Antigen valency controls the susceptibility of B cell activation to antibody feedback

A. Obraztsova[1,2,3], H. Wardemann[1], T. Höfer[2,3]

[1]German Cancer Research Center (DKFZ), B Cell Immunology, Im Neuenheimer Feld 280, 69120 Heidelberg, Germany
[2]German Cancer Research Center (DKFZ), Theoretical Systems Biology, Im Neuenheimer Feld 580, 69120 Heidelberg, Germany
[3]University of Heidelberg, Biosciences Faculty, Im Neuenheimer Feld 234, 69120 Heidelberg, Germany
a.obraztsova@dkfz.de

Abstract

Multivalent antigens appear in many immunological conditions, such as viral and bacterial infections and autoimmunity, and are remarkable for their ability to activate B cells by cross-linking B cell receptors. While B cell activation by cognate antigen has been much studied, the role of antigen valency remains to be defined quantitatively. To address this question, we developed a mathematical model linking B cell activation by antigens of varying valency to the abundance and affinities of B cell receptors and soluble competitor antibody. We found that suppression of the response to antigens with higher valencies requires higher concentrations of competitor antibody. To validate this finding experimentally we quantified antigen-induced activation of transgenic B cells expressing B cell receptors specific to an amino acid repeat motif (NANP) abundant on the surface of *Plasmodium falciparum* sporozoites. The activation by longer NANP repeat peptide tolerates higher concentrations of competitor antibody, thus confirming the theoretical prediction. This discovery is informative for improving the design of vaccines using multivalent antigens and provides a starting point for more comprehensive models of B cell responses *in vivo*.