Researchers unlock immune cell contributions that could lead to new therapies for endometrial cancer

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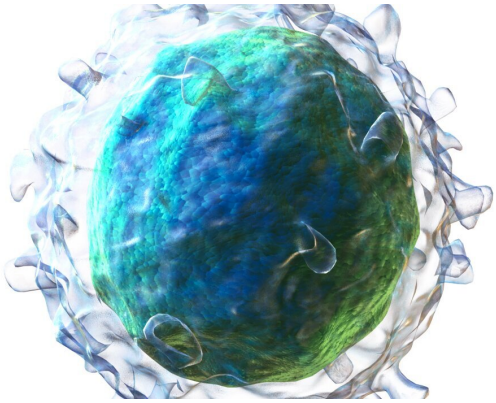

3D rendering of a B cell. Credit: Blausen.com staff (2014). "Medical gallery of Blausen Medical 2014". WikiJournal of Medicine 1 (2). DOI:10.15347/wjm/2014.010. ISSN 2002-4436. CC BY-SA 4.0

Endometrial cancer is the most common cancer of the female reproductive system. Patients who have active immune responses against cancer cells tend to have better outcomes, but much of what is known focuses on only one type of immune cell called T cells. In a new study published in *Cancer Research*, Moffitt Cancer Center researchers provide insight on the role of B cell immunity in endometrial cancer.

The immune system is composed of many different types of cells. T cells have a primary role of killing infected or cancerous cells and activating other immune cells. B cells produce antibodies to target cells for destruction. These antibodies are classified into 5 subtypes—IgM, IgD, IgG, IgE or IgA—and regulate different B cell processes and activity.

Interactions that occur between different immune cells and between immune and cancer cells can both negatively and positively impact cancer progression. Immune cells often infiltrate into or surround tumors, and patients who have higher levels of these infiltrating cells tend to have a better prognosis than those without the presence of active immune cells. Several different immunotherapies that activate the immune system to target cancer cells for destruction have been approved to treat patients with endometrial cancer; however, these agents focus solely on T cells.

With a goal of developing new treatment strategies that take advantage of other types of immune cells, Moffitt researchers aimed to better understand the role B cells play in endometrial cancer. They analyzed 107 endometrial cancer specimens for expression of specific antibodies. They discovered that all endometrial cancer subtypes displayed expression of IgA and IgG antibodies, with most tumors having higher levels of IgA. They also found that immune cell infiltration of endometrial tumors was associated with patient outcomes according to tumor subtype. For example, higher levels of B cells were associated with better outcomes among high-grade endometrioid and serous endometrial cancer subtypes, while higher levels of T cells were associated with improved survival among clear cell endometrial cancer subtypes.

The research team found that all endometrial cancer tumors expressed the antibody receptor pIgR, and after several laboratory experiments discovered that IgA bound to pIgR, activating a series of cell signaling pathways culminating in the stimulation of pro-inflammatory pathways, stress mechanisms and apoptotic cell death.

"This data suggests it may be possible to develop therapies that focus on B cells or antibodies to be used in combination with other approved T-cell

associated immunotherapies in endometrial cancer and possibly other gynecologic malignancies," said Jose Conejo-Garcia, M.D., Ph.D., chair of the Department of Immunology at Moffitt.

More information: Gunjan Mandal et al, IgA-dominated humoral immune responses govern patients' outcome in endometrial cancer, *Cancer Research* (2021). DOI: 10.1158/0008-5472.CAN-21-2376

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