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Overexpression of ARD1A gene reduces tumor size and number in mice

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Overexpression of the ARD1A gene (arrest-defective protein 1225) in mice reduced the number and size of both primary tumors and metastases, researchers report in a new study published online March 1in the *Journal of the National Cancer Institute*.

ARD1A blocks the expression of VEGFA (vascular endothelial growth factor A), an important mediator of blood vessel growth in tumors. It regulates VEGFA expression indirectly by acetylating the transcription factor that induces VEGFA expression— hypoxia inducible factor 1(HIF-1α). Acetylation by ARD1A triggers degradation of HIF-1a, which blocks VEGFA expression and blood vessel proliferation in tumors.

To better understand ARD1A's effect on VEGFA expression and on tumor growth, Goo Taeg Oh, D.V.M., Ph.D., Division of Life and Pharmaceutical Sciences, Ewha Women's University, in Seoul, Korea, and colleagues injected mice that overexpressed mARDIA with human gastric cancer and mouse melanoma cells. They then measured tumor growth, metastasis, and VEGFA expression.

The researchers found that the mARD1A-expressing mice had statistically significantly fewer intestinal polyps than controls. The growth and metastases of transplanted tumors were statistically significantly reduced in mice injected with mARD1A- overexpressing cells compared to mice injected with control cells. The group also confirmed that overexpression of mARD1A decreases VEGFA

expression and microvessel density in tumors and that HIF-1α only needs to be acetylated at one site to be degraded.

The authors write: "…We conclude that mARD1A225 presents a novel target in the regulation of HIF-1a stability and may have potent therapeutic effects in combination with currently approved anti-VEGFA treatments such as bevacizumab."

More information: jnci.oxfordjournals.org

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