Enzyme may drive breast cancer growth

18 May 2011

A recently discovered enzyme drives the production of a potent form of estrogen in human breast cancer tissue, researchers from the University of Illinois at Chicago College of Medicine have found.

The extra-strength estrogen, called estradiol, then drives the production of even more enzyme, in what may be a lethal feed-forward mechanism. Estradiol has been implicated in exacerbating tumor growth in breast cancer.

The research is published in the May issue of the journal *Molecular Endocrinology.*

Scientists had observed the increased production of an unknown protein in ovarian tissue in response to estrogen. UIC researchers under the direction of Geula Gibori, UIC professor of physiology and biophysics, then purified the protein and cloned its gene. Several laboratories established that it is an enzyme that converts a weak estrogen, estrone, to the much more potent estradiol.

The UIC researchers then examined the production of the enzyme in a line of breast cancer cells known to respond to estrogen levels.

"Estradiol up-regulates the very enzyme that produces estradiol, creating a positive cycle where this potent form of estrogen is being produced over and over again, sustaining its own production," said Aurora Shehu, UIC postdoctoral research associate in physiology and biophysics and first author of the study.

In human breast tissue, the researchers found a "dramatic" up-regulation in the cancerous cells but not in the surrounding benign tissue, said Gibori, who is principal investigator on the study. The surrounding tissue, however, is a rich source of the estrone that the enzyme needs to produce more estradiol, she said.

The researchers were able to show how estradiol turns on the gene that produces the enzyme, and that this activation also required at least one other known regulatory factor.

They found that tamoxifen, a drug widely used to inhibit breast cancer growth, prevents estradiol's stimulation of the enzyme and thus may shut down local production of estradiol in breast cancer cells.

"Breast cancer tumors with this enzyme are likely to be a much more aggressive and potentially deadly type of cancer," Gibori said. "Identifying this enzyme and how its expression is turned on gives medical researchers potential targets for disrupting the lethal production of estradiol in breast cancers."

The enzyme is a promising therapeutic target because blocking it may halt production only of the dangerous estradiol, which would reduce the side effects seen with other drugs that inhibit production of many estrogen-related compounds, Gibori said.

Provided by University of Illinois at Chicago