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**IMMUNE CELLULAR SYSTEM ACTIVATION AND HUMAN LEUKOCYTE ANTIGENS
EXPRESSION IN ITALIAN SCHIZOPHRENIC PATIENTS TREATED WITH CLOZAPINE**

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Clozapine is an atypical antipsychotic drug with absolute indications for the treatment of drug-resistant schizophrenia and of patients who are unable to tolerate traditional antipsychotic medications. Additionally, clozapine is considered more efficient than traditional antipsychotic drugs. However, its use has been limited mainly because of the idiosyncratic drug-induced agranulocytosis that occurs in approximately 1% of the population treated with the drug (Turbay et al, 1997).

Genes of the Major Histocompatibility Complex (MHC) are associated with susceptibility to different immune and nonimmune mediated diseases. Hence the effects of antipsychotic drugs on immune system are very likely linked to the drugs' immunological side effects, suggesting the existence of a possible immune system contribute to the clinical outcome (Pollmacher et al, 2000; Turbay et al, 1997).

The soluble Intercellular Adhesion Molecule-1 (sICAM-1) and the Tumor Necrosis Factor (TNF) are markers for the activation of the cellular immune system (Schwarz et al, 2000; Corti et al, 1998). Furthermore the T-Cell antigen Receptor (TCR) activates mature extrathymic T cells. TCR signaling commences with an early wave of protein tyrosine kinase activation, which is mediated by the Src kinases Lck and Fyn, the 70-kd zeta-associated protein kinase and members of the Tec kinase family. This early wave of protein tyrosine phosphorylation leads to the activation of downstream signaling pathways, which ultimately lead to the expression of genes that control cellular proliferation (Nel, 2002).

Recently it has been suggested that HLA -A2 and HLA-B35 antigens behave like independent predictors of clozapine responsiveness in Italian schizophrenic patients refractory to treatment (Marchini et al, 2001). The aim of this study is to correlate the activation of the cellular immune system, using both the levels of TNF and sICAM-1 and the TCR signaling pathways, to HLA antigens expression in Italian schizophrenic patients treated with clozapine.

References

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