Natural compound attacks HER2 positive breast cancer cells

February 18 2014

(Medical Xpress)—A common compound known to fight lymphoma and skin conditions actually has a second method of action that makes it particularly deadly against certain aggressive breast tumors, researchers at Duke Medicine report.

The compound is called psoralen, a natural component found in foods such as figs and celery, and researchers have long understood that it that works by disrupting DNA replication and causing cell death when activated by an energy source such as UV light.

Duke researchers have now identified another way the compound works to kill tumor cells, raising the potential for psoralen to be developed as an effective therapy for cancers that are particularly vulnerable to this second mode of action.

Reporting in the Feb. 14, 2014 issue of the journal *PLOS ONE*, the researchers detail how psoralen blocks the signaling pathway of the HER2 receptor, which is overproduced in 25 percent of breast cancers, plus ovarian, gastric and other solid tumors. When HER2 is overproduced, it fuels uncontrolled cell growth, leading to an aggressive form of cancer. Psoralen shut down this process in experiments using HER2 overexpressing breast cancer cell lines.

"This was very unexpected," said senior author Neil L. Spector, M.D., the Sandra Coates Associate Professor of Medicine at Duke. "The therapy has been known to kill cancer cells by causing DNA damage, but

it is also having a direct anti-tumor effect on HER2 overexpressing breast cancer cells by blocking HER2 signaling."

Psoralen also attacks another form of HER2 that is present in the nucleus of tumor cells. This form of the protein is resistant to cancer therapies such as lapatinib and trastuzumab that are otherwise effective in targeting HER2-positive cancers.

"Cancer drugs can recognize HER2 receptors when they are outside of the cell, but they don't recognize the truncated version inside the cell nucleus," Spector said. "We have shown that psoralen is effective in targeting this other form of HER2 that is resistant to current HER2-targeted therapies."

Spector said the benefits of psoralen remain dependent on its activation by an energy source, which has been an impediment to its use in solid tumors. Currently, psoralen is primarily used as a topical treatment in conjunction with UV light exposure in a process called PUVA. The treatment is used for skin conditions such as psoriasis and as a therapy for lymphoma by exposing treated blood to UV radiation during a dialysis-type procedure.

"The challenge all along has been to figure out a way of generating UV light deeper in the body," Spector said. That challenge is close to being resolved. In a previous publication, Duke investigators from the Pratt School of Engineering, working in collaboration with Spector and scientists from Immunolight, the company that has funded the research, reported the development of micron-sized particles that absorb energy from X-rays to emit UV light in and around cells, much like the cathode ray tube technology used in televisions.

The tiny particles are injected into tumors along with the psoralen, then targeted by low-dose X-ray that cause the micron particles to create the

UV light necessary to trigger psorlen's anti-tumor properties. Spector said the technology is being tested in animals, and may be approved for human trials as early as this year.

"A good part of four years has been trying to figure out how to overcome the biophysics challenge of generating enough energy inside the body to activate the particles and the drug," Spector said. "We've come a long way."

Provided by Duke University