Integrative multi-omics analysis of human atherosclerosis reveals an intraplaque hemorrhage associated network, which offers better prediction of disease stage

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Background

Initiation and progression of atherosclerotic lesions involve complex biological processes including lipid metabolism, inflammation, and hypoxia response. Unfortunately, a rigorous model to systematically and comprehensively describe the underlying mechanisms in plaque rupture is lacking. Therefore, we set out to compare the makeup of low- (n = 17) and high-risk (n=26) atherosclerotic carotid artery lesions from CEA patients, by integrally analyzing transcriptomics, proteomics and peptidomics datasets collected from CEA lesions. This integrative model is based on the sparse Partial Least Square Discriminant Analysis (sPLS-DA), a multivariate method for classification and feature selection.

Material

Stable plaque

- Large lipid core
- Thin fibrous cap
- High macrophage content

Unstable, Ruptured

- High microvessel density
- Intraplaque Hemorrhage
- Cap ruptured and thrombus

Workflow

Results

	Single-omics	Multi-omics
Balanced Error Rate	11.79%	11.04%
Selected Features	222	29
Gene Signatures	222	18
Protein Signatures	0	9
Peptide Signatures	0	9

Sample Distribution

Gene Expression

Network Visualization

Validation on Independent Cohorts

Atheroma vs Intact Advanced vs Early Ruptured vs Stable

Conclusion

- Integrative analysis of CEA omics shows competitive prediction power compare to single omics analysis.
- Result validation on independent cohorts shows multi-omics signatures can reflect not only the disease progression from stable to ruptured, but also through the whole disease.