Transcript Details

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Targeting Ribosome Maturation: A Preclinical Strategy for Triple-Negative Breast Cancer

Mr. Quigley:

You're listening to ReachMD, and this is an *AudioAbstract.* I'm Ryan Quigley, and today, we're diving into new research presented at the 2025 San Antonio Breast Cancer Symposium that explored whether interfering with ribosome production could suppress tumor growth in preclinical models of triple-negative breast cancer, or TNBC.

For some background, TNBC is one of the most challenging breast cancer subtypes to treat. Because it lacks hormone receptors and HER2 amplification, patients often rely on chemotherapy, which can be effective but still leaves many with residual disease or early relapse.

The ongoing need for better options has pushed researchers to look for new, targetable vulnerabilities in these tumors. One area of focus gaining traction is ribosome biogenesis. Many aggressive cancers, including triple-negative tumors, appear to depend heavily on this process.

Researchers analyzed data from The Cancer Genome Atlas and found that genes involved in ribosome biogenesis were expressed at higher levels in triple-negative tumors than in other breast cancer subtypes. And one protein in particular, fibrillarin, was consistently seen in higher levels in triple-negative tumors. This nucleolar protein helps process precursor ribosomal RNA into its mature form.

So to test whether interfering with this pathway could slow tumor growth, the researchers used two strategies. First, they blocked RNA polymerase I, the enzyme responsible for synthesizing the initial ribosomal RNA transcript. Then, they went further downstream and directly reduced fibrillarin expression using inducible shRNA.

Both approaches produced a clear effect across in vitro and in vivo models. In cell-based assays, tumor cell growth dropped substantially, and in mouse xenograft models, tumor growth was reduced significantly by either intervention.

However, only fibrillarin knock-down showed no evidence of genotoxic activity, with no detectable DNA damage in any of the preclinical models.

And across all experiments, fibrillarin knock-down predominantly caused cell-cycle arrest rather than apoptosis, even when combined with strong apoptosis inducers. This is an important finding as TNBC cells commonly have defects in apoptosis.

In fact, halting the cell cycle alone was enough to slow tumor progression. In fibrillarin-targeted xenografts, tumors showed almost no growth during the treatment window.

On the other hand, body weight and organ histology remained largely unaffected, which suggests minimal acute toxicity in this preclinical setting.

So why does this work matter?

These findings support ribosome biogenesis as a therapeutic vulnerability in TNBC. They also highlight fibrillarin as a potentially less damaging point of intervention compared with some RNA polymerase I inhibitors. And because fibrillarin's primary effect is cell-cycle arrest rather than cell death, this approach may be relevant for tumors that are inherently resistant to apoptosis—a frequent challenge in TNBC.

While these results are early and preclinical, they open the door to developing new classes of therapies that target ribosome maturation. For a breast cancer subtype with limited treatment choices and high relapse rates, this represents a promising direction for future drug

development.

This has been an *AudioAbstract* for *Project Oncology,* and I'm Ryan Quigley. To access this and other episodes in our series, visit ReachMD dot com, where you can Be Part of the Knowledge. Thanks for listening!

Reference

Jouines C, Lo Monaco P, Gaucherot A, et al. Fibrillarin-mediated ribosomal RNA maturation is a novel therapeutic vulnerability in triple-negative breast cancer. *Breast Cancer Res*. 2025;27(1):202. Published 2025 Nov 13. doi:10.1186/s13058-025-02163-x