

# Researchers develop a new cell and animal model of inflammatory breast cancer

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Inflammatory breast cancer (IBC) is a very aggressive, often misunderstood type of cancer that is diagnosed more frequently in younger women compared with other types of breast cancer. The five-year survival rate is between 25 and 50 percent—significantly lower than the survival rate for other types of breast cancer. The reason for the poor prognosis is that IBC usually grows rapidly and often spreads quickly to other parts of the body, including the brain, bone and lymph nodes. In an effort to better understand the biology of IBC, researchers at Fox Chase Cancer Center have developed a new cell and animal model that holds promise for providing a detailed understanding of the molecular mechanisms underlying the disease and for developing effective interventions.

"In order for us to improve the treatment of these [patients](#), we need to understand the biology of the disease—why these cells are so aggressive, invade very early on, and are resistant to standard treatments—and this starts with having good laboratory and preclinical models," says Massimo Cristofanilli, M.D., F.A.C.P., chairman of Fox Chase's department of medical oncology and senior investigator for the research, which will be presented at the AACR Annual Meeting 2012 on Wednesday, April 4.

The researchers developed a unique model that recapitulates the aggressive metastasis and cancer stem cell activity associated with poor outcomes in patients with IBC. Understanding of the molecular basis of IBC may help increase the research community's knowledge of the metastatic process of other types of breast cancers.

"Because there are only a few models of inflammatory [breast cancer](#), it's important to develop more models of this disease, and ours represents an ideal model to evaluate stem cell-targeting therapies," says Sandra Fernandez, Ph.D., assistant research professor at Fox Chase and lead author on the study.

To develop the new disease model, Fernandez, Cristofanilli and their colleagues developed an IRB-approved prospective protocol allowing for the collection of tissue and pleural fluid from patients with advanced IBC. The new cell line, known as FC-IBC02, was established from the pleural fluid collected from a 49-year-old patient whose cells lacked the protein HER2/neu, as well as receptors for the female hormones estrogen and progesterone. About 15 percent of breast cancer patients share these features and, as a result, they do not respond to hormonal therapies and certain medications that target these proteins. "Currently, the only option to treat these patients is chemotherapy," Fernandez says. "So it's important to have a specific model that we can use to test different drugs and see which ones work for this kind of disease."

Moreover, the researchers grew culture tumor cells derived from the patient's fluid and found that they contained a large amount of the protein tetraspanin CD151, which controls tumor cell migration and invasion. In addition, these cells formed multicellular spheroids that displayed markers of cancer stem cells, including the marker CD44. When injected into the mammary fat pad of mice, the tumor spheroids rapidly developed into tumors and spread to the lungs.

Furthermore, using the latest CytoScan HD arrays, the FCCC researchers found that these cells have multiple losses and gains across almost the whole genome, a phenomenon known as chromothripsis. In particular, FC-IBC02 cells have an amplification on chromosome 8q where the oncogene MYC is located and a deletion on chromosome 7p where tumor suppressor gene p53 is embedded. These analysis will

identify novel molecular targets to fight the disease. By culturing cells from a large pool of patients, they will look for promising targets that are commonly associated with IBC as well as test new stem cell-targeting drugs that could reduce metastasis.

"I think it's a major step forward for us as clinicians and scientists to develop better therapies and new diagnostic tools for patients with [inflammatory breast cancer](#)," Cristofanilli says. "We would like to translate our discoveries from bench to bedside very quickly, as these patients really need new treatments."

Provided by Fox Chase Cancer Center

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