

# Theory and Applications of Index Selection to Identify Responder vs Non-Responders to Chemotherapy Drugs

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## Abstract

The dream of personalized medicine is to use the genetic profile to individualize therapy. Index Selection (IS) is an established multivariate statistical technique developed in plant and animal breeding research designed to find signal sets of genes which operate together. We applied IS to the problem of discovering the genetic basis of chemotoxicity response in cancer therapy. 30 trios of immortalized CEPH cell lines from HapMap subjects with multiple doses of two chemotherapy drugs Docetaxel and 5-Fluorouracil to establish individual dose-response curves. 3,523,637 SNPs were available from the HapMap. A group of filters (MAF > 10% and tagSNPs;) and were performed to select the most promising SNPs. Only the additive effects of these SNPs are included in the IS model  $IS = b(z)z + b(m)m$ , where “z” represents a vector of quantitative traits, “m” is a vector of the selected SNPs, and “b” is the corresponding additive effects. In a preliminary analysis, 68 significant SNPs located within genes, out of 228,084 SNPs on chromosome 5 were included in an IS, which previously demonstrated strong linkage to chemotoxicity response. The correlation between the IS and the observed viability of Ceph cell lines was 0.814. This method holds promise to quantify the predicted individual response to chemotherapy.