S03-01 - **THE IMMUNOLOGICAL BACKGROUND OF MAJOR DEPRESSION: A GENETIC STUDY**

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Immune system dusfunction is a consistent finding in mood disorder research. One of the relevant metabolic pathways in this regard is the kynurenine pathway which forms a bridge between immune activation, serotonergic deficiency and disturbed NMDA-R function. Given the potential importance of the kynurenine pathway in the pathogenesis of MDD, a SNP based gene association analysis was undertaken, focusing on three major players in this pathway: the genes coding for Trytophan Hydroxylase 2 (neuronal THP, TPH2), Kynurenine-3-MonoOxygenase (K3MO), and Kynurenine AminoTransferase III (KATIII). In order to assess the potential role of these three genes, SNP maps covering the gene were constructed, and single SNP and haplotype association analyses were performed in a sample of 338 German patients with mood disorders and 310 control individuals matched for age, ethnicity and gender.

At the single SNP level, SNP rs1053230 in the K3MO gene shows borderline significant evidence for association. Looking at the haplotype analysis (using the Plink program), the KATIII gene showed significantly different overall haplotype distributions (OMNIBUS) between patients and control individuals for all windows (p-values between 1.75×10^{-5} and 0.006). These findings were mainly due to an overrepreseantation of the CGCTCT risk haplotype, with a frequency of 7,1% in bipolar patients, 5,3 % in MDD patients and 1,9% in healthy control individuals.

The identification of a KATIII risk haplotype for mood disorders should be considered preliminary. A next step would be to completely sequence the KATIII promoter, exons and intron-exon-boundaries in patients carrying the risk haplotype.

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