A 2-STAGE DESIGN FOR MINIMIZING THE OVERALL ADJUSTMENT FOR MULTIPLICITY IN MICROARRAY STUDIES FOR GxE

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Abstract: While genetics is believed to play an important role in many diseases, environmental factors likely modulate an individual’s genetic predisposition for disease. We present a method to address the interaction between environmental and genetic determinants for disease by computing a multiplicity adjusted lower bound on an “indirect” estimate for effect modifications. The “indirect” estimate, based on the main effects odds ratio for environmental exposure OR(E|D) and the population genotype (g), may be used to screen for plausible genes in a subsequent study aimed at “directly” identifying hidden interactions and complex associations between genetic and environmental factors. By eliminating stochastically discordant genes and thus minimizing the overall adjustment for multiplicity, our method will have significantly greater power to detect meaningful interactions between putative risk factors for disease compared with other data reduction methods.

Keywords: Gene-environment interaction, multiplicity, microarrays, discordant genes