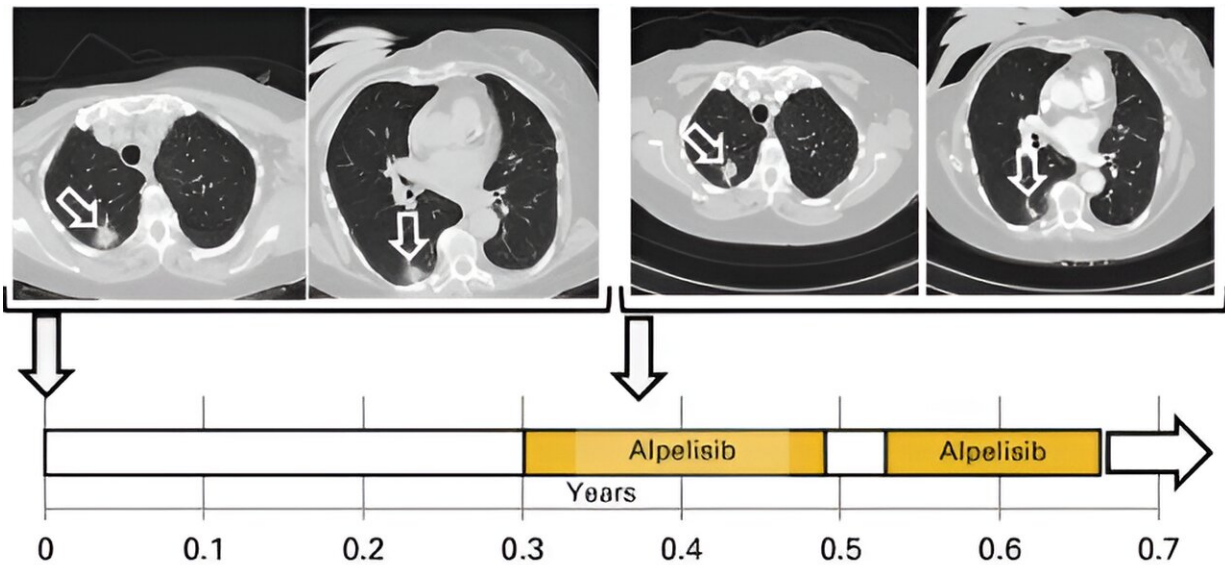# Researchers develop mechanism that predicts severity of aggressive form of breast cancer

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Clinical course of a patient with PDX+ metaplastic breast cancer after development of recurrent (metastatic) disease (day 0) where treatment was informed by prospective genomic and PDX-derived organoid-based drug profiling studies. Credit: *JCO Precision Oncology* (2024). DOI: 10.1200/PO.23.00724

Scientists at Huntsman Cancer Institute at the University of Utah (the U), the National Cancer Institute-designated cancer center for the Mountain West, have made a significant breakthrough in predicting the prognosis of triple-negative breast cancer (TNBC), a particularly

aggressive disease.

Their research, published in *JCO Precision Oncology* as part of the TOWARDS study, has led to the development of a new mechanism that accurately forecasts the aggressiveness of TNBC. This advancement could revolutionize the way doctors treat TNBC, allowing them to identify higher-risk patients and tailor precise treatments.

Currently, TNBC lacks reliable methods to predict recurrence after treatments like chemotherapy and surgery. Unlike other breast cancers, TNBC is challenging to treat because its tumor cells lack estrogen receptors, progesterone receptors, and high levels of HER2/neu protein, according to experts at the National Institutes of Health. This often results in a higher likelihood of relapse after treatment.

Researchers used a patient-derived xenograft (PDX) model, where biopsies of tumors from patients were implanted into mice to grow human tumors. Alana Welm, Ph.D., senior author of the study, senior director of basic science at Huntsman Cancer Institute, and professor of oncological sciences at the U, highlights the significance of this method, noting that it allows for an early and accurate assessment of the cancer's aggressiveness.

Cindy Matsen, MD, co-first author of the study, leader of the Breast and Gynecologic Disease Center at Huntsman Cancer Institute and associate professor in the Department of Surgery at the U, emphasizes the direct impact this research could have on patient care.

She describes the study as highly relevant to addressing a major challenge in breast cancer treatment, with the potential of creating more personalized treatment plans for patients with recurrent TNBC.

The study's mechanism was more accurate than existing methods in

predicting whether TNBC will recur. Welm notes, "By implanting a biopsy of the tumor into a PDX, we can discover how aggressive the cancer is. We hope to extend our new findings to improve the current standard tests used to predict whether the patients' cancer will recur."

"This study addresses a very pressing problem in the clinic," says Christos Vaklavas, MD, co-first author of the study, head of the breast cancer clinical program at Huntsman Cancer Institute, and associate professor of internal medicine at the School of Medicine at the U.

"PDX models help us not only predict with greater accuracy who will relapse and who will not, but also to treat recurrences with greater precision."

Matsen also underscored the practical benefits of the study. In the second phase, now underway as a clinical trial, scientists are testing specific drugs on PDX models. If these therapies prove effective, results will be shared with physicians, providing them with valuable insights on how to guide treatment decisions.

The study's results are crucial: if a tumor grows in the PDX model, it often indicates a highly aggressive cancer, which is significantly harder to treat. Matsen stressed the urgency of improving treatment strategies, noting the devastating impact of the cancer recurrence.

"This study gives us the opportunity to provide hope and to save more lives," Matsen says.

 More information: Christos Vaklavas et al, TOWARDS Study: Patient-Derived Xenograft Engraftment Predicts Poor Survival in Patients With Newly Diagnosed Triple-Negative Breast Cancer, *JCO Precision Oncology* (2024). DOI: 10.1200/PO.23.00724