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Treatment with AMD3100 beneficially affects pathology in 3xTg-mice model of Alzheimer's disease

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Senile plaques and neurofibrillary tangles cause synaptic dysfunction and loss of neurons in the brain of Alzheimer's disease (AD) patients, accompanied by inflammatory processes. Tumor necrosis factor α (TNF α), a multipotent cytokine, is considered as a "Master Regulator" of the immune response in the central nervous system and modulator of glutamate toxicity. This effect is enhanced when activated microglia cooperates to release the cytokine in response to CXCR4 stimulation which is increased in tissue of AD patients. CXCR4 is a chemokine receptor which belongs to the G-protein-coupled receptors family and is selective for the CXCL12 ligand. The axis of CXCR4/CXCL12 has a prime role in various physiological routes and mechanisms and release TNF α from astrocyte cell surface. Another mechanism which is being mediated by CXCR4/CXCL12 is homing and mobilization of hematopoietic stem and progenitor cells (HSPCs). Under basal conditions TNF α signaling negatively regulates HSPCs repopulating activity. AMD3100 is a FDA approved, small bicyclam molecule that reversibly and selectively blocks binding of CXCL12 to its receptor CXCR4. The binding of AMD3100 to CXCR4 mobilize HSPCs from the bone marrow into the blood. We chronically treated the triple transgenic mice model (3xTg-AD) which demonstrates age-dependent changes in TNF α mRNA levels with AMD3100. The data presented here suggests the potentiality of AMD3100, to modulate the TNF α , to improve the cognitive functions, to decrease pathology and to offer a chance of a cure for AD.

Biography

Beka Solomon has earned her PhD in 1976 from the Weizmann Institute of Science, Rehovoth, Israel. She has joined Tel-Aviv University in 1979 following Post-doctoral studies and training periods at Harvard Medical School and Brigham and Women's Hospital, Boston, USA. She is a Member of the Editorial Board of *Drugs of Today*, *Recent Patents on CNS Drug Discovery*, *Neurodegenerative Diseases* and *Journal of Alzheimer's Disease*. She was awarded the prestigious Zenith Award of the Alzheimer Association and received the Dana Foundation Award for Neuroimmunology. In 2007 she was included in Scientific American's List of 50 of the World's Leading Innovators.

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