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Gene expression profiles and protein-protein interaction network analysis in AIDS patients with HIV-associated encephalitis and dementia

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Central nervous system dysfunction is an important cause of morbidity and mortality in patients with Human Immunodeficiency Virus (HIV) infection and the Acquired Immunodeficiency Virus Syndrome (AIDS). Patients with AIDS may or may not present HIV-Associated Encephalitis (HIVE) with viral replication limited to cells of monocyte origin. In order to examine molecular mechanisms underlying HIVE-induced dementia, the GSE4755 affymetrix data were obtained from the Gene Expression Omnibus database and the Differentially Expressed Genes (DEGs) between the samples from AIDS patients with and without HIVE-associated dementia were identified. In addition, Protein-Protein Interaction (PPI) networks were constructed by mapping DEGs into PPI data to identify the pathways that these DEGs are involved in. The results revealed that the expression of 1528 DEGs, which are mainly involved in immune response, regulation of cell proliferation, cellular response to inflammation and cell-cell signaling. The Heat Shock Protein Alpha (HSP90A) and Fibronectin 1 (FN1) were detected as hub nodes with a degree of >130. In conclusion, the results indicate that HSP90A and FN1 have important roles in the pathogenesis of HIVE-associated dementia.

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Azidobupramine: A novel chemical tool to enlighten antidepressants' mode of action

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Antidepressants were discovered in the 1950s but their underlying molecular mechanisms are still incompletely understood. Revealing the identity of additional targets may contribute to a better understanding of the antidepressants' mode of action. The aim of this study was to develop a chemically modified antidepressant enabling the identification of alternative direct drug targets. For this purpose, azidobupramine, a structurally related analogue of imipramine, was synthesized featuring two additional chemical groups, one for Photo-Affinity Labeling (PAL) and the other for Copper (I) Catalyzed Azide Alkyne Cycloaddition (CuAAC). Using the serotonin transporter as model target, we demonstrate that azidobupramine is characterized by equilibrium dissociation constants (Ki) equivalent to those of clinically active substances. Furthermore, we show that azidobupramine forms chemical bonds with the transporter after UV light exposure in living cells. Thus, azidobupramine represents a promising and versatile tool for the discovery of novel direct antidepressant target sites in living systems.

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