# Loss of protein SPDEF allows prostate cancer cells to gain foothold at possible sites of metastasis

July 6 2012

Prostate cancer doesn't kill in the prostate — it's the disease's metastasis to other tissues that can be fatal. A University of Colorado Cancer Center study published this week in the *Journal of Biological Chemistry* shows that prostate cancer cells containing the protein SPDEF continue to grow at the same pace as their SPDEF- cousins, but that these SPDEF+ cells are unable to survive at possible sites of metastasis.

"It's as if these cancer cells with SPDEF can't chew into distant tissue and so are unable to make new homes," says Hari Koul, PhD, investigator at the CU Cancer Center and director of urology research at the University of Colorado School of Medicine, the study's senior author.

Koul and his group discovered the homesteading power of cancer cells that have lost SPDEF by introducing a gene into cells that makes them glow in the presence of a dye, and then introducing them into the bloodstream of animal models. Cells without SPDEF traveled through the blood and successfully attached to tissue, surviving and so fluorescing many weeks later when dye was introduced. However, cells with SPDEF flowed through the blood but were unable to successfully establish new colonies and so soon died out.

In fact, the protein SPDEF doesn't act directly to allow cells to attach at possible metastasis sites, but is a transcription factor that controls the

production (or lack thereof) of two other proteins MMP9 and MMP13. These two downstream proteins work to break down tissue, like a dissolving agent – they are the cleaning crew that clears space for new and different growth, and in the case of prostate cancer metastasis they chip the tissue footholds that cancer cells need to create micrometastases.

"Given that MMP9 and perhaps MMP13 are also involved in metastasis of several other cancers including lung, ovarian, breast and colon to name a few, our findings could potentially have far-reaching consequences outside prostate cancer," adds Koul

The group's continuing work points in two directions.

"First, we hope that the presence of SPDEF could help doctors recognize prostate cancers that don't require treatment." If future studies confirm the group's initial findings, the presence of SPDEF could predict prostate cancers that are unable to metastasize and so unable to kill. These cancers could be left to run their course without the use of treatments that sometimes carry difficult side effects.

"And second," Koul says, "we hope to regulate expression of this protein to remove prostate cancers' ability to metastasize."

Koul points to small molecules, gene therapy or nanodelivery as possible mechanisms for introducing SPDEF into cells that lack the protein.

"With this discovery we have opened a hopeful door into a future in which prostate and potentially other cancers are unable to metastasize," Koul says.

Provided by University of Colorado Denver