

Research Highlights

Highlights from the latest articles in biomarker research



Serum prostate-specific antigen: a new biomarker for breast cancer?

Evaluation of: Chang Y-F, Hung S-H, Lee Y-J *et al.* Discrimination of breast cancer by measuring prostate-specific antigen levels in women's serum. *Anal. Chem.* 83, 5324–5328 (2011).

Early detection is critical to reduce breast cancer morbidity and mortality. Current diagnostic methods (clinical examination and mammography) miss early-stage breast cancer in approximately 10% of postmenopausal and up to 40% of premenopausal women. The analysis of serum levels of prostate-specific antigen (PSA) are in general clinical use for the early detection of prostate cancer. It had been demonstrated that PSA can be measured in some, but not all women, owing to the low levels of the protein that are present in their serum (~1 pg/ml). The authors developed

an ultrasensitive PSA immunoassay that combines a sandwich immunoassay with a localized surface plasmon biosensor to reliably measure PSA down to 0.1 pg/ml.

In this study, the authors compared the PSA levels of eight women with and eight without breast cancer. They observed higher levels of PSA in serum in women with breast cancer. The receiver-operating characteristic curve demonstrated an area under the curve of 0.91. This is a promising preliminary finding. Important questions, if the findings are validated in an independent population, include: how available is this technology? What was the information on the women with breast cancer (e.g., stage and prior treatment)? Were the women matched regarding clinical variables (e.g., age and race)? A follow-up study could be conducted, which controls, as well as possible, for clinical variables.

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Molecular signatures of tumor-infiltrating immune cells are candidate prognostic biomarkers in breast cancer patients

Evaluation of: Ascierto ML, Kmiecik M, Idowu MO *et al.* A signature of immune function genes associated with recurrence-free survival in breast cancer patients. *Breast Cancer Res. Treat.* DOI: 10.1007/s10549-011-1470-x (2011) (Epub ahead of print).

Current concerns regarding breast cancer recurrence have led to growing interest in the use of neoadjuvant immunotherapy prior to conventional therapies. Previous

studies on breast cancer relapse have focused on tumor cells, rather than on infiltrating host immune cells. Recently, the clinical significance of tumor-infiltrating immune cells has been demonstrated in several human carcinomas including breast cancer. However, in breast cancer patients, the specific molecules, how they interact to prevent the attack of a tumor and prevent its recurrence remains to be fully defined.

In the current study, Ascierto *et al.* investigated the prognostic value of immune function genes. They collected total RNA

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from tumors of nine individuals with a 7-year relapse-free survival, and eight individuals who recurred within 5 years

of diagnosis. In all cases, the tumors were said to contain at least 10% infiltrating cells. Microarray analyses identified a five-gene panel (*IGK*, *GBPI*, *STAT1*, *IGLL5* and *OCLN*), distinct from two US FDA-approved panels (MammaPrint® and Oncotype Dx®), which predicted

disease recurrence with >85% accuracy. The authors propose that this observation suggests that neoadjuvant immunotherapy in patients with high risk of breast cancer relapse may reduce the recurrence of tumor, via induction of the immune function genes.

Urinary eosinophil protein X: a novel inflammatory biomarker that identifies children at risk of developing atopic disease

Evaluation of: Chawes BLK, Bønnelykke K, Bisgaard H. Elevated eosinophil protein X in urine from healthy neonates precedes development of atopy in the first 6 years of life. *Am. J. Respir. Crit. Care Med.* DOI: 10.1164/rccm.201101-0111OC (2011) (Epub ahead of print).

The identification of children at high risk of developing atopic disorders is important in order to provide targeted prevention, as well as individualized intervention and treatment. In addition, it is of research interest to determine whether

atopic disease(s) are active prior to the development of symptoms.

In this study, the authors measured eosinophil protein-X, leukotriene-C₄/D₄/E₄, and 11 β -prostaglandin-F₂ α in urine from more than 360 1-month-old children participating in the Copenhagen Prospective Studies on Asthma in Childhood (COPSAC) birth cohort. Thereafter, clinical information on the development of allergic sensitization, allergic rhinitis, nasal eosinophilia, blood eosinophilia, eczema, lung symptoms (significant cough, wheeze or dyspnea) and asthma were prospectively collected until the child was 6 years old.

The authors found that eosinophil protein-X levels were significantly

associated with development of allergic sensitization, nasal eosinophilia and eczema, but not with allergic rhinitis, asthma or blood eosinophilia. The other two markers were not associated with atopic phenotypes. Although the mechanism leading to eosinophilic activation prior to the manifestation of symptoms is not completely understood, the findings from this study suggest that activation of eosinophil granulocytes occurs early in life, prior to development of atopy-related symptoms. The authors concluded that urinary eosinophil protein-X is a novel and early inflammatory biomarker with the ability to identify children at risk of developing atopic disease.

Soluble amyloid precursor protein in cerebrospinal fluid is a promising diagnostic biomarker of incipient Alzheimer's disease

Evaluation of: Perneczky R, Tsolakidou A, Arnold A *et al.* CSF soluble amyloid precursor proteins in the diagnosis of incipient Alzheimer disease. *Neurology* 77(1), 35–38 (2011).

While up to 15% of patients with mild cognitive impairment (MCI) progress to Alzheimer's disease (AD) every year, some do not progress or may even revert to normal. The authors suggest that biologic markers to determine which individuals will progress would be useful in the early institution

of disease-modifying strategies. Based on reports that the soluble amyloid precursor proteins (sAPP) α and β mirror fundamental early events of AD pathogenesis and CSF concentration changes have been reported in AD, the authors determined if these proteins would better predict individuals with MCI who develop AD than the established biomarkers tau and amyloid- β_{1-42} .

The authors investigated 56 individuals with MCI at the time of CSF collection: 21 patients had progressed to probable AD (MCI-AD), 27 still had MCI and eight had reverted to normal.

Their results demonstrated that individuals who progressed to AD had higher sAPP β concentrations than those that did not, and that the best predictive model to differentiate individuals who progressed from those that regressed included sAPP β , tau and age.

Whether this information can be generalized to the population at large is unclear, as the authors indicate, owing to the limited sample of participants, recruitment at a specialized memory clinic, the lack of a control group and pathologic confirmation of the clinical end points (progression from MCI to AD and reversion from MCI to normal).

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