

Systems Biology Mining of APO Lipoprotein Metabolic Pathways

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ABSTRACT

We apply our systems biology approaches to the study of a transgenic APO E3 Leiden mouse model [1]. The APO E3 allele has been implicated in a variety of disorders of lipoprotein metabolism [2,3].

Metabolite levels in transgenic animals and their wild type counterparts were measured using both liquid chromatography/mass spectrometry and NMR technologies. Plasma lipoprotein levels were determined using chromatographic and mass spectrometry techniques, while the gene expression levels in liver tissue were determined using hybridization microarrays.

Preliminary results show differential levels of lipids possessing both structural and signaling functions. In order to perform correlation analysis and classification on metabolite data, we used standard statistical methods such as principal component analysis and canonical correlations, as well as newer methodologies such as support vector machines [4] and probabilistic relational models [5]. The latter, given its Bayesian nature, leads us to the next step in analysis, which is building pathway models based on combined metabolite and protein levels, as well as gene expression data.

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