$CD4^+$ T CELL PLASTICITY ENGENDERS ROBUST IMMUNITY IN RESPONSE TO IL-12 CYTOKINE THERAPY

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Inciting the cellular arm of adaptive immunity has been the fundamental goal of cancer immunotherapy strategies, specifically focusing on inducing tumour antigen-specific responses by $CD8^+$ cytotoxic T lymphocytes (CTL). However, there is an emerging appreciation that the cytotoxic function of $CD4^+$ T cells can be effective in a clinical setting. Harnessing this potential will require an understanding of how such cells arise. In this study we use an IL12-transduced variant of the 70Z/3 leukaemia cell line, LV12.2, in a B6D2F1 (BDF_1) murine model system to reveal a novel cascade of cells and soluble factors that activate anti-cancer $CD4^+$ killer cells. We show that natural killer T (NKT) cells play a pivotal role by activating dendritic cells (DC) in a contact-dependent manner; soluble products of this interaction, including MCP-1, propagate the activation signal culminating in the development of $CD4^+$CTLs that directly mediate an anti-leukaemia response while also orchestrating a multi-pronged attack by other effector cells. A more complete picture of the conditions that induce such a robust response will allow us to capitalize on $CD4^+$ T-cell plasticity for maximum therapeutic effect.