MedicalXpress

Loss of enzyme promotes tumor progression in endometrial cancer

December 7 2015

Scientists have shown for the first time why loss of the enzyme CD73 in human cancer promotes tumor progression.

The endometrial cancer study at The University of Texas MD Anderson Cancer Center provided key evidence for the importance of CD73's role in tumor growth. CD73 is the crucial enzyme for generating adenosine, a signaling molecule important for regulation of normal tissue function and stability or homeostasis.

Study results were published in today's online issue of the *Journal of Clinical Investigation*.

"Prior to our work, it had been generally thought that CD73-generated adenosine promoted cancer via suppressing the local immune response," said Russell Broaddus, M.D., Ph.D., professor in the Department of Pathology. "Our study reported the unexpected down-regulation of CD73 in carcinoma cells of advanced stage endometrial cancer."

In healthy tissues, CD73-generated adenosine is central to regulating tissue protection and physiology. Broaddus' team hypothesized that CD73-generated adenosine in endometrial carcinoma would protect the integrity of epithelial cells that make up the tumor. Such a scenario would mean that loss of CD73 would be crucial for tumor progression.

"Up to now, there has been little evidence to suggest that CD73-generated adenosine may have actions opposing disease

progression in human tumors," said Broaddus.

CD73 is over-expressed in a number of human tumors including breast and ovarian cancers and melanoma. There are exceptions as the enzyme is down-regulated in prostate, laryngeal and colon cancer.

Broaddus' team demonstrated that CD73-generated adenosine protects tissue integrity through a process known as actin polymerization. Actin is a multi-functional protein that is vital to many cellular functions, including the formation of cell-cell contacts. Polymerization is a process by which molecules are combined to form a chain or network.

"To our knowledge, this is the first study showing a mechanistic basis for why CD73 loss promotes tumor progression," said Broaddus. "We hope this will pave the way for different perspectives regarding CD73 and adenosine in cancer."

Provided by University of Texas M. D. Anderson Cancer Center