PRESS RELEASE

CONTACT:
Darien Sutton
215-898-3988 | dsutton@wistar.org

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Wistar Institute Researchers Discover New Combination Therapy Approach for Metastatic Ovarian Cancer

Zhang Lab Demonstrates Novel Combination of Beta Glucan and Interferon Gamma Results in Tumor Regression

PHILADELPHIA — (November 21, 2024) — The Wistar Institute's Nan Zhang, Ph.D., assistant professor in the Ellen and Ronald Caplan Cancer Center's Molecular and Cellular Oncogenesis Program, and lab have discovered a new approach to treating ovarian cancer that, in preclinical laboratory testing, shrinks tumors and improves survival rates while simultaneously making tumors more receptive to chemotherapy treatment. Their findings were published in *The Journal of Experimental Medicine* in the paper, "Myeloid activation clears ascites and reveals IL27-dependent regression of metastatic ovarian cancer."

"This is the first time researchers have been able to indirectly target ovarian cancer cells in peritoneal fluid by inducing an immune reaction, in preclinical models," said Zhang. "We look forward to taking this research further — particularly our findings on the role of IL27 — so we can continue to identify other strategies to improve this new anti-ovarian-cancer approach."

Ovarian cancer is the deadliest gynecological cancer; patients with metastatic ovarian cancer have a 30% chance of surviving for five years after their diagnosis. The danger of metastasis (when cancer spreads throughout the body) is exacerbated in ovarian cancer for two main reasons:

1. Ovarian cancer is naturally resistant to chemotherapy, so its presence anywhere is difficult to combat.

2. Ovarian cancer tends to metastasize through peritoneal fluid into the peritoneal cavity that's the larger space in the body that houses the stomach and intestines. Cancer in the peritoneal cavity is especially dangerous because the area is naturally immunosuppressive and limits the body's response to any tumors.

To combat the challenge of ovarian cancer, Zhang and his collaborators turned to a possible solution from nearly a century ago. In the late 1800s & early 1900s, New York surgeon William B. Coley achieved a cure rate greater than 10% for some cancers by injecting patients with dead pathogens. Scientists later reasoned that this anti-cancer effect was the result of the immune system's activation of myeloid cells those are the plentiful cells in the peritoneal cavity that when activated can mount a cancer-killing response.

Building on this concept, Zhang & team designed an approach that specifically activates myeloid cells within the peritoneal cavity through combination treatment with β-glucan, a pathogen-derived activator of myeloid cells, and interferon-gamma (IFNγ). Preliminary reports suggest the approach can work to reverse immunosuppression around tumors.

Their findings confirmed that this combination therapy worked when tested in preclinical lab models. After treating metastatic ovarian cancer models with both β-glucan and IFNγ, total tumor burden shrank substantially relative to controls. This disease reversal was consistent even in chemotherapy-resistant strains of ovarian cancer, which the team also modeled.

"Our work has opened the door to a possible new method of treating a particularly aggressive cancer," said Brennah Murphy, Ph.D., first author of the paper. "Ovarian cancer is infamous for resisting treatment, but we've shown — at the preclinical level — our treatment overcomes that resistance."

Co-authors: Brennah Murphy, Bryan S. Manning, Gauri Mirji, Alessio Ugolini, Toshitha Kannan, Daniel T. Claiborne, Yulia Nefedova, Andrew Kossenkov, Filippo Veglia, Rahul Shinde, and Nan Zhang of The Wistar Institute; Taito Miyamoto and Kohei Hamada of the Kyoto University Graduate School of Medicine; Yanfang Peipei Zhu of The Medical College of Georgia at Augusta University; Lu Huang of the University of Arkansas for Medical Sciences; and Rugang Zhang of the MD Anderson Cancer Center.

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