

Scaffold蛋白介导细胞信号转导专一性的定量分析

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细胞只使用相对有限的蛋白质组分传递大量的信号,因此不同的信号通常由相同的蛋白质组分传递。这些蛋白质组分是如何选择性的参与不同的信号通路,如何“高保真”的传递不同的刺激,从而产生特定的细胞应答,是目前细胞生物学领域中的研究热点和难点之一。鉴于Scaffold蛋白在确保信号转导专一性和保真性中的关键作用,本文基于酵母*S. cerevisiae*的生物学实验数据,建立了由Scaffold介导的MAPK(mitogen activated protein kinase, 丝裂原活化蛋白激酶)级联信号转导网络的数学模型,简单的数值模拟结果与酵母实验结果是一致的。利用文[1]给出的信号转导“专一性(specificity)”和“保真性(fidelity)”的精确的数学定义,计算了MAPK信号网络的专一性和保真性的解析解和数值解。用这些解可以定量分析细胞信号转导专一性、保真性与信号通路各种动力学参数(输入信号的强度和反应率、磷酸化和去磷酸化系数、降解系数等)之间的关系,从理论上阐述了隔离(sequestration)和选择性激活(selective activation)等机制是如何增强信号转导网络的专一性和保真性。从而有助于我们加深对细胞信号转导及其调控过程的系统理解,为揭示某些因细胞信号转导异常所致疾病的发生机理和寻找治疗药物提供新的思路。

The Quantitative Analysis of Specificity in Scaffold-mediated Cell Signaling

Cells use only a relatively limited number of component proteins to transmit a plethora of signals. Accordingly pathways that transduce distinct signals can share protein components. An important yet poorly understood problem in cell and developmental biology is how these component proteins selectively perceive different signaling pathways to transmit different stimuli with “high fidelity” so that distinct signals produce specific cellular response? Current data indicate that scaffold proteins play key roles in the maintenance of specificity and fidelity, hence, based on experimental data, the mathematical models of the yeast mating, invasive growth and stress-responsive MAPK cascades for scaffolding-mediated are developed, the results of numerical simulation are consistent with those of experiment data. Motivated by this perspective, we calculate the analytic solutions and numerical solutions of MAPK cascade networks by using the precise mathematical definition of “specificity” and “fidelity” in interconnected biochemical pathways proposed in literature[1], We can use these results to quantitatively analyze the relationship between “specificity”, “fidelity” and kinetic parameters in signaling pathways. It may help to understand cell signaling mechanisms and regulatory processes, and provide a rationale for revealing mechanisms of diseases caused by abnormalities of signal transduction, and novel tools for the prevention and treatment of disease.

关键词

信号转导(Cell Signaling); 数学模型(mathematical model); 专一性(specificity); 保真性(fidelity); scaffold 蛋白(scaffold protein)