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Dendritic Cells: Antigen Presenting Cells of T and B Lymphocytes

Cl-322 PRIMARY IMMUNE RESPONSE INDUCTION BY DENDRITIC CELLS

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Recently, we and others have identified antigens recognized by anti-melanoma cytotoxic T cells (CTL). These tumor-associated antigens provide potential targets for immunotherapy against melanoma. A key question is how immune responses against these antigens can be induced most efficiently. The potent antigen presentation capacity of dendritic cells renders them suitable for exploitation in the induction of these responses. We investigated the capacity of dendritic cells obtained from healthy donors to induce CTL responses against peptides derived from the melanocyte differentiation antigens gp100, tyrosinase or melan-A/Mart-1. For these purposes dendritic cells were generated by culturing highly enriched monocytes, obtained by centrifugal elutriation, in the presence of GM-CSF and IL-4 as described by Romani et al. (1994). When pulsed with peptides derived from the aforementioned antigens, these cells were able to induce a primary CTL response in vitro. Furthermore these CTL were capable of lysing melanoma cells, indicating that they recognized peptides derived from the melanoma differentiation antigens. These data demonstrate that CTL reactive with melanocyte differentiation antigens can be induced in healthy donors using dendritic cells.

While the powerful antigen presentation capacity of dendritic cells has been well documented, the mechanisms by which this is achieved have yet to be elucidated. We have employed the technique of differential display PCR in an attempt to identify novel proteins which are specific to dendritic cells and thus may account for the functional properties of these cells. This method allows for the selection of mRNAs which are differentially expressed in different cell types. Dendritic cell RNA, from at least three healthy donors, was compared to RNA from a panel of monocyte, B cell and T cell lines. Using multiple primer sets, numerous PCR products have been identified which appear to be specific to dendritic cells. Characterization of these cDNAs is ongoing and may provide insights into the role of dendritic cells in the induction of primary immune responses.