

Screens for linkage disequilibrium in association studies

Norbert Dahmen¹⁾ and Wolfgang Höppner²⁾

¹ CONGENICS AG, Nordkanalstraße 52, 20097 Hamburg, Germany;

² BioGlobe GmbH, Grandweg 64, 22529 Hamburg, Germany

The recruitment of families for traditional linkage studies is cumbersome and costly. In addition, linkage analysis suffers from a lack of power when compared to candidate gene association analysis. However, candidate gene studies are by nature restricted to a small subset of “suspects” and may miss potentially relevant genes not obviously connected to presumed mechanisms.

A novel approach to locate additional, relevant genes is to screen for linkage disequilibrium with genetic markers. The general study design is that of association studies without the need for whole family recruitment. One of the key features of linkage disequilibrium screens is the possibility to screen genome wide without the need for precise hypotheses about the nature of the genes involved. It is also possible to screen specified chromosomal areas, or to screen functionally related sets of genes from different chromosomal positions. The resolution is in the magnitude of the usable linkage disequilibrium and thus able to pinpoint to single genes or to gene clusters. Therefore the method is not only suitable for primary screens but also for the follow up of linkage analysis or other sources of low resolution genetic information.

In order to perform successful screens, ten issues need to be considered:

- Number of patients needed
- Selection of phenotype or endo-phenotype
- Size of linkage disequilibrium
- Number of genetic markers needed
- Selection of marker class
- Selection of markers
- Pooling vs. individual typing
- If pooling, size and number of pools
- Strategy for the detection of false positives
- Detection technology, e.g. MALDI-TOF.

Unlike some other commercial solutions relying solely on SNP high through-put technology, Congenics AG has adapted an approach integrating the advantages of using different marker classes and thereby dramatically reducing the rate of false positives. In addition, a proven four step strategy is used for the purpose of carving out true positives from initial positives.

It also comes with an inbuilt genomic control feature that allows for the detection of unwanted population structures (**Virtual Isolate Population™**).

Congenics AG and Bioglobe GmbH are now offering:

Congenics Total Screen™, primary, genome wide screen for linkage disequilibrium

Congenics Local Screen™. Screen for customer defined chromosomal areas.

Congenics Focal Screen™. Screen for customer defined sets of genes, or predefined sets, eg. Neurotransmission, apoptosis genes, cancer genes.

Prices are within the scope of academic research budgets or applications. Price quotes will be individual, based on effort, e.g. number of patients, confirmatory testing, clinical work (possible through partnering contract research organizations) and intellectual property agreements. Inquiries from academia, biotechnology and pharmaceutical companies are welcome.

Please contact:

info@bioglobe.net

+49 40 4606 93 10 (fax)

+49 40 4606 93 13 (phone, Prof. Höppner)