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Cancer Genome Scanning in Plasma: Detection of Tumor-Associated Copy Number Aberrations, Single Nucleotide Variants and Tumoral Heterogeneity by Massively Parallel Sequencing
By K.C. Allen Chan, et al.

This paper explores the use of massively parallel sequencing of plasma DNA in cancer patients for the scanning of genomewide genetic changes of cancers. The authors report successful genomewide profiling of copy number aberrations and point mutations in the plasma of the cancer patients. By detecting and quantifying the genomewide aggregated allelic loss and point mutations, they were able to determine the fractional tumor-derived DNA concentrations in plasma and correlate these values with tumor size and surgical treatment. The noninvasive profiling of the genomewide cancer-associated changes in plasma is a potentially powerful tool for cancer detection, monitoring and research.

***GALNT9* Gene Expression Is a Prognostic Marker in Neuroblastoma Patients**
By Nora Berois, et al.

Neuroblastoma shows extreme clinical, histologic, and genetic heterogeneity. Alterations in O-glycan profiles are a hallmark of cancer development; however, little is known in neuroblastoma. Increasing evidence suggests that some isoenzymes of the UDP-N-acetyl-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase family (which starts O-glycosylation) might be useful in correlating tumor markers with prognosis. In this article the authors assessed the brain-specific isoform *GALNT9* expression in a large cohort of primary neuroblastoma tumors and found *GALNT9* expression to be associated with higher overall survival, independent of the standard risk-stratification covariates. The results highlight that *GALNT9* expression could impact patient management as a prognostic factor or future molecular target for therapy.

Very Low PSA Concentrations and Deletions of the *KLK3* gene
By Santiago Rodriguez, et al.

PSA is a widely used biomarker for prostate cancer and is encoded by the *KLK3* gene. The authors of this study hypothesized that very low PSA levels might reflect gene inactivating mutations in *KLK3*. They sequenced all *KLK3*, and searched for gross inactivations in *KLK3* in the 30 individuals with the lowest PSA levels from a sample of 85,000 men from the prostate testing for cancer and treatment study. Three individuals were identified who displayed different large heterozygous deletions encompassing all *KLK3*. The clinical interpretation of the PSA test in individuals with a *KLK3* gene inactivation could lead to false negative findings for PSA used for screening, diagnosis or monitoring of prostate cancer.

TMPRSS2-ERG Fusion Transcripts in Matched Urine and Needle Rinse Material after Biopsy for the Detection of Prostate Cancer

By Phuong-Nhi Bories, et al.

The *TMPRSS2-ERG* fusion transcript is a highly specific marker of prostate cancer. However, the methods developed to detect the fusion transcripts in the urine lack analytical sensitivity. In this study the authors evaluated whether a double assay combining detection in both urine and prostate biopsy needle rinse material could improve the overall sensitivity. The sensitivity for fusion gene detection in paired samples was 89%. The low sensitivity in urine assay might be related to preanalytical issues such as a low number of tumor cells and their lysis during centrifugation. These results, if confirmed in additional studies, would support use of this new tumor marker as a detection tool.

Heterogeneity of Epidermal Growth Factor Receptor Status and Mutations of *KRAS*/*PIK3CA* in Circulating Tumor Cells of Patients with Colorectal Cancer

By Christin Gasch, et al.

In this study, circulating tumor cells from patients with colorectal cancer were analyzed for epidermal growth factor receptor expression and the presence of mutations in genes relevant for epidermal growth factor receptor inhibition. With the CellSearch system, at least 2 circulating tumor cells were detected in 24 of 49 patients with metastatic colon cancer and 7 of 32 patients with non-metastatic colon cancer. In 7 of 33 patients, circulating tumor cells with epidermal growth factor receptor overexpression were identified. Epidermal growth factor receptor gene amplification was found in 7 of 26 circulating tumor cells from 3 patients. *KRAS* and *PIK3CA* gene mutations were detected in 5 of 15 circulating tumor cells from one patient and 14 of 36 circulating tumor cells from 4 patients, respectively. The authors concluded that molecular characterization of circulating tumor cells demonstrates heterogeneity, probably explaining the variable response rates to epidermal growth factor receptor inhibition observed in patients with colorectal cancer.

Downregulation and Prognostic Performance of MicroRNA 224 Expression in Prostate Cancer

By Konstantinos Mavridis, et al.

The aim of this study was to profile the expression of microRNA-224 in benign and malignant prostate tumors to evaluate its potential as a biomarker, when measured using a reliable and cost-efficient quantification method. microRNA-224 was selected because of its reported aberrant expression in a broad spectrum of malignancies. The authors provide evidence that microRNA-224 is downregulated in prostate cancer and that its expression is gradually decreased as the malignancy progresses. In addition, the authors show that microRNA-224 expression is associated with a favorable prognosis and could prove to be a useful biomarker for prostate cancer.

SOX17 Promoter Methylation in Circulating Tumor Cells and Matched Cell-Free DNA Isolated from Plasma of Patients with Breast Cancer
By Maria Chimonidou, et al.

The detection of circulating tumor cells and cell-free DNA in peripheral blood of patients with cancer has been widely evaluated for the early detection of metastasis. In this study the authors addressed the question of whether a direct connection between the presence of circulating tumor cells and cell-free DNA occurs in breast cancer. They studied *SOX17* promoter methylation in circulating tumor cells and matched cell-free DNA isolated from plasma of 114 patients with breast cancer. The findings indicate a direct connection between the presence of circulating tumor cells and cell-free DNA in patients with operable breast cancer, after surgical removal of the primary tumor.

Comparative Assessment of Urinary Prostate Cancer Antigen 3 and _TMPRSS2:ERG_ Gene Fusion with the Serum [-2]Proprostate-Specific Antigen-Based Prostate Health Index for Detection of Prostate Cancer
By Carsten Stephan, et al.

This study compared urinary prostate cancer antigen 3, *TMPRSS2:ERG* gene fusion and the serum [-2]pro-prostate-specific antigen-based prostate health index for predicting prostate biopsy outcome in one cohort.
Serum samples and first-catch urine samples after digital rectal examination were collected from outpatients scheduled for prostate biopsy and who had prostate specific antigen concentrations between 0.5–20 micrograms per liter.
Both prostate cancer antigen 3 and the prostate health index performed significantly better than all other parameters. While prostate cancer antigen 3 showed the largest advantage in the repeat biopsy cohort, both measures performed comparably in the initial biopsy cohort and in the 2-10 microgram per liter prostate specific antigen range with negative digital rectal examination. The combination of both markers further enhanced the diagnostic power and the clinical utility.

Oral Cancer Diagnosis via a Ferrocenylnaphthalene Diimide-Based Electrochemical Telomerase Assay
By Kumiko Mori, et al.

In this article the authors describe an electrochemical telomerase assay with the aim of providing simple and rapid oral cancer diagnosis at an early stage. The assay is based on the electrochemical monitoring of the extended telomere DNA from the TS-primer on the electrode depending on the telomerase activity of the sample. The performance of the electrochemical telomerase assay was compared with that of conventional telomerase repeat amplification protocol. The electrochemical telomerase assay gave high hit rates for cancerous and normal cells, especially in exfoliated cells, supporting the suitability of this low invasive test for group examination for oral cancer.

Copy-Number and Expression Alterations of miRNAs in the Ovarian Cancer Cell Line OVCAR-3: Impact on Kallikrein 6 Protein Expression
By Jane Bayani, et al.
Kallikrein 6 has potential as an ovarian cancer biomarker due to its frequent overexpression in these cancers. However, the mechanisms that underlie its overexpression are unclear. Therefore the authors examined the copy-number status of microRNAs predicted to target Kallikrein 6, and their expression in a representative ovarian cancer cell line, using molecular cytogenetic analyses and microRNA profiling. Members of the hsa-let-7 family of microRNAs, predicted to target Kallikrein 6 were subject to copy-number loss and decreased expression. Transient transfection of hsa-let-7a into the ovarian cancer cell line resulted in the decreased protein expression of Kallikrein 6, demonstrating the ability of microRNAs to influence expression post-transcriptionally.

Multicenter Evaluation of [-2]Proprostate-Specific Antigen and the Prostate Health Index for Detecting Prostate Cancer
By Carsten Stephan, et al.

The prostate health index, calculated as [-2]proprostate-specific antigen divided by free PSA times the square root of total PSA was evaluated in the largest reported cohort so far using the World Health Organization calibration for free PSA and total PSA within the total PSA range of 1.6–8.0 micrograms per liter. In a total of 1362 men, 49% of whom had prostate cancer, the prostate health index had an area under the ROC curve for diagnosis of prostate cancer of 0.74, the largest of all parameters. The prostate health index was significantly higher in patients who had Gleason scores ≥7 as compared with Gleason scores <7. The prostate health index preferentially detected aggressive prostate cancer, implicating a future role for this biomarker in diagnosing clinically relevant prostate cancers.

Integrated Analyses of Proteins and Their Glycans in a Magnetic Beads-Based Multiplex Assay Format
By Danni Li, et al.

The authors of this paper developed a magnetic bead-based system for multiplex and integrated glycoprotein quantification by immunoassays, and glycan detection by the lectin immunosorbant assays. Using the previously described candidate prostate cancer biomarkers, tissue inhibitor of metallopeptidase 1, tissue plasminogen activator, membrane metallo-endopeptidase, and dipeptidyl peptidase-IV, the authors demonstrated that the multiplex integrated system was comparable to single immunoassays in the protein quantification and lectin immunosorbant assays in the glycan detection. The method simultaneously measures multiple proteins and generates integrated glycan information for the proteins from a single measurement. The method also helps conserve precious clinical samples and is useful for biomarker discovery and validation.