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News News News

Jellyfish Protein Gives New Glow to Tumor Imaging

Off Friday Island near Seattle, viewers used to delight as the ocean glowed with the fluorescence of hundreds of jellyfish. The jellyfish are now long gone, but about 10 years ago, the green fluorescent protein (GFP) was cloned from that Pacific jellyfish, *Aquorea victoria*, and is now used in laboratories around the world to monitor gene expression, protein localization, and protein–protein interaction.

GFP's newest use—the whole-body, real-time imaging of tumors—shows that, even in the intact animal, tumor growth, metastasis, and angiogenesis can be seen.

Robert Hoffman, Ph.D., president of AntiCancer Inc., San Diego, the company doing the work, said that they have been able to see the onset and progression of angiogenesis in mice that have been implanted with tumor cells that are genetically engineered to contain GFP. This process, Hoffman said, is revealing how a tumor metastasizes.

Once a tumor has been established in the mice, researchers put the animals in a simple light box, in which a blue light shines on the animals and causes the tumors and their metastases to emit a visible fluorescence. The vascularization of the tumor shows up dark against this background.

Hoffman said that even a single cell of a tumor can be visualized on the body surface, and slightly larger tumors within the intact body—about 50 cells, for instance—might be detected deep within a lung. If the animals are opened up, single tumor cells could be seen deep within the pancreas, lung, liver, or lymph nodes.

Metastases that express green fluorescent protein can be seen in the skull, scapula, spine, and liver of this mouse.

Photo from: Yang M, et al. Proc. Natl. Acad. Sci. USA 2000;97:1206–11

Hoffman said at the annual meeting of the American Association for Cancer Research that, for example, a tumor implanted in the right lung seems to follow a preferred metastatic pathway. "It goes down the lymphatics in a sort of single file, seeds on the diaphragm, and then crosses the diaphragm surface to the contralateral lung as well as the contralateral nodes." He said this metastatic march can be seen early, "and after 18 hours you already see cells in the lymphatics in the direction of the diaphragmatic surface."

Meng Yang, Ph.D., a scientist at the company, reported at a recent symposium that the depth to which metastases and micrometastases could be imaged depended on their size. A tumor 60 μm in diameter was detectable at a depth of 0.5 mm, while an 1800-μm tumor could be visualized at a depth of 2.2 mm.

At the moment, the GFP animal models are being used for the testing of new drugs that may have a benefit in cancer in humans, but Hoffman admits to a larger dream.

"Right now we're testing hundreds of drugs," Hoffman said in an interview. "But I think this technique could be applied to humans after the proper safety and efficacy studies. I think it would be safe, because the GFP is a reporter gene, like the neomycin resistance gene, which has been given safely to humans." He said he thinks it would be helpful to transduce a patient's tumor with GFP and follow the patient to see if there are any recurrences.

When the diagnostic capability of particular genes is better understood, he continued, GFP imaging may also be a good way to discover cancer early—just hook the GFP gene to the diagnostic gene and turn the blue light on the patient.

He added that there are no immediate plans to study GFP in humans, However, he said, "We're still an R&D company and we'd like to do it. If the proper partner came along, we'd be ready."

—Jean McCann