Critique of article

Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls.

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Nowadays, there are a lot of researches to improve of methods for the diagnostics of hereditary diseases (e.g. DNA Microarray[1]). Parallel studies aimed at finding the genetic causes of these diseases. Genome-wide association study (GWAS) - is a large-scale study of the human genome, in which there were studied seven hereditary disease (bipolar disorder (BD), coronary artery disease (CAD), Crohn's disease (CD), hypertension (HT), rheumatoid arthritis (RA), type 1diabetes (T1D), and type 2 diabetes (T2D)) by analyzing the genomes of 2000 representatives of each disease and the 3000 genomes controls[2]. In the results of the DNA and SNP loci have been identified in the genes that have a significant part in progresses of these diseases. GWAS - this is a very productive approach to the analysis of association of genetic polymorphisms with the disease, though it requires a large sample of individuals and search throughout the whole genome. These operations are technologically complicated and need a lot of time.

All of genetic ethnic differences are still completely unclear. Therefore it is unknown whether the frequency of a genetic disease depends on the ethnic group. In view of these ambiguities, the presence in the sample of representatives of various ethnic groups could possibly lead to wrong results: not full or noisy (false).

Together with a set of SNP, the cause of the disease may be the CNV (copy number variants). Therefore detected as a result set of GWAS SNV for each disease is not enough to describe the disease, because the sets of SNP are only genetic components of considered seven hereditary diseases. There were no word about CNV in the article (2007), but in 2010 the GWAS of CNV was published [3]. The study was about eight diseases and also 2000 genomes of representatives of each disease and the 3000 genomes controls.

Noteworthy, in the GWAS that were identified the SNP not only in the genes, but also, for example, in the desert regions of the genes (9p21 for Disease CAD and T2D). Further studies (not considered GWAS) recognized in this area 33 enhancer.[4] Thus, the cause of the genetic disease can be some changes not only in the gene encoding the important protein for metabolism, but also in the regulatory regions.

The obvious advantage of research GWAS - is that they do not rely on prior knowledge and not based on any hypothesis, therefore, can lead to the discovery of unexpected causes of diseases. Although

perhaps such studies should be carried out not on the full genome, but on a small section of it. The study on the complete genome are lost substantial funds (known previous data), which can help make searching quicker.Also studying SNP in every region of the genome may be redundant since some regions are inherited together (linked inheritance). Inclusion of this can simplify the search of genetic causes of hereditary diseases and may reduce the noise, if it can have the place to be.

The success of GWAS depends on the speed of the results, as it can accelerate the process of creations necessary medicines and new diagnostic methods. Therefore, the proposed additional modifications in search of significant SNP may play an important role.

Literature:

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2. The Wellcome Trust Case Control Consortium**.** Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. Nature 447 (2007).
3. The Wellcome Trust Case Control Consortium**.** Genome-wide association study of CNVs in 16,000 cases of seven common diseases and 3,000 shared controls.
4. Nature 464 (2010).
5. Olivier Harismendy et al., 9p21 DNA variants associated with Coronary Artery Disease impair IFNγsignaling response. Nature 470(2011).