عنوان مقاله:

Critical and synergy nodes in insulin-EGF signaling network

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خلاصه مقاله:

Signaling pathways are not isolated from their surroundings. They are also intervened by other signaling pathways known as crosstalk mechanism . One of the most important crosstalk mechanisms is the insulin-EGF network. Although insulin and epidermal growth factor (EGF) networks have some complexity in theirisolated forms, their complexities will grow in the crosstalk network. In this study, we used the analytical toolsof the systems biology workbench for elucidating some ambiguities of the insulin-EGF crosstalk. Based on sensitivity analysis, we reconstructed an elucidated model with 51 chemical reactions in comparison with the previous model with 111 chemical reactions. Interestingly, this reduced model reproduces the results of theoriginal model in synergy conditions. We noticed two controlling pathways with direct participation ofphosphorylated insulin and EGF receptors that involve Insulin Receptor Substrate (IRS) and Src kinase modules. Also, insulin pathway by producing phosphatidylinositol-3, 4, 5-triphosphate (PIP3), and EGF pathway by activation of GAB1, control the downstream events and lead to potentialities in the mitogenicsignal. Surprisingly, Shc and phosphatase SHP2-dependent reactions have no significant roles in the synergy conditions and are not involved in the reduced model. Regarding sensitivity analysis, all Ras/ERK cascade reactions are crucial for signal transduction and were kept in the reduced model

کلمات کلیدی:

Signaling pathways, crosstalk, computational modeling, systems biology, insulin-EGF networks,sensitivity analysis, targeted drug therapy