More research supports androgen treatment for breast cancer

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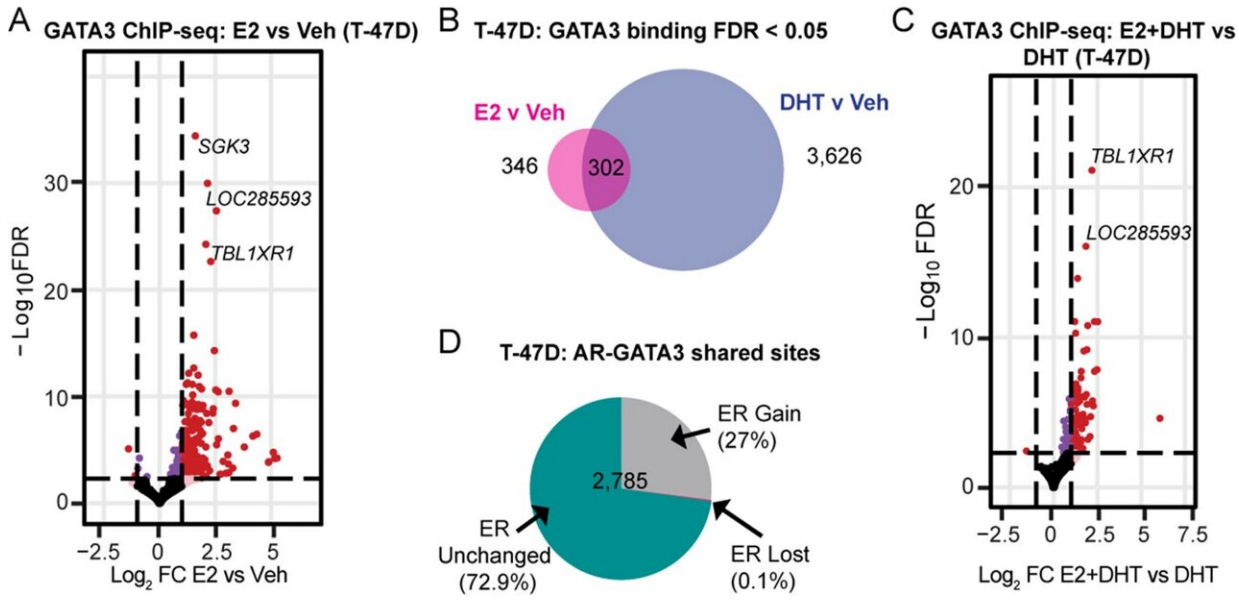

Hormone mediated changes in GATA3 chromatin binding in ER-positive breast cancer cells. A) FDR adjusted p-value and the log2FC of GATA3 chromatin binding events in T-47D breast cancer cells treated with E2 vs. Veh. B) Venn diagram showing the overlap of significantly enriched GATA3 binding sites with E2 or DHT. C) FDR adjusted *p*-value and the log_2FC of GATA3 chromatin binding events with simultaneous hormone treatment vs. DHT alone. D) Differential ER binding at AR and GATA3 shared sites. Credit: *Genome Biology* (2024). DOI: 10.1186/s13059-023-03161-y

A study by researchers from the University of Adelaide has provided

new insight into the fight against breast cancer.

The laboratory-based study was the work of co-senior authors Associate Professor Theresa Hickey and Dr. Amy Dwyer together with Professor Wayne Tilley of the Dame Roma Mitchell Cancer Research Laboratories, in collaboration with researchers at Cancer Research UK (CRUK), Cambridge Institute, University of Cambridge (U.K.) and the Imperial College of London.

"Our study employed a relatively new technology developed by the CRUK team, which was used to identify GATA3 (a transcription factor critical for the embryonic development of various tissues) as an important interacting partner of the androgen receptor in breast cancer," said Associate Professor Hickey.

The research, published in the journal *Genome Biology* , found that when the androgen receptor interacted with GATA3, it stimulated breast cancer cells to become more functionally mature.

"This study revealed an important means by which androgen receptor activity exerts anti-cancer activity in breast cancer," said Associate Professor Hickey.

"Discovering how the androgen receptor exerts anti-cancer activity in the breast is important because the opposite happens in the prostate where androgen receptor activity promotes cancer."

The finding supports work by the Dame Roma Mitchell Cancer Research Laboratory threesome, with Professor Tilley as senior author, published in *The Lancet Oncology* in February. That clinical study found that the androgen receptor stimulating drug enobosarm was effective against estrogen receptor-positive breast cancer, which constitutes up to 80% of all cases of this disease.

"Information from the GATA3 study supports the use of androgen receptor stimulating drugs for treatment of estrogen receptor positive breast cancer (as reported in the recent *Lancet Oncology* paper) and provides laboratory evidence to support this therapeutic strategy for other subtypes of disease that are not driven by the estrogen receptor. This includes the triple negative subtype of breast cancer," Associate Professor Hickey said.

"Drugs that stimulate the androgen receptor are not yet part of mainstream treatment for any type of breast cancer but is gaining momentum for the treatment of estrogen receptor positive disease.

"The GATA3 study provides evidence that this new therapeutic strategy will work by providing an explanation for how it works."

Associate Professor Hickey said she expected more developments to come from the study. "While the current study focused on interaction between the androgen receptor and GATA3, the new technology we used to identify this interaction revealed many other factors that interact with the androgen receptor in breast cancer cells," she said.

"We are currently investigating the importance of those other factors in mediating androgen receptor activity in breast cancer."

More information: Leila Hosseinzadeh et al, The androgen receptor interacts with GATA3 to transcriptionally regulate a luminal epithelial cell phenotype in breast cancer, *Genome Biology* (2024). DOI: 10.1186/s13059-023-03161-y

Provided by University of Adelaide