Melanoma Research Alliance

Prevention

The Melanoma Research Alliance (MRA) has invested almost $3 million in research to improve melanoma prevention. This research focuses on identifying the biological factors underlying the development and progression of melanoma. This includes studies of skin pigmentation biology and the identification of genetic risk factors, which will inform biologically-based strategies for prevention.

Skin pigmentation biology: Driving the development of melanoma prevention agents for high risk individuals

Individuals with mutations in a protein associated with red hair, called MC1R, have a 2-4 fold increase in risk for melanoma, because their skin has an ineffective protective response to UV radiation. MRA has funded studies to develop targeted topical prevention agents for this high-risk population.

One strategy is to manipulate the skin pigmentation pathways that are defective in this population. With MRA support, researchers identified a pathway that controls skin pigmentation and represents an attractive drug target. Several drugs were tested on the skin of redhead/fair skinned mice and were shown to stimulate pigment production. This work is continuing with funding from the National Institutes of Health.

In another related approach, a promising natural agent derived from broccoli sprouts, called sulforaphane, has the potential to compensate for the defective response to ultraviolet light that underlies the increased risk for melanoma suffered by individuals with mutations in MC1R. In laboratory studies, researchers showed that sulforaphane improved the skin's antioxidant response in addition to increasing pigment production after UV exposure. Future directions include clinical testing.

Melanoma genetics: Identifying genes associated with increased risk for melanoma

There are many unanswered questions about the genetic basis for melanoma risk, development, and progression. MRA-funded studies have identified genes that could predict an individual's risk of developing melanoma, forming the basis for more accurate estimates of individual disease risk and targeting high-risk individuals for early detection. In addition, this research will advance the understanding of how genetic mutations, chemical modifications of genes, and UV light exposure may interact in the development of melanoma.

While most melanomas are not hereditary, in families with multiple cases of melanoma, inherited risk factors may be playing a role. There are only two known hereditary melanoma risk genes, and the majority has not yet been identified. A MRA-funded team has undertaken a genetic analysis of families with multiple cases of melanoma and found a new melanoma risk gene. Identifying these factors in families will improve the understanding of melanoma initiation and progression more generally.

Another study to identify somatic risk genes (not inherited) uncovered five new risk genes that conferred and increased risk of melanoma of between 14-22%. In contrast to all previously documented predisposition genes, none of these appear to mediate their effect through phenotypic traits such as pigmentation or moles (nevi), suggesting additional mechanisms for targeting.

A new MRA-funded study will employ a new method of discovering melanoma risk genes using a unique collection of mouse models called the Collaborative Cross. This method will allow the more rapid identification of additional risk genes as well as those that might be protective against melanoma.