MedicalXpress

Master gene SRC-3 enables breast cancer growth, invasion

February 12 2010

The master gene called SRC-3 (steroid receptor coactivator 3) not only enhances estrogen-dependent growth of cancer cells by activating and encouraging the transcription of a genetic message into a protein, it also sends a signal to the cell membrane to promote cell motility or movement - a key element of cancer spread or metastasis, said Baylor College of Medicine researchers and collaborators in a report that appears in the current issue of the journal *Molecular Cell*.

The finding not only uncovers a new activity for SRC-3 at the cell's periphery, it also clears up a mystery about how the message that tells a cell to invade gets from the epidermal growth factor receptor (EGFR) to the activating enzyme called FAK (focal adhesion kinase) found on the cell's membrane, said Dr. Bert O'Malley, chair of molecular and cellular biology at BCM and the report's senior author.

"Two-thirds of breast cancers over express the gene SRC-3," said O'Malley, who is the 2008 National Medal of Science recipient. "The work represented in this paper shows that a coactivator gene (SRC-3) can produce an alternative form of its coactivator protein - a shorter form that is missing the part of the protein that keeps it in the nucleus. With that portion (called an exon) gone, it leaves the nucleus and goes into the cytoplasm (or general area of the cell) and travels to the membrane," he said.

"At the membrane, the enzyme PAK1 (p21-activted kinase 1) phosphorylates (attaches a phosphate molecule that activates the

coactivator) SRC-3, allowing it to function at the membrane," said O'Malley, responsible for identifying the first receptor coactivator and advancing the field in general.

The finding explains how the epidermal growth factor receptor at the membrane gets a signal to the enzyme that tells the cell to move - and ultimately grow, allowing the cancer to invade surrounding tissue, said O'Malley.

"Now we have a final picture as to why epidermal growth factor receptor and the estrogen receptor are the most dangerous combination of molecules overproduced in breast cancer," said O'Malley. "When they are both over functioning, people die quickly and are resistant to therapy."

More information: www.cell.com/molecular-cell/home

Provided by Baylor College of Medicine