How Eating Red Meat Can Spur Cancer Progression

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Researchers at the University of California, San Diego School of Medicine, led by Ajit Varki, M.D., have shown a new mechanism for how human consumption of red meat and milk products could contribute to the increased risk of cancerous tumors. Their findings, which suggest that inflammation resulting from a molecule introduced through consumption of these foods could promote tumor growth, are published online this week in advance of print publication in the *Proceedings of the National Academy of Sciences (PNAS).*

Varki, UC San Diego School of Medicine distinguished professor of medicine and cellular and molecular medicine, and co-director of the UCSD Glycobiology Research and Training Center, and colleagues studied a non-human cellular molecule called *N*-glycolylneuraminic acid (Neu5Gc). Neu5Gc is a type of glycan, or sugar molecule, that humans don't naturally produce, but that can be incorporated into human tissues as a result of eating red meat. The body then develops anti-Neu5Gc antibodies – an immune response that could potentially lead to chronic inflammation, as first suggested in a 2003 *PNAS* paper by Varki.

"We've shown that tumor tissues contain much more Neu5Gc than is usually found in normal human tissues," said Varki, who is also a faculty member of the Moores UCSD Cancer Center. "We therefore surmised that Neu5Gc must somehow benefit tumors."

It has been recognized by scientists for some time that chronic inflammation can actually stimulate cancer, Varki explained. So the researchers wondered if this was why tumors containing the non-human molecule grew even in the presence of Neu5Gc antibodies.

"The paradox of Neu5Gc accumulating in human tumors in the face of circulating antibodies suggested that a low-grade, chronic inflammation actually facilitated the tumor growth, so we set out to study that hypothesis," said co-author Nissi M.Varki, M.D., UCSD professor of pathology, and faculty member with the Moores UCSD Cancer Center.

Using specially bred mouse models that lacked the Neu5Gc molecule – mimicking humans before the molecule is absorbed into the body through ingesting red meat – the researchers induced tumors containing Neu5Gc, and then administered anti-Neu5Gc antibodies to half of the mice. In

mice that were given antibodies inflammation was induced, and the tumors grew faster. In the control mice that were not treated with antibodies, the tumors were less aggressive.

Others have previously shown that humans who take non-steroidal anti-inflammatory drugs (commonly known as NSAIDs) have a reduced risk of cancer. Therefore, the mice with cancerous tumors facilitated by anti-Neu5Gc antibodies were treated with an NSAID. In these animals, the anti-inflammatory treatment blocked the effect of the Neu5Gc antibodies and the tumors were reduced in size.

"Taken together, our data indicate that chronic inflammation results from interaction of Neu5Gc accumulated in our bodies from eating red meat with the antibodies that circulate as an immune response to this non-human molecule – and this may contribute to cancer risk," said Varki.

Additional contributors to the paper are Maria Hedlund and Vered Padler-Karavani, UCSD Departments of Medicine and Cellular and Molecular Medicine. The study was funded in part by a grant from the National Cancer Institute, of the National Institutes of Health.

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