TuSalud

An Understudied Type of Breast Cancer Poses a Lurking Threat

Matthew Sikora, of University of Colorado Cancer Center, seeks better answers for lobular breast cancer, which can be harder to detect.

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University of Colorado Cancer Center member Matthew Sikora, PhD, is a national leader in research into an understudied subtype of breast cancer that's on the rise in American women, is often more difficult to detect than other forms of breast cancer, and has sharply lower survival rates several years after diagnosis than the most common type of breast cancer.

Sikora's latest research — bolstered by foundation funding — seeks ways to potentially open up a new treatment option for people with this challenging cancer type, known as lobular breast cancer or invasive lobular carcinoma (ILC), representing about 15% of all breast cancer cases.

Sikora is an associate professor in the CU Anschutz Department of Pathology. His lab focuses on ILC, he serves on the scientific advisory board of the Lobular Breast Cancer Alliance, and he has helped to build the Front Range ILC Patient Network, an advocacy group that includes patients, caregivers, researchers, and clinicians.

→ Seeking a Unique Treatment for Lobular Breast Cancer

'Very different challenges'

A key difference between ILC and other forms of breast cancer is how it presents itself in the breast, Sikora says.

"Rather than forming the typical lump or mass that a woman might think of finding on a self exam, lobular tumors don't typically form a lump," he says. "When you look on the diagnostic image, rather than seeing a solid field of tumor, the ILC cells radiate through the breast in this very characteristic single-file pattern. So, because it rarely forms a mass, it doesn't show up as well in mammography because there's nothing solid to pick up."

ILC often is mistakenly called "a disease of older women, but that's largely because it doesn't get detected until later," Sikora says. "The all-too-common anecdote about ILC is that women have

negative mammography for years, then one day they show up with a speck in the breast, and then they go in for a biopsy and they have a breast full of cancer."

Also, ILC is "much harder to excise surgically," Sikora says. "The surgeon often doesn't know where the tumor stops, so women with ILC more often have to go back in for re-excision. And it metastasizes in weird places that other breast cancers usually don't go, including in the abdomen, through the gut, and around the gynecologic organs, so it presents very different challenges."

VIDEO: Watch the 2024 Lobular Breast Cancer Awareness Day program at the CU Cancer Center:

Cast aside for many years

In a report released October 7, the American Cancer Society estimated that 33,600 women in the United States will be diagnosed with ILC this year. The ACS report warned that incidence of ILC rose an average of 2.8% per year between 2012 and 2021 in the U.S., a far steeper increase than all other forms of breast cancer combined (0.8% per year).

The ACS report said ILC survival rates after seven years are significantly lower than for most other breast cancers. It also said that ILC is "very understudied" in comparison to other breast cancer types, "probably because of a very good short-term prognosis," and cited "a critical need for more study of this unique breast cancer subtype."

Meanwhile, the National Cancer Institute estimates that ILC may in fact account for 47,500 diagnoses in the U.S. annually.

Sikora agrees that ILC has not been adequately studied, and says the varying estimates of incidence underscore the need for a better understanding of the disease. He suspects that ILC has been "grossly under-diagnosed" in less affluent and rural areas far from high-volume medical centers.

ILC "has been cast aside for many, many years as something that's low risk and unremarkable. But we're learning that patients with ILC face the highest risk of long-term recurrence. After patients finish their five or so years of standard anti-estrogen therapy, they think they're all clear, but that's when lobular cancer recurrences tend to tick up. It's a very long-term psychological burden that these patients face."

→ Medical Student Receives Award for Lobular Breast Cancer Research

Focusing on a hidden weakness

Sikora has received ongoing support from the Dynami Foundation, which underwrites research into ILC and other breast cancer types, in his work to better understand lobular cell biology and why

these cancers are different from others, including $50,000 for his latest project to identify promising new therapeutic approaches to the disease.

Sikora has been focusing on PARP inhibitors, a class of drugs that are designed to target a dysfunction in the repair of DNA in cancer cells, thereby killing them. ILC patients usually aren't given PARP inhibitors because their cancer doesn't present the kinds of DNA repair dysfunctions that these drugs can exploit, he says.

But Sikora's new research suggests ILC actually has a hidden DNA repair weakness that could make certain PARP inhibitors effective as a treatment option beyond anti-estrogen therapy. In lab experiments and animal models, Sikora and his team tested a PARP inhibitor called talazoparib and found it effectively stopped ILC growth.

"We think ILC potentially will be hyper-responsive to a combination of PARP inhibitors, either combined with certain anti-estrogens or with related DNA-repair-targeted drugs that are currently in clinical trials," Sikora says. "So Dynami is helping us break new ground in trying to identify what types of therapies ILC may respond to."

→ CU Cancer Center Breaks Down the Divide Between Research and Community

Overcoming a barrier

It's been a long road for Sikora on the hunt for ILC answers. He recalls writing grants to study ILC 15 years ago as a post-doc. "I received some reviewer comments that said things like, 'Why are you studying this? This is a low-risk disease.' So we've overcome a barrier over the last 15 years to get the community to acknowledge that this, in fact, is something that needs to be studied."

Sikora and Front Range ILC have also been involved in periodic outreach events, including tours of his lab and poster sessions.

On October 15, from 1:30 to 4 pm, Front Range ILC and the Sikora Lab commemorated Lobular Breast Cancer Awareness Day at an outreach event in the Krugman Conference Hall at CU Anschutz to talk about ILC research at the CU Cancer Center and support people with ILC. Click here to register to attend in person or via a live video link.

"The goal of these events is to reach women with ILC, who have been differentially diagnosed with lobular cancer from other types of breast cancer for decades, but only recently have they been recognized as perhaps needing different treatment," Sikora says. "A lot of these women are hungry to learn anything they can about their disease. We want them to know there are people on our campus who are trying hard to understand their disease. We want to update them on what we're learning and how we hope it will impact their care eventually."

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