IMAGING

Genetic probe illuminates metastases

A novel genetic imaging probe improves detection of micrometastases when injected into mice. The system, developed by researchers at The Johns Hopkins Medical Institute, is composed of two DNA components: one is a genetic regulator, called PEG-3 promoter; the other encodes a 'reporter' protein, which produces an easily detectable signal, but only when the regulator allows it. Importantly, the PEG-3 promoter is only active in tumor cells, but not in normal cells. This activity limits expression of the reporter protein and its characteristic signal to tumor tissue.

"We specifically wanted something that would have the following properties: firstly, be systemically delivered; secondly, be specific for cancer—but any cancer; and thirdly, have a clear path to translation," explains Martin Pomper, senior investigator of the study.

In animal models of human melanoma and breast cancer, Pomper's team tested two different types of reporter genes. One illuminated tumors by producing light, whereas the alternative version trapped radionucleotides inside tumor cells. In both cases, signals derived from the probes correlated with the location of metastases identified by histological analyses of the tissues. The tumor-specific activity of the PEG-3 promoter had been shown previously in a range of cancers *in vitro*.

In certain tissues, such as the lung, the radionucleotide-based technique was even more sensitive than the current clinical standard for cancer staging (PET with ^{18}F-fluorodeoxyglucose). This finding suggests that tumors might be detected before their tissue of origin or subtype is identified.

The plasmid is delivered via a nanoparticle and remains stable in cells only for a limited amount of time. With this approach, the researchers hope to avoid problems frequently associated with more stable, viral delivery methods, such as carcinogenesis and accumulation of viral particles in the liver. Importantly, the probe was taken up equally by tumor and lung tissue. The plasmid was even detected, although at lower levels, in tissues that are usually hard to access through systemic application, such as the brain or bones. The authors point out, however, that delivery to poorly vascularized, primarily necrotic areas within tumors might be limited.

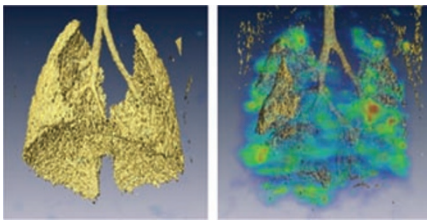

Image courtesy of Hyo-eun (Carrie) Bhang

According to Pomper, the construct could be useful for preoperative planning, intraoperative management, or therapeutic monitoring. His team will now test it in a variety of cancers, while trying to further improve the delivery vehicle. "Ultimately we intend to move this to the clinic as rapidly as possible," Pomper adds.

Christoph Schmitt

Original article Bhang, H. C. *et al.* Tumor-specific imaging through progression elevated gene-3 promoter-driven gene expression. *Nat. Med.* **17**, 123–129 (2011)