1. No.
   2022G003

2. Title
   Elucidation of Mechanism on Hormone Therapy-Induced Oxidative Stress in Prostate Cancer and Application

3. Period
   2022-2024

4. Summary

   Aberrant activation of androgen receptor signaling plays an important role in resistance to hormone therapy in prostate cancer. We found that intracellular oxidative stress levels are increased by hormone therapy in prostate cancer. Therefore, we aimed to elucidate the mechanism and role of oxidative stress in the development of resistance to hormone therapy in prostate cancer.

   In prostate cancer LNCaP cells, we found increased oxidative stress in peroxisomes in a hypoandrogenic environment, and intracellular oxidative stress was decreased by suppression of PPARA expression induced by androgen signaling inhibition. Therefore, we investigated the usefulness of novel therapies targeting PPARα and its signaling and found that inhibition of PPARα signaling by knockdown of PPARA and PPARα inhibitor suppressed cell proliferation and enhanced cellular sensitivity to enzalutamide.

   Intracellular oxidative stress induced by hormone therapy is mainly generated in peroxisomes via an induction of PPARA expression, indicating that inhibition of the PPARα pathway may enhance the therapeutic effect of hormone therapy. In the future, we would like to pursue novel therapies targeting PPARα and its signaling for clinical application.