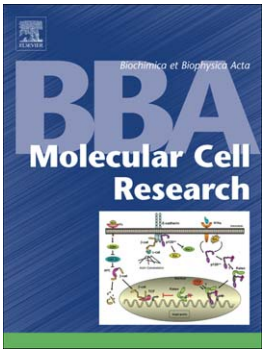

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GDNF family ligand dependent STAT3 activation is mediated by specific alternatively spliced isoforms of GFRα2 and RET

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Abstract:

Neurturin (NRTN), a member of the GDNF family of ligands (GFL), is currently investigated in a series of clinical trials for Parkinson's disease. NRTN signals through its cognate receptor GFRα2 and co-receptor RET to induce neurite outgrowth, but the underlying mechanism remains to be better understood. STAT3 was previously shown to be activated by oncogenic RET, independent of ligand and GFRα. In this study, we demonstrated that NRTN induced serine[727] but not tyrosine[705] phosphorylation of STAT3 in primary cortical neuron and neuronal cell lines. Remarkably, STAT3 phosphorylation was found to be mediated specifically by GFRα2c and RET9 isoforms. Furthermore, serine but