New clues to how cancer spreads

June 27 2011

Cancer cells circulating in the blood carry newly identified proteins that could be screened to improve prognostic tests and suggest targets for therapies, report scientists at the Duke Cancer Institute.

Building on current technologies that detect tumor cells circulating in blood, the Duke team was able to characterize these cells in a new way, illuminating how they may escape from the originating tumors and move to other locations in the body.

The circulating tumor cmoponents include proteins normally seen when embryonic stem cells begin to specialize and move through the body to develop organs such as the heart, bones and skin, the Duke scientists reported this month in the journal *Molecular* Cancer Research.

The discovery may enhance the accuracy of blood tests that detect circulating cancer cells, giving doctors better information to gauge how a patient's disease is responding or progressing.

"By developing a better blood test based on our findings, we may be able to identify molecular targets for therapy tailored to an individual patient's cancer," said Andrew J. Armstrong, M.D., ScM, assistant professor of medicine at Duke and lead author of the study.

The Duke team isolated tumor cells from blood samples of 57 patients, including 41 men with advanced prostate cancer and 16 women with metastatic breast cancer.

In the tumor cells of more than 80 percent of the prostate cancer patients and 75 percent of those with breast cancer, the researchers detected a group of proteins normally seen during embryonic development when stem cells begin to assume distinct roles.

As stem cells morph to build tissue and organs, they switch back and forth in what is known as epithelial-mesenchymal transition (EMT) and it's opposite, mesencymal-epithelial transition (MET). Cancer cells have that same ability, changing from an epithelial cell similar to the organs from which they arose, to a mesenchymal or connective tissue-like cell. This EMT may underlie much of the treatment resistance and ability of cancer cells to spread.

Current FDA-approved blood tests that detect circulating tumor cells flag molecules associated with epithelial transitions; however, the Duke team found additional markers associated with mesenchymal origins, adding new targets that could be used to enhance the usefulness and sensitivity of the tests.

"Cancer is a hijacking of that normal embryonic stem cell process," Armstrong said. "It reactivates this silent program that is turned off in adult cells, allowing tumor cells to move throughout the body and become resistant to therapy."

Armstrong said the involvement of EMT/MET processes in tumor growth is a relatively new finding that is gaining acceptance among cancer scientists. The discovery by the Duke team adds strong evidence that the EMT/MET processes are underway when a patient's cancer is spreading.

"In my opinion this work presents some of the most compelling data for the existence of epithelial-mesenchymal transitions in human cancer," said Mariano A. Garcia-Blanco, professor of medicine, molecular

genetics and microbiology, and senior author in the work.

"This work should pave the way for studies to understand the mechanisms underlying these transitions in humans and their importance in disease progression and therapy," said Garcia-Blanco, who is also director of the Duke Center for RNA Biology.

The Duke team additionally noted that tumor cells appear to be most dangerous when they can easily transition between EMT and MET in a stem cell-like phase of changability that enables them to grow, spread and resist treatment.

That finding could provide new opportunities for novel therapies that target these morphing mechanisms.

"This is not just for a biomarker, it's a direction to take therapies as well," Armstrong said. "It's a new horizon."

Provided by Duke University Medical Center