

2 Abstract

Neurotrophins are growth factors. In mammals, they exert a broad range of modulatory effects on developing as well as on mature neurons. Neurotrophin-mediated signals are transduced by either the neurotrophin receptor $p75^{\text{NTR}}$ or the receptor tyrosine kinases TrkA, TrkB and TrkC. Whereas signaling via the Trk-receptors is quite well understood, even 10 years after its identification there was little known about the function and signaling pathways of $p75^{\text{NTR}}$. The aim of this work was therefore to identify intracellular interactors of $p75^{\text{NTR}}$. A biochemical approach was chosen, as was previously applied to related proteins of the TNFR-family. Three different purification strategies were used: 1) purification of the $p75^{\text{NTR}}$ -interactor complex in the presence of its extracellular ligands, 2) affinity purification via the intracellular domain of $p75^{\text{NTR}}$ and 3) enrichment of the $p75^{\text{NTR}}$ -interactor complex in characterized subcellular fractions.

In addition, new antisera against $p75^{\text{NTR}}$ were generated and characterized. One antiserum recognized additional $p75^{\text{NTR}}$ -like signals on Western blot. Surprisingly, these signals remained strongly detectable in brain homogenates of a partial as well as a complete $p75^{\text{NTR}}/-$ knock out mouse. The $p75^{\text{NTR}}$ -like antigens were expressed exclusively in the central nervous system, were strongly downregulated during postnatal development and showed calcium-dependent segregation during centrifugation. In addition, a $p75^{\text{NTR}}$ -like binding site was detected in dissociated dorsal root ganglia of the complete $p75^{\text{NTR}}$ knock out mouse. The $p75^{\text{NTR}}$ -like antigens were purified, identified as the N-terminus of the microtubule associated protein MAP1B and the homology to $p75^{\text{NTR}}$ was investigated.