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Collaborative study looks for clues on hard-to-treat breast cancer

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Some types of breast cancer can be successfully treated with drugs such as tamoxifen, but treatment for a type of breast cancer more common in young and black women is still limited to radiation and general chemotherapy. Called triple negative breast cancer, this type of cancer is the focus of a 20-month, $8.6-million research project that aims to find new diagnostic tools and options for drugs.

The project takes advantage of one of the most comprehensive collections of breast cancer clinical samples in the U.S. -- the Clinical Breast Care Project located at the Walter Reed National Military Medical Center in Bethesda, Md., and the Windber Research Institute in Winder, Pa.

Researchers will explore these samples using advanced proteomics technology at the Department of Energy's Pacific Northwest National Laboratory and EMSL, DOE's Environmental Molecular Sciences Laboratory in Richland, Wash. Led by PNNL proteomics researcher Richard D. Smith, the study is funded by the Department of Defense.

"Triple negative cancers are more likely to hit young women and African American women. That's a health disparity issue. We need a better understanding of this disease," said team member Karin Rodland, a cancer biologist at PNNL. "And what's been holding that up has been getting enough samples to thoroughly examine how triple negative cancers operate."

Because the Army has such a large population of women that receive health care for years, as well as a higher percentage of black women than the general U.S. population, the Walter Reed-Windber breast cancer repository will provide many high quality samples with well-documented health histories.

One of the first things doctors check when a woman is diagnosed with breast cancer is whether her cancer will grow in response to any or all of three hormones: one that stimulates cell growth and two sex hormones, estrogen or progesterone -- cancers that can be treated with particular drugs. But many other breast cancers don't respond. Called triple negative breast cancers, these types represent a wide variety of cancers and are typically more aggressive and harder to treat.

The research team will profile the complement of proteins -- known as the proteome -- that the breast cancer tissues produce, looking for proteins that triple negative cancers share. The shared proteins could suggest new options for drug therapies. In addition, comparing how aggressive the cancers are to the complement of proteins the cancers make or other metabolic products could lead to new diagnostic tools.

In addition to finding leads on diagnostic tools and therapies, the study might reveal proteins and molecular pathways that have gone astray and led to the cancer in the first place.

A recent, unrelated study reported in the news from the journal *Nature* re-grouped breast cancers into 10 sub-groups based on the cancer's genes and which genes were turned on or off in the cancerous cells. But genes are like a raw movie script -- how the movie turns out depends on many details beyond the words in the script. This new study will look beyond genes to see how cancer cells translated their scripts into live action.

The PNNL research effort will draw on the unique instruments and

expertise developed at PNNL and EMSL in support of DOE-funded research in biofuels and bioremediation, which are also applicable to biological questions related to human health.

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