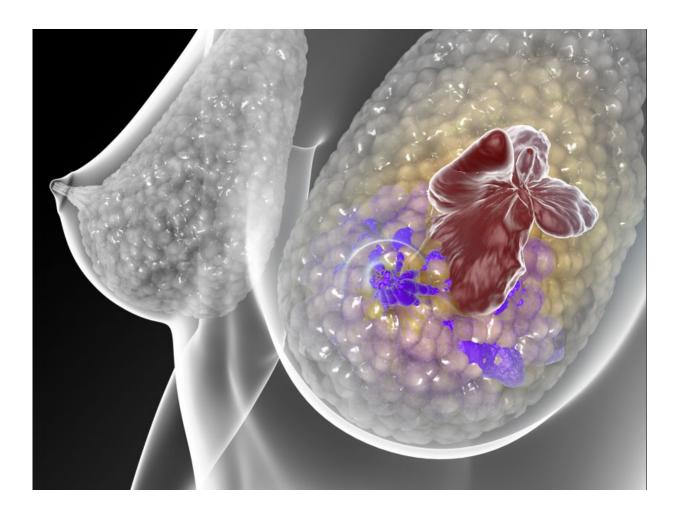


## Scientists probe obesity's ties to breast cancer risk

August 20 2015, by Emily Willingham, Healthday Reporter



Obesity is known to be a major risk factor for breast cancer, especially in postmenopausal women. Compared to women with normal body mass index, obese women tend to be diagnosed with larger tumors, with greater risk of lymph node metastases and recurrence. Credit: C. Bickel / Science Translational Medicine



Obesity is a well-known risk factor for breast cancer, but researchers haven't figured out what connects the two. A new study suggests the link may be due to a change in breast tissue structure, which might promote breast cells to progress to cancer.

The findings, based on research with <u>tissue</u> from mice and humans, emphasize the need to encourage a healthy weight in women who have breast cancer and in general. The results may also have implications for <u>breast cancer detection</u> and breast reconstruction surgeries, the researchers reported in the Aug. 19 issue of *Science Translational Medicine*.

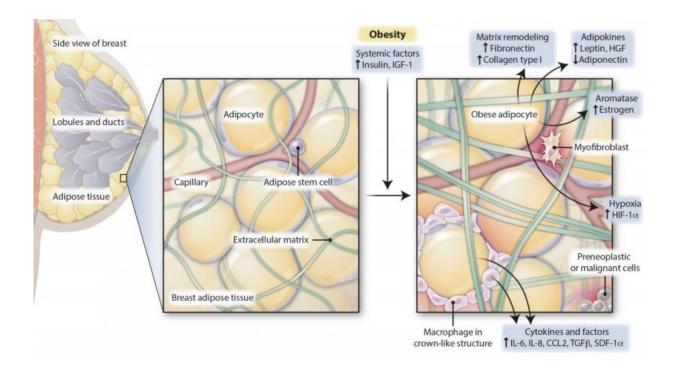
The authors of an editorial accompanying the paper said the findings could be key to solving the puzzle of how obesity leads to breast cancer or worsens outcomes for women with the disease. This kind of information could open the way to treatments that target those pathways, according to Lisa Arendt, a research assistant professor, and Charlotte Kuperwasser, an associate professor, at Tufts University in Boston.

"Unfortunately, therapeutics specific for <u>obese women</u> with breast cancer are limited," Arendt and Kuperwasser wrote. They said that obesity accounts for as much as one-fifth of all cancer deaths among women.

The processes underlying the obesity-breast cancer link had left specialists stumped, although some had proposed obesity-related differences in hormones or inflammation. But obesity-related stiffening of breast tissues was not high on the list.

In the new work, Cornell University doctoral student Bo Ri Seo and colleagues looked at breast fat tissue in humans and mice. They found that in obesity, the web-like network of fibers holding fat cells in place is more rigid than normal.





Obesity induces both local and systemic changes implicated in breast cancer progression. These include changes in insulin levels, secretion of adipocytederived hormones, increased local estrogen concentrations, secretion of cytokines and other growth factors, and hypoxic conditions. Now, Seo et al. have identified an additional mechanism by which increased collagen and fibronectin deposition within obese adipose tissue contribute to extracellular matrix stiffness, which promotes breast tumor progression. Credit: H. McDonald / Science Translational Medicine

Curious about whether obesity-related genetics might play a role, the researchers compared tissues of mice that were genetically obese and mice that became obese from overfeeding. Regardless of how they became obese, their tissues still were stiffened, the investigators found.

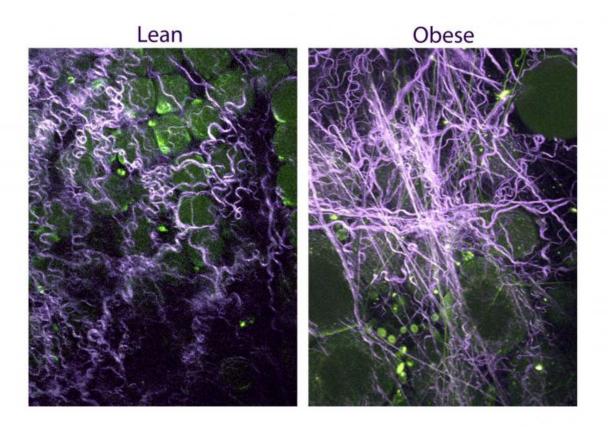
The researchers also ruled out a common inflammation-related molecule as playing a role. They concluded that the stiff structure itself seemed to



be the relevant factor.

To assess that idea further, the study authors also exposed precancerous <u>breast cells</u> to these stiff fibrous networks from obesity-related tissue samples. Cells growing under these conditions were more likely to become completely cancerous compared to those grown in non-obesity-related samples.

Finally, the researchers turned to the obvious question: Would weight loss reduce this stiffening effect?



Lean vs. obese tissue is shown. Credit: Cornell University



When the researchers placed obese mice on a diet, the fibrous network thinned out a little, "hinting that weight loss can potentially reverse this tissue stiffening," the study authors explained in a journal news release.

Another question is how obesity leads to the stiffer tissues. Arendt and Kuperwasser said that low oxygen in the denser tissues might be one explanation. And, they noted, it's still possible that an inflammatory process plays a role.

Dense breast tissue on a mammogram is associated with a higher probability of developing breast cancer, Seo and her co-authors pointed out. But fat tissue might mask this kind of density, they added, suggesting that for obese women, more focused, high-resolution imaging might be called for to detect hidden areas of density.

The study authors also noted that using donor <u>breast tissue</u> to regenerate breasts after complete breast removal is becoming a possibility. If donor tissue from obese women might carry a risk of promoting cancerous changes in breast cells, that factor may need to be considered, they suggested.

Obesity-related breast cancer rates are likely to increase as obesity rates keep rising, Arendt and Kuperwasser warned. Currently, weight loss is the only recommendation for obesity in women diagnosed with breast cancer.

Diabetic women who take the drug metformin have a lower risk of developing breast cancer. For this reason, this diabetes drug is also being tested in clinical trials as treatment for obesity-associated breast cancer, the editorialists said.

But little research has addressed how weight loss might affect risk for developing <u>breast cancer</u> in the first place. One recent study, Arendt and



Kuperwasser wrote, found no effect of short-term <u>weight loss</u> on this risk in postmenopausal women.

**More information:** Obesity-dependent changes in interstitial ECM mechanics promote breast tumorigenesis, *Science Translational Medicine* 19 Aug 2015: Vol. 7, Issue 301, pp. 301ra130 . DOI: 10.1126/scitranslmed.3010467

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