

Skin Homing Cytotoxic T-Cells Mediate Destruction of Melanocytes by Apoptosis in Vitiligo

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Vitiligo is a disease associated with the loss of skin pigmentation of affected areas of the skin in susceptible individuals. There is ample evidence suggesting that the disease is mediated by a specific subset of white blood cells known as T lymphocytes. These cells play a very important role in our immune system by protecting the body from undesirable invaders that will cause harm to the body. They are able to distinguish between our own tissues and destroy any potential invaders. However, in vitiligo, it is believed that certain T cells infiltrate the skin and start to attack the body's own melanocytes which provide skin pigmentation. It is unclear why a body's immune system suddenly starts to turn against its own tissues. In addition, it is yet to be determined why this auto immune reaction is directed towards particular cells (melanocytes) in the skin. This attack leads to melanocyte destruction and loss of skin pigmentation. In many patients, the destruction does not lead to inflammation in affected individuals as seen in other auto immune diseases. Therefore, the main goal of our project was to determine how the melanocytes are destroyed and to identify and characterize the specific T cells responsible for the destruction.

To address this, we exposed T lymphocytes obtained from blood samples donated by vitiligo patients to whole antigens prepared from normal melanocyte and nonmelanocyte cells such as human fibroblast. For comparison, we treated T lymphocytes obtained from non-vitiligo volunteers as described above. The cells from both groups were collected, treated with reagents that will help us to identify specific T cells that responded to melanocyte antigen, and analyzed in our laboratory using a method known as flow cytometry.

Our experiments revealed that a subset of T lymphocytes known as cytotoxic T cells, from a majority of vitiligo patients, responded to melanocyte antigens by expressing markers (CD69, CD71, CD25 and HLA-DR) on their surface. Expression of these proteins is indicative of activated cells. However, this observation was not made with cells from non-vitiligo volunteers. We also looked for specific proteins that help these activated T cells move towards the skin to find melanocyte, many of which eventually become targets for destruction. We observed that in a majority of the cases, exposure to antigens induced 10-fold higher expression of a skin homing protein (CLA) in vitiligo patients than our nonvitiligo volunteers. In addition, the activated T cells expressed high levels of a protein known as Fas ligand on their surface. This protein is used by activated cytotoxic T cells to attach to Fas, another protein which is expressed on target cells, and induces them to destroy themselves. The target cells in our study are melanocytes, which have been shown and confirmed by our group to express high levels of Fas.

Taken together, our results demonstrate that T lymphocytes from vitiligo patients respond to melanocyte antigen and become activated. These activated cells also show an increased expression of Fas ligand and a skin homing protein on their surface that helps the cells to migrate to the skin area where they probably induce the melanocytes to destroy themselves. We have isolated specific T cells from vitiligo patients and are growing them in large numbers. In our next series of experiments, we will expose different kinds of dye-labeled melanocytes to the activated cells and determine the level and method of melanocyte destruction. In addition, we will determine the cytokines that are produced by these cells which are suspected to have a hand in the destruction of melanocytes in susceptible individuals.