Modeling migration and search strategy of immune cells.

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Cytotoxic T-lymphocytes (CTLs) and natural killer (NK) cells are the killer cells of the immune system and migrate actively within the tissues to find and eliminate potential dangers such as virus-infected and tumor cells. Upon target cell encounter, the killer cells form a tight connection with them called the immunological synapse that enables killing. However, how migration is regulated in these cells for a rapid finding of their target remains a central question in immunology. In this work we analyzed the migration of primary human CTLs and NK cells in 2 dimensions in the absence of external cues to mirror the early immune response where no signals guide the killer cells to their target. Our analysis of the mean square displacement and the velocity autocorrelation showed that CTLs and NK cells perform a persistent random walk. Additionally, cell shape analysis enabled us to establish a model for killer cell migration where the movement of the cell is determined by several independent internal “force generators”. Each of them can switch between an active and an inactive state independently. We found a correlation between the number of the “force generators” and the duration of their activity to the number and life time of lamellipodia. Furthermore numerical simulations revealed that the search time in a given space depends on the behavior of cells upon contact with boundaries. Thereby we found that a minimal search time can be reached depending on the persistence of the cells. We believe that simulation of migration and search strategy of killer cells will ultimately lead to an improved understanding of the immune response.