

IS-05

„Genomweite Assoziationsanalysen bei
komplexen Krankheiten -
genome wide association analyses (GSA) for
complex diseases“

Koordinatorin:

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In order to locate genetic factors contributing to a complex disease measures of correlation between a genetic marker and an unknown disease locus are used. These measures are the common segregation of a marker and a disease in families, i.e. linkage, or Linkage disequilibrium (LD), if the probability for the existence of a specific marker allele together with a specific disease allele in a population gamete differs from the product of individual probabilities. Linkage is more suitable to identify rare variants causing a Mendelian subtype of a complex disease. For biallelic markers within a “common disease – common variant hypothesis” association analysis is more appropriate.

We can distinguish two major approaches. Depending on the context, either the first or the second approach is more efficient. The first is a *genome scan*, i.e. the systematic grid search of the whole genome with a map of genetic markers. The other approach is to investigate *candidate genes*. Thereby, the focus is set on genes for which their function on the pathway to the phenotype can evidently be assumed. In both approaches the genotypes of the relevant functional component of the candidate genes are not always observed. We therefore need to use the information on genetic markers that lie in close proximity to the candidate gene in question, e.g. in the same haplotype block.

This session will highlight pressing issues of this rapidly evolving research area since the technological tools for GSAs with 500 000 SNPs are already available to molecular biologists. 5 presentations discuss the interplay between biometry, clinic, epidemiology, genetics and pharmacology. Wichmann's talk will demonstrate first successes with the use of *large population based cohorts* and at the same time address areas of further research needs in epidemiology, biostatistics and medical informatics. Wojnowski will give some insights in study planning for a “common monogenic disease” from the viewpoint of a pharmacologist. Thomas will highlight in this central talk the next necessary step in integrating genome wide techniques with prior biological knowledge – the up-to-date missing link between pure candidate gene approaches and GSAs. Sax discusses optimal data integration from disease related collections and biomaterial collections. Finally Schulz discusses the optimal way to get the necessary information on the phenotype side, i.e. which clinical data are necessary for successful GSAs. In summary, large cohorts with optimal biomaterial and data collections as well as high quality phenotypic and genotypic data and their data integration is necessary for GSAs with many questions left often to further research.

Vorträge:

1. Epidemiologe Prof. Wichmann, GSF
Thema: Genome-wide association studies - first experiences with study planning, data management and statistical analysis (Wichmann H.-E. et al)
2. Pharmakologe Wojnowski, Pharmakogenetik, Mainz
Thema: Optimizing parameters for a cardiovascular genomewide association study
3. Biometriker Duncan Thomas
Thema: Integrating prior genomic information into genome-wide association studies
4. Medizin-Informatiker – Sax, Göttingen
Thema: Data-related Challenges of Genotype - Phenotype studies

5. Bioinformatiker Schulze, Mannheim

Thema: Exact phenotype definition for complex genetic traits: Novel strategies to establish valid diagnostic entities in psychiatric genetics in the age of high-throughput genotyping and brain imaging