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Research team identifies a new way to treat prostate cancer

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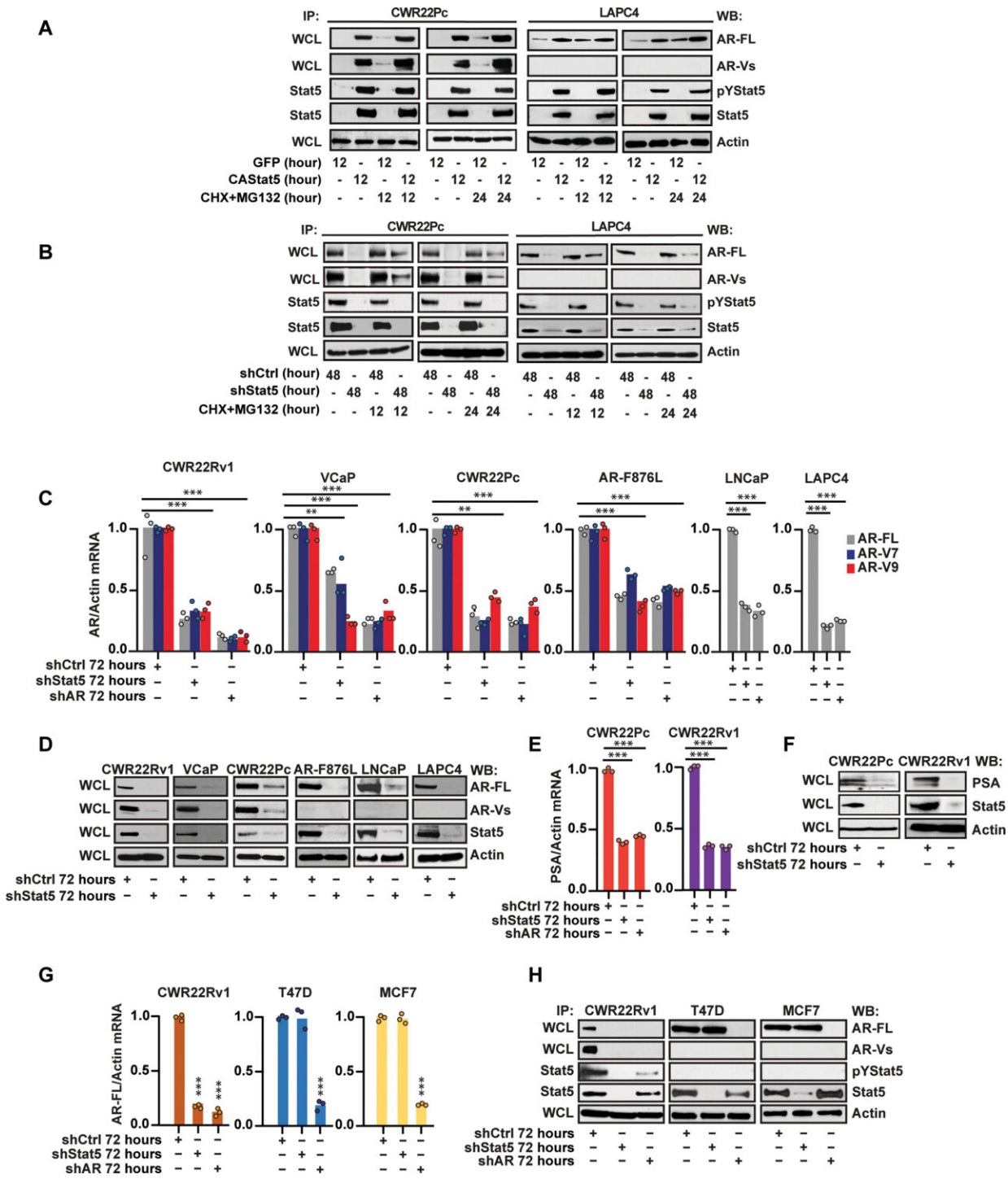

Active Stat5 increases protein levels of full-length androgen receptor (AR-FL) and AR variants (AR-Vs) through the induction of AR mRNA levels in PC. Credit: *Science Advances* (2024). DOI: 10.1126/sciadv.adi2742

The American Cancer Society estimates there are nearly 300,000 new cases of prostate cancer every year in the U.S., and approximately one in eight men will be diagnosed with prostate cancer in their lifetime. Prostate cancer is often treated with androgen deprivation therapy, which lowers testosterone levels to shrink tumors. However, this treatment has side effects including sexual dysfunction and weight gain, and it eventually results in castrate-resistant prostate cancer, a deadlier form that grows even when testosterone levels are low.

Now, new research published in *Science Advances* suggests there may be a workaround to improve prostate cancer therapy.

"We want to develop a new therapeutic approach for androgen deprivation in a way that is more patient-friendly," says Marja Nevalainen, MD, Ph.D., a translational medicine physician-scientist and senior author on the study. Using a clever trick of cell signaling, her research curbs tumor growth through a different route.

Androgen deprivation therapy works by decreasing activity of the androgen receptor, a key protein involved in both testosterone signaling and prostate tumor growth. However, the androgen receptor eventually develops mutations that stop androgen deprivation therapy from working. Dr. Nevalainen wondered if she could avoid mutations and target the androgen receptor and associated tumor more directly by blocking activity at Stat5, a protein involved in boosting androgen receptor levels and promoting prostate cancer growth.

Using a drug that inhibits Stat5, Dr. Nevalainen measured androgen receptor levels and prostate cancer growth in cell cultures and human tumors in vitro and grafted into mice. She found that inhibiting Stat5 significantly slowed tumor growth and decreased androgen receptor levels. Because Stat5 inhibition suppresses the androgen receptor, Dr. Nevalainen believes that this approach may carry a lower risk of

inducing castrate-resistant prostate cancer because the androgen receptor is less likely to mutate or develop other genetic adaptations.

The next steps will involve translating this research into humans. Nevalainen says a new drug influencing Stat5 activity is beginning to be tested in Phase II clinical trials.

More information: Cristina Maranto et al, Stat5 induces androgen receptor (AR) gene transcription in prostate cancer and offers a druggable pathway to target AR signaling, *Science Advances* (2024). DOI: 10.1126/sciadv.adi2742

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