

Novel approaches for treating neurodegenerative diseases

Merja Voutilainen

University of Helsinki, Finland

The prevalence of neurodegenerative diseases such as Amyotrophic lateral sclerosis (ALS) and Parkinson's disease (PD) is growing rapidly. Current treatments cannot stop the progression of the disease, thus there is an urgent need for new therapies. Neurotrophic factors (NTFs) are secretory proteins that regulate the survival of neurons, neurite growth and branching. They have been explored as novel drugs for the treatment of ALS and PD but their efficacy in clinical trials has been poor. CDNF is a protein with NTF properties that protects and restores dopamine (DA) neurons in animal models of PD and increases motor coordination and protects motoneurons (MNs) in rodent models of ALS. CDNF was safe and showed therapeutic effects in PD patients in Phase I/II clinical studies. However, a major limitation of NTFs and CDNF is the need for direct delivery into the brain. Drug delivery across the blood brain barrier (BBB) is a key unmet need in neurological drug development. I have shown that a novel CDNF fragment protects MNs and DA neurons in vitro and in vivo. Furthermore, our data show that CDNF fragment can pass through the BBB as measured by three different methods and has a neurorestorative effect in genetic mouse model of ALS and in 6-OHDA rat model of PD when administered subcutaneously. The ultimate goal of my research is to understand the mode of action and therapeutic effect of novel BBB penetrating CDNF-derived polypeptides. The innovative aspect of this study is the new ground-breaking concept for treating neurodegenerative diseases.