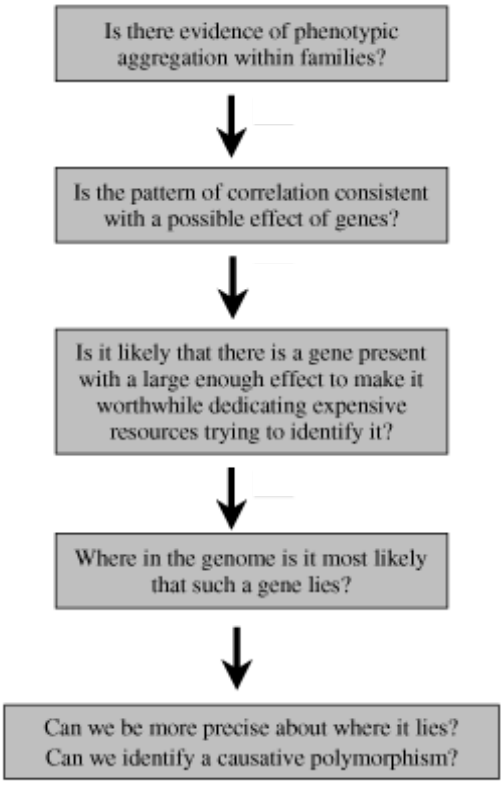
# Project 1: Genetic Epidemiology Flowchart

## Introduction

In this project, you will start from a selected "complex disease" or "complex trait" of interest (cfr. group formations in class) and you will describe the trait and discuss it in the context of different types of analyses that are possible within genetic epidemiology:




The last part of the flowchart above relates to "genetic association studies". For this component you may find the "Catalog of GWAS" for published genome-wide association studies useful. The link to this catalog is http://www.genome.gov/gwastudies/#searchForm.

## Your report should contain answers to the flowchart questions

and includes information about

- whether or not the trait is heritable (with references)
- familial aggregation (is there an increased risk for siblings of affected individuals? Is there an increased risk for other types of relatives? What is this risk increase if it exists?)
- mode of inheritance (is there evidence for one gene? Dominant? Recessive? Is there evidence for multiple genes?)

Moreover,

- do subtypes of the disease exist? How are these subtypes defined? Using clinical parameters? Using genetic parameters?
- Does the disease have different realizations depending on geography (e.g., Asia versus Europe)
- Does the disease have different realization depending on other non-genetic factors (i.e., is there evidence for gene-environment interactions)?
- How was information about relevant genes retrieved? How were these genes identified? Via which methods? First via linkage analysis and then via genetic association modeling? Or directly via association analysis? Can you give more details about the linkage analysis (design, markers, method)?
- Has genetics been used for this disease to enhance disease management or to improve diagnosis? If so, how?

Lastly, dig into the literature and search for genome-wide association analyses for your trait (main effects, gene-gene interaction studies, gene-environment interaction studies) and report about them. We will discuss in class which of these can serve as a basis for Project 2.

# Project 2: Genetic Association in Detail

## Introduction

Project 1 has given you the relevant background information to dig into genome-wide or smaller scaled genetic association studies related to your chosen trait.

For the selected study (decided upon in class, together with the instructor), **write a report** by giving an answer to the following questions:

- Describe the biological question(s) dealt with in the study.
- What is the design of the study? (markers, subjects). Is it different from the designs seen in class? If so, what was the motivation to select a different design?
- Which quality control procedures have been put in place? Are they in line with the Travemunde criteria? If not, was there a motivation given in the paper for adopting a different criterium, or can you come up with a motivation yourself? Be critical.
- How did one make use of the concept of LD (linkage disequilibrium)? Was it used to reduce the number of tests? Was it used after the analysis to identify causal variants?
- What type of association test was carried out? Single locus at the time? Haplotype-analysis was considered as well? What is the possible advantage of performing a haplotype analysis? What are the drawbacks?
- Was there a need to correct for population stratification? What is population stratification? How did one correct for it? Are there other ways?

- Were the genetic association results supported by a replication analysis or a validation analysis? If so, what did it involve? What are the factors causing a non-replication? May it also be the existence of gene-gene interactions? Was there evidence for gene-gene or gene-environment interactions?
- What are the final conclusions of the study and how much trust can be given to them (when looking at the replication/validation results)?
- What type of follow-up analyses do the authors advocate? Can you place these in the context of (modern) "genetic epidemiology"?


## Useful references


- Psychiatric GWAS Consortium Coordinating Committee, Cichon S, Craddock N, Daly M, Faraone SV, Gejman PV, Kelsoe J, Lehner T, Levinson DF, Moran A, Sklar P, Sullivan PF (2009). Genomewide association studies: history, rationale, and prospects for psychiatric disorders. Am J Psychiatry. 166(5):540-56.
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