Serendipity points to new potential target and therapy for melanoma

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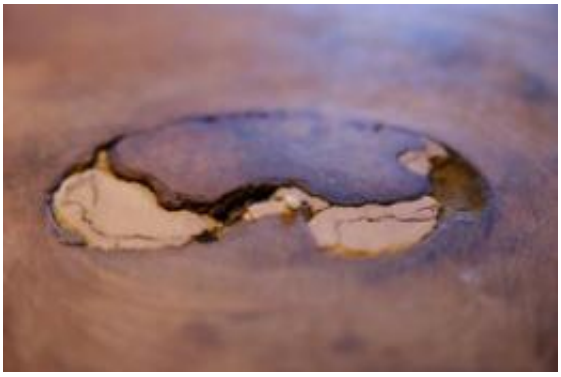

MicroRNA-26a suppresses melanoma — its loss promotes it. Image: Flickr/ume-y

(Medical Xpress)—A University of Colorado Cancer Center study in this month's edition of the *Journal of Investigative Dermatology* describes a new target and potential treatment for melanoma, the most dangerous form of skin cancer. MicroRNA can decide which genes in a cell's DNA are expressed and which stay silent. Melanoma tends to lack microRNA-26a, which makes the gene SODD go silent.

"It's a double negative," says Yiqun Shellman, PhD, investigator at the CU Cancer Center, associate professor at the CU School of Medicine, and the study's co-senior author. "miR-26a works to stop the growth of cancer. You turn off this thing that should stop growth, and you have growth."

When Shellman, David Norris and colleagues reintroduced microRNA -26a to melanoma cell lines that lacked it, they saw a marked decrease in cancer cell survival. MicroRNA-26a killed melanoma cells while leaving healthy cells unharmed.

In fact, the discovery started back a couple steps. First the group compared microRNA expression in healthy cells to that of microRNA expression in melanoma cells. "We hoped the difference between microRNA expression in healthy and melanoma cells would show which ones were contributing to tumorgenesis," Shellman says.

The microRNA most consistently different between healthy and cancerous cells was 26a. The discovery of how it works and what exactly it does was serendipitous. "We started by testing the effect of microRNA-26a on known gene targets to see if it was effecting the expression of logical, cancer-causing pathways, but none of them seemed affected in melanoma," Shellman says. "We were working with the SODD gene in an unrelated project, and SODD has a putative but not high-scored binding site for miR-26a, and thought, why not test it? Sure enough, it turned out to be the target – microRNA-26a downregulates this gene."

Shellman hopes this robust finding in cell cultures will help pave the way for future work with microRNA-26a as a therapeutic target in animal models and eventually a human trial.

"The first step is to further pinpoint the genetic signatures of the patients likely to benefit from microRNA-26a replacement therapy," Shellman says, noting that only some and not all melanoma cells were killed by miRNA replacement. "Maybe it's simply the downregulation of microRNA-26a itself, or maybe we can use SODD expression as the biomarker," Shellman says.

Once Shellman and colleagues discover the characteristics of a melanoma susceptible to microRNA-26a treatment, they hope funding will allow the lab to follow the promising therapy up the evolution from cells to humans.

More information: www.nature.com/jid/journal/vao … ull/jid2012400a.html

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