SENSORS AND PROBES

Cancer cells report

An early biomarker of cancer reports from inside the mouse.

Cancer is a silent operative, preferring not to reveal itself until it is well established and beyond control. Early detection may be the key to understanding and fighting the disease, but the problem is enormous: how do you spot a handful of rogue cells that are, after all, just altered versions among trillions of the body's own?

Various cancers are associated with genetic changes that can be used to identify tumor cells. These biomarkers have helped in animal imaging studies, but they fail to capture early stages or pinpoint cancer cells precisely. Norman Sharpless of the University of North Carolina, Chapel Hill, and his coworkers offer a bright new tool based on an unlikely biomarker.

The *p16Ink4a* (also called *Cdkn2a*) gene is associated with cancer, but it has mainly been used as a reporter of aging. As cells age, suffer DNA damage or express cancer-causing genes, p16Ink4a accumulates until it reaches a level that halts cell division. A fulcrum between aging and cancer, p16Ink4a holds the scales that weigh increased tumor risk in older animals on one side and the ability of stem cells to repair tissues on the other.

The Sharpless group specifically replaced part of the *p16* (*Cdkn2a*) gene associated with tumor suppression with the luciferase gene. Transgenic mice expressing the resulting p16Ink4a-Luc reporter received a shot of D-luciferin under the skin, which luciferase acts on to produce light. Imaging revealed that it is a superb marker of aging in mice.

By breeding the reporter mice with various cancer-prone mice, the researchers made an important discovery: p16Ink4a-Luc lit up breast, skin and blood cell malignancies and even spontaneous tumors—14 types in all—as tight, bright spots. The reporter detected cells with a cancerous pathology an average of 62 days before they could be found by touch or by eye.

The reporter's remarkable sensitivity was explained by the finding that cells surrounding a tumor express *p16Ink4a* and help to point the finger on their neighbor. For the same reason, all tested cancers could be detected regardless of genetic origin. The reporter is also activated by cellular stress, but tumors are brighter than background luminescence from stress or age; it has also revealed that average cellular age does not predict the propensity for cancer.

Early results suggest that p16Ink4a can even light up internal cancers and metastases. The new reporter will be a powerful tool for early detection and long-term tumor tracking.

Tal Nawy

RESEARCH PAPERS

Burd, C.E. *et al.* Monitoring tumorigenesis and senescence *in vivo* with a $p16^{INK4a}$-luciferase model. *Cell* **152**, 340–351 (2013).