

Next generation genetics in allergy

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The past 4 years have seen tremendous developments in human genetics of complex diseases. Genetic technology has made quantum leaps in recent years and these technologies are now being applied to medical genetics. Based on knowledge derived from the Human Genome Project and the Haplotype Map Project (HapMap), which mapped genetic variation to the human genome, the so-called single nucleotide polymorphism (SNP) chips have been developed. This technology allows testing hundreds of thousands (or even millions) of polymorphisms (SNPs) in a single experiment in an individual. Applying this technology to large populations leads to 'genome-wide association studies' (or GWAS), as the first wave of these kinds of studies was called. In 2007, the first GWAS on asthma was published and a few more studies focusing on intermediate or asthma-related phenotypes followed. As of 2010, GWAS data exist for asthma and related traits, immunoglobulin E regulation, eosinophilia, and atopic eczema. The last years of genetics were like living the big gold rush, in which everybody who could afford SNP chips, and had a claim (e.g. a well phenotyped disease population), would dig for the genome and surely find treasures.

No doubt, GWAS has changed our views on genetics of complex diseases and novel insights into the genetic architecture of diseases have been achieved. At the same time, GWAS has failed to 'solve complex diseases' as was the expectation of many inside and outside the medical field. In reality, only a small fraction of the heritability of complex diseases can be explained with major susceptibility signals identified by today's GWAS. However, it was necessary to perform these GWAS to gain the insight that a large fraction of the heritability of complex diseases cannot be explained by common polymorphisms alone.

It becomes clear that GWAS is not the end of the developments in human genetics of complex diseases. Rather, GWAS was a first, but important, step in understanding the role of the genome and its variation in the susceptibility to allergy. The road from genetics to clinical bedside in allergy may be long and winding,

but within a few years and a few GWAS, a number of dogma-changing insights have already been gained. The major susceptibility loci for asthma hold genes never linked to the disease before; genetic susceptibility for asthma in childhood and adulthood asthma differs significantly. Susceptibility for atopic sensitization and asthma as well as atopic eczema does not overlap, although the major asthma locus also increases the risk for Morbus Crohn, a disease not easily related to asthma and allergies at first sight. Different ethnicities may have different diseases causing variants harboured in diverse genes. Taken together, there is now genetic evidence that asthma is a different disease in different ethnicities, genders and at different ages.

New challenges lie ahead. For this series, we have invited those groups that have contributed substantially to the field of allergy genetics with their own GWAS. Experts like Kathleen Barnes [1], Hakon Hakonarson [2], Young-Ae Lee [3] and Stephan Weidinger [4] have been asked to comment on the status of GWAS and what will be next in the field of asthma and allergy genetics and their responses can be found in this issue. Miriam Moffatt [5] and Carole Ober [6] have already done so previously. Working on the cutting edge of these developments, the authors of the reviews in our series have the insight to comment on where the field of allergy genetics can, should and will move. It is time to review what GWAS has achieved and what to do with our enormous datasets, new analytical tools, the technology we hold now in our hands (and that which is appearing on the horizon) and the new ideas and insights that came out of this round of GWAS. Rome was not built in a day and the genome will not be understood in an instant.

References

- 1 Barnes KC. Genomewide association studies in allergy and the influence of ethnicity. *Curr Opin Allergy Clin Immunol* 2010; 10:5.
- 2 Swarr DT, Hakonarson H. Unraveling the complex genetic underpinnings of asthma and allergic disorders. *Curr Opin Allergy Clin Immunol* (in press).
- 3 Esparza-Gordillo J, Marenholz I, Lee YA. Genome-wide approaches to the etiology of eczema. *Curr Opin Allergy Clin Immunol* (in press).
- 4 Weidinger S, Baurecht H, Naumann A, Novak N. Genome wide association studies on IgE regulation. Are genetics of IgE also genetics of atopic disease? *Curr Opin Allergy Clin Immunol* (in press).
- 5 Moffatt MF. Genes in asthma: new genes and new ways. *Curr Opin Allergy Clin Immunol* 2008; 8:411–417.
- 6 Ober C, Chupp GL. The chitinase and chitinase-like proteins: a review of genetic and functional studies in asthma and immune-mediated diseases. *Curr Opin Allergy Clin Immunol* 2009; 9:401–408.