Researchers Carolyn Larabell, Sophie Lelievre, Donna Hamamoto, Mina Bissell and Werner Meyer-Ilse at LBNL recently developed the methodology to label proteins in hydrated cells for examination in the x-ray microscope (XM-1). Using this approach, they have obtained images at higher spatial resolution (40 nm to 50 nm) than light microscopy and can examine samples 10 μm thick in a liquid environment at atmospheric pressure. To label proteins, they used a commercially available probe, FluoroNanogold™ (Nanoprobes, Inc., Stony Brook, NY), which has both fluorescein (FITC) for visualization in the light microscope and 1.4 nm Nanogold™ particles which readily enter permeabilized cells. The gold particles can subsequently be enhanced with silver to create aggregates visible in the x-ray microscope. The researchers have used this technique to label proteins in the cytoplasm and nuclei of human mammary epithelial cells.

It is important to point out that immunolocalization analyses in the x-ray microscope also reveal information about the underlying structural components of the nuclei. Although the skeletal components of the cytoplasm, referred to as cytoskeleton, have been well characterized, comparable nuclear structures remain controversial. The controversy results from the fact that examples of nuclear structure are based on electron microscopy of cells that have undergone extensive chemical extractions, and critics claim the resulting matrix is an artifact of these preparation techniques. Using x-ray microscopy, researchers can examine hydrated, whole cells and examine nuclear architecture without subjecting the cells to the chemical processing steps required for electron microscopy. Therefore, x-ray microscopy has the potential to be very instrumental in addressing this controversy. Ultimately, with the use of stereo images and tomographic reconstructions of cells, researchers will be able to obtain unique, three-dimensional information about protein localizations with respect to cell architecture in hydrated cells at 4 to 5 times the resolution of light microscopy. They will be able to examine the distribution of these proteins in normal cells and compare these data with the patterns of distribution of that same protein in tumor cells to elucidate structural differences that may contribute to, or be the product of, tumorigenesis.

4. DISEASE PREVENTION

New Sensor Provides Instant Litmus Test for Pathogens (LBNL). A new class of colorimetric sensor materials has been invented that makes it possible to instantaneously and inexpensively detect a wide range of biological toxins and common disease-causing organisms. Building on earlier discoveries in their laboratory, researchers at the Lawrence Berkeley National Laboratory have developed a thin film consisting of receptor molecules attached to a film of linked diacetylene molecules. The film transmits blue light. The surface receptor molecules are designed to very selectively bind specific pathogens causing the film molecules to reorganize and the film to turn red. Pathogens thus far detected with good sensitivity include an influenza virus, cholera toxin, botulinum toxin, and the *E. coli* toxin produced by the bacteria responsible for 200 deaths per year in the United States alone, as noted in the recent contamination of fruit drinks and fast food hamburgers. Existing tests for all of these pathogens require at least a 24-hour culture. With further development (150 companies have inquired) the sensors can be