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

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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.

Methods

![Diagram of Methods]

- 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

![Diagram of Results]

Of the 35 genes differentially expressed in EAT vs SAT by FC>3 and p<0.05

<table>
<thead>
<tr>
<th>Gene</th>
<th>q-value</th>
<th>p-value</th>
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<tbody>
<tr>
<td>ITGB8</td>
<td>0.94</td>
<td>0.0005</td>
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<tr>
<td>MMP13</td>
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<td>0.014</td>
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<td>ITGAL</td>
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<td>ITGAM</td>
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</tr>
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<tr>
<td>ITGB8</td>
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<td>0.0074</td>
</tr>
<tr>
<td>ITGB8</td>
<td>0.90</td>
<td>0.0074</td>
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</tbody>
</table>

Of the 35, 14 are correlated with CAD severity measured by Gensini score

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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