

Sehgal, R. N. M, and I. J. Lovette. 2003. Molecular evolution of three avian neurotrophin genes: Implications for proregion functional constraints. *Journal of Molecular Evolution* 57: 335-342.

Neurotrophin proteins are essential for the survival, differentiation, and maintenance of neurons in the peripheral and central nervous systems. Recent studies have shown that the unprocessed proforms of the neurotrophins are preferential high-affinity ligands for p75(NTR) and potent inducers of p75(NTR)-mediated cell death. Here, we explore differences in the selective constraints acting on the proregions of the three avian neurotrophin genes-NT-3, BDNF, and NGF-in an explicit phylogenetic context. We found a 50-fold difference in levels of constraint as estimated by d(N)/d(S) ratios, with the NGF proregion showing the lowest degree of constraint and BDNF the highest. These patterns suggest that the high conservation exhibited by the BDNF proregion results from intense functional constraints that are relaxed in NGF and somewhat relaxed in NT-3. The proregion of BDNF is likely to have a function that differentiates it from the corresponding regions of the NGF and NT-3 genes, suggesting that BDNF is the avian neurotrophin most likely to be used both in its precursor and mature forms in vivo.