Deactivating a cancer growth promoter

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Three enzymes called phosphatases that shut down a molecule called SRC-3 (steroid receptor coactivator 3) could provide a new pathway for fighting cancer, particularly tumors of the breast and prostate, said researchers at Baylor College of Medicine in a report that appears in the current issue of the journal *Molecular Cell.*

"This kind of information provides a target for the production of drugs against cancer," said Dr. Bert O'Malley, chair of molecular and cellular biology at BCM. "One can already find drugs that stimulate or inhibit phosphatases in other disease processes."

O'Malley and his colleagues had already determined that SRC-3 is an oncogene or cancer-promoting gene as well as a master switch in the cell. Phosphorylation or adding a phosphate molecule activates its cancer-promoting activities. In this study, the researchers identified three phosphatases that promote removal of the phosphate and thus halt the activity of SRC-3.

Of the three identified, PDXP, PP1, and PP2A, PP1 not only stops SRC-3 activity, it also stops the degradation of the co-activator. SRC-3 then builds up in cells, but without the phosphate, it is a dead molecule that does not function and may even further inhibit tumor growth.

Providing new avenues for fighting cancer is an important outcome of basic science, said O'Malley, who is also associate director for basic research in The Dan L. Duncan Cancer Center at BCM. "In cancer right now, many drugs work the same way. They are toxic to all cells. Because

the cancer cell grows faster, the drug is more toxic, but there is nothing selective about the process. In the past decade, we have realized that there has to be a better, more intellectual approach to cancer. In fact, some already exist."

For example, the drug Herceptin targets breast cancer cells that carry the protein Her2/neu. Finding drugs that stop the activation of SRC-3, found at high levels in some breast tumors, could provide another avenue of treatment that could target just the cancer cells.

One study, published by Dr. C. Kent Osborne, director of the Lester and Sue Smith Breast Center at BCM, showed that women whose tumors have both the Her2/neu protein and high levels of SRC-3 are less likely to be helped by drugs such as tamoxifen and more likely to die quickly of their disease. Finding a way to stop Her2/neu and shut down SRC-3 could make the tumor cell's growth controllable, O'Malley said.

Source: Baylor College of Medicine