ABSTRACT

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Zinc induced activation of breast cancer cell lines and the involvement of MAP kinase

The aim of this work was to investigate the effect of zinc on various signalling pathways in breast carcinoma cell lines MCF7 and TamR cells. The differences between signalling pathways in MCF7 cell line and TamR cells were evaluated with a special focus on a role of MAP kinase, which activation is believed to be linked with malignant diseases.

An effect of zinc on various cellular kinases in 0, 2, 5, 10, 15 and 20 minute of zinc treatment was analyzed in MCF7 cells transfected by wild and mutant type of ZIP 7, TamR cells and TamR cells pre-treated with MAP kinase inhibitor (PD) using the methods of western blotting and fluorescent microscopy.

We show here the dependence of activation of pMAP kinase and other important oncogenic kinases (such as Lyn, Src and STAT3) on zinc release into cytoplasm. According to our results, MAP kinase is activated very upstream and it can stimulate many important protein kinases as Src Y^{418}, STAT3 S^{727} and Lyn Y^{396} in tamoxifen-resistant breast cancer cells. On the other hand the dependence of activation of pAKT Y413 on pMAP kinase wasn't proved. We conclude that the inhibitors of the zinc release from the perinuclear storages could specifically suppress the zinc dependent activation and invasiveness of breast cancer. Therefore, zinc transporters could serve as new targets in treatment of tamoxifen resistant breast cancer in future and it is worth further investigation.