

Researchers identify protein that contributes to racial disparities in prostate cancer

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Drs. Dhyan Chandra, left, and Rahul Kumar led the Roswell Park research team that has proposed a new strategy for treating prostate cancer in some men.
Credit: Roswell Park Cancer Institute

Cancer researchers have long known that prostate cancer tends to be more common, more aggressive and more resistant to existing treatments

in African-Americans than in Caucasian-Americans, but they're only beginning to understand why. A Roswell Park Comprehensive Cancer Center study published today points to cellular factors that appear to be driving these disparities—mitochondrial differences that prevent formation of the cancer-killing "death wheel" apoptosome protein complex—and proposes a strategy for overcoming these factors with new therapeutic targets.

The new work, led by Dhyana Chandra, Ph.D., and published in *Cancer Research*, a journal of the American Association for Cancer Research (AACR), provides the first concrete evidence that [mitochondrial dysfunction](#) and an inability to generate apoptosome formation are key factors behind higher [prostate cancer](#) incidence and poorer outcomes in African-Americans.

Many African-American men lack a key mitochondrial protein known as cytochrome c—the main protein that facilitates the formation of the desirable "death wheel" effect against cancer cells. Cytochrome c deficiency can occur in people of any race or background, but is common among people of African ancestry. Dr. Chandra and his team report in their new study that African-American males tend to have high expression of the cancer promoters c-Myc and NF-κB, leading to the inhibition of cytochrome c.

"Our findings shed light on why our current therapeutic agents for firstline prostate cancer treatment, chiefly docetaxel, do not provide much benefit for many African-American men," says Dr. Chandra, Professor of Oncology in the Department of Pharmacology and Therapeutics at the Buffalo-based cancer center. "But importantly, they also provide strong evidence that new therapeutic strategies can be developed to address and exploit these mechanisms."

The team, which included Rahul Kumar, Ph.D., a postdoctoral

researcher with Dr. Chandra's lab and first author on the new publication, determined that inhibiting the cancer-promoting proteins c-Myc and NF- κ B can restore cytochrome c in the prostate cancer cells of those with [cytochrome c](#) deficiency, thereby enhancing apoptosome production to kill prostate cancer cells.

Existing drugs approved for other applications can be used to inhibit c-Myc and NF- κ B. The team plans to pursue clinical trials to assess the effectiveness of this approach as treatment for prostate [cancer](#).

The study, "Cytochrome c-deficiency Confers Apoptosome and Mitochondrial Dysfunction in African-American Men with Prostate Cancer," is published in *Cancer Research*.

More information: Rahul Kumar et al. Cytochrome c-deficiency Confers Apoptosome and Mitochondrial Dysfunction in African-American Men with Prostate Cancer, *Cancer Research* (2019). [DOI: 10.1158/0008-5472.CAN-18-2383](https://doi.org/10.1158/0008-5472.CAN-18-2383)

Provided by Roswell Park Cancer Institute

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