

P03-04

GENOMICS, TRANSCRIPTOMICS AND METHYLOMICS: ALTERNATIVE APPROACHES FOR THE ANALYSIS OF SEROTONIN SYSTEM AND ANTIPSYCHOTIC RESPONSE

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Serotonin receptors blockade is the major basis for the action of atypical antipsychotic drugs. Genetic factors affecting the density and/or function of serotonergic receptors, transporters and enzymes may therefore affect antipsychotic response. This exploratory study investigates the effect of ten polymorphisms from HTR1A, HTR1D, HTR2A, HTR3A, HTR3B, HTR4, HTR6, SLC6A4, TPH1, TPH2 genes on antipsychotic response in a sample of 289 patients with DSM-diagnosis of schizophrenia. Clinical Response was assessed using Brief Psychiatric Rating Scale (BPRS). Response was determined as 20% reduction improvement of BPRS compared to baseline. Selection of the biological relevant interactions, regardless the phenotype was performed using different statistics strategies regardless the phenotype to investigate epistasis within the serotonin system. The test for relevant interaction selection showed that 5HT4 and 5HT6 can be in epistatic relationship. The single locus analysis of these two receptor polymorphisms showed no significant results and the logistic regression model incorporating both genes, the clinical and demographic variables was not significant. Even this result is not significant, this strategy aimed to investigate the epistatic effect among genes could be useful for finding relevant biological interaction among genetic variants. Furthermore we are currently analyzing the methylation level of HTR2A in responders and non-responders, this epigenetic analysis will be very valuable in adding more information to the classic pharmacogenetic studies.