

Microtubules are hollow cylindrical protein polymers that together with intermediate filaments and actin filaments comprise the cytoskeleton of eukaryotic cells. In neurons, microtubules participate in many vital functions, such as the axonal transport of intracellular cargo and the differential distribution of proteins to distinct neuronal domains. In the experimental part of my thesis, I investigated the intracellular distribution of microtubule-associated protein 2B (MAP2B) in rat neurons. Together with MSc Patrik Hollos we identified a novel dendrite targeting motif from MAP2B.

MAP2 is the most abundant microtubule-stabilizing protein in the mature mammalian brain. The high molecular weight isoforms of this protein, MAP2A and MAP2B, are strictly targeted to the neuronal somata and dendrites. The molecular mechanisms behind this specific distribution are still largely unknown. We investigated this targeting by creating several deletion mutants from rat MAP2B, which were then fused with green fluorescent protein (GFP) and transfected to rat hippocampal neurons. The intracellular distribution of these mutants was studied with fluorescent microscopy and quantified by measuring the GFP fluorescence intensity in dendrites and axons. We identified a MAP2B deletion mutant of 67 amino acids that is sufficient to target the GFP tag to dendrites..

In the literature review part of my thesis, I explored the significance of microtubules to neurons and their dysfunction in neurodegeneration. Mounting evidence suggests that microtubule dysfunction is among the earliest pathological changes in many neurodegenerative diseases. A common feature in these diseases is the destabilization of neuronal microtubules, leading to impaired axonal transport and thus deterioration of the distal parts of axons. Pharmacological stabilization of microtubules has therefore been investigated as therapy for neurodegeneration, with some promising results.

Avainsanat: microtubule, neuron, neurodegeneration