HER-2-Targeted T Cells May Have a Role in Ovarian Cancer Treatment

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(PhysOrg.com) -- Ovarian cancer is the most lethal reproductive cancer for women, with just one-fifth of women diagnosed with advanced disease surviving five years. It is frequently reported that less than one-third of ovarian cancers overexpress the HER-2 protein, which is the molecular target of trastuzumab (Herceptin).

However, with more sensitive detection methods, Daniel J. Powell, Jr., PhD, a research assistant professor of Pathology and Laboratory Medicine and Obstetrics and Gynecology at the University of Pennsylvania School of Medicine, and colleagues found that virtually all ovarian cancers express HER-2. The novel findings suggest that therapy targeting HER-2 may have a role in ovarian cancer treatment in the future, and may improve the outcome for women with ovarian cancer the way it has for women with HER-2 expressing breast cancer.

The team used three different assays to test for HER-2 expression in ovarian cancer cell lines and patient tumor samples. “What we found is that ovarian cancers ubiquitously express HER-2, and generally at higher levels than normal ovary tissue,” says Powell, whose group presented their findings Tuesday, April 20th at the American Association of Cancer Research meeting.

Although the results of previous clinical trials testing trastuzumab in women with advanced ovarian cancer have been lackluster, Powell thinks responses could be improved by using genetically engineered immune cells to deliver a toxic hit to tumor cells expressing HER-2. The

modified T cells express an engineered protein - called a chimeric immune receptor -- that combines a portion of an anti-HER-2 antibody with a portion of a killer T-cell receptor to stimulate cell-killing activity. “The chimeric immune receptor is not simply binding the HER-2 protein; it also uses the power of killer T cells coming in behind to further mediate the anti-tumor response,” Powell explains. “Also, the chimeric immune receptor that we are using is able to distinguish recognition of ovarian cancer from normal targets, despite the fact that the normal cells do express HER-2.”

The new results support testing of anti-HER-2 T-cell therapy in ovarian cancer, but Powell cautions that more research is needed to understand how to deliver the cells safely.

Provided by University of Pennsylvania School of Medicine