

# Researchers reveal a chemo-resistant cancer stem cell as cancer's 'Achilles' heel'

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Scientists at Mount Sinai School of Medicine have discovered a subpopulation of cells that display cancer stem cell properties and resistance to chemotherapy, and participate in tumor progression. This breakthrough could lead to the development of new tests for early cancer diagnosis, prognostic tests, and innovative therapeutic strategies, as reported in *Cancer Cell*.

Resistance to chemotherapy is a frequent and devastating phenomenon that occurs in cancer patients during certain treatments. Unfortunately, tumors that initially respond to chemotherapy eventually become resistant to it, contributing to tumor progression and death. The study reveals that these new cancer "stem" cells, which have not been differentiated into more specific cell types, are capable of multiplying despite being exposed to chemotherapy, while differentiated cells die.

Led by Carlos Cordon-Cardo, MD, PhD, Chair of Pathology, and Josep Domingo-Domenech, MD, PhD, Assistant Professor of Pathology at Mount Sinai, the research team generated cellular models of drug resistance by treating prostate tumor cell lines with increasing doses of the common [chemotherapy drugs](#), including docetaxel. They identified a cell population expressing markers of embryonic development. In addition, these cells displayed cancer stem [cell functions](#), including the capacity to initiate tumor cell growth. Next, the team evaluated human tissue samples of prostate cancer and found that patients with more aggressive or [metastatic tumors](#) had more of these cancer "stem" cells.

"This is the first time these so-called cancer [stem cells](#) of prostate have been identified as the basis for [drug resistance](#) and tumor progression, indicating that they are cancer's 'Achilles Heel,'" said Dr. Cordon-Cardo. "These findings are the culmination of more than six years of innovative research, which has led to the successful unveiling of cancer characteristics that are critical to understanding how the disease works and progresses."

The study also defines a new therapeutic strategy for patients with prostate cancer, consisting of a combination of standard chemotherapy and two pharmacological agents that inhibit key signaling pathways associated with embryonic development and cell differentiation. Results showed that chemotherapy eliminated differentiated tumor cells, whereas the signaling pathway inhibitors selectively depleted the cancer stem cell population. Some of these inhibitors are already in clinical trials, and some are FDA-approved.

"By targeting these newly identified cancer 'stem' cells, we are attacking the foundation of tumor growth, rather than treating the symptoms of it," said Dr. Domingo-Domenech. "The novel discovery of this [cell population](#) could lead to the development of new tests for early [cancer diagnosis](#), prognostic tests, and innovative therapeutic strategies."

Ongoing studies suggest that this new cell type exist in other tumor types such as breast cancer, colon cancer, bladder cancer and lung cancer. Dr. Cordon-Cardo's team is studying these disease areas to determine the presence and impact of these [cancer cells](#).

Provided by The Mount Sinai Hospital

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