

P003 Characterization of symmetric complexes of nerve growth factor and the ectodomain of the pan-neurotrophin receptor, p75^{NTR}

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Nerve growth factor is the ligand for two unrelated cellular receptors, TrkA and p75^{NTR}, and acts as a mediator in the development and maintenance of the mammalian nervous system. Signaling through TrkA kinase domains promotes neuronal survival, whereas activation of the p75^{NTR} “death domains” induces apoptosis under correct physiological conditions. However, co-expression of these receptors leads to enhanced neuronal survival upon NGF stimulation, possibly through a ternary p75^{NTR}:NGF:TrkA complex. We have expressed human p75^{NTR} ligand-binding domain as a secreted glycosylated protein in *Trichoplusia ni* cells. Following assembly and purification of soluble p75^{NTR}:NGF complexes, mass spectrometry, analytical ultracentrifugation and solution X-ray scattering measurements are indicative of 2:2 stoichiometry, which implies a symmetric complex. Molecular models of the 2:2 p75^{NTR}:NGF complex based on these data are not consistent with the further assembly of either symmetric (2:2:2) or asymmetric (2:2:1) ternary p75^{NTR}:NGF:TrkA complexes.