A unifying mathematical framework for experimental TCR-pMHC kinetic constants

J. Faro Rivas; M. Castro Ponce; C. Molina París

Abstract-

Receptor binding and triggering are central in Immunology as T cells activated through their T cell receptors (TCR) by protein antigens orchestrate immune responses. In order to understand receptor-ligand interactions, many groups working with different experimental techniques and assays have generated a vast body of knowledge during the last decades. However, in recent years a type of assays, referred to as two-dimensional or membrane-to-membrane, has questioned our current understanding of the role of different kinetic constants (for instance, on- versus off-rate constants) on TCR-ligand interaction and subsequent T cell activation. Here we present a general mathematical framework that provides a unifying umbrella to relate fundamental and effective (or experimentally determined) kinetic constants, as well as describe and compare state-of-the-art experimental methods. Our framework is able to predict the correlations between functional output, such as 1/EC50, and effective kinetic constants for a range of different experimental assays (in two and three dimensions). Furthermore, our approach can be applied beyond Immunology, and serve as a «translation method» for the biochemical characterization of receptor-ligand interactions.

Index Terms- Computational models; Kinetics; Lymphocyte activation

Citation:
Faro, J.; Castro, M.; Molina-Paris, C. "A unifying mathematical framework for experimental TCR-pMHC kinetic constants", A unifying mathematical framework for experimental TCR-pMHC kinetic constants, vol.7, pp.46741-1-46741-12, .