New method monitors early sign of oxidative stress in cancer

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(PhysOrg.com) -- The growth of cancerous tumors is fueled, at least in part, by the buildup of free radicals -- highly reactive oxygen-containing molecules.

It stands to reason, then, that cancer should respond to treatment with antioxidants, which inhibit the rogue radicals, or with pro-oxidants, which go the opposite direction, increasing "oxidative stress" on cancer cells to the point of vanquishing them.

But experiments with such treatments have had mixed results, possibly because patients differ in their "redox profiles," or oxidative stress levels. Being able to monitor a marker of oxidative stress that is associated with the activation of tumor cell growth pathways, particularly at an early stage, and then tailor treatments accordingly would allow for more targeted studies and might improve the odds of success with antioxidants and pro-oxidants, said University of Michigan chemical biologist Kate Carroll.

A new method developed by Carroll and postdoctoral research fellow Young Ho Seo makes such monitoring possible and reveals that different individuals and even different tumor types have different redox profiles. The method and the research behind it are described in a paper scheduled for online publication in the Proceedings of the National Academy of Sciences during the week of Sept. 7.

The new method detects sulfenic acid in proteins -- a tipoff to early

oxidative stress and to a specific protein modification associated with cell growth pathways. Sulfenic acid is produced when a particular oxidant, hydrogen peroxide, reacts with the protein building block cysteine. But because the chemical modification involved is so small and transient, it has been difficult to detect. To get around that problem, Carroll and Seo used a chemical probe that "traps" sulfenic acid and tags it for recognition by an antibody. The antibody is labeled with a fluorescent dye that glows when observed with a fluorescence microscope.

The researchers then used the method to assess sulfenic acid levels as a marker of oxidative stress in several systems, including a panel of breast cancer cell lines.

"For each line, we saw a very distinct pattern of sulfenic acid modifications," indicating different oxidative stress levels and hinting at differences in the underlying molecular events associated with tumor growth," said Carroll, assistant professor of chemistry and a research assistant professor in the Life Sciences Institute. "Whether the patterns we see will correlate with response to antioxidant treatment or other therapies that modulate oxidative stress level remains to be seen, but now we at least have a way to investigate that question."

Next, Carroll's group wants to determine which specific proteins in the cell are being modified and what roles, if any, those proteins play in the disease process. "Some of the modified proteins may not play any role, but I'm sure it will turn out that many of them do," Carroll said. "Once we find out which proteins are involved, we can target them directly rather than using global treatments like antioxidants."

The U-M Office of Technology Transfer is working on commercialization of the technology. Patent protection has been applied for, and the compounds used in this research soon will be commercially

available.

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