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Effect of therapeutic concentration of lithium on living HEK293 cells; alteration of overall protein composition

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Despite abundant clinical use of lithium (Li) in pharmacotherapy of bipolar disorder, important questions regarding its mechanism of action remains open. One of the organs most adversely affected by Li therapy is the kidney. In order to characterize the long-term effect of Li on live cells, Human embryonic kidney (HEK293) cells were cultivated for 7 and 21 days in the presence of 1 mM LiCl and overall protein composition and alteration of Na^+/K^+-ATPase level was determined by proteomic analysis, immunoblot assays and radioligand binding. We have also tested biophysical state of plasma membrane (PM) lipid bilayer after Li treatment. Resolution of post-nuclear fraction by 2D-ELFO indicated decrease of 8 proteins after 7 days of Li exposure. This number was increased to 21 after 21 days of Li exposure. Identification by MALDI-TOF MS/MS indicated major reorganization of energy metabolism proceeding in mitochondria and cytosol and alteration of cytoskeleton structure, cellular response to calcium, ubiquitin conjugation pathway, protein synthesis, gene expression and mRNA processing; 5 proteins functionally related to oxidative stress were decreased. Identification of altered proteins by LFQ method revealed the decrease of 4 calcium binding proteins functionally linked to apoptosis and cell adhesion. Na+/K+-ATPase was significantly increased in PM isolated from HEK293 cells exposed to Li for 7 and 21 days. Biophysical analysis of isolated PM by fluorescence probes indicated significant effect of Li on the surface, polar head-group region of PM lipid bilayer. Hydration of this area of PM was decreased.

Biography

Miroslava Vosahlikova has completed her PhD from Charles University in Prague. She is a Junior Scientist in Laboratory of Biochemistry of Membrane Receptors, Department of Biomathematics, Institute of Physiology of the Czech Academy of Sciences in Prague. She has published in reputed journals.

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