Synopsis of Original Research Paper

Dendritic cells differently respond to haptens and irritants by their production of cytokines and expression of co-stimulatory molecules.

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After application of haptens to the skin, Langerhans cells (LCs), i.e., immature dendritic cells (DCs) in the skin, move to secondary lymphoid organs to sensitize naive T cells. During this process, LCs become mature DCs with augmented expression of various co-stimulatory molecules and class II MHC antigens. In this scenario, however, critical questions remain as to what kind of chemicals can induce this maturation process through what kind of mechanisms. To clarify these questions, we used monocyte-derived $CD1a^+$ DCs instead of LCs since LC maturated in in vitro culture, spontaneously. After we confirmed that monocyte-derived DCs showed at least phenotypic characteristics and a response to TNFa similar to LCs, we added various chemicals, i.e., dinitrochlorobenzen (DNCB), trinitrochlorobenzen (TNCB), $NiCl_2$, $ZnCl_2$, sodium lauryl sulfate (SLS), or benzalkonium chloride (BC), to a culture of purified monocyte-derived CD1a+ DCs. Among them, only $NiCl_2$ and DNCB significantly increased the surface expression of CD54, CD86, HLA-DR antigen, and IL-1b production, while SLS, BC, or $ZnCl_2$ could not augment them, except for weak augmentation of CD86 expression by SLS. Among these three molecules, the increase in the expression of CD86 induced by $NiCl_2$ or DNCB was most remarkable, being observed in DCs from almost all the subjects we examined. TNCB could also induce responses similar to those with DNCB, but the number of the subjects whose DCs responded to it was far less than that of the subjects whose DCs responded to $NiCl_2$ or DNCB. In spite of the augmented CD86 expression on DCs treated with DNCB or $NiCl_2$, they induced different responses of DCs in their expression of CD54 and HLA-DR and the production of IL-6 and TNFa. In addition, the up-regulation of CD86 expression on DCs treated with DNCB was significantly suppressed by either anti-IL-1b or anti-TNFa antibody, while that by $NiCl_2$ was relatively insensitive to these antibody treatments. Finally, the protein kinase C inhibitor, H7, but not staurosporin, could suppress the augmentation of CD86 expression on DCs induced either by $NiCl_2$ or by DNCB. These data suggest that DCs respond to some haptens by changing their expression of several co-stimulatory molecules and their production of cytokines with a resultant change in potency of antigen presenting function. They also suggest that these chemicals stimulate DCs by different mechanisms. By these responses, DCs may modulate the final immune response to chemicals.