Skin sentry cells promote distinct immune responses

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A new study reveals that just as different soldiers in the field have different jobs, subsets of a type of immune cell that polices the barriers of the body can promote unique and opposite immune responses against the same type of infection. The research, published online on July 21st by Cell Press in the journal *Immunity,* enhances our understanding of the early stages of the immune response and may have important implications for vaccinations and treatment of autoimmune diseases.

Dendritic cells serve as sentries of the immune system and are stationed at the body's "outposts," like the skin, where they are likely to encounter invading pathogens. When dendritic cells encounter pathogen-associated antigens (molecules that trigger an immune response), they process the antigen and present it to other responding immune cells in an effort to inititate a cellular cascade resulting in clearance of the pathogen. This is a critical part of the immune response because many responding immune cells cannot "see" antigen and initiate the proper protective response unless the antigen is properly presented by a dendritic cell.

"There are at least three different types of dendritic cells in the skin," explains senior study author, Dr. Daniel Kaplan from the University of Minnesota. "Despite studies examining these cells, the basic question of whether skin resident dendritic cells have unique or redundant functions remains unresolved." Dr. Kaplan and colleagues developed a model of yeast infection that is limited to the superficial layer of the skin and studied antigen-specific immune responses in mice lacking specific subsets of skin dendritic cells.

The researchers discovered that direct presentation of antigen by one type of dendritic cell, Langerhans cells, was necessary and sufficient for the generation of antigen-specific T helper-17 (Th17) cells but not the generation of cytotoxic lymphocytes (CTL). T helper cells play a key role in orchestrating the immune response, whereas CTLs can directly destroy infected cells. While Th17 cells play productive roles in indirectly eliminating pathogens when their response is dysregulated, they have been implicated in autoimmune disease, Meanwhile, another subset of dendritic cells was required for the generation of antigen-specific CTLs and inhibited the ability of other dendritic cells to promote Th17 cell responses.

"Our work demonstrates that dendritic cells in the skin promote distinct and opposing antigen-specific responses," concludes Dr. Kaplan. "This has important implications for vaccination strategies that selectively target dendritic cell populations. In addition, the requirement for Langerhans cells in the development of Th17 cells suggests these cells may participate in the early pathogenesis of Th17 cell-mediated skin diseases such as psoriasis."

Provided by Cell Press

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