Metastatic 'switch' could lead to cancer therapies

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(Medical Xpress)—What kills cancer patients often isn't the primary tumor; it's when the tumor metastasizes—or spreads the cancer to other areas of the body.

Focusing on colorectal cancer, a leading cause of cancer death worldwide, a multidisciplinary research team has shed new light on how these cancer cells metastasize by identifying a key chemical signaling factor that triggers the process.

What's more, they have engineered a low-cost, surgery-free genetic "switch" that turns metastatic behavior of colorectal cancer cells on and off, allowing for easy, repeatable study of this process.

The research is detailed in the Journal of Clinical Investigation, published Sept. 4, and was led by Huanhuan Joyce Chen, a graduate student under Xiling Shen, assistant professor of electrical and computer engineering and a field member of biomedical engineering. Shen is a co-author with Steven Lipkin, associate professor of medicine at Weill Cornell Medical College. The work was also highlighted online by the company Qiagen.

The researchers found that particular signaling mechanisms called chemokines induce metastasis of colorectal cancer cells. Chemokines are "motility factors" because they help cells move throughout the body. They are known, for example, to be important in the body's immunoresponse, which requires immune cells to travel quickly to areas

of inflammation or infection.

The researchers established a link between a particular chemokine receptor, called CCR9, and its ligand chemokine CCL25, to the metastatic behavior of colorectal cancer cells. Normal expression of these chemokines keeps the cancer cells in the gut, but once the cells lose CCR9 expression, they can spread. In other words, cancer cells hijack the signaling mechanism.

This discovery in itself, Shen said, could form the basis for targeted anti-metastatic therapies.

A barrier to cancer research, however, is the lack of good animal models to test therapies, Shen said, and human clinical trials often fail as a result.

So Chen used her engineering background to take things a step further: She made a mouse with a CCL25 and CCR-9 metastatic "switch" that could be turned on and off after cancer cells were injected into the mouse. At first, the cells expressed the CCR9 receptor, and the tumor only formed in the gut. Turning off the switch made the cells lose the signaling mechanism, and metastasis occurred.

This switch could eliminate the traditional way scientists study metastasis: expensive, low-throughput surgical implantation of metastasized cancer cells. With the switch, metastasis can be studied and repeated by a simple injection of colorectal cancer cells.

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