

Stress Proteins in Autoimmune Depigmentation

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In most patients, it appears that the loss of pigmentation in Vitiligo involves an autoimmune response to pigment cells in the skin. These pigment cells come under attack as though they were infectious organisms that need to be cleared from the body. Since pigment cells are the only source of melanin, parts of the skin that have come under attack will lose pigment and turn pale white.

It is not understood what triggers such an autoimmune response. Patients often report being exposed to some form of stress shortly before the vitiligo has appeared. This can be stress in the form of overexposure to sunlight, cuts or bruises to the skin, contact with phenolic chemicals or even emotional stress. These factors will initiate a protective response by skin cells involving synthesis of so-called stress proteins. These proteins can 'chaperone' existing proteins in the cell and prevent premature cell death. Of course, if the cell has encountered too much stress, even the stress proteins cannot help them and the cells will die. In that case, the stress proteins are released, still chaperoning the proteins released from the cells that just died. When immune cells encounter such stress proteins, they know there is something wrong and that a cleanup must be done. In response to this signal, they take up the stress proteins and present the cellular proteins to the immune system. This can trigger an immune response that is specific for the proteins that were just released by the dying cells.

We know that pigment cells make a number of proteins that are relatively easily recognized by the immune system. It appears that these proteins are indeed recognized by lymphocytes that subsequently enter vitiligo skin and kill remaining pigment cells, leading to further depigmentation. Thus, we believe that stress proteins are important factors involved in initiating vitiligo. Indeed, we have been able to show in the lab that many parts of the immune response occur more efficiently when stress proteins are present. Pigment cells will start to express sticky molecules that make them more recognizable for lymphocytes entering the skin, whereas other skin cell types do not express these molecules. Lymphocytes more efficiently recognize the pigment cells after the latter have been exposed to stress proteins. And in an earlier phase, dendritic cells, the 'messengers' of the immune system, will more efficiently take up and process proteins that are later presented to lymphocytes.

Surprisingly, we found that when we artificially over-expressed stress proteins in pigment cells, it did not protect them from subsequent stress. They died just as frequently as they would have without the extra stress proteins. This appears to be an even greater problem when we used a cell line derived from a vitiligo patient.

These recent experiments are helping us understand why vitiligo can develop in response to stress. It also helps us to think about ways of preventing the development of white skin. Of course, avoiding stress should be a big help. But the experiments also suggest that we can possibly interfere with the abundance of stress proteins in the skin to prevent the autoimmune response that follows. We hope to continue our investigations and need your continuing support as we search for a cure.