Prostate cancer
Reflex testing with serum, urine and tissue biomarkers: Which, when and how viable?

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Biochemical and genomic markers in prostate cancer
Prostate cancer is the most common non cutaneous cancer diagnosed and the second top cause of cancer deaths in men worldwide, with current over diagnosis, biopsies with negative or indolent cancers cause complications and may have a minimal effect on patient survival, so finding suitable genomic and biochemical markers to detect men at high risk of Prostate adenocarcinoma and differentiate clinically insignificant and aggressive tumors to enable us for the better therapeutic plans is critical.

DNA markers
Several genes have been identified as mutated in a prostate cancer and seems to be frequently in charge of hereditary type of that disease, Genes like BRCA1, BRCA2, HOXB13, and the mismatch repair genes (e.g., MSH2).Specific region of the androgen-regulated gene transmembrane protease, serine 2 (TMPRSS2) with v-ets erythroblastosis virus E26 oncogene homolog (ERG) or ets variant 1 (ETV1) were found to be nearly 100% specific. In prostate tissue sample, α-Methylacyl coenzyme A racemase (AMACR) gene, is upregulated in malignant ones. AMACR immunostaining is frequently done on prostate needle biopsy specimens to confirm the malignancy. Single nucleotide polymorphisms (SNPs) of various genes or loci related to prostate cancer. Although these relation shows week increases in risk of malignancy but in multiplicatively it can be valuable. In current practice genetic testing alone can only is useful for screening or risk assessment of PSA. NADiA is an immunoassay developed for detection of nucleic acid in serum. It assays by means of immuno-polymerase chain reaction with 2 monoclonal antibodies employed.

RNAmarkers
miRNAs are small non-coding RNAs, which negatively regulate the gene expression. Urine miR-187 is an independent predictor of prostate cancer at prostate sample. Clinical usefulness of miRNAs in urine is under investigation, and unfortunately series of small studies considered different sampling methods like whole urine, urinary pellet and the cell-free urinary or after a prostate massage. But these data show that measurement of urinary miRNAs may be valuable as biomarkers especially in subset of early Prostate cancer. Prostate cancer antigen 3 (PCA3) is non-coding RNA that can be measured by quantitative amplification (reverse transcription polymerase chaining reaction [RT-PCR], specimens must be got next to prostate massage; but, lately suggested novel molecular PCA3 combined to ERG can also be got without prostate massage (EXO106 score)

Epigenetic alteration
Epigenetic Alteration define as changes in gene function that do not involve changes in the DNA sequence, it refer to refers to changes in a chromosome that affect gene activity and expression. many hypermethylated genes have been showed in prostate cancer, including Glutathione-S-transferase π, etinoic acid receptors beta 2, adenomatous polyposis coli and RAS association domain family protein isoform A.

Biochemical marker in blood

At first, Prostate-Specific Antigen was used for monitoring patients after treatment of prostate cancer. PSA is a member of the kallikrein gene family. Some important genes of this family of family are as fellow: the pancreatic/renal kallikrein (hKLK1), human kallikrein 2 (hKLK2), and PSA (hKLK3) genes. PSA starts as a zymogen, termed preproPSA. Cleavage of prepro PSA make a proPSA. Lastly, cleavage of proPSA result in active form of PSA. In prostate cancer we have additional tissuehK2 that have a great role in 4Kscore test (Opko Health Inc.), four kallikrein forms (tPSA, fPSA, intact PSA, and hK2) to calculate risk of prostate cancer. other kallikrein genes like KLK4, KLK14, and KLK15 have likely prostate cancer predictability. encouraging novel test based on prostate-specific antigen (PSA) named the Prostate Health Index (PHI), PHI mathematically calculate the risk of prostate cancer by means of total PSA, free PSA and [-2] proPSA.

PSA begins as a zymogen, termed preproPSA, Cleavage of preproPSA results in an inactive proenzyme called proPSA. Cleavage of proPSA by hK2 result in the active form of PSA. PSA has a two form in blood complexed PSA and free PSA, three proteins that are recognized to bind to PSA are ACT, A2M, and α1-protease inhibitor (API). Free PSA in blood includes three isoforms: proPSA, BPH-associated PSA (BPSA), and intact fPSA. The leader of PSA and named proPSA or [-7]proPSA. This precursor amino acid chain is cleaved by hK2, and produce active PSA. Partial subtraction of the 7–amino acid precursor made different formulas of proPSA, contain proPSAs with [-2]proPSA, [-4]proPSA, and [-5]proPSA. These enzymes include most of the circulating fPSA in patients with prostate cancer. Although Several PSA isoforms have been recognized with greater risk of prostate cancer but [-2] form of proPSA (p2PSA) demonstrate better accuracy rather than total PSA. The prostate health index (phi) is a formula includes all 3 PSA forms (total PSA, free PSA, and p2PSA) with following formula: (p2PSA/free PSA) x square root (PSA).

The glycoprotein prostate-specific membrane antigen (PSMA) in serum, urine, or tissue is an old biomarker of prostate cancer. While PSMA is secreted by epithelium of the prostate tissue but it secretes central nervous system and intestine. Recently of three alternatively spliced variants of PSMA, PSM′, defined as a probable new biomarker in prostate cancer but data in this field up to now is rare.

Tumor circulating cell

During last decades, circulating tumor cells have long been hyped as promising biomarkers especially by detection of PSA mRNA in prostate cancer. At the present time, there is only one FDA-approved methodology for identifying circulating tumor cells: CellSearch .it measures antibodies against EpCAM for circulating tumor with antibodies against CD45 (negative) and cytokeratins 8, 18, and 19 (positive). circulating tumor amount of 5 or additional cells per 7.5 mL of blood predict poor prognosis in prostate cancers. In recent studies it showed that possibility that immune system markers may aid to reproduce the presence of prostate cancer and its probable metastatic ones. Endoglin is another immune system marker, a transmembrane glycoprotein also known as CD105. It proposed to have a role in angiogenesis and lean towards to be in vascular endothelial cancerous cells. Active androgen receptor alternatives, consequential of different splicing of the human androgen receptor gene, is a promising biomarker, for example AR-V7 mRNA status in circulating tumor cells. It can predict drug