Shining light on cells' inner workings

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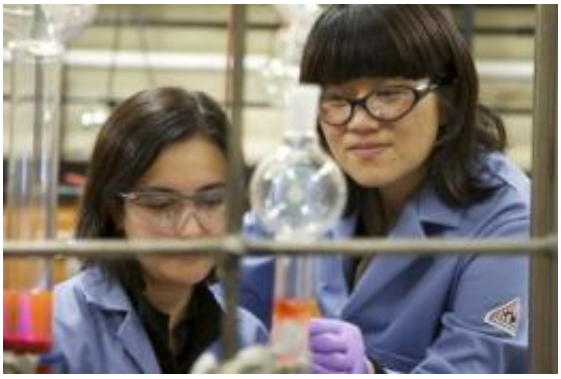

Nazmiye Yapici, left, and Lanrong Bi

(Phys.org) -- Lanrong Bi and Nazmiye Yapici are shining new light on the hidden processes within cells. For their groundbreaking research, Bi, an assistant professor of chemistry at Michigan Technological University, and PhD candidate Yapici have received the Bhakta Rath Research Award.

The Rath Award recognizes research by faculty and doctoral students to meet the nation's needs and contribute to emerging technologies.

Inside our cells are processes that make or break us. They are tied to tiny organelles, such as mitochondria, nuclei and lysosomes. To get a glimpse of those organelles, technologists infuse tissue samples with special dyes and observe them under powerful fluorescent microscopes.

When the dyes work, you can see a glowing image of the organelle. That image may someday be able to tell you if a cell is about to become cancerous or the patient is coming down with Alzheimer's disease. Until now, however, those dyes had certain limitations.

Working together, Bi and Yapici have developed fluorescent dyes with powerful new properties: they work in acidic conditions, and they can trace hydroxyl radicals (also known as free radicals), very unstable molecules that are associated with a whole range of pathologies, from heart disease to AIDS.

"It's difficult to monitor a cell's interior pH, because if a cell goes acidic, the commercial dye breaks down," said Bi. "But we have developed two dyes that become fluorescent under acidic conditions, which would make it much easier to monitor cells in a diseased state."

This property makes these dyes especially useful in imaging lysosomes, which serve as the cell's waste disposal system and have an interior pH of about 4.5. And there's a good reason to look at lysosomes. "Their morphology changes as cells become cancerous," Bi said. "This could be used for very early diagnosis, when it's difficult to tell if a cell is cancerous or not."

Using a different type of fluorescent dye, Bi and Yapici have also been able to verify the presence of free radicals in mitochondria--organelles that generate most of the cell's energy--within colon cancer cells. "We do more than label mitochondria," said Bi. "We are focusing on detecting oxidative stress, which is characteristic of many pathologies, including Parkinson's, stroke and cancer."

The fluorescent dyes could be used for quick, safe, inexpensive diagnostic tests, Bi said. "Just put a cell sample on a slide, add the dye, and wait 30 minutes for it to go to the specific organelles," she said.

Then look at it under a microscope.

"These novel fluorescent probes will have great potential for biomedical applications," said James Russo of Columbia University in supporting their nomination for the Rath Award. "This project is especially exciting because the new compounds already show a dramatic improvement over a probe that is currently on the market."

Yapici has been key to this research, Bi said. "She is an absolutely outstanding student," she said. "She works very hard; to demonstrate one fluorescent dye, she will test it under 2,000 experimental conditions. And we will meet at two or three o'clock in the morning to do our work, because not many people are working on the fluorescent microscope at that time."

Yapici has also been a willing collaborator, working with colleagues at Columbia and Northwestern universities on recent papers as well as with faculty in other departments at Michigan Tech.

Bi expressed her appreciation to her department chair, Professor Sarah Green. "A paper Sarah wrote back in 1990 in this area inspired me," she said. "She is a pioneer in this field." And she also thanked Bruce Seely, dean of sciences and arts, for his assistance, saying, "He gives pre-tenure faculty a great deal of support."

More information: Their work is described in the papers "New Rhodamine Nitroxide-Based Fluorescent Probes for Intracellular Hydroxyl Radical Identification in Living Cells," authored by Yapici, et al. and published in *Organic Letters*, 2012, Vol 14., No. 1; and "Determination of Intracellular pH Using Sensitive, Clickable Fluorescent Probes," authored by Yapici, et al., and published in *Bioorganic & Medicinal Chemistry Letters*, April 2012, Vol. 22, No. 7.