Circulating Tumor Cells Present EMT Marks in Human Cancers

During normal development, epithelial cells can morph into a mesenchymal state, travel to their destination, and then flip back into an epithelial form. Many recent *in vitro* and animal studies have suggested that this "epithelial-mesenchymal transition" (EMT) and the converse mesenchymal-epithelial transition (MET) play a crucial role in metastasis of solid tumors.

That theory has been questioned because it has proven difficult to detect signs of EMT in human cancers. However, 2 studies published in June provide supporting evidence by detecting EMT markers in human circulating tumor cells (CTC).

Duke University scientists collected CTCs expressing EpCAM, an epithelial marker, from 41 men with castration-resistant prostate cancer and 12 women with metastatic breast cancer. More than 80% of CTCs from the men expressed multiple epithelial proteins such as cytokeratin and E-cadherin; mesenchymal proteins including vimentin, N-cadherin, and O-cadherin; and the stem cell marker CD133. Similarly, more than 75% of CTCs from the women expressed cytokeratin as well as vimentin and N-cadherin [Mol Cancer Res 2011 Jun 10 (Epub ahead of print)].

The researchers hypothesize that cells showing such combined markers may be in transition between states and thus particularly adept at metastasis. "These measurements don't prove plasticity for these cells, but they do provide supporting evidence for EMT in human cancer," says first author Andrew Armstrong. He and Mariano A. Garcia-Blanco co-led these studies, which will be followed up with analyses of metastatic tumors from the same patients.

Separately, researchers at the Hellenic Oncology Research Group in Athens studied the expression of two EMT markers, twist and vimentin, in cytokeratin-expressing CTCs of 25 metastatic and 25 early breast cancer patients. Among CTCs from patients with early disease, 77% expressed vimentin and 73% expressed twist; those figures rose to 100% for both markers in patients with metastatic disease.

"The high incidence of these cells in patients with metastatic disease compared to early stage breast cancer strongly supports the notion that EMT is involved in the metastatic potential of CTCs," the scientists reported (Breast Cancer Res 2011;13:R59). ■

Astronomy Research Suggests Tumor Tools

While studying how stars and black holes emit and absorb radiation, Ohio State University astronomers discovered that heavy metals such as iron emit low-energy electrons when exposed to X-rays at specific energies.

Working with radiation oncologists and medical physicists, the scientists now plan to examine whether heavy-metal nanoparticles might allow doctors to obliterate tumors with low-energy electrons while sparing healthy tissue.

"If we could target heavy-metal nanoparticles to certain sites in the body, X-ray imaging and therapy could be more powerful, reduce radiation exposure, and be much more precise," predicts astronomy professor Anil Pradhan.

At the International Symposium on Molecular Spectroscopy in June, senior research scientist Sultana Nahar announced findings of computer simulations of the technique using gold and platinum nanoparticles. Once injected into the body, the nanoparticles, coated with tumor antigens, would target and latch on to the tumor. The nanoparticles, the thinking goes, would absorb the X-rays. A large number of relatively low-energy electrons would then break free, killing the malignant cells. The researchers constructed models with gold and platinum because those metals have been used safely in humans.

Typical X-ray machines, such as CT scanners, generate X-rays at a wide spectrum of energies, so the research team, which includes colleagues at Thomas Jefferson University Medical College, will work to develop an easy-to-use, low-cost device to deliver mono-energetic X-rays in hospitals. ■

NOTED

- The National Cancer Institute has added an **International Collaboration in Clinical Trials portal** (www.cancer.gov/clinicaltrials/international) as a resource for cancer researchers across the world. In addition to connecting users with U.S. cancer centers and international clinical trials, this site offers step-by-step instructions and explanations for concerns that arise among research groups.
- In **Citeline's 2011 Annual Review of Trends in Pharmaceutical Research and Development,** cancer drugs led the way, accounting for 28% of all drugs in the research and development pipeline. Of the 2,719 cancer therapies, 773 are immunologic agents.
- Scientists from the University of Liverpool have unlocked the **genome of the naked mole rat**, a creature whose life expectancy is 7 times longer than that of other rodents such as mice and which displays a unique resistance to cancer.
- The government of Australia's New South Wales is dedicating $30 million (Australian) to 7 **Translational Cancer Research Hubs** that aim to stimulate collaboration among doctors, researchers, and clinicians.
- iTunes released the "Genome Wowser," an **iPad application that puts the human genome at one's fingertips**. Developed by the Center for Biomedical Informatics at the Children's Hospital of Philadelphia, this app is said to let you navigate the entire genome with the ease and convenience of web tools such as Google Maps.
- **Phase III clinical trials:** Roche intends to submit pertuzumab for FDA approval following its CLEOPATRA phase III clinical trial, which concluded that patients with HER2-positive metastatic breast cancer who took the drug with Herceptin and docetaxel experienced a significantly better survival rate than those who were treated with Herceptin and docetaxel alone. Novartis claimed success in a phase III clinical trial involving its Afinitor (everolimus) for treating postmenopausal breast cancer.

CANCER DISCOVERY

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