

Impact of Melanocyte Autoantigen Presentation in Vitiligo

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Our research is focused on understanding why the immune system attacks melanocytes (the skin cell that is responsible for pigmentation) in vitiligo, causing them to be lost from the skin. Using recombinant DNA technology, we will target special proteins to epidermal melanocytes of genetically altered mice (called transgenic mice). In these mice, artificial DNA is introduced into their natural DNA. As a result of this genetic alteration, the skin melanocytes of these transgenic mice will express novel proteins that are not normally associated with melanocytes. This is termed a "neoantigen" or a novel antigen that cannot be recognized by the immune system because it is foreign. The animals will then be tested to determine whether the immune system can be induced to attack these novel melanocyte-associated proteins (or "neoantigens"). We predict that the immune system of these transgenic mice can be caused to attack the melanocytes expressing these special proteins, resulting in these mice developing vitiligo. This vitiligo may be similar to that which occurs in humans, and will allow us to test which immune white blood cell populations (either helper or cytotoxic T-lymphocytes or B-lymphocytes) are involved in the pathophysiology of vitiligo. It will also allow us to create a model system that will be useful in screening potentially new treatments that may arrest vitiligo. These transgenic mice that develop vitiligo will be useful research tools to better understand the vitiligo which occurs in humans, because we will be able to perform detailed immunologic studies in a controlled manner over time, which is difficult to perform in humans afflicted with this disease.

Currently, we have assembled the recombinant DNA constructs that will be used to create the transgenic mice. We are testing this DNA in cultured melanocytes, and have found that this DNA works as predicted in this cell type. We are now in a position to create these genetically altered mice, and begin to test our theories on how the immune system attacks melanocytes in vitiligo.