Researchers identify a protein that may help breast cancer spread, beat cancer drugs

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New research from UC Davis Cancer Center shows that a protein called Muc4 may be the essential ingredient that allows breast cancer to spread to other organs and resist therapeutic treatment. The study, which appears in the April 1 issue of *Cancer Research*, is one of the first to characterize the role of Muc4 in the disease.

Kermit Carraway, senior author of the study, knew that Muc4 was not always expressed in primary breast cancer tumors, yet it could be present in lymph node metastases. He suspected that it may have a specialized function in the process of metastasis.

"Breast cancer deaths are caused by metastasis, not by the primary tumor," explained Carraway, an associate professor of biochemistry and molecular medicine. "It's at that point that the disease also becomes difficult to treat. We think that Muc4 may be packing a one-two punch by promoting the release of breast cancer cells from the primary tumor and then inhibiting their death."

Muc4 is member of a group of proteins called mucins, which are commonly found in fluids such as tears and mucus. They have a known role in protecting epithelial cells, from which breast cancer cells are derived. When separated from their surrounding cell matrix, epithelial cells tend to die. Metastasizing breast cancer cells, however, can survive this detachment.

"Because breast cancer cells can lose their adhesive properties and still

thrive, we suspected that Muc4 may be somehow allowing them to leave their cellular framework, travel to secondary sites and withstand treatment," Carraway explained.

To test his suspicions, Carraway and his team conducted two experiments. They started by comparing breast cancer cells that express Muc4 with those for which Muc4 production is blocked. The researchers then exposed both types of cells to chemotherapy drugs. The Muc4-producing cells survived.

They repeated the experiment with breast cancer cells and epithelial cells that do not naturally express Muc4 but were engineered to do so. Both sets of cells avoided cell death and effectively resisted chemotherapy.

"Our results lead us to believe that Muc4 is somehow disrupting normal links between epithelial cells," said UC Davis graduate student Heather Workman, lead author of the study. "We now need to refine our understanding of this disruption process in order to find ways to interfere with it. There currently are no drugs that target Muc4, and this research will help change that."

Carraway is now preparing to test metastasizing breast cancer tumor cells for the overexpression of Muc4.

"If we find that Muc4 is all over metastasizing breast cancer cells, it will confirm that we are on the right track," he said.

While Carraway's current focus is on breast cancer, his findings could have relevance to other cancers that show aggressive properties. For example, Muc4 is also expressed in pancreatic, lung and ovarian tumor cells.

"Muc4 is likely a central cellular mechanism for metastasis of many

cancers, and we will be continuing this important work to prove that," he said.

Source: University of California - Davis - Health System