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TITLE

Pharmacogenomics of Alziemer's Disease

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Recent advances in genomic medicine can contribute to accelerating our understanding on pathogenesis of dementia, improving diagnostic accuracy with the introduction of novel biomarkers, and personalizing therapeutics with the incorporation of pharmacogenetic and pharmacogenomic procedures to drug development and clinical practice.

Most neurodegenerative disorders, including Alzheimer's disease(AD),share some common features, such as a genomic background in which hundreds of genes(more than 200 genes) might be involved, genome-environment interactions, complex pathogenic pathways, poor therapeutic outcomes and chronic disability.

The AD population exhibits a higher genetic variation rate than the control population with absolute and relative genetic variations of 40-60% and 0,85- 1,89%, respectively. AD patients also differ in their genomic architecture from patients with other forms of dementia. Functional genomic studies in AD revealed that age of onset, brain atrophy, cerebrovascular hemodynamics, brain bioelectrical activity, cognitive decline, apoptosis are associated with AD- related genes.

Pioneering pharmacogenomics studies also demonstrated that the therapeutic response in AD is genotype-specific, with apolipoprotein E(APOE 4/4 carriers the worst responders to conventional treatments. Pharmacogenetic and pharmacogenomic factors may account for 60-90% of drug variability in drug disposition and pharmacodynamics.

The main aim of a cost-effective treatment is to halt disease progression via a modification of the functional cascade involving AD genomics, transcriptomics, proteomics and metabolomics. Unfortunately, the drugs available for the treatment of dementia are not cost-effective.

The incorporation of pharmacogenetic/pharmacogenomic protocols to AD research and clinical practice can foster therapeutics optimization by helping to develop cost-effective pharmaceuticals and improving drug efficacy and safety.

Biography

In the years 1978-1981 doctoral studies at Wroclaw Medical University Psychiatric Clinic crowned with conferring a doctor's degree and a scientific award from the Medical University Rector in 1981 Title of doctoral thesis: Behaviour of arginase activity in the cerebrospinalis fluid and blood serum of schizophrenic patients treated with neuroleptic drugs and in experimental tests on animals.

2001-2004 -grant from the Polish Ministry of Health Research Committee entitled:" Significance of AGE products in early diagnosis and clinical progress of Alzheimer's disease" A project run jointly by the Psychiatric Clinic and the Polish Academy of Sciences Institute of Immunology and Experimental Therapy in Wroclaw.Principal Investigator: Jerzy Leszek, M.D., Ph.D.

2000- 2003-Medical University grant towards the cost of the project entitled: Oxidation stress in Alzheimer's disease. Assessment of the activity of supraoxide dismutase(SOD-1) and of the catalase, peroxidase and reductase of the glutathione-the connections with the patient's age and the stage of the disease.