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Molecular Signatures of Carotid Plaques

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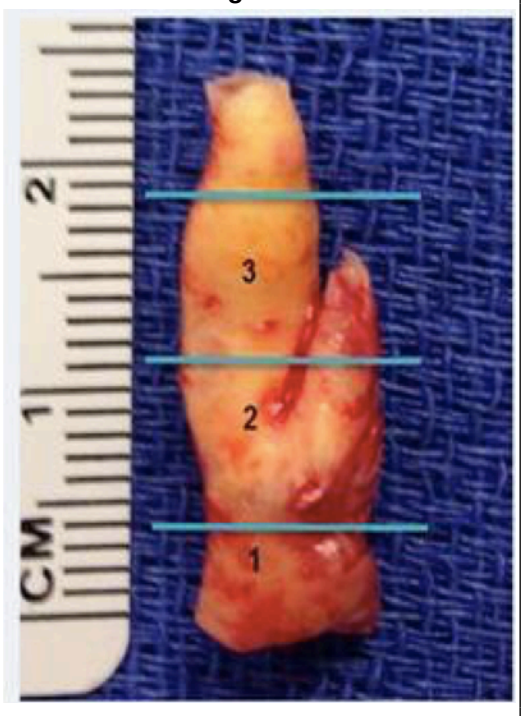
Introduction

Our ability to predict which atherosclerotic plaques are at higher risk to become symptomatic is limited, resulting in numerous unnecessary interventions. A better understanding of the molecular signatures associated with rupture-prone plaques, and the development of peripheral biomarkers could help guide management

Figure 1.

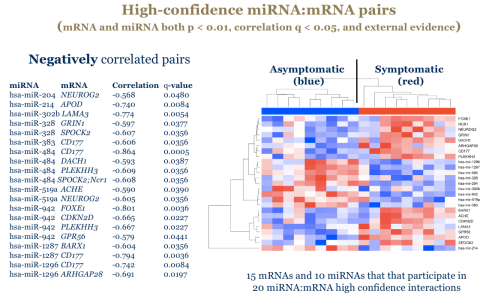


Carotid plaque specimen segmentation into pre-bifurcation (1), bifurcation (2), and post-bifurcation segments

Methods

Thirty-eight carotid plaques (26 symptomatic, 12 asymptomatic), obtained from carotid endarterectomies at our institution, were dissected into pre-bifurcation, bifurcation, and post-bifurcation segments. All were used for protein expression. In addition, 9 symptomatic, and 9 asymptomatic plaques were used to identify mRNA:miRNA interactions in the post-bifurcation segments. Furthermore, peripheral blood from 9 patients with symptomatic plaques, and 9 patients with asymptomatic plaques, as well as 3 normal controls were used to evaluate peripheral miRNA expression.

Figure 2.

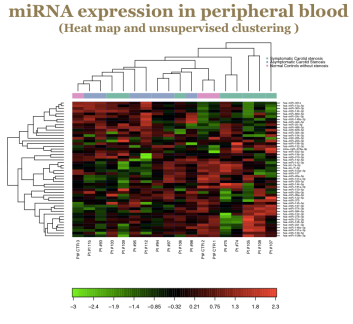


High Confidence miRNA:mRNA pairs

Results

Protein expression profiles revealed increased levels of IL-1ß , IL-6, IL-8, and cleaved caspace-3 in symptomatic compared to asymptomatic plaques, and in the distal, compared to the proximal plaque segments (post-bifurcation> bifurcation> pre-bifurcation). Further analysis of the post-bifurcation segments revealed three high-confidence miRNA:mRNA pair interactions (negatively correlated) that were differentially expressed between symptomatic and asymptomatic plaques: hsa-miR-214/APOD, hsa-miR-484/DACH1, hsa-miR-942/GPR56 ($p < 0.001$, correlation $q < 0.05$). Evaluation of peripheral blood miRNA expression revealed 7 miRNAs to be differentially expressed between symptomatic, and asymptomatic plaques, and 13 miRNAs to be differentially expressed between symptomatic plaques and controls.

Figure 3.



miRNA expression in peripheral blood

Conclusions

The current study identifies a number of novel potential biomarkers for carotid plaque vulnerability. Prospective evaluation of these markers in a large number of patients with carotid stenosis is warranted to establish their clinical applicability

Learning Objectives

By the conclusion of this session, participants should be able to: 1) discuss the importance of biomarkers in the risk stratification of carotid stenosis, 2) describe some of the most important novel biomarkers presented in this study