Ovarian cancer stem cell study puts targeted therapies within reach

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Researchers at Yale School of Medicine have identified a key link between stem cell factors that fuel ovarian cancer's growth and patient prognosis. The study, which paves the way for developing novel targeted ovarian cancer therapies, is published online in the current issue of *Cell Cycle*.

Lead author Yingqun Huang, M.D., associate professor in the Department of Obstetrics, Gynecology & Reproductive Sciences, and her colleagues have demonstrated a connection between two concepts that are revolutionizing the way cancer is treated.

First, the "cancer stem cell" idea suggests that at the heart of every tumor there is a small subset of difficult-to-identify tumor cells that fuel the growth of the bulk of the tumor. This concept predicts that ordinary therapies typically kill the bulk of tumor cells while leaving a rich environment for continued growth of the stem cell tumor population.

The second concept, dubbed "seed and soil," defines a critical role for the tumor cells' "microenvironment," which is the special environment required for cancer cell growth and spread.

"Both concepts have particular relevance for the treatment of adult solid tumors such as ovarian cancer, which has been notoriously difficult to diagnose and treat," said co-author Nita J. Maihle, M.D., professor in the Department of Obstetrics, Gynecology & Reproductive Sciences and a member of Yale Cancer Center. "Ovarian cancer patients are plagued by

recurrences of tumor cells that are resistant to chemotherapy, ultimately leading to uncontrolled cancer growth and death."

In this study, Huang and her colleagues were able to define a molecular basis for the interplay between these two concepts in ovarian cancer. They did this by using sophisticated gene sequencing methods to demonstrate a regulatory link between the stem cell factor Lin28 and the signaling molecule bone morphogenic protein 4 (BMP4).

"These results are supported by the latest molecular ovarian cancer prognosis data, which also suggest an active role for the tumor microenvironment in ovarian carcinogenesis," said Huang and Maihle. "Together these studies reveal new targets for the development of cancer therapies."

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