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Keywords
Integrins, Adipose Tissue, Coronary Artery Disease, Transforming Growth Factor beta, Gene Expression, Inflammation

Comments
Medical student Nancy Lee participated in this study as part of the Senior Scholars research program at the University of Massachusetts Medical School.

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Expression of ITGB8 in Epicardial Adipose Tissue is Highly and Directly Correlated with the Severity of Coronary Atherosclerosis

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Background

Obesity and its associated cardiovascular diseases have reached epidemic proportions. Prior studies suggest that in those with increased visceral adiposity, immune cells in visceral adipose tissue (VAT) establish chronic local inflammation that results in ectopic lipid deposition in peripheral organs and insulin resistance.

Epicardial adipose tissue (EAT) has been advanced as a possible direct link between obesity and cardiovascular disease. In patients with coronary artery disease (CAD), EAT has been shown to express increased levels of inflammatory cytokines.

What is not currently understood is whether or not inflammatory gene expression influences the development of atherosclerosis or is a compensatory response to established disease.

Objectives

The purpose of this study was to determine:
- Whether there are differences in gene expression between EAT and subcutaneous adipose tissue (SAT)
- If gene expression in EAT of patients with and without CAD differs
- If there is a difference, whether these differentially expressed genes participate in the inflammatory pathways.

Methods

- **CONTROL** (valve surgery)
  - Consent
  - Chart review
  - Fasting bloodwork
  - EAT, SAT, and at time of surgery
  - Microarray + qRT-PCR
  - Histology & IHC
- **CASE** (CABG surgery)
  - Comparison of gene expression in cases and controls

**Is Subcutaneous Fat Different than Epicardial Fat?**

- Informed consent obtained from controls (pts without CAD) and cases (pts with CAD) scheduled for elective cardiothoracic surgery.
- 500 mg EAT and SAT collected at the time of surgery, fixed for microscopy and frozen for RNA extraction.
- RNA was hybridized to Affymetrix Human Gene 1.0 ST chips.
- Genes w/ FC>3 in EAT vs. SAT were identified.
- Gensini scores for participants determined through review of cardiac catheterization data.
- Probe intensities for these resultant genes were then correlated with the severity of atherosclerosis in each patient as determined by the Gensini score.

Results

**Comparison of EAT and SAT**

- Of these, 35 genes differentially expressed in EAT vs SAT by FC>3 and p<0.05
- Of the 35, 14 are correlated with CAD severity measured by Gensini score

**Correlation with CAD Severity**

- Of the 14 genes correlated with CAD severity, EAT expression of ITGB8 had the strongest positive correlation. Importantly, this relationship did not persist in SAT, suggesting it was an effect specific to EAT.

Conclusion

Expression of ITGB8 was found to be directly correlated with CAD severity. Integrin αvβ8 (ITGB8) has been previously shown to be expressed by fibroblasts and functions to activate immunomodulating TGFβ. TGFβ signaling has also been correlated with advanced atherosclerosis. We speculate that EAT expression of ITGB8 may have pro-inflammatory effects, possibly through activation of TGFβ, and stimulating recruitment of dendritic cells or T cells to secondary lymphoid organs in EAT. Whether or not this is the case is a goal of future studies.

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