Growth factor predicts poor outcome in breast cancer

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The response to insulin-like growth factor 1 (IGF-I) in breast cancer cells predicts an aggressive tumor that is less likely to respond to treatment, said researchers at Baylor College of Medicine in a report that appears in the current issue of the *Journal of Clinical Oncology.* The finding gives impetus to the movement to tailor cancer treatments to attributes of the various tumors.

"These findings come at a critical time," said Dr. Adrian Lee, associate professor in the Lester and Sue Smith Breast Center at BCM. "Our goal is to identify biomarkers that will help predict which patients will respond to therapy against insulin-like growth factor. Several inhibitors of the IGF pathway are in patient studies right now. There's a large movement to understand which patients will respond to these drugs. This is a step toward that goal?

In this study, Lee and his colleagues stimulated breast cancer cells with IGF-I in the laboratory and defined how more than 800 genes in the cells responded to the growth factor. They then examined samples of patient breast tumors with this "gene signature" and correlated the gene signatures with the fate of the patients.

"We have technology now to allow us to globally assess what IGF is doing in breast cancer at the whole gene expression level," said Lee. "This is one of the first studies to do that. We know that IGF is bad in cancer, but now we can globally understand it in a more comprehensive manner. It could lead to finding biomarkers for patients response" to breast cancer treatments.

"We found that IGF-I is a major regulator of cell growth and cell survival," said Lee. "It also regulates DNA repair."

This has major implications for anti-cancer treatments that seek to cause DNA damage and tumor cell death.

"If you have something regulating DNA repair, you want that turned off," said Lee.

They found that tumors in which IGF (insulin-like growth factor) affected the way in which genes were activated or translated into messages were more aggressive and more likely to grow. They also found that the effect of IGF was independent of whether the tumor was affected by estrogen or not.

"This is very important," said Lee. "Once patients are resistant to hormone treatment (as with tamoxifen), their treatment options are limited. A treatment that inhibited receptors for IGF might give them another option."

Currently, the Breast Center is studying the effects of an IGF receptor antibody combined with a drug called exemestane (Aromasin® or an aromatase inhibitor that blocks estrogen production) in postmenopausal women. One group of women take the combination and the other takes exemestane.

Bioinformatics – the ability to analyze large amounts of data – proved key to the study, said Lee. In fact, the first author, Dr. Chad J. Creighton of BCM, is a bioinformatician, said Lee.

Source: Baylor College of Medicine