Possible predictive biomarker for patients who may respond to autophagy inhibitors

April 8 2013

Autophagy, the process by which cells that are starved for food resort to chewing up their own damaged proteins and membranes and recycling them into fuel, has emerged as a key pathway that cancer cells use to survive in the face of assault by chemotherapy and radiation. Using drugs to shut down that survival mechanism shows great promise, especially when combined with targeted agents and standard chemotherapies, but until recently, it has been unclear which patients' cancers would respond to that combination therapy.

A team led by researchers from the Perelman School of Medicine at the University of Pennsylvania will present findings (Presentation #1679A) during the AACR Annual Meeting 2013 showing that colon cancer and lung cancer cell lines which expressed a gene known as helicase-like transcription factor (HLTF) tended to be impervious to the effects of the autophagy inhibition drug hydroxycholoroquine (HCQ), a drug originally used as an antimalarial agent. Cells where HLTF is silent, however, appeared to be sensitive to HCQ, which led the team to test HLTF expression in a group of colon cancer patients treated with two chemotherapies (the FOLFOX regimen plus bevacizumab) and HCQ. They found that low expression of HLTF predicted those who would respond to the combination therapy.

Since previous studies have shown that HLTF gene silencing is common in 20 to 40 percent of many epithelial cancers, the Penn team is hopeful their findings could lead to the development of a predictive biomarker to identify patients with other cancers who are most likely to respond to

drug therapies involving autophagy inhibitors.

The study will be presented by Ravi Amaravadi, MD, in the Autophagy and Cell Death poster session, Hall A-C, Poster Section 23, at the at the Walter E. Washington Convention Center, 801 Mt Vernon Pl NW, Washington, DC 20001, on Monday, April 8, 2013.

Provided by University of Pennsylvania School of Medicine