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FOR RELEASE: December 10, 2008

## LIGHT SHINES FOR POTENTIAL EARLY CANCER DIAGNOSIS TECHNIQUE

EVANSTON, Ill. --- A team led by a Northwestern University biomedical engineer has developed a new optical technique that holds promise for minimally invasive screening methods for the early diagnosis of cancer.

The researchers have shown for the first time that nanoscale changes are present in cells extremely early on in carcinogenesis. Their technique, partial-wave spectroscopy (PWS), can detect subtle abnormal changes in human colon cancer cells even when those same cells appear normal using conventional microscopy.

The study will be published online by the Proceedings of the National Academy of Sciences.

A simple yet sensitive method, PWS quantifies the statistical properties of cell nanoscale architecture by using the signal generated by light waves striking the cell.

PWS can provide information not only about individual cells, but it also can look inside the cell and see the cell's fundamental "building blocks," such as proteins, nucleosomes and intracellular membranes, and detect changes to this cell nanoarchitecture. Conventional microscopy cannot do this, and other techniques that can (to some degree) are expensive and complex.

"Imagine a cell as a house and the cell's fundamental building blocks as bricks," said Vadim Backman, professor of biomedical engineering at Northwestern's McCormick School of Engineering and Applied Science.

"Our technique can see not only the sizes of the house's bricks but the details of those bricks. And it can show when those bricks are in trouble even when the house looks normal. Conventional microscopy can see the individual houses but not the bricks that make up the house. That's a significant difference," said Backman, who led the research.

Backman and his colleagues studied both human colon cancer cell lines and cells from a colon cancer animal model. In both cases, the PWS technique showed that an increase in the disorder of cells on the nanoscale parallels genetic events in the early stages of carcinogenesis.

"We have to look at cell morphology at the nanoscale," said Backman. "Cells are not just a bag of molecules -- the nanoarchitecture can control many important cellular processes and activities."

The team studied three variants of malignant human cells, each exhibiting a different degree of aggressive behavior. (In all three, the malignancy resulted from genetic alteration.)

Using PWS, the researchers were able to distinguish each cell line. They found architectural disorder in all three but of varying degrees; the most aggressively malignant cell line showed the most intracellular disorder. When viewed using microscopy, all three cell lines looked

normal, and each was indistinguishable from the others. The same trend was found in the researchers' study of cells from an animal model.

"If the PWS screening technique for colon cancer is validated by appropriate clinical trials, there is the potential for preventing many thousands of cancer deaths each year," said Allen Taflove, professor of electrical engineering and computer science at Northwestern, who collaborated with Backman in conducting computer simulations of how light interacts with the complex structure of a cell and is an author of the paper.

In addition to cancer research, PWS could find use in biomechanics (to study the nanoscale architecture of polymers, materials or tissue), tissue engineering and stem cell research.

"Anywhere you use microscopy you could use PWS and get more information," said Backman. "PWS can work with virtually anything, and it can detect features as small as 20 nanometers."

Authors of the PNAS paper from Backman's research group are lead author and graduate student Hariharan Subramanian; research associate Prabhakar Pradhan, a theoretical physicist who predicted that PWS should work; and Yang Liu, a former graduate student and now an assistant professor at the University of Pittsburgh who performed the first experiments to demonstrate PWS.

Other authors are Ilker Capoglu, Xu Li, Jeremy Rogers and Alexander Heifetz, from Northwestern University; and Dhananjay Kunte and Hemant Roy, M.D., from NorthShore University HealthSystem (formerly Evanston Northwestern Healthcare).

The PNAS paper is titled "Optical Methodology for Detecting Histologically Unapparent Nanoscale Consequences of Genetic Alterations in Biological Cells."

The work was supported by the National Institutes of Health and the National Science Foundation.

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