

analytical specificity and reliable quantification. Here we developed the first Selected Reaction Monitoring (SRM) assay for the multiplexed measurement of cancer biomarkers in human bile. For this purpose, 8 potential biomarker candidates previously highlighted by proteomic analysis were selected. Equal volumes of bile collected from patients presenting with malignant and non-malignant biliary stenosis were stacked on the top of a SDS-PAGE gel. Proteins were then digested in-gel with trypsin and proteotypic peptides of each candidate biomarker were quantified by nanoLC-SRM on a 5500-QTrap mass spectrometer (ABSciex) using heavy synthetic peptides as standards (PEPotecTM, ThermoFisher). SRM data were finally analysed using Skyline software and manual validation. The developed assay proved to be valuable and reliable to quantify all the selected candidates. Moreover, the results confirmed the simultaneous overexpression of some of the proteins in bile samples from malignant stenoses. Overall, our data demonstrate the ability of SRM to quantify cancer biomarkers in human bile and emphasize the interest of using multiplexed SRM assays to assess the diagnostic potential of a panel of bile biomarkers in differentiating biliary stenoses. Work supported by the PRIME-XS consortium.

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The changing face of epidemiology of systemic fungal infections

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Abstract

Invasive fungal diseases (IFDs) are an increasingly common complication in critically ill patients in Europe and are frequently fatal. Because of changes in treatment strategies and the increased use of antifungal prophylaxis, the epidemiology of IFDs has changed substantially in recent years and infections due to *Candida* species are no longer the majority in many institutions. In contrast, the emergence of non-*Candida* IFDs such as aspergillosis, ucrmycosis and fusariosis has increased. Rates of IFD-related mortality in Europe depend on the pathogen, geographical location and underlying patient characteristics, with rates ranging from 28 to 59% for *Candida* infections and from 38 to 80% for invasive aspergillosis. Early initiation of antifungal therapy is critical for improving outcomes; however, this is complicated by the difficulty in diagnosing IFDs rapidly and accurately. Choice between agents should be based on a variety of factors, including spectrum of activity, adverse events, drug interactions, route of administration, clinical efficacy of individual agents and local epidemiology.

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Anti-tumor effects of the human monoclonal anti-nuclear antibody on the HEp-2 cells

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Abstract

Function of autoantibodies from patients with autoimmune diseases in malignancies development is not clear yet. It has been reported that a cell-penetrating lupus autoantibody, 3E10, which was isolated from a mouse model of systemic lupus erythematosus (SLE), has been a potential targeted

therapy for DNA-repair deficient malignancies. We have got four human monoclonal antinuclear antibodies from patients with autoimmune disease, 3B5, 3C1, 3E8 and 4F3. Our data showed that four antibodies could combine HEp-2 cells and display different nuclear types as antinuclear antibody (ANA). Also, these four ANAs can inhibit HEp-2 cells proliferation. We think these antibodies may be potential antibody drugs to cancer therapy. However, the function and mechanism are not clear. Further study, we want to clarify the effects of four ANAs on proliferation of various cancers cells and to investigate the mechanism of four ANAs affecting various cancers cells proliferation and their targets. This may be a new mechanism of malignancies development in patients with autoimmune diseases, and provide novel angle of autoantibody function study.

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Rapid saline test for varicella zoster virus

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Abstract

Varicella zoster virus (VZV) is a ubiquitous human herpesvirus typically causing childhood varicella (chickenpox) at which time a life-long latent infection is established in ganglionic neurons throughout the neuraxis. Reactivation of latent virus, typically in the elderly and immunocompetent usually causes zoster (shingles) but can also result in serious neurologic disease. In cases of vasculopathy, meningoencephalitis and myelitis where VZV is suspected, diagnosis requires detection of virus DNA or antibody in CSF. In collaboration with NASA, VZV DNA was found in saliva of health astronauts suggesting asymptomatic virus reaction due to the stress of spaceflight. This led to a series of studies indicating virus DNA can be found in saliva of patients with VZV associated neurologic disease. With the goal of eliminating the need for lumbar puncture to diagnose VZV associated neurologic disease; we developed a rapid saliva test for the detection of VZV DNA in saliva that can be used in space as well as on Earth. Herein the test and its potential application will be present.

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Novel approaches for the supportive extracorporeal therapy of sepsis: Towards personalized treatment

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Abstract

Sepsis and sepsis-associated multiple organ failure are associated with extensive tissue damage caused by over-activation of the innate immune system and by the excessive release of inflammatory mediators. The development of targeted therapies for sepsis remains a major challenge due to the complex network of inflammatory mediators involved in the septic process.

Early detection and timely therapeutic intervention are crucial for improved outcome of patients with sepsis. Currently however, the diagnosis of sepsis mostly relies on general symptoms. Taking into account the extreme heterogeneity of septic patients, the application of supportive extracorporeal therapies to modulate the concentration of inflammatory mediators requires diagnostic tools to monitor the inflammatory profile of the patients in order to identify the optimal time window for application of supportive therapies.

Here, we report on the development of extracorporeal adsorption systems for cytokine modulation and on the development and validation of a novel array technology to detect markers of inflammation (interleukins 6 and 10,