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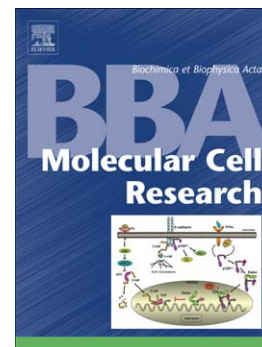
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GDNF family ligand dependent STAT3 activation is mediated by specific alternatively spliced isoforms of GFR α 2 and RET

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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 GFR α 2 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 GFR α . In this study, we demonstrated that NRTN induced serine⁷²⁷ but not tyrosine⁷⁰⁵ phosphorylation of STAT3 in primary cortical neuron and neuronal cell lines. Remarkably, STAT3 phosphorylation was found to be mediated specifically by GFR α 2c and RET9 isoforms. Furthermore, serine but

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