High-fat diet in pregnancy increases breast cancer risk over generations in animal study

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Feeding pregnant female mice a diet high in fat derived from common corn oil resulted in genetic changes that substantially increased breast cancer susceptibility in three generations of female offspring, reports a

team of researchers led by scientists at Georgetown Lombardi Comprehensive Cancer Center.

Their study, published online today in *Breast Cancer Research*, suggests a research direction for examining the diet of pregnant women, says the study's senior author, Leena Hilakivi-Clarke, PhD, professor of oncology at Georgetown Lombardi.

"It is believed that environmental and life-style factors, such as diet, plays a critical role in increasing human breast cancer risk, and so we use animal models to reveal the biological mechanisms responsible for the increase in risk in women and their female progeny," says Hilakivi-Clarke.

A high-fat diet is linked to excess inflammation, and a number of epidemiological studies have made the connection between inflammation and risk of cancer, she says.

Hilakivi-Clarke has found in earlier studies that mice that eat a high fat diet when they are pregnant have "daughters" that are at excess risk of the cancer. This study, however, found that if pregnant mice were switched to a high fat diet during their second trimester when the germ line mediating genetic information from one generation to another forms in the fetus, an increase in breast cancer risk is also seen in "great granddaughters.

A gene screen revealed a number of genetic changes in the first (daughter) and third (great granddaughter) high-fat mice generations, including several genes linked in women to increased breast cancer risk, increased resistance to cancer treatment, poor cancer prognosis and impaired anti-cancer immunity. The researchers also found three times as many genetic changes in third generation than first generation mammary tissue between high-fat diet progeny and the control group's

offspring.

"The soil in the breast, so to speak, remained fertile for breast cancer development in our high-fat experimental mice," Hilakivi-Clarke says.

The amount of fat fed to the experimental mice matched what a human might eat daily, says Hilakivi-Clarke. In the study, both the control mice and the mice fed chow with high levels of corn oil ate the same amount of calories and they weighed the same. "But our experimental mice got 40 percent of their energy from fat, and the control mice got a normal diet that provided 18 percent of their energy from fat," she says. "The typical human diet now consists of 33 percent fat."

Pregnant mice in the experimental arm ate the high-fat diet starting at gestation day 10, the time when a daughter's ovarian eggs (and so their germ cells) begin to develop. This corresponds roughly to a woman's second trimester. By comparison, eating a high-fat diet before and during pregnancy increase breast cancer risk in the subsequent two generations, but does not cause inheritable changes in the germ cells, Hilakivi-Clarke says.

"Studies have shown that pregnant women consume more fats than non-pregnant women, and the increase takes place between the first and second trimester," she says.

"Of the 1.7 million new cases of breast cancer diagnosed in 2012, 90 percent have no known causes," she says. "Putting these facts, and our finding, together really does give food for thought."

More information: Nguyen M. Nguyen et al, Maternal intake of high n-6 polyunsaturated fatty acid diet during pregnancy causes transgenerational increase in mammary cancer risk in mice, *Breast Cancer Research* (2017). DOI: 10.1186/s13058-017-0866-x

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