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EMBARGOED FOR RELEASE Thursday, Oct. 9, to correspond with publication in the October issue of the scientific journal *Photochemistry and Photobiology*.

Editors, reporters please note: Color photos are available showing areas of gene activation in lab animals. The photos and other material related to the new research can be viewed on the World Wide Web at http://www-leland.stanford.edu/group/Contag/

LAB MICE GLOW WHEN GENES TURN ON

STANFORD — Borrowing glow-in-the-dark chemistry from fireflies, researchers have developed a technique enabling them for the first time to observe gene activation as it occurs in a living mammal.

In a series of experiments performed in mice and rats, the Stanford scientists used ultrasensitive cameras to detect light emitted when certain genes were turned on, even deep within the animals' tissues.

The technique may find use as a way of monitoring gene therapies, tracking infectious processes in various diseases, possibly including AIDS, and studying gene expression in animals as they grow and develop, said Christopher Contag, acting assistant professor of pediatrics and director of bioluminescence research at Stanford University School of Medicine.

"This is a powerful approach for looking at any number of things, because you can study gene regulation in a living animal over time, in superficial or deep tissues," said Contag, who describes the technique in the October issue of the scientific journal *Photochemistry and Photobiology*.

Natural bioluminescence, such as the glow of fireflies, happens when the enzyme luciferase reacts with an energy-rich chemical called luciferin to generate light. Contag and his co-workers used the firefly luciferase gene and a genetic promoter to generate a molecular "light switch" that revealed when gene activation occurred in their experimental systems.

One set of experiments tested the use of luciferase as an indicator light for monitoring gene therapy. The idea behind gene therapy is to transfer healthful genes into patients with diseases caused by genetic defects, such as cystic fibrosis.

(more — glow)

Contag's group transferred the luciferase gene into the lungs of rats. After injecting luciferin into the rats, the researchers were able to detect, from outside of the animal, light coming from the lungs. The glow indicated that the luciferase gene was active.

The new technique will help researchers know when they have succeeded in transferring a potentially therapeutic gene into lab animals. In the past, this has often required removing tissue for biopsy or conducting a postmortem to look for the products of the transferred gene. "But then you no longer have that animal to study to find out if the therapy was effective, so you need other groups of animals in order to evaluate efficacy," Contag said.

By linking the luciferase gene to a therapeutic gene, researchers can now use a sensitive imaging device as a noninvasive way to monitor the success of gene transfers in living animals.

"You can reduce the number of animals used for experiments tenfold while getting more information more quickly," Contag said. "This will help streamline development of many types of therapies, including DNA-based gene therapies and gene vaccines."

His group performed another set of experiments in mice genetically altered to carry the luciferase gene in their chromosomes. In these transgenic mice, created by Dr. John Morrey at Utah State University, expression of the luciferase gene is controlled by the regulatory region of the genome of HIV (the virus associated with AIDS).

The Stanford researchers used a chemical signal to switch on the HIV regulatory region, then detected the glow of luciferase activity in the cells of various tissues. They were able to detect luciferase activity both in the skin and in deeper tissues, such as the colon. Weak signals originating from especially dense tissues, such as the liver, might not be detectable, Contag noted.

The HIV regulatory region in this experimental model is more than just a convenient tool for developing the technology, he added. Scientists around the world are hoping to develop a mouse model for studying replication of the AIDS virus. The ability to study HIV in a small animal, rather than using chimpanzees or other primates, would be a major breakthrough for AIDS researchers. "But to have an indicator light in these animals that tells you where and when the virus is replicating — in the living animal, in real time — would be truly amazing," Contag said.

(more — glow)

"Such a tool would have tremendous impact on antiviral drug development," he said.

In their studies, Contag's group also used luciferase as an indicator of HIV replication in cell cultures. This technique could be used to develop a rapid assay for screening large numbers of potential antiviral drugs, Contag said.

Other areas in which he plans to use the molecular light-switch technique include studies of tumor progression, gene expression in cancer cells, cancer therapies, and host responses to bacterial and viral infections.

Contag's co-authors on the paper include six scientists associated with the Department of Pediatrics at Stanford: research assistant Stanley D. Spilman; visiting scholar Dr. Pamela R. Contag, CEO of Xenogen Corp.; research assistant Brian F. Eames (now at UCSF); assistant professor Dr. Phyllis Dennery; Dr. David Stevenson, the Harold K. Faber Professor; and assistant professor Dr. David A. Benaron. Also collaborating in the work was Masafumi Oshiro of Hamamatsu Corp., which provided the photonic detection systems.

The work was supported in part by the California Universitywide AIDS Research Program, the Stanford Office of Technology Licensing, the Office of Naval Research, the Baxter Foundation, Mary L. Johnson, and the Packard Fund at Lucile Packard Children's Hospital at Stanford.