Regulation by proteins outside cancer cells points to potential new drug target

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Protein interactions outside breast cancer cells can send signals to the cancer cells to permanently stop proliferating, a new study showed in the School of Medicine at The University of Texas Health Science Center San Antonio.

"Because this protein cascade is outside the cells, it is likely amenable to therapeutic manipulation," said lead author Yuzuru Shiio, M.D., Ph.D., assistant professor of biochemistry at the university's Greehey Children's Cancer Research Institute. "I hope our study will ultimately lead to a therapeutic strategy to reprogram cancer cells to a state of permanent dormancy."

He cautions that the finding was observed in cell cultures and is still far from human cancer therapy. Dr. Shiio is also a member of the Cancer Therapy & Research Center (CTRC) at the UT Health Science Center, a National Cancer Institute Designated Cancer Center.

Upon successful chemotherapy, cancer cells either die or permanently stop proliferation. The latter phenomenon is called senescence and is poorly understood, Dr. Shiio said.

Using cultured breast cancer cells as a model, the team found that upon chemotherapeutic drug treatment these cells released factors that stop proliferation. By analyzing which proteins are released under this stress, the team discovered that a protein called IGFBP3 (insulin-like growth factor binding protein 3) is a key player in cancer senescence. The team

then studied other proteins that work together with IGFBP3 outside of the cancer cells.

Using powerful, large-scale analysis called proteomics, the researchers literally picked out the increased abundance of this one protein, IGFBP3, among a thousand other proteins outside of the cells. It was like finding a proverbial needle in a haystack.

The study is published in this week's *Proceedings of the National Academy of Sciences*.

Provided by University of Texas Health Science Center at San Antonio