In vitro mechanisms involved in the regulation of cell survival by lithium chloride and IGF-1 in human hormone-dependent breast cancer cells (MCF7).


Source
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Abstract
Lithium, the lightest of all solid elements, has been used for the treatment of bipolar disorder since 1970s and prescribed to millions of women worldwide. Lithium chloride (LiCl) has been considered to be a potent inhibitor of glycogen synthase kinase-3β (GSK-3β), a serine/threonine kinase that is involved in the control of cell proliferation, differentiation, and apoptosis. In addition, GSK-3β has been found to be inhibited endogenously by insulin-like growth factor-1 (IGF-1), a potent mitogen that plays an important role in the survival, growth, and differentiation of normal and neoplastic cells. Although both IGF-1 and LiCl have the ability to inhibit GSK-3β, the specific signaling difference that mediates the survival of breast cancer cells was not clear. Therefore, in the present study, MCF-7 cells (human breast cancer cells) were treated with or without IGF-1 or LiCl in the presence or absence of LY294002 or PD98059 (pharmacological inhibitors) for 24h. As the expression of signaling proteins is crucial in the maintenance of cell survival and apoptosis, we analyzed the cells using immunoblotting procedure. In summary, our results have shown that LiCl and IGF-1 mediates cell survival by inhibiting GSK-3β but differ in their mechanisms. IGF-1 involves PI3K/Akt or MAPK pathways whereas LiCl is completely independent of these pathways. IGF-1 upregulates anti-apoptotic proteins whereas LiCl downregulates apoptotic proteins in order to maintain cell survival.

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