Researchers identify priority targets for immunotherapy in epithelial ovarian cancer

August 14 2014

(Medical Xpress)—Researchers at Roswell Park Cancer Institute (RPCI) have found that the expression pattern of a unique class of tumor-associated antigens, known as the MAGE cancer-testis antigens (CTAs), correlates with clinical outcome in epithelial ovarian cancer. Based on their findings, the researchers have identified priority targets for ovarian cancer immunotherapy.

Epithelial ovarian cancer is the most lethal gynecologic cancer in women and has a relapse rate of 85%.

"The MAGE family of proteins is part of a class of CTAs that may serve as a target for directed immunotherapy in ovarian cancer and other types of cancer," said senior author Kunle Odunsi, MD, PhD, FRCOG, FACOG, M. Steven Piver Professor of Gynecologic Oncology and Executive Director of the Center for Immunotherapy at RPCI. "To achieve the important goal of tumor-directed immunity for ovarian cancer immunotherapy, it is critical to determine the extent to which this family of CTA molecules is expressed in these tumor cells."

Dr. Odunsi and his colleagues examined the expression pattern of five MAGE molecules using genetic and immunohistochemical screens in tissue samples of 400 patients with ovarian cancer. They analyzed immune responses by determining whether antibodies present in 285 serum samples recognized the same five molecules. Their results revealed that aberrant expression of MAGE-A1 was present in 15% of epithelial ovarian cancers, expression of MAGE-A3 was present in 36%,

expression of MAGE-A4 was present in 47%, expression of MAGE-A10 was present in 52%, and expression of MAGE-C1/CT7 was present in 16%.

"Approximately 78% of ovarian tumor tissue showed expression of at least one of these five CTAs," Dr. Odunsi said.

Researchers also noted strong co-expression of MAGE-A1 and MAGE-A4, MAGE-A1 and MAGE-C1, and MAGE-A4 and MAGE-A10. MAGE-A1 and MAGE-A10 expression were associated with poor progression-free survival, while MAGE-C1/CT7 was associated with improved progression-free survival, although this improvement diminished with the co-expression of MAGE-A1 or MAGE-A10.

According to Dr. Odunsi, these results suggest that MAGE-A1, MAGE-A10 and MAGE-C1 are possible prognostic factors for ovarian cancer. In addition, "as MAGE-A4 exhibits a relatively high frequency of expression and appears to direct a major pattern of co-expression of other MAGE antigens, we also propose MAGE-A4 as a priority target for ovarian cancer immunotherapy," he said.

RPCI researchers are also conducting clinical trials, including vaccination studies and adoptive cell therapy, using another CTA known as NY-ESO-1. "Because not all ovarian tumors express NY-ESO-1, it is critical to identify other potential targets for immunotherapy," Dr. Odunsi noted. "The current study supports the development of MAGE-directed immunotherapies to provide alternative modalities for patients whose tumors do not express NY-ESO-1 or whose responses against NY-ESO-1-expressing tumors are no longer sufficient."

The RPCI Center for Immunotherapy is actively studying MAGE CTAs to translate the current laboratory findings into clinical studies with the goal of providing further treatment options to patients with ovarian

cancer, as well as patients with other cancers that express MAGE molecules, including melanoma, breast cancer and lung cancer.

The study, published online ahead of print in the peer-reviewed journal *PLOS One*, is "Expression and Immune Responses to MAGE Antigens Predict Survival in Epithelial Ovarian Cancer."

Provided by Roswell Park Cancer Institute