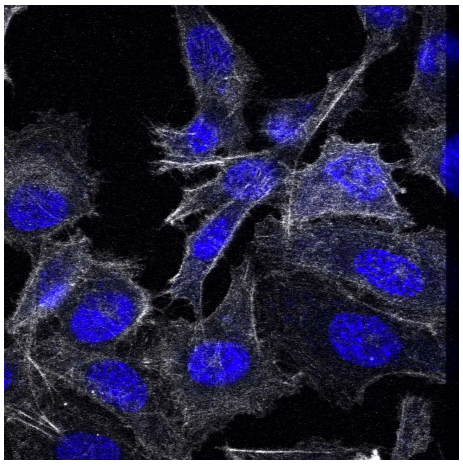
# A therapeutic target to prevent or treat castration-resistant prostate cancer

## Unmet Need

Prostate cancer is the second leading cause of cancer death in American men. Androgen deprivation therapy has been the standard of care for initial management of advanced prostate cancer, but resistance to therapy often develops, leading to an advanced, castration-resistant prostate cancer. The incidence of prostate cancer is increasing worldwide and there is an urgent need for better diagnostic strategies to distinguish between indolent and aggressive tumors, and to develop more efficacious treatment options for highly aggressive tumors.

## Technology

Researchers at Duke have reported a new therapeutic target for prostate cancer intended to prevent or treat the development of castration-resistant prostate cancer. They have uncovered how activation of olfactory receptor OR51E2, also known as Prostate Specific G-protein Receptor (PSGR) drives the progression of treatment-resistant prostate cancer. Using *in silico* and *in vitro* approaches, they were able to identify and validate biologically relevant modulators of the human OR51E2 receptor that are likely involved in prostate carcinogenesis. Activation of the OR51E2/PSGR receptor by a group of endogenous metabolite-ligands induced trans-differentiation of cancer prostate cells into neuroendocrine phenotype (NEtD), a characteristic of castration-resistant prostate cancer. Selected ligand 19-hydroxyandrostenedione (19-OH AD) acted as a highly potent agonist, which we believe drives and contributes to cancer resistance seen in the treatment induced castration-resistant prostate cancer. Furthermore, 9- and 13-cis retinoic acid were identified as an effective antagonist and



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**Publication(s)**

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**External Link(s)**

• From the lab of Dr. Tatjana Abaffy
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tested in heterologous cell expression system and also in the prostate cancer cell line. Both agents were able to suppress OR51E2 expression and activation, decrease several NE-markers and significantly inhibit cellular proliferation. These antagonists and inverse agonists may be used as therapeutic agents either alone, or in combination therapy, and may also serve as potential pharmacophores for a novel drug design.

## Additional Applications

This receptor OR51E2 and its agonist 19-OH AD together with other newly identified endogenous ligands/agonists can also be used as biomarkers to stratify prostate tumors.

## Advantages

- Provides a novel therapeutic strategy for treating castration-resistant prostate cancer
- Inventors have identified effective compounds that target OR51E2
- This technology also offers a method of diagnosing prostate cancer