Specific oligoclonal T-cell recruitment within epicardial adipose tissue of patients with acute coronary syndrome: evidence for a local, immune-mediated, pathogenetic mechanism


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**Background**

Potential role of Epicardial Adipose Tissue (EAT) in acute coronary syndromes (ACS)

- EAT has a close functional and anatomic relationship with epicardial coronary arteries.
- EAT is different from other fat depots (smaller adipocytes size, different fatty acid composition, high protein content).
- Release of proinflammatory cytokines, and chronic inflammatory cell infiltration with macrophages, lymphocytes, and basophils, have been demonstrated in EAT of patients with coronary artery disease (CAD), although without any distinction between chronic and acute manifestations of the disease.\(^1\)\(^2\)
- EAT of patients with ACS is characterized by a specific secretion of resistin, produced in an inflammatory milieu, that increases in vitro endothelial cell permeability, thus highlighting a potential pathogenetic role of EAT in ACS.\(^3\)

**Objectives**

The present study aims to address whether a specific, immune-driven T-lymphocyte recruitment within EAT might be implicated in acute coronary syndrome (ACS)

**Methods**

T-cell receptor (TCR) repertoire analysis using CDR3 BV-BC spectratyping\(^4\)

EAT samples (obtained during coronary artery bypass grafting, or cardiac surgery for MVD)

Peripheral blood mononuclear cells (PBMC)

NST-ACS 30 patients

Stable angina (SA) 27 patients

Mitral insufficiency with normal coronary arteries (MVD) 12 patients

**Results**

We found T-cell clonotype expansions in EAT as compared with peripheral blood from each ACS patient.

The TCR repertoire in EAT samples of ACS was restricted

- TCRs enriched in epicardial adipose tissue distribute differently in ACS, SA, MVD

- A disproportionately high expression of TCR-BV6.2, BV7, and BV10 was observed, as they were found in 73%, 38% and 44% of EAT samples, respectively (compared with an expected 0.1%, 4% and 1%, in a random use of TCR gene segments)\(^5\) (Figure 3).

- Although the size of the repertoire used by SA and MVD was comparable to that of ACS patients, it was characterized by different T-cell receptors (Figure 3).

- SA patients expressed preferentially TCR-BV3 that was observed in 63% EAT samples (44% when a R.E.I. ≥5 was considered), while BV10 (4%) and BV6.2 (20%) were less frequent.

- MVD expressed TCR-BV3 (R.E.I. ≥5 =17%) and BV7 (36%), but none had BV10 or BV6.2.

**Conclusions**

For the first time, T-cell receptor repertoire was investigated directly into EAT surrounding diseased coronary arteries. Using this approach, we demonstrated that coronary plaque instability is associated with immune-driven T-cell recruitment, not only within the plaque, but also in the surrounding adipose tissue, and that T-cells bearing selected TCRs might be involved in the pathogenesis of ACS.

**References**