

Melatonin Hypothesis of Vitiligo

Andrzej Slominski, M.D., Ph.D.

Associate Professor of Pathology

The University of Tennessee Health Science Center

Vitiligo is a disfiguring cutaneous disease characterized by progressively enlarging areas of depigmentation. Current therapies for vitiligo are generally unsatisfactory. We have postulated that vitiligo may be related to local malfunction in the cutaneous involvement of the hormone melatonin. This hypothesis is based on the action of melatonin in the maintenance of skin pigmentation; therefore, either defective local synthesis, degradation or action could result in vitiligo. In the first step of testing the above hypothesis we have produced a detailed characterization of molecular apparatus governing the synthesis of melatonin in the human skin and in cultured cutaneous cells.

It is known that melatonin is the product of a multistep metabolic pathway that starts with the hydroxylation of the aromatic amino acid L-tryptophan, involves production of neurohormone/neurotransmitter serotonin, its transformation to biologically active N-acetylserotonin that serves as direct precursor of melatonin. This transformation includes several steps in a process that is regulated enzymatically. The most important step is the hydroxylation of L-tryptophan by the enzyme tryptophan hydroxylase that is necessary for the production of serotonin. A second important regulatory step is the acetylation of serotonin catalyzed by N-acetyltransferase, which generates N-acetylserotonin. The third and final step also critical is the enzymatic methylation of N-acetylserotonin by HIOMT that produces melatonin. The process of L-tryptophan transformation to melatonin requires expression of all these three separate enzymes.

We therefore used methods of molecular biology to determine expression of the genes, coding the three critical enzymes in a number of biological specimens. These included normal and malignant human keratinocytes and melanocytes and samples of tissues including human and rodent skin.