

## Ingenuity<sup>®</sup> Science Spotlight:

Articles featured in the Ingenuity Science Spotlight represent some of the best and most diverse examples of how IPA<sup>®</sup> has contributed to research across multiple platforms, research areas, and research goals.



### Identification of pathways for atherosclerosis in mice: integration of quantitative trait locus analysis and global gene expression data.

Wang SS, Schadt EE, Wang H, Wang X, Ingram-Drake L, Shi W, Drake TA, Lusis AJ. Circulation Research 2007 Aug 3;101(3)

[http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17641228&ordinalpos=6&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_ResultsPanel.Pubmed\\_RVDocSum](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17641228&ordinalpos=6&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum)

Quantitative trait locus analysis is a powerful tool for mapping regions of the genome that contain genes involved in specifying complex disease phenotypes such as atherosclerosis. Previous studies by Paigen et al (Am J Hum Genet. 2005; 77:1-15) mapped loci that segregate with atherosclerotic lesion development. However, identification of the underlying genes that segregate with that phenotype has been difficult because these regions harbor hundreds of genes. By combining QTL analysis with whole-genome-expression array analysis, a research team led by Dr. Aldons Lusis of UCLA's Department of Human Genetics was able to identify candidate genes that mapped to atherosclerosis QTLs. IPA analysis of the expression of genes highly correlated with atherosclerotic lesions enabled the team to conclude that many of these genes were enriched for known pathways involved in lesion development, including cholesterol metabolism, mitochondrial oxidative phosphorylation, and inflammation.

This approach enabled the research team to narrow in on disease-relevant pathways and candidate genes that underlie the complex molecular genetics of atherosclerosis. Importantly, these studies also demonstrated that monitoring genome-wide gene expression changes in peripheral tissues could capture system-wide disruptions that contribute to the development of disease phenotypes such as atherosclerosis. This approach provides a valid strategy for identifying novel therapeutic targets and biomarkers for the treatment and monitoring of complex cardiovascular diseases such as atherosclerosis.