Therapeutic potential of nitric oxide signaling pathway agonists against castration resistant prostate cancer

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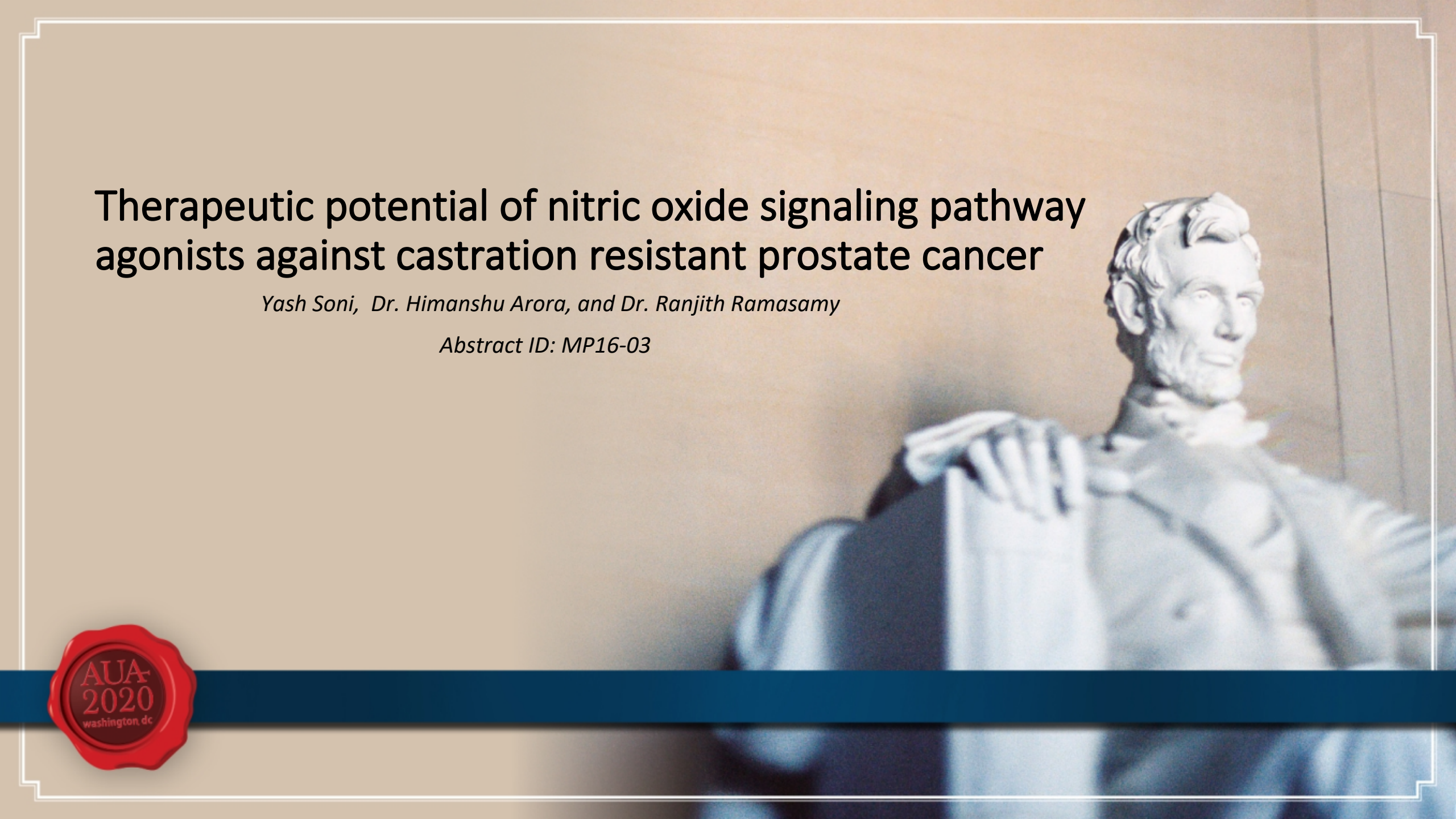

Hypothesis, Objective, and Methods

- **Hypothesis**: Although GSNO and Tadalafil both act via the nitric oxide pathway, GSNO can decrease CRPC tumor burden via tumor microenvironment.
- **Objective:** To evaluate if exogenous Tadalafil (PDE5 inhibitor), a known inducer of cGMP, could affect the tumor microenvironment and suppress Prostate Cancer growth in a similar way that GSNO does.
- **Methods:** CRPC murine models were divided into 3 groups (Control, GSNO, Tadalafil). Tumor weights and sizes were collected and protein analysis was done via western blot.

Results and Conclusion

- **Results**
  - No significant difference in tumor volumes was seen between controls and PDE5i treated mice.
  - GSNO treated mice showed a decrease in AR in 3/5 mice while having a generally increased GAPDH. PDE5i showed a decrease in AR in only 2/5 mice
- **Conclusions**
  - Although both GSNO and Tadalafil are acting through the nitric oxide signaling pathway, their effects on reducing castration resistant prostate cancer are independent.
  - inhibition of PDE-5 leading to a build-up of cyclic GMP does not regulate CRPC and therefore confirming the mechanism of NO donor action (GSNO) on the tumor microenvironment.