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ACHIEVEMENTS

Breaking the Code: Researchers Decipher How SCLC Powers Its Deadly Advance

Share:

Dr. Leanne Li and Prof. Jin-Shing Chen with their research team members.

Small cell lung cancer (SCLC) remains one of the most aggressive and treatment-resistant cancers. Patients are often diagnosed only after extensive metastasis has occurred, and current therapies provide limited long-term control, resulting in an average survival of less than a year.

Prof. Jin-Shing Chen of the Department of Surgery at National Taiwan University Hospital (NTUH) and his research team contributed to a major international study that disclosed key biological mechanisms driving SCLC's aggressive behavior. Their groundbreaking findings were published online in *Nature* on February 12, 2025. This study reveals, for the first time, that SCLC tumors generate their own electrical activity, which in turn directly induces metastasis and progression. The discovery opens potential new avenues for targeted therapies against this lethal cancer.

The study was spearheaded by Dr. Leanne Li's laboratory at the Francis Crick Institute in the UK. It brought together top-tier research teams from the University of Cambridge, MIT, Harvard Medical School, Dana-Farber Cancer Institute, and UT Southwestern Medical Center, together with NTUH—all globally recognized for excellence in both basic and clinical research.

Dr. Li, an NTU alumna who earned her MD at NTU and trained under Prof. Chen at NTUH, reflected on their collaboration: "Prof. Chen's transformative work in lung cancer research and patient care in Taiwan has been a constant source of inspiration to me. Collaborating with my mentor from my alma mater—also Taiwan's leading thoracic surgeon—is a true honor."

The New Discovery: Cancer Cells with an Internal Power Grid

SCLC tumors are composed of neuroendocrine (NE) cells and non-neuroendocrine (non-NE) cancer cells. The study found that NE cells are capable of generating intrinsic electrical signals, much like neurons communicating within the brain. More crucially, this self-generated electrical activity was found to directly drive tumor aggressiveness and metastatic potential. Meanwhile, non-NE cells support the tumor by supplying energy, creating a dynamic interplay between different cancer cell populations that fuels SCLC growth.

Prof. Chen likened the phenomenon to a new kind of self-sufficiency in cancer cells:

"Most cancer cells are like cars—they need external fuel or power to operate. If you cut off the supply, you slow them down. But SCLC is different. It's as if it has installed its own solar panels, creating an internal power grid. This ability to generate and sustain its own energy makes it uniquely aggressive and extraordinarily difficult to treat."

Targeting Electrical Activity to Halt Cancer Progression

To test whether inhibiting the tumor's electrical activity could slow its growth, researchers administered tetrodotoxin (TTX)—a neurotoxin that blocks electrical signaling—to SCLC cells. Although TTX did not immediately kill the NE cells, it significantly reduced their ability to form tumors over time. Furthermore, analysis of clinical SCLC patient samples revealed that higher levels of tumor electrical activity correlate with poorer patient prognosis, confirming the critical role of this mechanism in disease progression.

Dr. Li added: "While previous research hinted that some cancer cells express neuron-like genes, this is one of the first direct demonstrations that electrical signaling actively drives cancer aggressiveness. They believe the mechanisms disclosed here in SCLC may also apply to other highly metastatic cancers."

Looking ahead, Dr. Li's and Prof. Chen's teams plan to explore how cancer cells harness electrical and metabolic systems for growth and survival—and whether targeting these systems can yield new therapeutic strategies.

The NTU research team is committed to building on these findings by investigating similar electrophysiological mechanisms in other cancer types and assessing whether disrupting these self-sustaining neural networks could lead to revolutionary treatments against some of the most difficult-to-treat malignancies.

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