Can “Self-Tanning” Mice Help Us Avoid Skin Cancer?

In the summer, many people flock to beaches, pools, BBQs, and backyards, using any excuse to spend time outdoors. More outdoor time during the day means more UV exposure from the sun. The body’s natural response to this sun exposure is **tanning,** a biological process that occurs when your skin darkens as it produces more **melanin** (skin pigment molecules) in response to the UV rays.

Melanin acts as a shield for the nucleus of a skin cell, protecting the DNA inside from damaging sun exposure). People with naturally darker skin have higher levels of melanin in their untanned skin than people with naturally fairer skin. Therefore, people with darker skin are naturally more protected from the sun than those with lighter skin, as shown in **Figure 1**. If a dark-skinned person and a fair-skinned person are both exposed to the same source of UV radiation, the person with fair skin may experience tanning while the dark-skinned person does not. This is because fair skin does not have much natural protection and the body responds by producing more melanin.

So if tanning helps protect skin cells it must good, right? Well, sort of. The problem is that prolonged and intense UV exposure can eventually get through the protective melanin barrier and cause DNA damage. What happens when DNA is damaged? Well, over time, the damage can add up and eventually trigger skin cancer. In other words, while tanning may increase your skin’s natural protection against further UV damage in the short-term, it could be increasing your long-term risk of skin cancer.

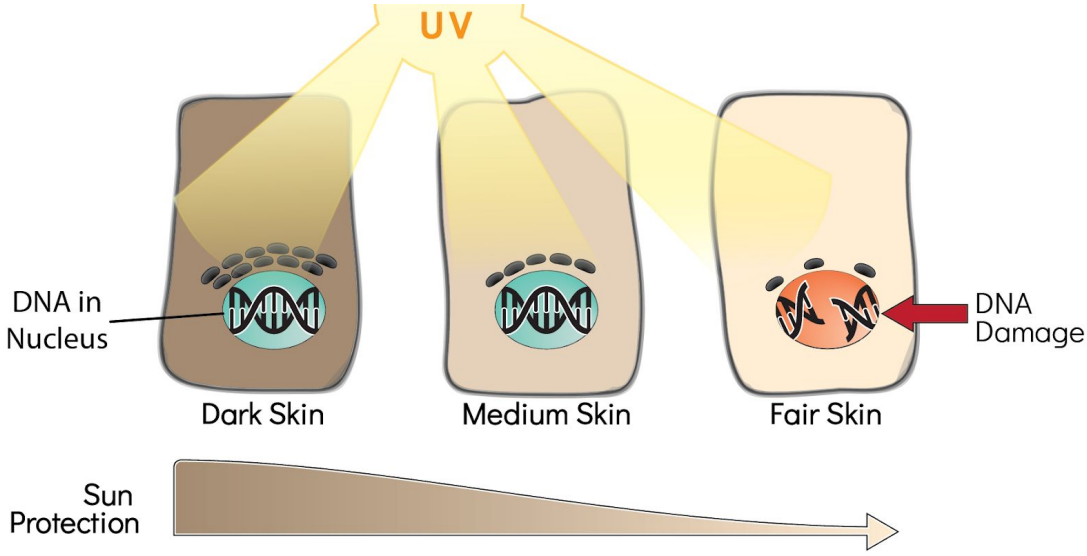

Figure 1. A Melanin Shield. Melanin, represented by small black dots, is found in different amounts in different skin tones. Melanin molecules arrange themselves like a shield over the nucleus of the skin cell, protecting it from damage from UV rays. Darker skin cells have higher melanin concentrations and are therefore more strongly protected from UV rays than fairer skin cells are. *Source:* Adapted from *Michael et al.*, 2017.

But what if there was a way you could get the short-term protective benefit of tanning without sun exposure? That'd be pretty cool, right? Scientists hypothesized that if they could somehow make skin cells produce more melanin, they could increase protection from the sun without the risk of damaging DNA with UV rays. Could they develop a drug to increase pigment production without the sun? Yes!

The new drug in this study is topical, which means that it is put on the skin from the outside. Once absorbed by cells, it induces pigment production in the skin by increasing the amount of a protein called MITF. MITF is a transcription factor that acts as the conductor of a cellular orchestra, increasing the production of enzymes that in turn produce melanin. Thus, when there are higher levels of MITF, there are higher levels of melanin-producing enzymes, and a greater amount of melanin in the cells. The scientists tested this drug on the skin of mice and found that after daily application, the skin of the mice turned darker (see **Figure 2**). They hypothesize that the darker skin induced by the drug increase protect the mice against skin cancer.

Figure 2. Tanned Mice. Mice treated with no drug (left four mice) or the newly developed drug (right four mice) for seven days. Those treated with the drug develop darker skin pigmentation that can protect against damaging UV rays. *Source:* Mujahid *et al.,* 2017.

The mice in this study make good model organisms for humans because they induce the same molecular process of tanning (via MITF), but there are some differences between mice and humans that make drug development challenging. The scientists in this study created different versions of the drug and tested them on human skin samples to see which one would work the best. Some of their results are shown in **Figure 3**.

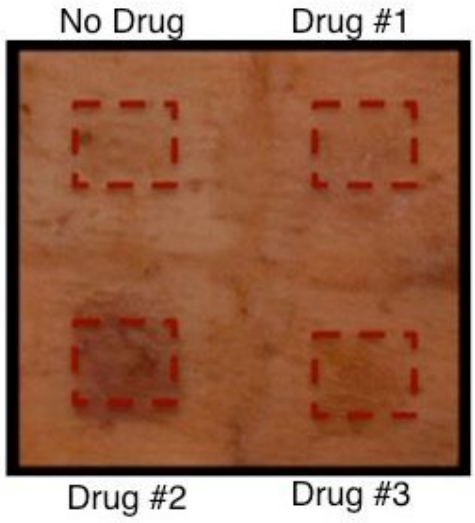

Figure 3. Drug Applied to Human Skin. Multiple versions of the drug were applied to human skin samples. There are different tanning effects depending on how well the drug is absorbed by human skin. Here, Drug #2 produces the strongest effect. *Source:* Mujahid *et al.,* 2017.

Moving forward, scientists hope that this study can provide the basis for the development of a drug that could make the skin tan at the molecular level in humans without the damaging side effects of sun

exposure. It is important to note, however, that no matter what, tanned skin is not as strong of a protectant against skin cancer as SPF sunscreen. The drug alone will not completely protect against skin cancer but will be only slightly protective, and the researchers warn that if their drug is ultimately successful, it should not be a substitute for sunscreen. What the researchers hope, however, is that if the drug is available, it will lead to decrease the usage of tanning bed and unsafe UV exposure that leads to skin cancer by providing a sunless alternative.

References

Mujahid, Nisma, Yanke Liang, Ryo Murakami, Hwan Geun Choi, Allison Dobry, Jinhua Wang, Yusuke Suita, Qing Yu Weng, Jennifer Allouche, Lajos Kemeny, Andrea Hermann, Elisabeth Roider, Nathanael Gray, and David Fisher. 2017. "A UV-Independent Topical Small-Molecule Approach for Melanin Production in Human Skin." *Cell Reports* 19(11): 2177–84. doi: https://doi.org/10.1016/j.celrep.2017.05.042

Michael, Helen T., and Glenn Merlino. 2017. "A Topical Solution to the Sunless Tanning Problem." *Trends in Molecular Medicine* 23(9): 771–73. doi: https://doi.org/10.1016/j.molmed.2017.07.010

Bite Scientist Profiles

Steph Guerra is a recent graduate of Harvard University with a doctorate in Biological and Biomedical Sciences. Her thesis work focuses on developing more effective treatments for lung cancer patients. She is a former co-director of Science in the News and works with this organization and others to facilitate scientist involvement in science outreach and policy.

Melissa Kelly is a Biology teacher at Brockton High School in Brockton, MA. She has been teaching for eleven years and recently earned a license in Special Education. Her goal is to make science fun and relevant while challenging her students to think critically about the world around them and their role in it.

_v2: Edits for clarity 10/3/19