Daniela M. Moutinho et al., J Trauma Stress Disor Treat 5:4
http://dx.doi.org/10.4172/2324-8947.C1.006

Searching for the human VGF-derived antidepressant neuropeptide TLQP-62 receptor: HSPA8/ TLQP-62 complex

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Chronic mental disorders, as schizophrenia, bipolar disease or major depression, affect about 10% of the world population. DISC1 (DIsrupted In SChizophrenia 1) protein is truncated in a Scottish family with a high prevalence of Chronic Mental Illness and forms insoluble aggregates in a subset of cases of mental disease[1]. DISC1 regulates the expression of VGF, a neuropeptide precursor with potent antidepressant and neurotrophic properties[2].

This neuropeptide, specific of the central and peripheral nervous systems, is synthesized in neuronal cells of the cortex, hypothalamus, hippocampus and cerebellum. It is the precursor for multiple peptides with different activities in synaptic plasticity, neurogenesis, glucose and energy balance, among others. VGF's involvement in affective disorders have been described and the VGF-derived 62 amino acid peptide TLQP-62 shows an acute antidepressant effect in behavioural mice models of depression enhancing neurogenesis at the hippocampus[3][4][5]. To better understand TLQP-62 role in the nervous system and its antidepressant properties, efforts to find a receptor and to unveil its structure and signalling pathway are being made.

To search for a possible TLQP-62 receptor in the human brain, a crosslinker is used to link biotinylated TLQP-62 to the possible receptor present in human hippocampus homogenate and human neuroblastoma derived cells SHSY-5Y. The putative receptor is trapped in an avidin column and identified by separation in SDS-PAGE and western blotting, followed by mass spectrometry.

We found HSPA8 to be a binding partner of TLQP-62. This constitutively express chaperone is critical for cell survival and is downregulated in patients suffering from depression and schizophrenia[6]. Thus, this protein seems to be an interesting target for further studies concerning chronic mental disorders molecular mechanisms and treatments.

Biography

Daniela Moutinho is a PhD student of the Marie Curie Research Training Network IN-SENS "Deciphering inter and intracellular signaling in schizophrenia", focusing on exploring the connection between DISC1 and VGF proteins in chronic mental disorders, by performing proteomic studies on cellular models.

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