Studies on Melanocytes Cultured from Vitiligo Patients

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During the past year we have been investigating the hypothesis that melanocytes cultured from patients with vitiligo express altered levels of molecules essential for cell survival, and as a result, are susceptible to undergoing cell death when challenged. There is a family of cellular proteins that either prevent or help a cell undergo programmed cell death (ie., apoptosis) when confronted with a toxic or stressful situation. These proteins are called the BcI-2 family of apoptosis regulators and consist of the pro-apoptotic mediators Bax and BcI-Xs (that prevent cells undergo death) and the anti-apoptotic mediators BcI-2, Bcl-XI, and MeI-1(that help cells undergo death). Our recent work has indeed demonstrated that the levels of some of these proteins in many melanocytes cultured from patients with vitiligo are significantly different than the amount expressed by melanocytes cultured from unaffected individuals. Specifically, it appears that the pro-apoptotic molecule Bax and/or the anti-apoptotic molecules BcI-2 be either increased or decreased respectively in cultured vitiligo melanocytes. This specific change in expression patterns for these molecules could conceivably render the vitiligo melanocytes vulnerable to cell death when challenged.

We have been testing various inducers of cell death on the survival of normal melanocytes in culture and are beginning to compare the effect of these inducers on vitiligo melanocytes. Normal human melanocytes in cultures can be induced to undergo cell death (i.e., apoptosis) when challenged with ultraviolet light (UVB), the phenolic derivative 4-tertiary butyl phenol (4-TBP), and Staurosporine (a kinase inhibitor). The data demonstrating that UVB and 4-TBP can damage melanocytes is very interesting. There are many anecdotal stories from patients with vitiligo that correlate the onset of their disease with extensive exposure to sunlight (UVB) resulting in severe sunburns or with topical exposure to compounds containing phenolic/ catecholic derivatives. We are currently carrying on a series of experiments to determine if melanocytes cultured from patients with vitiligo that express altered levels of the BeI-2family of apoptosis regulators are more susceptible to cell death than normal melanocytes after exposure to UVB and 4-TBP. If this hypothesis is demonstrated, it will help us understand why some people's exposure to sunlight (UVB) resulting in severe sunburns or to compounds containing phenolic/ catecholic derivatives develop vitiligo.