Lithium ions: a novel treatment for pheochromocytomas and paragangliomas.

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Abstract

BACKGROUND: Operative resection is the only curative treatment for patients with pheochromocytomas, paragangliomas, and other catecholamine-producing neoplasms. Activation of glycogen synthase kinase 3beta (GSK3beta) is thought to promote tumor growth and neuroendocrine (NE) peptide secretion in NE neoplasms. Thus, we hypothesized that inhibition of this signaling pathway with lithium chloride (LiCl), a well-known GSK3beta inhibitor, could be a potential therapeutic strategy to control tumor growth and hormone production. METHODS: Pheochromocytoma PC-12 cells were treated with varying concentrations of LiCl (0 to 30 mM). Levels of active and inactive GSK3beta and NE peptides chromogranin A (CgA) and Mash1 were determined by Western blot. Cellular growth was measured by MTT cell-proliferation assay. RESULTS: At baseline, PC-12 cells had increased active GSK3beta signaling. Treatment of PC-12 cells with increasing dosages of LiCl resulted in dose-dependent inhibition of GSK3beta. Importantly, LiCl inhibited pheochromocytoma cellular proliferation significantly. Furthermore, inhibition of GSK3beta by LiCl was associated with marked suppression of CgA and Mash1 levels. CONCLUSIONS: These data suggest that GSK3beta inhibition may be a novel strategy to treat pheochromocytoma and other catecholamine-producing neoplasms.

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