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Regulation of CD4$^+$ T cells by LFA-1/ICAM-1 interactions

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Increasing evidence points to important roles for accessory molecule interactions not only in T cell activation but also in the development of T cell effector functions, survival, and migration. Determining the influence of individual accessory molecules on CD4$^+$ T cell responses has been complicated by the fact that most mammalian cell types express a wide variety of cell-surface accessory molecules and potentially secrete various immunomodulatory molecules such as cytokines and chemokines. Thus, even with mammalian cell lines transfected with genes encoding defined cell surface molecules, it is difficult to exclude the possibility that the observed results are not influenced by other accessory molecules or cytokines. To simplify the analysis of individual accessory molecules, we use a system involving the expression of defined mammalian accessory molecule ligands and MHC class II molecules in nonmammalian, Drosophila cell lines. These cell lines are used as antigen presenting cells (APC) to present ovalbumin peptide to naïve D011 TCR transgenic CD4$^+$ T cells. This approach has been used to further dissect the varied effects of LFA-1/ICAM-1 interactions in CD4$^+$ T cell responses. In addition to showing an inhibitory effect of LFA-1/ICAM-1 interactions on IL-4 production during primary responses, we found a requirement for LFA-1 interactions in the production of diabetogenic CD4$^+$ cells in a murine model for type 1 diabetes. Though the mechanisms responsible for this effect are not yet clear, the differential production of key chemokines suggest that regulation of cell recruitment may be involved. We have also shown strong synergism between LFA-1 and the TNF receptor family member CD27 in providing costimulatory signals for the activation of naïve CD4$^+$ cell responses. In this latter system, our focus is on defining the unique contribution of the two receptors to cell growth and survival.

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