UT SOUTHWESTERN MEDICAL CENTER NEWS

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Loss of gene function in certain prostate cancer cells makes them more aggressive, UT Southwestern researchers find

DALLAS – Feb. 2, 2010 – Prostate cancer cells are more likely to spread to other parts of the body if a specific gene quits functioning normally, according to new data from researchers at UT Southwestern Medical Center.

Certain prostate cancer cells can be held in check by the *DAB2IP* gene. The gene's product, the DABIP protein, acts as scaffolding that prevents many other proteins involved in the progression of prostate cancer cells from over-activation. When those cells lose the DAB2IP protein, however, they break free and are able to metastasize, or spread, drastically increasing the risk of cancer progression in other organs as the cells travel through the bloodstream or lymph system.

The study in mice, published in the Jan. 11 issue of the *Proceedings of the National Academy of Sciences*, found that eliminating the DAB2IP scaffolding in human carcinoma cells caused them to change from epithelial cells to mesenchymal cells – a hallmark of metastatic cancer.

"Cells undergoing an epithelial to mesenchymal transition (EMT) experience biological changes that enable them to move freely and spontaneously throughout the body," said Dr. Jer-Tsong Hsieh, director of the Jean H. & John T. Walker Jr. Center for Research in Urologic Oncology at UT Southwestern and the study's senior author. "By restoring DAB2IP function in cancer cells in mice, we reversed their ability to change and metastasize."

Dr. Hsieh said identifying the DAB2IP protein in human cells might serve as a biomarker, helping physicians identify patients who could have more aggressive, metastatic forms of prostate cancer.

EMT is known to play an important role in embryo implantation, embryogenesis and organ development, and tissue regeneration, as well as in cancer progression and metastasis. For cancer progression, EMT is believed to facilitate the migratory and invasive ability of cancer cells.

"Carcinoma cells undergo several changes that enable them to spread," said Dr. Hsieh, also professor of urology. "The majority of human visceral tumors derived from carcinomas are primarily made up of epithelial cells. When they acquire mesenchymal phenotypes, they lose cell-to-cell adhesion and become more mobile throughout the body."

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In the current study, Dr. Hsieh and his team first shut down the *DAB2IP* gene expression in prostate epithelial cells in mice and found that the prostate cancers did indeed metastasize to lymph nodes and other organs in mice. When the researchers restored the *DAB2IP* genetic function to metastatic prostate cancer cells, the EMT process reversed, thereby inhibiting the cancer cells' ability to spread.

"Based on the outcome of this paper, we believe the assessment of DAB2IP in these cancer cells can be a valuable prognostic biomarker for risk of the aggressiveness of certain prostate cancers," said Dr. Daxing Xie, urology postdoctoral researcher and lead author of the study. "Further understanding of the DAB2IP function could also provide potential therapeutic strategies for treating prostate cancer."

Other UT Southwestern researchers involved in this study were Crystal Gore and Michael Long, research technicians; Dr. Jun Liu, postdoctoral researcher; Rey-Chen Pong, senior research associate; Dr. Ralph Mason, professor of radiology; Dr. Guiyang Hao, postdoctoral researcher; Dr. Wareef Kabbani, assistant professor of pathology; Dr. Xiankai Sun, assistant professor of radiology in the Advanced Imaging Research Center; and Dr. David Boothman, professor of radiation oncology and pharmacology and associate director of translational research in the Harold C. Simmons Comprehensive Cancer Center.

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