TRILATERALE PARTNERSCHAFTEN - VOLKSWAGENSTIFTUNG

In silico screening and experimental validation of new drug targets for the treatment of co-morbid multifactorial diseases

Multifactorial diseases (MD) are one of the most important problems of modern society. Most of all drugs used to treat them achieve therapeutic effect in 30 - 60% of cases, while in other cases patients experience lack of therapeutic effect or suffer from side effects of drug therapy (Meyer, 2013). The situation is complicated by the high prevalence of co-morbid conditions in one patient requiring separate approaches to the treatment of each of the associated diseases. From this perspective, the studies of the molecular mechanisms of disease co-morbidity become extremely important.

Through the use of new genomic, proteomic and other "omic" technologies, new opportunities to study MDs emerge, this includes various aspects of their combined manifestation. One of the variant of co-morbidity, called syntropy (frequent combination of diseases in one individual caused by interaction of common, syntropic, genes) attracts special attention (Puzyrev, Freidin, 2009). Taken into account frequent co-occurrence of syntropic disease, their analysis can be fruitful in terms of revealing common markers of exposure and new drug targets to treat combinations of diseases.

The project aims to discover new drug targets for co-morbid diseases in humans using such frequently co-morbid pathologies as asthma and hypertension. A computer search will be carried out to fulfil the target. For genes for potential drug targets identified insilico, we will estimate the probability of the effect of promoter single nucleotide polymorphisms (SNPs) on the efficiency of transcription factor binding. The SNPs with highest possible functional effect will be further explored for their association with asthma, hypertension, and a combination of the diseases. To identify pathogenetic significance of regulatory variants of the studied genes, we will carry out an assessment of their impact on the level of expression of different categories of patients.

A rodent model of asthma and hypertension co-morbidity will be established and the common genes for asthma and hypertension will be investigated to reveal their pathophysiological impact on the development of the diseases. RNA-interference and other approaches will be used to reveal potential therapeutic relevance of common genes.

Overall, the study will examine molecular features of common co-morbidity of asthma and hypertension and will also identify potential drug targets for the treatment of these conditions.

The project will be carried out by a collaborative group of partners based in Institute of Cytology and Genetics (Novosibirsk, Russia), Research Institute for Medical Genetics (Tomsk, Russia), Bogomoletz Institute of Physiology (Kiev, Ukraine), and Bielefeld University (Bielefeld, Germany).

Further information:
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