

Topical treatment may prevent melanoma

April 26 2011

While incidents of melanoma continue to increase despite the use of sunscreen and skin screenings, a topical compound called ISC-4 may prevent melanoma lesion formation, according to Penn State College of Medicine researchers.

"The steady increase in [melanoma](#) incidence suggests that additional preventive approaches are needed to complement these existing strategies," said Gavin Robertson, Ph.D., professor of pharmacology, pathology, dermatology and surgery, and director of Penn State Hershey Melanoma Center.

Researchers targeted the protein Akt3, which plays a central role in 70 percent of melanoma by preventing cell death and has the potential to prevent early stages of melanoma.

"The Akt3 signaling pathway is deregulated in the majority of melanomas, making it a promising target which, if inhibited, could correct the apoptotic -- or cell death -- defect in melanocytic lesions, thereby preventing this disease," Robertson said.

Isothiocyanates were identified as inhibitors of Akt3. These are naturally occurring compounds found in cruciferous vegetables like broccoli and brussels sprouts that have anticancer properties. Unfortunately, previous research showed they have low chemotherapy potency on [melanoma cells](#) because high concentrations are needed to be effective. To create a more potent version, Penn State Hershey Melanoma Center researchers previously developed isoselenocyanates (ISC-4), by replacing sulfur with

selenium.

Researchers have now found that repeated topical application of ISC-4 can reduce tumor [cell expansion](#) in laboratory-generated human skin by 80 to 90 percent and decrease [tumor development](#) in mice skin by about 80 percent. The research also showed that the use of the compound is safe. The research was recently reported in *Cancer Prevention Research* and featured on the journal cover.

To be an effective preventative agent, a substance needs to kill the melanoma cells while having little effect on normal cells. Researchers learned that ISC-4 kills melanoma cells two to five times more effectively than it kills normal cells. In addition, examination of the treated skin showed no obvious damage to skin cells or skin structure, and treated animals did not show signs of major organ-related toxicity. This indicates a potential for use as a topical application.

"ISC-4 prevented melanoma by decreasing Akt3 signaling that led to a three-fold increase in apoptosis rates," Robertson said. "Thus, topical ISC-4 can delay or slow down melanocytic lesion or melanoma development in preclinical models and could impact melanoma incidence rates, if similar results are observed in humans."

Currently, surgical excision is used to remove melanocytic lesions or prevent development into more aggressive cancer. Topical ISC-4 treatment could potentially be an alternative to surgery for some patients.

"Topical or localized treatments, such as those we propose for ISC-4, could permit the use of high local concentrations with minimal toxicity and be useful for treating cutaneous lesions not amenable to surgical removal or other currently available approaches," Robertson said.

"With more than \$1 billion spent on sunscreen every year in the United

States, the market for skin cancer prevention is enormous and continues to grow," Robertson said. "Addition of agents such as ISC-4 to sunscreens, body lotions or creams could have a profound impact on this market for preventing melanoma."

Provided by Pennsylvania State University

Citation: Topical treatment may prevent melanoma (2011, April 26) retrieved 7 July 2024 from <https://medicalxpress.com/news/2011-04-topical-treatment-melanoma.html>

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