Immunization Under Stress: Limits B Cell Clonal Expansion and Promotes Selection of Higher Affinity Antibody Variants

N. Ben-Shalom[1], E. Sandbank[2], S. Ben-Elyiahu[2], N.T. Freund[1]
[1]Department of Clinical Microbiology and Immunology, Sackler Faculty of Medicine, Tel Aviv University, 6997801 Israel; [2]The Sagol School of Neurosciences, Gordon Faculty of Social Sciences, Tel Aviv University, 6997801 Israel
noamb1@mail.tau.ac.il

Adrenergic signaling plays a central role in physiological regulation, including modulation of processes in the immune system. However, the effects of adrenergic activation on antibody-mediated immune response remain unknown. Here, we investigate the effects of stress-induced β-adrenergic receptor activation on the B cell response at molecular and the systemic levels. We find that β-adrenergic agonist treatment of B cells from four convalescent SARS coronavirus-2 donors, reduced both membrane IgG expression and clonal expansion when the cells were stimulated *ex vivo* with spike receptor binding domain (RBD). Interestingly, B cells cultured in the presence of β-adrenergic agonist exhibited stronger binding to RBD, compared to B cells clones from control cultures, suggesting that clones under stress exhibit higher affinity. As a corollary, following ovalbumin immunization in mice, physiological stress during germinal center reaction phase increased the levels of antigen specific serum IgG, while reducing B cell clonal expansion and membrane IgG expression. These effects were completely abolished by treatment with the selective β2 adrenergic antagonist, ICI-118, 551. Our study suggests that under stress conditions selection of high affinity variants comes in the expense of clonal expansion.