

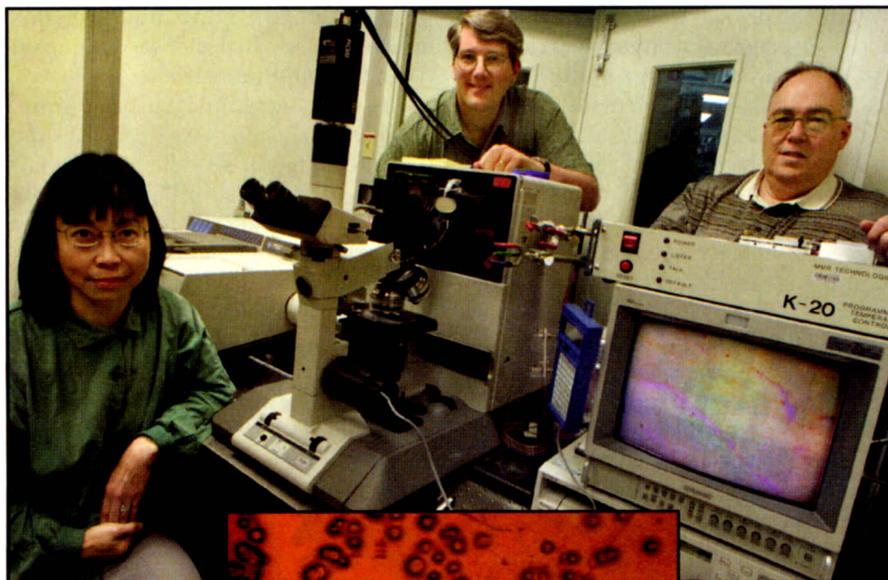
Synchrotron light exposes living cells

BERKELEY, Calif. — How do you non-destructively peer into the machinery of the living human cell? Standard biomedical methods involve killing cells, averaging the result of many observations,

or introducing tagged proteins or dyes that affect their chemistry and delay results. Now a research team at Lawrence Berkeley National Laboratory has developed a variant of Fourier transform

infrared (FTIR) spectromicroscopy that allows them to follow molecular changes in human cells as they occur, without disturbing them.

The key to the technique is the lab's



Hoi-Ying Holman (left) monitors the spectra of living human cells with the Advanced Light Source's high-brightness infrared beamline, designed and built by Michael C. Martin (center) and Wayne McKinney (right).

and bleomycin, which induce single- and double-strand breaks in DNA, respectively, caused distinctive changes in the spectra of the cells.

Another experiment exposed lung cells to low-intensity doses of x-rays. Findings suggest that radiation studies based on less-sensitive dye-labeling techniques may have overestimated the effects of low doses on nuclear plant workers. "It is far too early to know if our results will have any impact on regulatory agencies," Holman said.

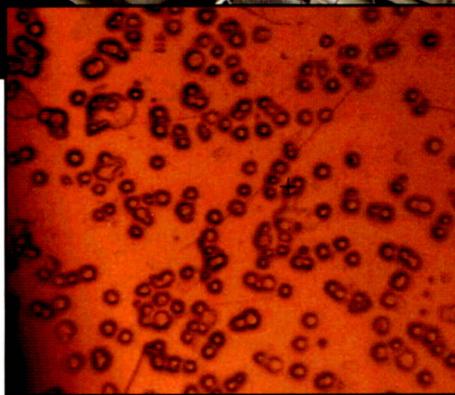
Other researchers will use the beamline to study changes in human cells. Plans are under way to evaluate the efficacy of radiotherapy for cancer, as are studies of oxidative cellular stress in atherosclerosis, diabetes, rheumatoid arthritis and degenerative diseases such as amyotrophic lateral sclerosis.

Synchrotron-radiation-based FTIR spectromicroscopy also may lead to the development of unique medical tools. The researchers are beginning to correlate spectra changes to specific cellular activities, and similar work could be used to produce a categorized database of cellular spectra from which diagnostic systems could be tailored.

"Once we have identified which specific IR absorptions change for a specific disease or contaminant," Martin said, "one could fairly easily and inexpensively build a solid-state laser-based system to measure specifically these wavelengths in individual cells from a patient." □

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synchrotron-powered Advanced Light Source. Electrons that race around the facility's magnetic storage ring with energies of 1.9 GeV give up photons that serve as the 450- to 10,000- cm^{-1} light source. Because the beam is so bright, it can be focused with little loss into diffraction-limited spot sizes of 10 μm — roughly the size of a mammalian cell — with a Magna 760 FTIR bench from Nicolet Instrument Corp. of Madison, Wis. Moreover, because the light comes in 2-ns pulses, the researchers can monitor rapid changes in the absorption spectrum of an individual cell.



Synchrotron-radiation-based Fourier transform IR spectromicroscopy can monitor real-time changes in the spectra of living human cells such as these lung fibroblasts. Images courtesy of Lawrence Berkeley National Laboratory.

Hoi-Ying Holman, the principal investigator in developing the technique, and her colleague Michael C. Martin, who described their work in March at the annual meeting of the American Physical Society in Minneapolis, have used synchrotron radiation-based FTIR to identify cells by type, by cytomorphic phase and by chemistry.

In recent experiments, the researchers monitored real-time changes in living human liver cells as they introduced dilute hydrogen peroxide and the antibiotic bleomycin, two typical oxidizing agents in the environment. They found that H_2O_2