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Protein shines light on cancer response

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A technique that specifically “tags” tumors responding to chemotherapy may offer a new strategy for determining a cancer treatment’s effectiveness within days of starting treatment, according to a new study by Vanderbilt-Ingram Cancer Center investigators.

Appearing online ahead of print in *Nature Medicine*, the researchers report the identification of a small protein that specifically recognizes tumors responding to chemotherapy. They show that the protein, when tagged with a light-emitting molecule, can be used to visualize cancer response in mice just two days after starting therapy.

Improved monitoring of tumor response could help customize patient treatment and also speed up the development of new cancer drugs, said senior investigator Dennis Hallahan, M.D., the Ingram Professor of Cancer Research and chair of Radiation Oncology at Vanderbilt University Medical Center.

Currently, response to chemotherapy is determined by measuring changes in tumor size with imaging techniques like CT (computed tomography) and MRI (magnetic resonance imaging).

“It takes two to three months of cancer therapy before we can determine whether the therapy has been effective for a patient,” he said. “If we can get that answer within one to two days, we can switch that patient to an alternative regimen very quickly.”

Rapid assessment of tumor response is especially important now,

Hallahan says, given recent advances in molecular targeted therapies – chemotherapy medications that specifically interfere with the growth and proliferation of cancer cells while avoiding damage to healthy cells.

“We now have so many molecular targeted drugs to choose from, and that number is growing every year, so we are now at a point where a patient can be switched from one regimen to another,” he said. “But we need the tools to make the decision to use an alternative therapy with the patient.”

To find a rapid and noninvasive method to assess cancer response to these therapies, Hallahan focused not on tumor size, but molecular and cellular changes in responding tumors.

From a panel of billions of protein fragments, or peptides, Hallahan and colleagues identified one that specifically bound to tumors responding to therapy. To this peptide, they attached a light-emitting molecule and injected these labeled peptides into mice that had been implanted with human tumors.

Using specialized imaging cameras that detect light in the near-infrared range (invisible to the human eye), the investigators saw that tumors responding to therapy were “brighter” than non-responding tumors. The peptide detected response in a wide range of tumors – brain, lung, colon, prostate and breast – within two days of initiation of treatment.

“The key word here is ‘days,’” Hallahan said. “This will allow us to minimize the duration of treatments with ineffective regimens in cancer patients.”

The next step will be to move the technology into humans. The imaging technique used in mice (near-infrared) is not sensitive enough to penetrate deeply into human tissues, so the researchers are adapting the

technology to an imaging modality commonly used in humans, called PET (positron emission tomography).

“This imaging peptide will enter clinical trials within about 18 months,” Hallahan said. “The purpose, when we bring it into people, is to ask a very simple question: can we image responding cancers in people as well as we can in mice?”

If so, he says that he suspects that such molecular imaging methods could help accelerate the development of new chemotherapeutic drugs.

“In the pharmaceutical industry, we’ll have a patient on a drug for months before we can re-evaluate the size of the tumor,” Hallahan said. “If we can get that answer within a couple of days, it will speed cancer drug development in the early phases of clinical trials.”

Source: Vanderbilt University Medical Center