

Pathways for skin immunity directed against lipids and other non-protein antigens

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Human group 1 CD1 molecules (CD1a, CD1b, CD1c) are expressed prominently in dendritic cells, and mediate presentation of non-protein lipid antigens to T cells. Langerhans cells are epidermis-resident dendritic cells that play a pivotal role in skin immunity. These cells are unique in their abundant expression of the CD1a protein, but its role in skin immunity remains to be determined. The principal investigator of this project previously isolated Langerhans cells from the human skin, and observed their striking ability to activate microbial lipid-specific T cells. To extend this finding further, this project has aimed to address whether CD1a-positive Langerhans cells mediate lipid-specific immune responses *in vivo*. To accomplish this, we have attempted to reconstitute by a transgenic technology CD1a-dependent immunity in mice that have deleted genes for CD1a. Generation of mice carrying the human *CD1A* genome has been completed, and we found that the human CD1a protein was expressed specifically in epidermal Langerhans cells. In addition, microbial lipid-specific, CD1a-restricted T cell responses were readily detected in these mice, suggesting that the positive selection for CD1a-restricted T cells indeed occurred as in humans. Therefore, these mice provide a valuable opportunity for our evaluating CD1a function *in vivo*.