skull and the transmission of light at two wavelengths is measured. The procedure, which takes a few seconds per measurement, is then repeated on the other side of the brain. "What they find is a huge change in differential absorption at those two wavelengths when there's a stroke, or bleeding." says Yodh. The light-absorption signal, measured with a cheap and portable system, could serve as an early warning telling physicians when a CT scan is urgently needed.

The Holy Grail in this field, as Chance puts it, is developing light-based systems that could detect breast tumors and even determine whether a tumor is malignant or benign based solely on its response to light. Many researchers are skeptical that this will ever be done, if for no other reason than because of the near impossibility of getting sufficient resolution out of tissue more than a few centimeters thick.

Both Gratton and Bruce Tromberg of the University of California, Irvine, however, are working on systems to do just that. Gratton says they have demonstrated that absorbed and scattered light can reveal tumors, but "the real question is can we see all tumors?" As for the task of distinguishing malignant from benign tumors, he describes it as "another order of magnitude." Blood oxygenation might be one basis for the distinction, he says; it may be lower in malignant tumors because the tissue is growing faster. The cells' mitochondria—which are more abundant in cancers—could also provide a clue, because the density of mitochondria should affect light scattering. "We're trying to understand fundamentally what it is about tissue that changes" in a cancer, says Tromberg, "and why it looks like it does."

In spite of the technical hurdles, researchers persist because they believe optical imaging will be simplicity itself in practice. Benaron describes one vision: "If someone comes into an office and says 'I have this lesion,' you stick a light probe onto it and image the lesion. And the computer, using the absorption and scattering characteristics, can tell you whether this is normal or a cancer. That's more than just a pipe dream."

–Gary Taubes

BIOMEDICINE

Firefly Gene Lights Up Lab Animals From Inside Out

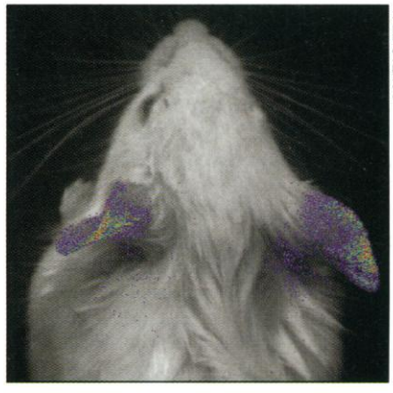
What better way to look inside your resident lab animal than to put a light source inside it and detect the light seeping out? A team of researchers at Stanford University has done just that by genetic engineering.

In a proof of concept, physician and engineer David Benaron, virologist Christopher Contag, and microbiologist Pamela Contag spliced the gene for luciferase, the enzyme that puts the fire in fireflies, into a salmonella bacterium. The photos below, made with no more than a souped-up video camera, show mice infected with the glowing salmonella. Taken 5 hours apart, they trace the course of the infection when untreated (top pair) and when treated with antibiotics (bottom pair).

A transgenic mouse created by John Morrey of Utah State University represents the next step: an animal with the luciferase gene in every cell of its body. The photo at right shows the glow that appears in the ears of this mouse when the gene is turned on. In this mouse, the luciferase gene is tied to a genetic switch that, in human cells, is activated when HIV, the AIDS virus, is replicating. Mice aren't susceptible to HIV infection, but the Stanford researchers simulated its effect with a chemical known as DMSO, which turns on the genetic switch and, with it, the light. "We can image in the intact animal where and when the gene is activated by watching the lights," says Benaron. He adds that with the right animal model for HIV infection—which is still "a huge step," says Contag—the scheme might be used, for instance, to test HIV drug treatments. "We would no longer have to wonder if the drug is effective in vivo; we could watch the virus replicate and see what happens when we give an antiviral," says Benaron.

He adds that the spatial resolution of the technique is limited to roughly 10% of the depth—which means that a glowing cell 5 centimeters deep can be resolved to within a half-centimeter. Even so, Benaron sees unlimited potential. "You can use bioluminescent approaches to study processes in vivo which cannot otherwise be visualized at any resolution," he says. "You could use it to study gene expression in real time. Want to know when a gene turns off and on during development? Add luciferase. Or evaluate genetic therapy. Right now we have no real-time information on genetic therapy. This would give you a way to track genetic therapies in vivo."

–Gary Taubes



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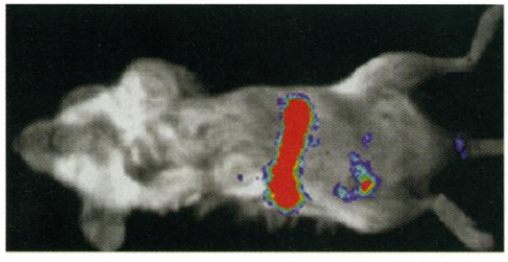

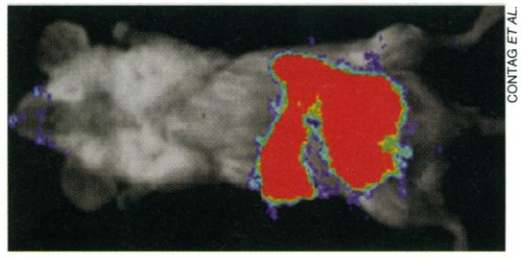

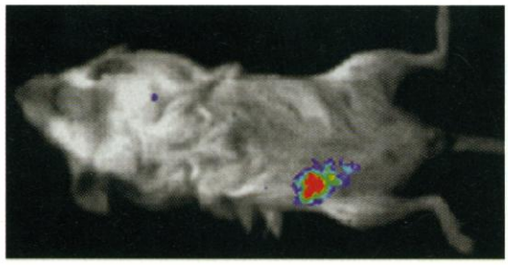

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