Researchers discover cancer stem cell pathway in endometrial cancer

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A team of Cleveland Clinic researchers have discovered a key pathway that leads to recurrence and treatment resistance in endometrial cancer, providing the potential for much needed new therapies for women with limited options.

For the past 25 years, standard therapy for endometrial and ovarian cancers has included surgery and the chemotherapy drug cisplatin. While these treatments typically are initially successful, the cancer often recurs and becomes resistant to cisplatin, leaving patients with limited treatment options.

The Cleveland Clinic team studied the unique role of an immune regulatory protein, called CD55, which is abundant on the surface of endometrioid ovarian cancer and uterine cancer cells. Using human cells and patient-derived tissue models, they found CD55 to be the most prevalent on cancer stem cells, a subgroup of aggressive cancer cells that are thought to be responsible for recurrence and spread of many types of cancer.

The researchers discovered that high levels of CD55 caused cancer stem cells to be more aggressive and resistant to cisplatin than non-stem cell cancer cells. The CD55 pathway is unique in that it controls both stem cell self-regulation/growth and therapeutic resistance, while other mechanisms control just one or the other.

In addition, when CD55 was removed from cells, they became sensitive to cisplatin in cell culture models and in pre-clinical mouse models. The researchers hope that blocking the protein will enhance cisplatin treatments and that high expression of CD55 could be used as a biological marker of aggressive gynecologic cancers. The team plans to complete further preclinical testing followed by a clinical trial in patients with CD55-expressing endometrial cancers.

The study was co-led by Justin Lathia, Ph.D., and Ofer Reizes, Ph.D., both of the Department of Cellular & Molecular Medicine in Cleveland Clinic Lerner Research Institute. Dr. Reizes holds the Laura J. Fogarty Endowed Chair for Uterine Cancer Research at Cleveland Clinic.

"We have discovered a unique role for the CD55 complement signaling pathway in cancer as a target which offers an opportunity to prevent recurrence and associated mortality in endometrial cancer patients. Fortunately, there is already an FDA investigational drug that can inhibit the CD55 signaling pathway," Dr. Lathia said. "We hypothesize that using this drug in combination with cisplatin will improve treatment outcomes."

"Endometrial cancer is the most common gynecologic malignancy in the United States, yet research in this area is understudied and underfunded," Dr. Reizes added. "We hope that our study will lead to much needed new therapy options for women with treatment resistant, relapsed disease."

Provided by Cleveland Clinic