



HERE COMES THE SUN

Gender inequity

Differences in male skin may explain greater frequency of cancers

STORY HIGHLIGHTS:

- ▶ Murine research illuminates gender differences in skin
- ▶ UV exposure causes females' skin to pinken, but not males'
- ▶ Males develop ~50 percent more tumors than females

By **BOB ROEHR**

STAFF CORRESPONDENT

Columbus, Ohio — Differences in the biochemistry of male skin make it significantly more likely to develop tumors when exposed to ultraviolet (UV) B, studies in a murine model show.

The key differences are in the inflammatory and antioxidant responses.

“Historically, the thought has been that men get twice as much skin cancer because they have jobs requiring them to be out in the sun more, getting more damage. We really thought that our study was going to support that hypothesis. It ended up not,” says Tatiana Oberyszyn, Ph.D., an assistant professor at the Ohio State University Medical Center.

The first clue came almost immediately, Dr. Oberyszyn says, and it wasn't subtle. As have most investigators conducting skin research, she has found that researchers can work

more easily with female hairless mice because they are much less likely to fight than are males, so she uses females for most studies. By 24 to 48 hours after exposure to UV light the sunburn effect turns the skin of female hairless mice noticeably pink.

“The first time we did the male mice, they were not pink at all, especially compared to the female mice. I asked Jennifer Thomas-Ahner, the graduate student working on the project, to check the lights to make sure they are working properly,” Dr. Oberyszyn tells *Dermatology Times*.

“That was a bit of a surprise; we never anticipated that the male mice wouldn't respond as well as the females,” she says.

Dr. Oberyszyn says a decade of work with the outbred Skh-1 mouse model has established “a clear link between acute inflammation and tumor development.” If a compound decreased parameters of inflammation, “We could pretty much predict it would decrease tumor development. What this new research suggests is that with male mice, that may not be true.”

At 48 hours, the females had a fivefold greater increase in skin fold thickness from baseline than males, a marker of edema. They also had three times the increase in myeloper-

oxidase activity, a measure of neutrophil infiltration. Both are key markers of an inflammatory response.

Dr. Oberyszyn and her assistant also found that antioxidant activity in both males and females declined after exposure to UVB, but females

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had significantly more antioxidant activity, both at baseline and after exposure to UVB. This suggests to Dr. Oberyszyn that males either are more susceptible to the formation of 8-oxo-dG adducts or have a less effective oxidative repair capacity.

The initial work led to a longer study that exposed male and female mice to the same dose of UVB three times a week.

Based on the tumor count model, male mice had ~50 percent more tumors than female mice at every time point from week 16 forward. Histology showed that the male's

tumors were more likely to be malignant (38.5 percent vs. 18.2 percent) and were more likely to be fully invasive squamous cell carcinomas (14.6 percent vs. 2.9 percent).

Future research includes oral and topical application of antioxidants “to see if we can make male mouse skin look more like female mouse skin” and its response to UVB exposure.

The research suggests to Dr. Oberyszyn that men probably are not receiving the same inflammatory signals as women to get out of the sun, which “probably contributes to their staying out longer.” It also suggests that an anti-inflammatory approach that may help prevent the development of skin tumors in women may not have the same efficacy in men.

“It is possible that with male skin you need a combination of antioxidants as well as anti-inflammatories,” she says. While females also may benefit from antioxidants, the best ratios of the two agents may be gender-specific.

The focus of skincare, she says, should include encouraging both men and women to be smart and to use sunscreen. **DT**