

Efficient Survival Multifactor Dimensionality Reduction Method for Detecting Gene-Gene Interaction

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Background and Objective: The problem of identifying SNP-SNP interactions in case-control studies has been studied extensively and a number of new techniques have been developed. Little progress has been made, however in the analysis of SNP-SNP interactions in relation to censored survival data.

Methods: We present an extension of the two class multifactor dimensionality reduction (MDR) algorithm that enables detection and characterization of epistatic SNP-SNP interactions in the context of survival outcome. The proposed an Efficient Survival MDR (ES-MDR) method handles censored data by modifying MDR's constructive induction algorithm to use logrank Test.

Results: We then applied ES-MDR to genetic data of over 470,000SNPs from the OncoArray Consortium. We use onset age of lung cancer and case-control (n=27,312) status as the survival outcome. We also adjust for subject's nicotine level through smoking. We identified that chr17_41196821_INDEL_T_D and rs11692723_C is the top SNP-SNP interaction that associated with lung cancer onset age.

Discussion and Conclusions: ES-MDR is capable of detecting interaction models with weak main effects. These epistatic models tend to be dropped by traditional linear regression approaches. With improved efficiency to handle genome wide datasets, ES-MDR will play an important role in a research strategy that embraces the complexity of the genotype-phenotype mapping relationship.

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