



## The Trouble with TNBC

[Triple Negative Breast Cancer](#) (TNBC) is difficult to treat because of what it lacks. The term "triple-negative breast cancer (TNBC) is just a definition of what [the cancer] isn't." explains Komen Scholar Dr. Jennifer Pietenpol, Director of the Vanderbilt-Ingram Cancer Center and Professor of Molecular Oncology at Vanderbilt University. TNBC tumors lack the receptors – estrogen (ER), progesterone (PR), and human epidermal growth factor 2 (Her2) – that drive the majority of breast cancers. The absence of these receptors means that TNBC tumors are unlikely to respond to the therapies that target them, including hormone therapies like tamoxifen and Her-2 targeted therapies like trastuzumab (Herceptin).



The lack of targeted therapies for TNBC poses a significant barrier to the treatment of this aggressive subtype, which accounts for approximately 15% of all breast cancers and disproportionately affects women with a [BRCA](#) mutation and African American women. With few treatment options and cytotoxic chemotherapy (kills both normal and cancer cells) as the standard care, there is an urgent need to create therapies specifically targeted for patients diagnosed with TNBC.

## A TNBC Signature

With a grant given by Komen, and partially funded by the Milburn Foundation, Dr. Pietenpol and her research team have identified six different subtypes of TNBC and are working to develop therapies that target the subtypes. By studying nearly 600 cases of TNBC, the Vanderbilt-Ingram Cancer Center researchers were able to uncover the unique genetic differences among different TNBC tumors. These differences led the researchers to assign "genetic signatures" to the different triple negative tumors, which they are using to develop TNBC-targeted therapies.

Collaborating with researchers at MD Anderson Cancer Center, the Pietenpol group analyzed how the newly discovered TNBC subtypes responded to different chemotherapy regimens. Only about 28% of patients with TNBC have a complete response to existing treatments and it is not fully understood what differentiates these patients from the rest.<sup>1</sup> The collaborative study between two cancer centers confirmed that response rates to treatment varied substantially by subtype. ***Oncologists now have more molecular information that will help them better identify which investigational treatment regimens will be most effective for each subtype of TNBC.***

## A New Tool for TNBC

Recognizing the urgency of those patients living with TNBC, Dr. Pietenpol and colleagues turned their attention to developing a web-based tool that can help other researchers determine TNBC subtypes in the samples they are studying. The tool, called [TNBCtype](#), was released in 2011 and has been used by over 1000 scientists from 17 countries around the [world](#)<sup>2</sup>.

<sup>1</sup> Masuda H, Baggerly KA, Wang Y, Zhang Y, Gonzalez-Angulo AM, Meric-Bernstam F, Valero V, Lehmann BD, Pietenpol JA, Hortobagyi GN, Symmans WF, and Ueno NT. Differential response to neoadjuvant chemotherapy among 7 triple-negative breast cancer molecular subtypes. [Clin Cancer Res](#). 2013; 19: 5533-40.

<sup>2</sup> Chen X, Li J, Gray WH, Lehmann BD, Bauer JA, Shyr Y, and Pietenpol JA.. TNBCtype: A Subtyping Tool for Triple-Negative Breast Cancer. [Cancer informatics](#) 2012;11:147-56.



### What's Next?

In the coming year, Dr. Pietenpol and her collaborator, Dr. Vandana Abramson, will oversee two clinical trials that will test new, targeted treatments for the TNBC subtypes. **To Dr. Pietenpols' knowledge, one of the trials would be the first of its kind, with TNBC patients assigned to a treatment group based on a predictive biomarker test (predicts who will most likely respond to a given therapy) and, as a result, matched to a targeted combination treatment.**

Both trials – one of which is currently open and accruing patients – will test the safety and tolerability of using two new drugs that target the TNBC signatures. The new drugs will be used in combination with existing standard-of-care treatments in patients with metastatic TNBC. The trials will be offered through the [Translational Breast Cancer Research Consortium](#), a Komen supported collaborative group founded in 2005 to conduct innovative and high-impact clinical trials for breast cancer.

[Learn](#) more about TNBC

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