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## "EpiProState": Prostate cancer detection by DNA methylation assessment in liquid biopsies

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**Introduction & Objectives:** Prostate Cancer (PCa) is the most incident cancer in males, in Europe and USA. Despite the high sensitivity of serum prostate-specific antigen (PSA), the gold standard PCa screening tool, the lack of cancer specificity of this approach is a limitation causing overdiagnosis of non-life-threatening PCa. Thus, there is an urgent need for development and implementation of more trustworthy screening biomarkers. Due to its early onset, cancer specificity and biological stability, DNA methylation have called attention as epigenetic-based biomarkers. Additionally, their accessibility in body fluids makes them an attractive target to be studied in liquid biopsies.

We aimed to explore the detection value of eight methylated gene promoters ($APC_{me}$, $FOXA1_{me}$, $GSTP1_{me}$, $HOXD3_{me}$, $RAR\beta2_{me}$, $RASSF1A_{me}$, $SEPT9_{me}$ and $SOX17_{me}$) in liquid biopsies of PCa patients.

**Materials & Methods:** Plasma samples from 121 PCa patients diagnosed at IPO-Porto and 135 asymptomatic blood donors, for control purposes, were collected once written informed consents were provided. After circulating cell-free DNA (ccfDNA) extraction from plasma samples, sodium-bisulfite modification and whole-genome amplification was performed followed by measurement of promoter methylation levels of the selected genes by multiplex qMSP. Biomarker's detection performance was evaluated (Ethics approval IPOPFG-CES 120/2015).

**Results:** Except for $APC_{me}$, all tested genes were significantly hypermethylated in ccfDNA of PCa patients. Promoter methylation levels of these genes, individually, were able to depict PCa with sensitivities between 12%-80% and specificities between 43%-99%. Remarkably, the best gene-panel ("EpiProState"), constituted by $FOXA1_{me}$, $RAR\beta2_{me}$, $RASSF1A_{me}$ and $GSTP1_{me}$, detected PCa with 72% sensitivity, specificity and accuracy.

**Conclusions:** We conclude that "EpiProState" panel assessed in liquid biopsies might be a promising tool for PCa screening.