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Strategies of Antibody Optimization During an Immune Response

Abstract:

At the onset of an infection by a pathogen, antibodies either neutralize the invader by binding to it, or tag it to be destroyed by the immune system. Either way, the capacity of recognition of a pathogen by antibodies is of paramount importance in providing a successful defense. Since this capacity is not always optimal, the immune system strives to create new antibodies possessing a high binding affinity towards the pathogen.

This is accomplished by an antibody evolution process which is launched at the appearance of the intruder. This process includes targeted mutation of the gene encoding the antibody binding region. Those events happen in localized structures called germinal centers, which form in lymphoid tissue during an immune response. There, antibody producing cells undergo fast rounds of proliferation, diversification and selection.

The accepted dynamics of germinal center growth is traditionally based on records of cross-sectional germinal center areas. Due to the broad distribution of these areas detected within single tissue sections, we argue that this inference is too simplified (Wicksell corpuscle problem). We conclude that mathematical modeling of germinal center dynamics and hence dynamics of the antibody optimization process should strive to grasp the dynamics and regulation of the whole ensemble of germinal centers rather than that of individual germinal centers. We then introduce a new mathematical model and discuss its results and implications.