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Years of research have shown that the immune system is capable of recognizing and destroying melanoma. Immune responses against melanoma can develop spontaneously in rare cases, but usually require immunotherapeutic intervention. However, immune cells that are destructive to melanoma sometimes cross-react with melanocytes; the pigment-producing cells in the skin that give rise to melanoma. This leads to autoimmune destruction of melanocytes, also known as vitiligo. Importantly, melanoma patients that develop vitiligo have a much better prognosis, especially late stage patients where overall survival is nearly doubled. This relationship between improved responses to melanoma and vitiligo has been observed in the clinic for over 30 years, but has only been reported as a correlation.

In our lab, we use a mouse model to study the immune response to melanoma. Using the melanoma tumor itself, in combination with an immunotherapy and surgery, we have shown that we can induce a robust immune response against the tumor in a model that mimics the clinical setting. We also found that this method of treating the mice resulted in a long-lived immune response- but only with the concurrent development of vitiligo. This novel finding elucidated a causal relationship between tumor immunity and autoimmunity. We also were surprised to find that vitiligo was able to induce a new immune response against melanocytes, even in the absence of melanoma. It had been suggested that cells induced to kill melanoma could cross-react with melanocytes. However, it has not been previously considered that cells induced by vitiligo would be able to kill melanoma cells.

This project focuses on understanding what role vitiligo plays in maintaining the immune response against melanoma in the long-term. The vitiligo-induced killer cells may be critical in preventing metastatic melanomas, however, further investigation is required to determine their anti-melanoma functions. Additionally, vitiligo may enhance the repertoire of melanocyte-reactive immune cells, which will make it more difficult for melanomas to escape detection by the immune system.

The conclusions from this project will be extremely informative for treating melanoma patients in the clinic. These studies will greatly enhance our current interpretation of clinical outcomes. Additionally, conclusions from this project will help guide future clinical treatments, possibly involving combinations of current vitiligo-inducing therapies with available melanoma immunotherapies. Thus, this project could provide information that has rapid, long-lasting effects on treatment designs for melanoma patients.