Lack of RNA 'editing' leads to melanoma growth and metastasis

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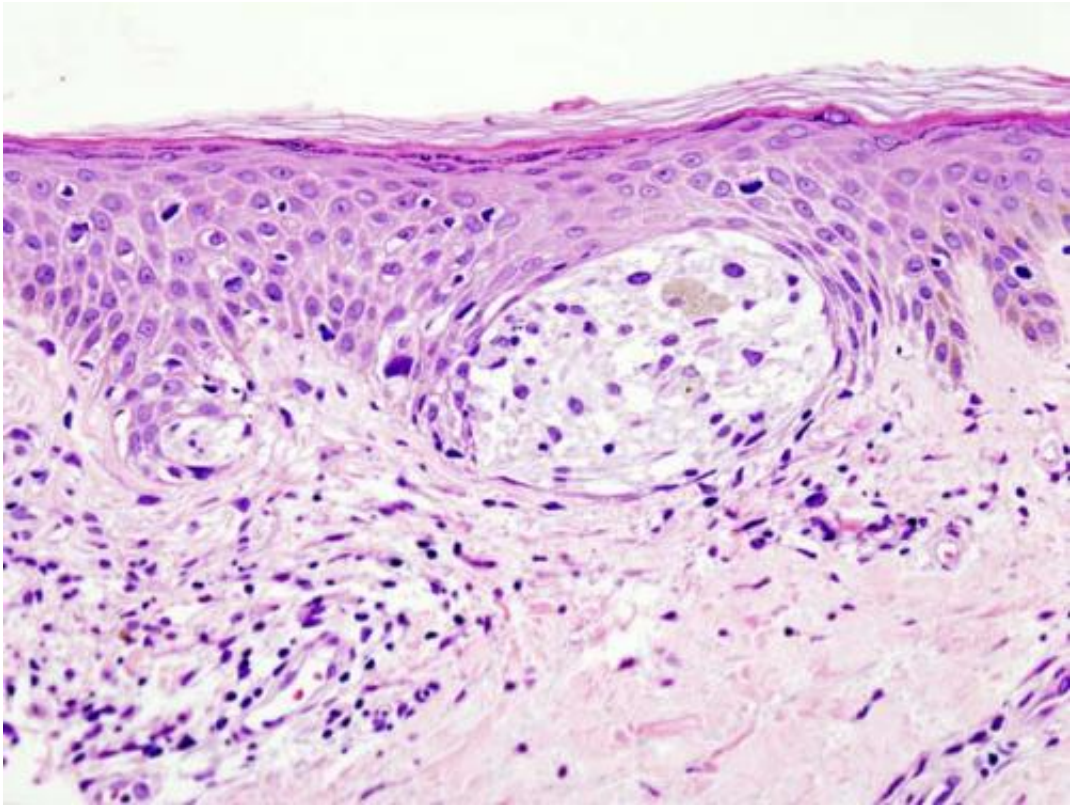

Melanoma in skin biopsy with H&E stain—this case may represent superficial spreading melanoma. Credit: Wikipedia/CC BY-SA 3.0

The importance of RNA editing in melanoma has been demonstrated by scientists at The University of Texas MD Anderson Cancer Center. The study revealed that a lack of RNA editing, a process by which information inside RNA molecules is transformed, leads to tumor

growth and progression through manipulation of proteins.

Study lead Menashe Bar-Eli, Ph.D., professor of Cancer Biology, reported a previously unknown target for CREB (cAMP response element-binding protein), a transcription factor that regulates other transcription factors involved in melanoma development. Transcription factors are proteins that turn genetic instructions on and off.

"We found that CREB regulates ADAR1, an enzyme involved in RNA editing," said Bar-Eli, whose study findings appear in this month's issue of *Nature Cell Biology*. "CREB negatively regulated ADAR1, promoting melanoma tumor growth and metastasis."

"When we discovered that CREB negatively regulated ADAR1, we looked further into how the loss of ADAR1 expression contributes to the cancer spread."

Bar-Eli's team evaluated the RNA editing functioning of ADAR1 in microRNAs (miRNAs). MicroRNAs are small, non-coding molecules that have been linked to several types of cancer. Bar-Eli identified adenosine-to-inosine RNA editing in three miRNAs. RNA editing occurs only in the non-metastatic (ADAR1-positive), but not in the metastatic melanoma cells (ADAR1-negative).

Manipulation of the miRNAs by silencing the naturally occurring or wild-type version of a miRNA and overexpressing an "edited" miRNA confirmed the significance of RNA editing in tumor growth and metastasis.

"We found that increased wild-type miRNA led to increased tumor growth and cancer spread," said Bar-Eli. "In contrast, overexpression of the edited miRNA led to decreased tumor growth and metastasis. The biological functions of edited mi RNAs are different from unedited

forms, as they recognize a different set of genes. These results demonstrate a previously unrecognized role for RNA editing in melanoma progression."

The team's investigation involved study of cell lines, mice and data from The Cancer Genome Atlas (TCGA). The TCGA is a research program supported by the National Cancer Institute and National Human Genome Research Institute within the National Institutes of Health that is looking at genomic changes in more than 20 different types of cancer.

More information: Reduced adenosine-to-Inosine miR-455-5p editing promotes melanoma growth and metastasis, dx.doi.org/10.1038/ncb3110

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