

Research Group: ChemSynBio Lab

Project: DISCOVERY OF A NEW PATHWAY FOR THE ACTIVATION OF THE NEURONAL GROWTH FACTOR BDNF INVOLVED IN ALZHEIMER'S DISEASE

Brief description:

Brain-derived neurotrophic factor (BDNF) is an essential factor of the nervous system and plays an important role in synaptic formation and neuronal survival. On the other hand, a decrease in BDNF levels is believed to be involved in the onset of Alzheimer's disease and neuronal aging. Therefore, it is crucial to understand the molecular mechanisms responsible for maintaining optimal levels of BDNF in the brain.

BDNF is initially synthesized as an inactive form known as proBDNF, and its activation requires the action of an enzyme called plasmin. Plasmin cleaves a small peptide from proBDNF, resulting in the release of mature and active BDNF (mBDNF). Notably, the brain has been found to contain another enzyme called neurotrypsin, which shares similarities with plasmin and trypsin, an enzyme commonly found in the digestive system. Although the exact reason for the presence of neurotrypsin in the brain remains unknown, it is understood that mutations in this enzyme can lead to mental retardation.

Preliminary laboratory data suggests that neurotrypsin may play a role in activating BDNF into its mature form. The discovery of neurotrypsin's involvement in BDNF activation could open up an entirely new field of research focusing on diseases like Alzheimer's disease as well as neuronal aging. Furthermore, it has the potential to pave the way for exploring novel therapeutic approaches to treat dementia. The primary objective of this Master Thesis proposal is to determine the specific role of neurotrypsin in the activation of BDNF.

Objective:

The primary objective of this Master Thesis proposal is to determine the specific role of neurotrypsin in the activation of BDNF.

Technical skills:

This research will involve initially the expression and purification of neurotrypsin followed by the biophysical characterization of the efficiency of proBDNF activation by plasmin, trypsin, and neurotrypsin at different times and concentrations. This activation will be measured through SDS-PAGE, western blot, and mass spectrometry. Once the activation is characterized, the study of the effect of active BDNF on cell cultures will be initiated.

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