

Deriving a germinal center lymphocyte migration model from two-photon data.

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Abstract

Recently, two-photon imaging has allowed intravital tracking of lymphocyte migration and cellular interactions during germinal center (GC) reactions. The implications of two-photon measurements obtained by several investigators are currently the subject of controversy. With the help of two mathematical approaches, we reanalyze these data. It is shown that the measured lymphocyte migration frequency between the dark and the light zone is quantitatively explained by persistent random walk of lymphocytes. The cell motility data imply a fast intermixture of cells within the whole GC in approximately 3 h, and this does not allow for maintenance of dark and light zones. The model predicts that chemotaxis is active in GCs to maintain GC zoning and demonstrates that chemotaxis is consistent with two-photon lymphocyte motility data. However, the model also predicts that the chemokine sensitivity is quickly down-regulated. On the basis of these findings, we formulate a novel GC lymphocyte migration model and propose its verification by new two-photon experiments that combine the measurement of B cell migration with that of specific

chemokine receptor expression levels. In addition, we discuss some statistical limitations for the interpretation of two-photon cell motility measurements in general.

Beteiligte Forschungseinheiten

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