finding of increased levels of circulating TEM in humans and the relationship to animal findings could help in understanding new research directions for targeting plaque progression.