PRESS RELEASE

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Wistar Scientists Identify Connection Between Nervous System and Aggressive Prostate Cancer

PHILADELPHIA — (THURSDAY, SEPT. 24, 2026) — A new study from The Wistar Institute has found a link between the nervous system and the rapid development of neuroendocrine prostate cancer (NEPC), an aggressive form of the disease. Published in *Oncogene*, the study found high levels of neuromedin U (NMU), a kind of neurotransmitter, present in prostate cells at the very early phase of NEPC formation, which support tumor progression by blocking the immune response. These findings could present a target for therapy for what is now a virtually untreatable disease.

"We already know that the immune system and cancers communicate with each other, which has led to transformative therapies for cancers that had once been thought of as untreatable," said **Dario C. Altieri, M.D.,** president & CEO, director of the Ellen and Ronald Caplan Cancer Center and Robert and Penny Fox Distinguished Professor at The Wistar Institute, and senior author on the study. "This study reveals that cancer is also communicating with the nervous system, potentially opening the door to new therapies for cancers that currently lack effective therapeutic options."

Prostate cancer is typically survivable, with a 98 percent survival rate five years after diagnosis according to the American Cancer Society. But NEPC is a specific type of prostate cancer that is considered immunologically "cold," meaning it does not respond to currently available treatments, including newer classes of immunotherapy drugs.

NEPC is different because it doesn't have any T cells, which is one way that our immune system responds to cancer. T cells can also be trained by immunotherapy to more aggressively attack tumor cells. "But immunotherapy only works if you have immune cells within the tumor," said **Michela Perego, Ph.D.**, research assistant professor in the Altieri lab and first author of the study. "With NEPC, you can't target T cells because there are no T cells. We wanted to understand why."

In a murine model, researchers looked at activity in tissue cells before cancer developed and found an excessive amount of NMU. This neurotransmitter usually does not play a pathological role in the

human body, and is a key part of critical functions like regulating blood pressure, stress response and keeping hormones in check. But in NEPC, an overabundance of NMUs effectively block T cell migration to the prostate by activating neutrophils that suppress T cells: NMU-activated neutrophils work for the cancer before the cancer really forms by suppressing T cells that would normally lead the charge to mount an immune response.

Researchers were able to change NPEC in a simulated microenvironment to target NMU for destruction. “By blocking the communication between the destructive NMUs working for NPEC, we were able to disarm them, and allow the T cells back in,” said Perego. “It reinforced anti-tumor immune response and restored sensitivity to immunotherapy.”

Disrupting this pathway to stop the overproduction of NMU in NEPC could open new avenues for treatment, she added. “They could turn cold tumors hot, and when used together, make these tumors new targets for immunotherapy and present a new way to approach cancer that has proven nearly impossible to stop or slow down.”

“Neuromedin U turned out to be a lynchpin,” said Altieri. “The tumor uses it to build a shield of protective immune cells around it, and when the signal is removed, the shield comes down. For a cancer with limited options, identifying a target that reopens the door to immunotherapy is something we want to better understand.”

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