Medical Xpress

Scientists uncover protein that thwarts tumor invasion

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Researchers at UT Southwestern Medical Center have determined that cancer cells lacking a key protein are more invasive and more likely to metastasize, providing a possible drug target to combat certain tumor types.

"Further down the line we could create a drug that would bring COMMD1 protein levels back to normal, or even above normal, in the tumor to hopefully affect cancer cell invasion," said Dr. Ezra Burstein, assistant professor of internal medicine and molecular biology and senior author of the study appearing in the June issue of the Journal of Clinical Investigation. "If the cancer cells have already started invading other organs, maybe further invasion would be halted or even regressed."

Dr. Burstein is a member of a research team that years ago discovered the COMMD family of proteins and its abilities. They discovered that one of those proteins, COMMD1, inhibits NF-kB, a key factor that activates genes involved in inflammation and that is often involved in helping cancer cells survive. COMMD1 also regulates a protein called HIF, which plays a role in the survival of cells in areas of low oxygen, a common feature of cancer. For example, enhanced HIF activity is associated with tumor growth, metastasis and poor clinical outcomes for cancer patients.

Because COMMD1 has this dual role in regulating both NF-kB and HIF, the researchers thought that COMMD1 might be inactivated or repressed in tumors. This study supports their hypothesis, as the scientists found

decreased amounts of this protein in a variety of human cancers and the decreased expression of COMMD1 also was associated with more invasive cancers.

COMMD1 suppression in cancer cells leads to enhanced activity of both NF-kB and HIF, a one-two punch that makes the cancer more invasive, Dr. Burstein said.

In a review of 63 patients with endometrial cancer, the researchers determined that those whose tumors had the lowest levels of COMMD1 had the worst clinical outcomes.

Using mice, it was also discovered that the COMMD1-deficient cells were more invasive when implanted. The researchers then generated mouse melanoma cells that produced an overabundance of COMMD1, and injected those cells back into healthy mice. The number of metastatic lung tumors that resulted was greatly reduced when the cells expressed greater levels of COMMD1.

These results indicate that COMMD1 restrains the metastatic potential of an invasive cancer cell line, Dr. Burstein said.

"This is the first study that clearly links COMMD1 to human disease and substantiates what we would've expected based on the prior work we have done on this protein," he said. "COMMD1 is yet another player in the very important and complicated cancer invasion process."

The next step, Dr. Burstein said, will be to investigate what changes in the tumor environment may be responsible for reducing levels of COMMD1 in cancer cells.

Provided by UT Southwestern Medical Center