SCIENCE FOR THE BENEFIT OF HUMANITY

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A Novel Hierachical Multivariate Statistical Approach for Decision-Making in Clinical Trials and Personalized Medicine

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Technology Summary

Common diseases typically reflect disturbance in complex biological systems. Thus, finding the treatment with the best risk/benefit ratio may entail relating many genetic, genomic, and proteomic variables to composite phenotypes. Traditional statistical methods have limitations because they are usually based on models specified by relatively few parameters.

Dr. Knut M. Wittkowski from The Rockefeller University has developed a novel non-parametric method for scoring multi-dimensional data, including flexible models and computational methods to process large data sets. This scale-independent method, termed muStat, can integrate information on diplotypes (sequences of adjacent SNPs), gene expression pathways (e.g., microarray data), protein profiles, and complex phenotypes (e.g., efficacy measures and adverse experiences). When applied to a study population, muStat can identify subpopulations at risk for side effects/adverse events or treatment failure and suggest new biological pathways. Confirming these pathways (e.g., in animal studies), muStat can then lead to rationally targeted studies for drug safety, efficacy, and approval. Since no unrealistic simplifying assumptions (linearity, normality, independence, etc.) need to be made, time-consuming empirical 'validation' is avoided. Thus, muStat can analyze and interpret data sets through scoring systems and decision rules tailored specifically to a particular patient, thereby advancing predictive, preventive, and personalized medicine.

Advantage

- Provides objective results independent of subjective and/or questionable assumptions.
- Can be applied to large datasets, e.g. thousands of subjects.
- Can integrate hundreds of genetic, genomic, proteomic, and phenomic variables
- Generate scores and decision functions without the need for empirical validation.

Area of Application

- Animal studies (genetic analyses in in- or outbred populations)
- Clinical trials (complex phenotypes, side effect profiles, overall benefit)
- Observational studies/GWAS (identifying drug targets and risk factors for side effects from Ph III data)
- Diagnostic support / personalized medicine

Stage of Development

- This method has been used in numerous biological studies and clinical trials using the analysis server for non-profit use in research (http://muStat.rockefeller.edu) and the free evaluation software (http://cran.r-project.org, http://csan.insightful.com). Demonstrations of the use of the muStat server in a client-server architecture can be arranged upon request. Two recent applications confirmed drug targets for epilepsy (www.ncbi.nlm.nih.gov/pubmed/23438886) and suggested early intervention with ion channel modulators as the first causal treatment for autism spectrum disorders (http://www.nature.com/tp/journal/v4/n1/abs/tp2013124a.html

Patent Information:

U.S. Patent 7,664,616.

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