1. **No.**

   FP01801019

2. **Title**

   Smoking and oxidative stress in castration resistance of prostate cancer

3. **Period**

   2016-2018

4. **Summary**

   We investigated the relationships and roles between cigarette smoking and oxidative stress in castration resistance of prostate cancer. As a result, basic research using prostate cancer cells revealed that tabacco smoke condensate induced AR variants expression, resulting in activated AR signaling through oxidative stress and phosphorylation of Akt in prostate cancer 22Rv1 cells. Cellular resistance to enzalutamide was augmented by tabacco smoke condensate. In clinical studies, smoking was a risk factor of biochemical recurrence after radical prostatectomy. Meanwhile, serum testosterone and the prognosis in primary ADT was comparable between current smokers and non-smokers while serum testosterone before ADT was higher in current smokers. Genetic polymorphism in GSTM3 encoding antioxidant enzyme was associated with the prognosis in primary ADT. On the other hand, the prognosis when treated with novel AR axis-targeting agents including enzalutamide and abiraterone for castration-resistant prostate cancer in current smokers was worse than that in non-smokers, which may be explained by higher expression rate of AR variants in castration-resistant prostate cancer. According to the findings obtained in this research, cessation of smoking would be recommended for prostate cancer patients.