

T细胞活化的动力学模型

张伟、杨先清、漆安慎
北京师范大学物理系

T细胞表面DIGs (detergent-insoluble glycolipid-enriched domains) 在细胞活化过程中的作用正成为研究的热点问题, 为了证实受触发的TCR (T cell receptor) 向DIG中聚集的重要性, 以及PTKs (protein tyrosin kinases) 参与T细胞活化信号转导的机制, 提出了一个定性的理论模型, 在TCRs的连续触发模型基础上, 研究了T细胞活化早期TCR与其特异性配体的相互作用机制, 及辅助受体CD4/CD8在细胞膜上“免疫突触”形成过程中的作用, 解释了不同配体对最终T细胞活化结果的影响。研究表明, TCR与配体的结合亲和力、TCR与配体复合物的离解率、以及辅助受体间的相互作用是T细胞的活化过程中的重要参数, 对于一定的T细胞克隆, 其特异性配体与其TCR-pep复合物的离解率, 决定了这一配体究竟是显效剂抑或是拮抗剂。辅助受体CD4/CD8参与识别配体的同时, 又可以通过它与TCR-pep复合物的相互作用, 改善配体对T细胞刺激信号的强度, 影响最终的活化结果。通过模型, 证明了TCR与配体复合物在DIG中的聚集是细胞活化的重要事件, DIG中的PTKs保证了活化信号的转导。

A DYNAMICAL MODEL DESCRIBING T CELL ACTIVATION

The function of DIGs (detergent-insoluble glycolipid-enriched domains) in the immune response has become a focus of discussion in immunology. A theoretical model is proposed in this paper which accounts for the interaction of TCR with its ligand to confirm the importance of the immunological synapse and the mechanism of sufficient PTKs recruitment in T cell activation. This model relies on a serial triggering model. The mechanism of interactions between the antigen-specific TCRs and their antigenic ligands is explored. The function of the co-receptors during the formation of the immunological synapse and the recognition of the antigen by the TCR is investigated. It is theoretically studied that subtle changes of ligands would influence the outcomes of T cell receptor ligation. Using this model, it is shown that the access affinity of TCR with ligand, the ligand dissociation rate from TCR-pep complex and the co-receptors play important roles in determining the outcomes of T cell activation. With respect to the certain ligand and certain T cell clone, the dissociation rate determines the ligand agonist or antagonist. In addition, through the interaction of CD4/CD8 with TCR-MHC/pep, the co-receptors change the dissociation rate of the complexes and consequently affect the outcomes of the immune response. The model proved that the oligomer of TCR-pep/MHC complexes in the DIGs is important while the sufficient PTKs within DIGs assure the signal transduction.

关键词

亲和力(Affinity); TCR; DIGs; PTKs