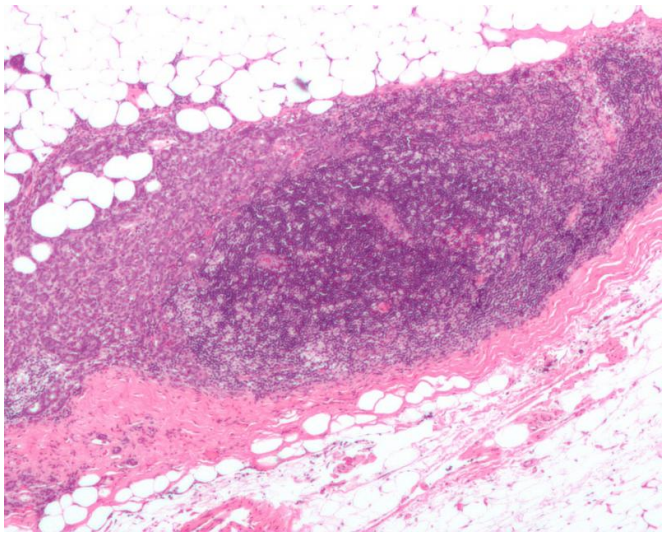
When—not what—obese mice ate reduced breast cancer risk

26 January 2021



Micrograph showing a lymph node invaded by ductal breast carcinoma, with extension of the tumour beyond the lymph node. Credit: Nephron/Wikipedia

Restricting eating to an eight-hour window, when activity is highest, decreased the risk of development, growth and metastasis of breast cancer in mouse models, report researchers at University of California San Diego School of Medicine, Moores Cancer Center and Veterans Affairs San Diego Healthcare System (VASDSH).

The findings, published in the January 25, 2021 edition of *Nature Communications*, show that time-restricted feeding—a form of intermittent fasting aligned with circadian rhythms—improved metabolic health and tumor circadian rhythms in mice with obesity-driven postmenopausal breast cancer.

"Previous research has shown that obesity increases the risk of a variety of cancers by negatively affecting how the body reacts to insulin levels and changing circadian rhythms," said senior author Nicholas Webster, Ph.D., professor at UC San Diego School of Medicine and senior research career scientist at VASDSH. "We were able to increase insulin sensitivity, reduce hyperinsulinemia, restore circadian rhythms and reduce tumor growth by simply modifying when and for how long mice had access to food."

Breast cancer is the second most common cancer among women in the United States, after skin cancers. One in eight women will develop breast cancer in their lifetime.

Researchers used female mouse models mimicking postmenopausal hormone conditions to investigate whether time-restricted feeding of obese mice affected the development and growth of tumors and reduced breast cancer metastasis to the lungs. Three groups were compared in different mouse models. One group had 24-hour access to food. A second had food access for eight hours at night when mice are most active and a third group had an unrestricted low-fat diet.

Both obesity and menopause can disrupt circadian rhythms, which in turn can lead to the development of insulin resistance, predisposing individuals to chronic diseases like cancer.

Data indicates that elevated insulin levels in obese mice are driving the accelerated tumor growth. Artificially elevating insulin levels accelerated tumor growth, whereas reducing insulin levels could mimic the effect of the time-restricted feeding. The results suggest that the antitumor effect of time-restricted feeding is due to improving metabolic health and lowering the levels of insulin, said Manasi Das, Ph.D., postdoctoral fellow in the Webster lab and first author.

"Time-restricted eating has a positive effect on metabolic health and does not trigger the hunger and irritability that is associated with long-term fasting or calorie restriction," said Das. "Through its beneficial metabolic effects, time-restricted eating

may also provide an inexpensive, easy to adopt, but effective strategy to prevent and inhibit breast cancer without requiring a change in diet or physical activity."

Exploring the ability of time-restricted eating to prevent breast cancer in women, or cancer in general, could affect a wide range of patients, said Webster, suggesting that clinical trials are warranted.

"The increase in risk of breast cancer is particularly high in women who are overweight and have been through menopause. For this reason, doctors may advice women to adopt weight loss strategies to prevent tumor growth," said Das. "Our data suggests that a person may benefit from simply timing their meals differently to prevent breast cancer rather than changing what they eat."

More information: Manasi Das et al. Time-restricted feeding normalizes hyperinsulinemia to inhibit breast cancer in obese postmenopausal mouse models, *Nature Communications* (2021). DOI: 10.1038/s41467-020-20743-7

Provided by University of California - San Diego