Computational analysis of the effect of CCR7 and structures on T cell localization in lymph nodes

Humayra Tasnim, Janie R. Byrum, G. Matthew Fricke, Melanie E. Moses, and Judy L. Cannon

## Abstract

T cells play a vital role in eliminating pathogenic infections. To activate, T cells need to encounter dendritic cells (DCs) bearing cognate antigen in lymph nodes (LNs). Some studies have suggested that DC colocalization with high endothelial venules may facilitate T cell-DC interaction. Our work previously demonstrated that LNs contain “hotspots”, locations that are visited more frequently than can be explained by chance, that induce differential T cell motion. However, it was not previously clear what structures or signals contribute to hotspots, modulating T cell movement. Movement of T cells in LNs may be influenced by multiple cells types and structures in the LNs, including DCs, T cells crawling along fibroblastic reticular cells (FRCs), as well as entry points from high endothelial venules (HEVs). Here we use novel computational methods to determine whether T cell motility is influenced by DCs, FRCs, and/or HEVs. Mutual information is employed as an analysis tool, in addition to direct measurements, to determine whether T cells colocalize with DCs, FRCs, or HEVs. We then analyze whether a key motility chemokine receptor, CCR7, affects T cell colocalization with DCs and motility in LN hotspots. Our results show that mutual information analysis can shed light on T cell interactions with LN cell types and structures. We find that CCR7 deficiency has a marginally significant impact on the colocalization of naïve T cells with DCs. These results demonstrate that novel analytical approaches that combine in vivo imaging of T cell motion in LNs using two photon microscopy with computational modeling can reveal fresh insights into determinants that drive T cell motion leading to productive T-DC interactions.