Researchers advance findings on key gene related to cancer metastasis

February 4 2014, by Annie Deck-Miller

(Medical Xpress)—New evidence reported by researchers at Roswell Park Cancer Institute (RPCI) lends support to the hypothesis that the SSeCKS/AKAP12 gene is a key inhibitor of prostate cancer metastasis. The data are some of the first to demonstrate this dynamic in transgenic animal models, with promising implications for development of targeted therapies for prostate cancer and perhaps for other solid-tumor cancers.

A team led by Irwin H. Gelman, PhD, noted that aggressive prostate cancers in humans typically turn off or delete two major regulatory genes, SSeCKS/AKAP12 and Rb. To explore this dynamic, the researchers developed a transgenic animal model to study the effects on prostate cancer progression of deleting these two genes. They report in *Cancer Research*, a peer-reviewed journal published by the American Association for Cancer Research, that the loss of these two genes and associated protein products leads to early prostate cancer. Moreover, more than 80 percent of the transgenic models in their study developed metastatic lesions in lymph nodes near the prostate.

"This correlates with our earlier finding that SSeCKS/AKAP12 inhibits the chemotaxis of metastatic prostate tumor cells—that is, their ability to move on to another environment in response to chemical attractants," said Dr. Gelman, the John & Santa Palisano Chair in Cancer Genetics at RPCI. "Thus, our data suggest that SSeCKS plays a role in preventing the early dissemination of prostate cancer cells to metastatic sites. Importantly, we show that humans whose prostate cancers have turned off or deleted the SSeCKS/AKAP12 gene have significantly higher rates

of metastasis formation compared to cases where SSeCKS/AKAP12 levels are sustained."

While the SSeCKS/AKAP12 gene is deleted in about a third of metastatic prostate cancers, precluding benefit from targeted therapies exploiting this vulnerability, the remaining two-thirds of such tumors may be treatable with drugs that induce the reactivation of SSeCKS/AKAP12 production. Dr. Gelman and colleagues are now looking to identify the genomic signatures controlled by SSeCKS/AKAP12 in the suppression of metastasis pathways—at the level of the tumor cells themselves and in the cells that form the metastatic microenvironment.

"At least 93 percent of cancer patients die because of complications due to metastatic cancers, yet the vast majority of pathways studied and therapies developed address the biology of primary cancers," Dr. Gelman noted. "This current research is important in that it addresses specific mechanisms of cancer metastasis, with the result that genetic tests and therapies derived from such studies will have a higher chance of affecting cancer patient survival."

More information: "A Transgenic Mouse Model for Early Prostate Metastasis to Lymph Nodes." Hyun-Kyung Ko, Shin Akakura, Jennifer Peresie, David W. Goodrich, Barbara A. Foster, and Irwin H. Gelman. *Cancer Res* February 1, 2014 74:945-953; DOI: 10.1158/0008-5472.CAN-13-1157

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