

# DERMASCOPE

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The Sun Care Issue

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# The Science of Prevention

by Laura Brockway-Lunardi, Ph.D.

Skin cancer is the most common cancer in the U.S. with more than two million Americans diagnosed annually. Basal cell carcinoma and squamous cell carcinoma make up the majority of these cases. The third type, melanoma, arises from pigment producing cells called melanocytes. The ability to spread widely to other parts of the body is a unique characteristic of melanoma that the other skin cancers do not readily possess. This characteristic makes melanoma the deadliest, accounting for only four percent of skin cancers but 80 percent of skin cancer-related deaths. The number of new cases of melanoma is increasing steadily and dramatically. In the U.S. alone, the incidence of melanoma has tripled over the past three decades. In 2010, approximately 70,000 new cases were diagnosed.

Despite major advances in reducing incidence and mortality for a number of cancers, the statistics for melanoma have remained stubbornly high. As a catalyst to accelerate progress and transform the outlook for this disease, the Melanoma Research Alliance (MRA) was launched in 2007 by Debra and Leon Black, under the auspices of the Milken Institute. This unique non-profit finds and funds cutting-edge research to better prevent, detect and treat melanoma. MRA has funded more than \$33 million to 74 projects in 10 countries; an important component of this research program focuses on the understanding of the causes of melanoma towards innovative prevention strategies.

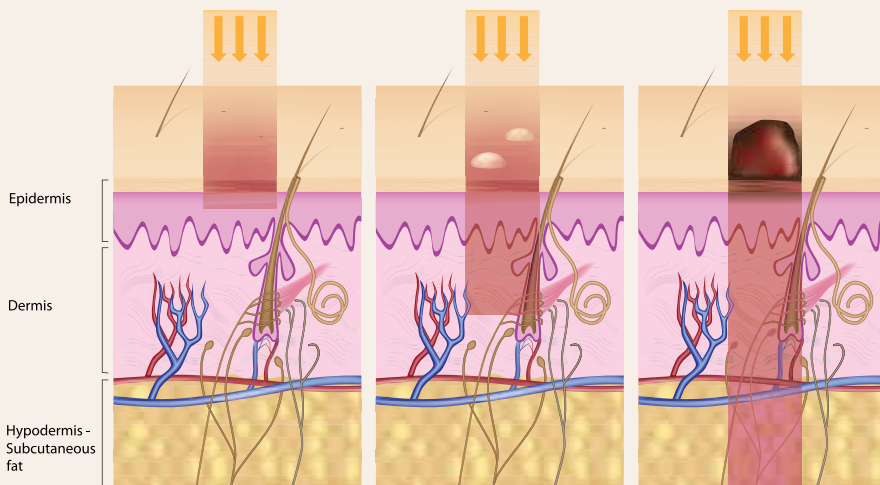
Research has clearly demonstrated the link between UV exposure from the sun and tanning beds and skin cancer. Scientists supported by MRA and others are now beginning to uncover key insights about biology of the skin and how it responds to UV radiation on a cellular basis. In addition, research is identifying the genetic risk factors that make certain people more susceptible to skin cancer. These efforts will accelerate the development of the next generation of prevention efforts.

## UV Radiation Promotes Skin Cancer

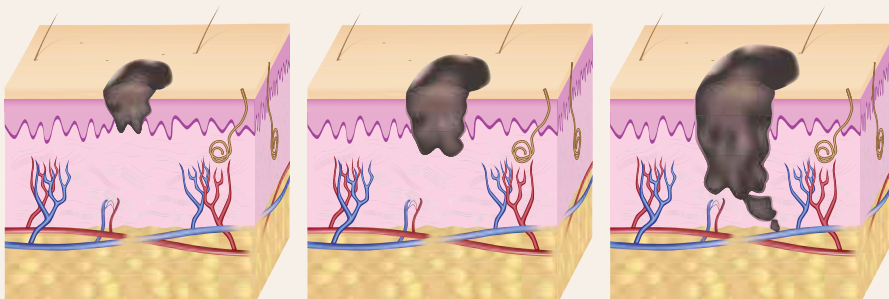
Exposure to UV rays from the sun or tanning beds is the most modifiable risk factor for all skin cancers, including melanoma. Because of this, skin cancer is often called the most preventable cancer. A person's risk for melanoma doubles if he or she has had five or more sunburns in their lifetime. The use of tanning beds increases a person's chance of developing melanoma by as much as 75 percent. UV rays are a part of sunlight that is an invisible form of radiation. UV rays can penetrate and change the structure of skin cells and can cause skin cancer and premature skin aging. UVA rays are the most abundant source of solar radiation at the earth's surface and penetrate beyond the top layer of skin. UVB rays are less abundant at the earth's surface and penetrate less deeply into the skin but can also be damaging and are primarily responsible for causing sunburn. Scientists have evidence that both UVA and UVB rays can increase a person's risk for developing skin cancer. Most people associate sunburn with skin damage, but even developing a tan is a sign of skin damage. A tan develops when the skin tries to protect itself from exposure to UV rays. Skin aging and cancer are often

delayed effects that show up many years after exposure. In a recent study reporting on the genome sequencing of a melanoma patient's tumor sample, scientists revealed a pattern of mutations that is indicative of UV damage, providing additional, biological evidence for the link between UV damage and melanoma.

## Stages of Sunburn:



## Stages from Sunburn to Skin Cancer:



## Sun Protection

Given the clear link between UV and skin cancer, public health agencies around the world recommend that individuals minimize their exposure. One way is to use sunscreen, which has been shown to prevent both squamous cell carcinoma and melanoma skin cancer. A randomized, controlled trial conducted in Australia, a country with one of the highest melanoma rates in the world, showed that, among adults, regular application of SPF15+ broad-spectrum sunscreen during a five-year period reduced the incidence of new primary melanomas for up to 10 years afterwards. Sunscreen is the form of sun protection most often used by people of all ages. However, its use is often suboptimal, and improvements in formulations and labeling are in development to aid consumers. The current SPF scoring system – developed in 1962 – refers to degree of protection against burning UVB radiation. The U.S. Food and Drug Administration (FDA) is

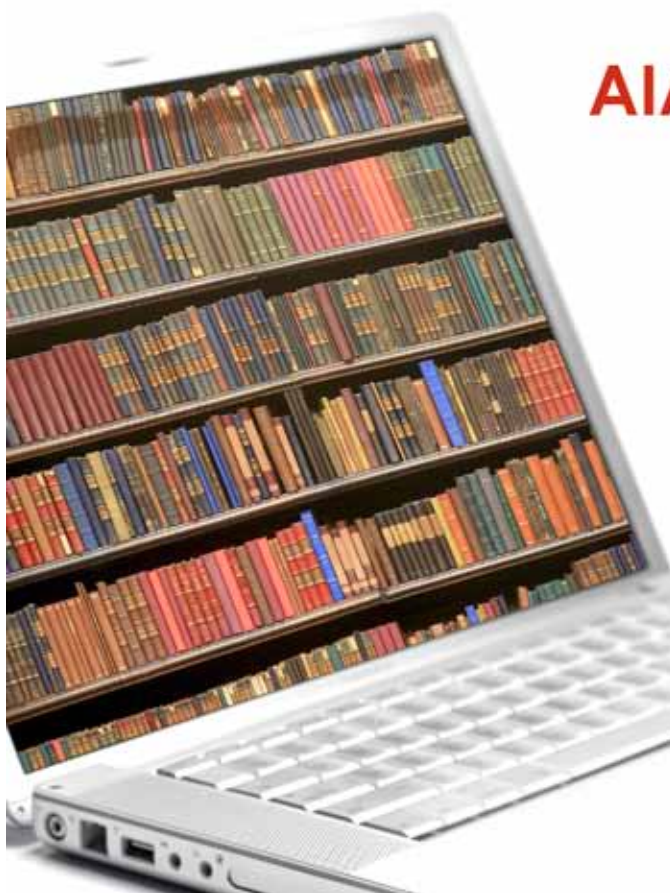
working to develop and implement an updated system to include the level of UVA protection. Additional guidelines will established standards for testing the effectiveness of sunscreen products and require labeling that accurately reflects test results. For example, sunscreens that demonstrate protection against both UVA and UVB may be labeled "broad spectrum." Only those with SPF of 15 or greater can claim to reduce the risk of skin cancer and premature skin aging. They would also limit the maximum SPF value on sunscreen labels to "SPF 50+" because there is not sufficient data to show that products with SPF values higher than 50 provide greater protection for users than products with SPF values of 50. Finally, the new requirements specify water resistance claims.

### Indoor Tanning

In addition to sun protection, individuals can reduce their risk of skin cancer – as well as skin aging, and skin and eye damage – by avoiding indoor tanning devices. Melanoma is the number one new cancer diagnosed in young adults, and scientists attribute this trend to the increasing use of tanning beds among this age group, particularly young women. Of the 28 million people who frequent tanning salons, 75 percent are girls and women ages 16 to 29. As previously mentioned,



indoor tanning has been shown to increase the risk of melanoma by up to 75 percent. The risk increases with greater years of use, number of sessions or total hours of use. The World Health Organization classifies tanning devices as cancer-causing, and other scientific authorities such as the FDA have pronounced tanning devices as causing serious health risks including skin cancer. As a result of this serious public health concern, legislative efforts in the U.S. and around the world have aimed to limit access to tanning beds, particularly for minors. France, Germany, Austria, Finland, Britain, England and Wales ban indoor tanning for minors. Brazil prohibits use of tanning devices for anyone for cosmetic purposes throughout the country. In March 2010, the FDA held a hearing to consider increased regulations on tanning devices in the U.S. including a potential ban for minors, but the announcement



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of their decision has yet to be made. In parallel, efforts have been pursued at the state and local level; in 2011 California was the first state to ban access to tanning beds for minors.

### New Prevention Agents

While important efforts are ongoing to reduce the incidence of skin cancer through public health campaigns, research is needed to develop bio-

logically-based prevention strategies. It is known that individuals with red hair have a two to four fold increase in risk for melanoma, because their skin has an ineffective protective response to UV radiation. This is due in part to mutations in a protein associated with red hair, called MC1R, which is a protein on melanocytes that regulates pigment production. By teasing out the cellular pathways controlled by MC1R and find-

ing ways to modify them, scientists are beginning to develop topical prevention agents for this high-risk population. Several candidate agents have been tested in genetically engineered mouse models and were shown to successfully stimulate pigment production. However, drugs that work in mice may not be feasible in humans because human skin is more difficult to penetrate. This work is ongoing to further cultivate additional agents. In another related approach, a promising natural agent derived from broccoli sprouts, called sulforaphane, has been shown to hold the potential to compensate for the defective response to UV 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. If successful, these research programs will set the stage for developing topical agents that could mitigate risk for melanoma development in high risk skin types.

### Risk Assessment

There are many unanswered questions about the genetic basis for melanoma risk, development and progression. It is clear that traits such as skin type, hair and eye color and number of moles are associated with melanoma risk. Melanomas are highly mutated, making analysis of important genetic factors complex. Scientists are working to elucidate the underlying genetic factors that influence this risk and reveal the interactions between genes and environment. Studies funded by MRA and others have identified genes that could predict an individual's risk of developing melanoma, which would aid in targeting high-risk individuals for prevention and early detection measures. Those with a family history of melanoma, particularly those with first-degree relatives with the disease, have an increased risk independent of pig-





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mentary characteristics. Only a few hereditary melanoma risk genes have been identified to date. In research supported by MRA, a recent analysis of families with multiple cases of melanoma found a new melanoma risk factor manifested as a mutation in a gene called MTF. In another study focused on non-inherited genetic factors, investigators uncovered five new risk genes. 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. If successful, these projects will identify genes that could predict an individual's risk of developing melanoma, and will advance the understanding of how genetic mutations, chemical modifications of genes, and UV light exposure may interact in the development of melanoma.

### Public Awareness

Research continues to advance the understanding of melanoma. In addition, the MRA has been engaged in a series of public awareness initiatives urging people to protect themselves from the sun's damaging rays, avoid indoor tanning, and be aware of changes in their skin. Recognition of changes in the skin is the best way to detect melanoma early.

This includes promotion of the ABCDEs of melanoma (moles or growths that are Asymmetrical, have an irregular Border, exhibit changes in Color, have a Diameter larger than the size of a pencil eraser, or have Evolved in size or thickness). With the incidence of melanoma on the rise, it is clear that no one organization or individual can overcome this deadly disease. Research foundations, together with health care providers, companies, policymakers and others who counsel individuals on the importance of skin health must work together toward the day when no one will suffer or die from melanoma. **D**



Laura Brockway-Lunardi, Ph.D. joined MRA as the scientific program director in May 2009 where she is responsible for the grant-making program, scientific meetings, scientific outreach, as well as contributing to advocacy and communications activities of the organization. Prior to MRA, she has held several professional positions in biomedical research policy and scientific programs. Dr. Brockway-Lunardi was a science and technology policy fellow at the National Academy of Sciences. She received her doctorate in physiology from the University of Alabama at Birmingham and bachelor's degree in biology with honors from Florida State University.

An advertisement for Dermascope.com. On the right side, a woman with dark hair pulled back, wearing a white high-necked top, is looking towards the left. Her right hand is raised, with her index finger pointing towards a list of items. The list is contained within a semi-transparent blue rectangular box that has a slight 3D effect. The background is a light blue gradient. At the bottom of the advertisement, the website address is displayed in large, bold, blue and red letters.

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