

Study presents novel treatment strategy to tackle metastatic intra-abdominal cancer

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Researchers from the National Cancer Centre Singapore (NCCS) have found a potential new strategy to treat peritoneal carcinomatosis, a metastatic form of intra-abdominal cancer, where patients are presented with limited treatment options and poor overall survival. Published in *Cell Reports Medicine* on 15 February 2022, the findings provide a way to identify more effective treatments for patients with metastatic intra-

abdominal cancers by targeting what fuels cancer cells.

A widely accepted scientific hypothesis is that [cancer](#) ("seed") spreads onto the organ surfaces ("soil") through a series of complex interactions in the body. Most cancer treatments directly target the "seed" such as through the use of chemotherapy, which inhibits cancer cell division. In the last nine years, immunotherapy has become increasingly popular as a means of cancer treatment, altering the "soil" by enlisting the body's immune system to target [cancer cells](#). In this latest research from the Laboratory of Applied Human Genetics at NCCS, findings show it is possible to target "water" to create an arid environment thus making it inhospitable for tumor cell growth.

The team of researchers, led by NCCS clinician-scientist Assistant Professor Chin-Ann Johnny Ong, identified that ascites, excess fluid ("water") present in the abdomen of patients with metastatic intra-abdominal cancers, can be directly targeted to remove the fuel that drives cancer growth. By interrogating the proteins in ascites, the team found that PAI-1 (plasminogen activator inhibitor 1) is a good marker of response to direct inhibition and could potentially curb cancer cell proliferation. Prior to the team's discovery, PAI-1 was not known to be related to the growth of intra-abdominal cancers.

Using biological samples from 150 intra-abdominal cancer patients, Asst Prof Ong and team further identified a panel of three biomarkers that could predict patient outcomes as well as responsiveness to PAI-1 therapy. The findings were confirmed with models incorporating the tripartite combination of "seed," "soil" and "water."

"Our study not only highlights a novel treatment strategy for peritoneal carcinomatosis, it also provides the foundation for the development of a new translational research therapeutic program at NCCS. In addition, the concept of targeting water beyond the traditional view of seed and soil

potentially paves the way for a paradigm shift in how cancers can be treated." said Asst Prof Ong, a Consultant in the Department of Sarcoma, Peritoneal and Rare Tumours (SPRinT), Division of Surgery and Surgical Oncology at Singapore General Hospital and National Cancer Centre Singapore, who treats patients with peritoneal carcinomatosis and is the Principal Investigator of the study.

The research team is currently working with multiple [government agencies](#) and pharmaceutical partners to harness the research findings of this study to realize the potential of targeting "water" in cancer patients.

More information: Chin-Ann J. Ong, Ligand-Mediated PAI-1 Inhibition in a mouse model of peritoneal carcinomatosis, *Cell Reports Medicine* (2022). [DOI: 10.1016/j.xcrm.2022.100526](https://doi.org/10.1016/j.xcrm.2022.100526). [www.cell.com/cell-reports-medi ... 2666-3791\(22\)00026-X](https://www.cell.com/cell-reports-medicine/abstract/S2666-3791(22)00026-X)

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