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Titel des Beitrags:
A systems biology framework identifies molecular underpinnings of coronary heart disease.

Abstract:
Genetic approaches have identified numerous loci associated with coronary heart disease (CHD). The molecular mechanisms underlying CHD gene-disease associations, however, remain unclear. We hypothesized that genetic variants with both strong and subtle effects drive gene subnetworks that in turn affect CHD. We surveyed CHD-associated molecular interactions by constructing coexpression networks using whole blood gene expression profiles from 188 CHD cases and 188 age- and sex-matched controls. Twenty-four coexpression modules were identified, including 1 case-specific and 1 control-specific differential module (DM). The DMs were enriched for genes involved in B-cell activation, immune response, and ion transport. By integrating the DMs with gene expression-associated single-nucleotide polymorphisms and with results of genome-wide association studies of CHD and its risk
factors, the control-specific DM was implicated as CHD causal based on its significant enrichment for both CHD and lipid expression-associated single-nucleotide polymorphisms. This causal DM was further integrated with tissue-specific Bayesian networks and protein-protein interaction networks to identify regulatory key driver genes. Multitissue key drivers (SPIB and TNFRSF13C) and tissue-specific key drivers (eg, EBF1) were identified. Our network-driven integrative analysis not only identified CHD-related genes, but also defined network structure that sheds light on the molecular interactions of genes associated with CHD risk.