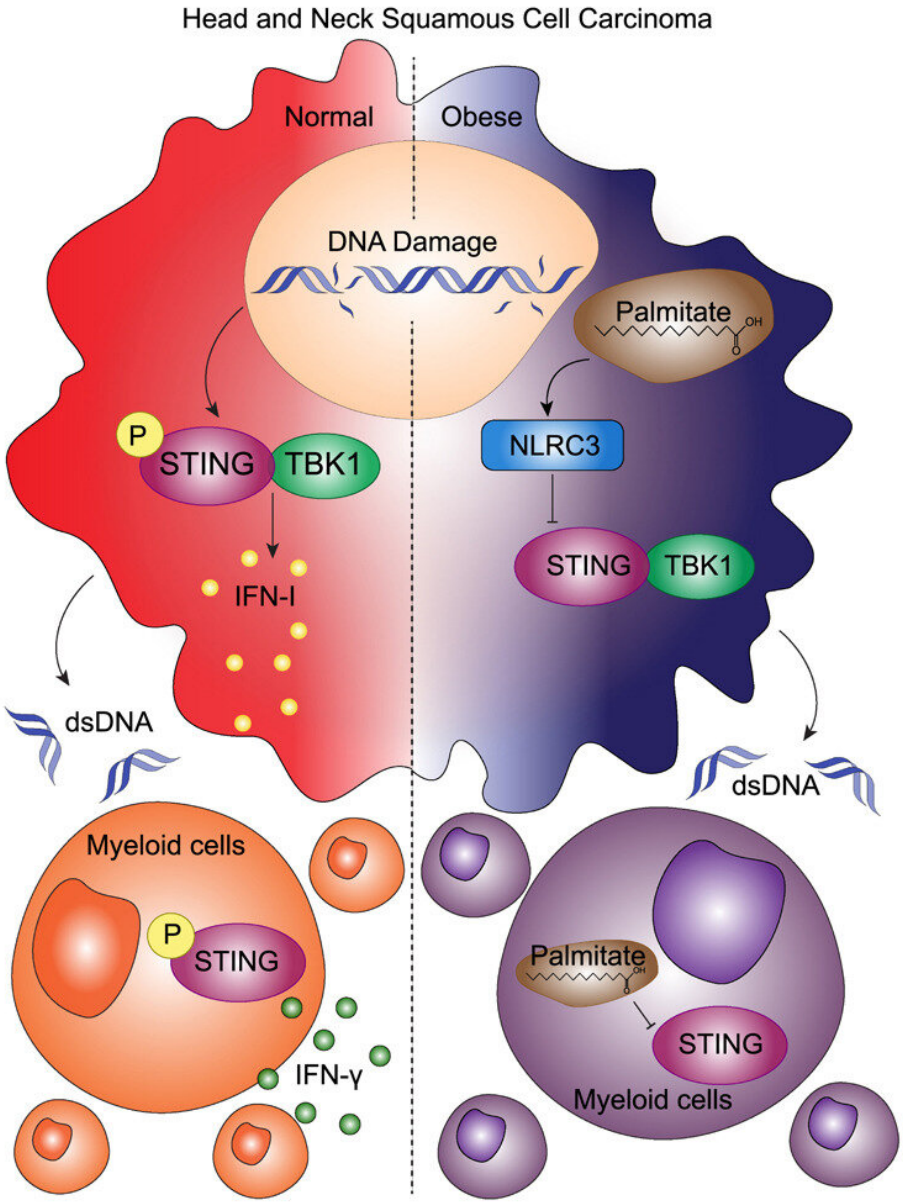
Study links obesity with dampened immune detection of oral cancers

May 16 2023, by Anna Megdell



Credit: *Cell Reports* (2023). DOI: 10.1016/j.celrep.2023.112303

A team from the University of Michigan Rogel Cancer Center and School of Dentistry, led by Yu Leo Lei, D.D.S., Ph.D., have identified a mechanism in mice for how obesity affects some oral cancers' ability to escape from the immune system.

This study, published in *Cell Reports*, found that obesity helps to establish a type of tumor microenvironment that promotes tumor progression. How exactly this happens lies in the relationship between the saturated fatty acids, the STING-type-I interferon pathway, and NLRC3.

"We tend to think about the increased risks for gastrointestinal tumors, breast cancer, pancreatic cancer, and ovarian cancer when it comes to obesity," said Lei, a pathologist-immunologist and lead author of this study. "Multiple recent prospective cohorts involving millions of individuals from several continents revealed a previously underappreciated link between obesity and oral cancer risks."

"Myeloid cells in obese mice were insensitive to STING agonists and were more suppressive of T cell activation compared to the myeloid cells from leans hosts," explained Lei. This feature drove the loss of immune subsets that were crucial for anti-tumor immunity in the tumor microenvironment.

The team found that saturated fatty acids can block the STING pathway, which is induced by cytosolic DNA and promotes antigen-presenting cell maturation, by inducing a protein called NLRC3.

Lei says this is the first study establishing a mechanistic link between

obesity with oral cancer immune escape. "We're excited about the translational implications," he continued.

Obesity is a common comorbidity in cancer patients. Two recent studies found that oral cancer patients who were on statins—medicines that lower cholesterol—showed improved overall and cancer-specific survival. "This study establishes a mechanistic link for those observations and highlights the potential of targeting fatty acids metabolism in remodeling the host anti-tumor immune response," said Lei.

Next, Lei's team will explore how obesity regulates other immune-activating pathways and identify novel intervention targets for better oral cancer prevention in high-risk individuals. More work must be done before this can move to the clinic.

Additional study authors include Blake Heath, Ph.D.; Wang Gong, research Investigator at the School of Dentistry; and Hülya Taner, D.D.S.-Ph.D. candidate.

More information: Blake R. Heath et al, Saturated fatty acids dampen the immunogenicity of cancer by suppressing STING, *Cell Reports* (2023). DOI: 10.1016/j.celrep.2023.112303

Provided by University of Michigan