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Sugar Molecule Links Red Meat Consumption and Elevated Cancer Risk in Mice

Neu5Gc, a non-human sugar found in red meat, promotes inflammation and cancer progression in rodents

While people who eat a lot of red meat are known to be at higher risk for certain cancers, other carnivores are not, prompting researchers at the University of California, San Diego School of Medicine to investigate the possible tumor-forming role of a sugar called Neu5Gc, which is naturally found in most mammals but not in humans.



Red meat is rich in Neu5Gc, a non-human sugar found to promote inflammation and cancer progression in rodents.

In a study published in the Dec. 29 online early edition of the *Proceedings of the National Academy of Sciences*, the scientists found that feeding Neu5Gc to mice engineered to be deficient in the sugar (like humans) significantly promoted spontaneous cancers. The study did not involve exposure to carcinogens or artificially inducing cancers, further implicating Neu5Gc as a key link between red meat consumption and cancer.

“Until now, all of our evidence linking Neu5Gc to cancer was circumstantial or indirectly predicted from somewhat artificial experimental setups,” said principal investigator Ajit Varki, MD, Distinguished Professor of Medicine and Cellular and Molecular Medicine and member of the UC San Diego Moores Cancer Center. “This is the first time we have directly shown that mimicking the exact situation in humans — feeding non-human Neu5Gc and inducing anti-Neu5Gc antibodies — increases spontaneous cancers in mice.”

Varki’s team first conducted a systematic survey of common foods. They found that red meats (beef, pork and lamb) are rich in Neu5Gc, affirming that foods of mammalian origin such as these are the primary sources of Neu5Gc in the human diet. The molecule was found to be bio-

available, too, meaning it can be distributed to tissues throughout the body via the bloodstream.

The researchers had previously discovered that animal Neu5Gc can be absorbed into human tissues. In this study, they hypothesized that eating red meat could lead to inflammation if the body's immune system is constantly generating antibodies against consumed animal Neu5Gc, a foreign molecule. Chronic inflammation is known to promote tumor formation.

To test this hypothesis, the team engineered mice to mimic humans in that they lacked their own Neu5Gc and produced antibodies against it. When these mice were fed Neu5Gc, they developed systemic inflammation. Spontaneous tumor formation increased fivefold and Neu5Gc accumulated in the tumors.

“The final proof in humans will be much harder to come by,” Varki said. “But on a more general note, this work may also help explain potential connections of red meat consumption to other diseases exacerbated by chronic inflammation, such as atherosclerosis and type 2 diabetes.

“Of course, moderate amounts of red meat can be a source of good nutrition for young people. We hope that our work will eventually lead the way to practical solutions for this catch-22.”

Study co-authors include Annie N. Samraj, Oliver M. T. Pearce, Heinz Läubli, Alyssa N. Crittenden, Anne K. Bergfeld, Kalyan Banda, Christopher J. Gregg, Andrea E. Bingman, Patrick Secrest, Sandra L. Diaz and Nissi M. Varki, all at UC San Diego School of Medicine.

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Disclosure: Ajit Varki and Nissi Varki are co-founders and have equity interest in SiaMab Therapeutics, Inc., a biotech company with an interest in Neu5Gc and anti-Neu5Gc antibodies. In addition, Ajit Varki is a member of SiaMab Therapeutics, Inc.'s Board of Directors and is a Scientific Advisor to the company. The terms of this arrangement have been reviewed and approved by the University of California, San Diego in accordance with its conflict of interest policies.

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