“Smart Bomb” Nanoparticle Strategy Impacts Metastasis

July 7, 2008

Debra Kain

A new treatment strategy using molecular "smart bombs" to target metastasis with anti-cancer drugs leads to good results using significantly lower doses of toxic chemotherapy, with less collateral damage to surrounding tissue, according to a collaborative team of researchers at the University of California, San Diego. By designing a "nanoparticle" drug delivery system, the UC San Diego team, led by Moores UCSD Cancer Center Director of Translational Research David Cheresh, Ph.D., has identified a way to target chemotherapy to achieve a profound impact on metastasis in pancreatic and kidney cancer in mice.

In a study to be published online the week of July 7 in advance of publication in the *Proceedings of the National Academy of Sciences (PNAS)*, Cheresh, professor and vice chair of pathology, and members of his team report that the nanoparticle carrying a payload of chemotherapy homes in on a protein marker called integrin ###3 - found on the surface of certain tumor blood vessels where it is associated with development of new blood vessels and malignant tumor growth.

The team found that the nanoparticle/drug combination didn't have much impact on primary tumors, but stopped pancreatic and kidney cancers from metastasizing throughout the bodies of mice. They showed that a greatly reduced dosage of chemotherapy can achieve the desired effect because the drug selectively targets the specific blood vessels that feed the cancerous lesion and kills the lesion without destroying surrounding tissue. The destruction of healthy tissue is a side-effect when chemotherapy is administered systemically, flooding the body with cancer-killing toxins.

"We were able to establish the desired anti-cancer effect while delivering the drug at levels 15 times below what is needed when the drug is used systemically," said Cheresh. "Even more interesting is that the metastatic lesions were more sensitive to this therapy than the primary tumor."

The study is an example of an initiative that joins researchers from UC San Diego's Health Sciences and the Jacobs School of Engineering to improve health care through innovative technologies. Engineers and oncologists working together designed a nanoparticle - a microscopic-sized particle of 100 nanometers, made of various lipid-based polymers - which delivers the cancer cell-killing drug doxorubicin to the network of blood vessels supporting the tumor that express the ###3 protein.

"Doxorubicin is known to be an effective anti-cancer drug, but has been difficult to give patients an adequate dose without negative side effects," Cheresh said. "This new strategy represents the first time we've seen such an impact on metastatic growth, and it was accomplished without the collateral damage of weight loss or other outward signs of toxicity in the patient."

Cancer metastasis is traditionally much more difficult to treat than the primary tumor, and is what usually leads to the patient's death. Because metastasis is more reliant on new blood vessel growth, or angiogenesis, than established tumors are, Cheresh theorized that targeting the anti-cancer drug to the sites of new blood vessel growth has a preferential effect on metastatic lesions.

"Traditional cancer therapies are often limited, or non-effective over time because the toxic side effects limit the dose we can safely deliver to the patient," said Cheresh. "This new drug delivery system offers an important advance in treating metastatic disease."

Additional contributors to the study were Eric A. Murphy, Bharat K. Majeti, Leo A. Barnes, Milan Makale, Sara M. Weis and Wolfgang Wrasidlo, all of the Department of Pathology and Moores UCSD Cancer Center. The study was supported by the National Institutes of Health and the National Cancer Institute Nanotechnology Alliance.

Media Contact: Debra Kain, 619-543-6163