help for differentiation into plasma cells. Our results also indicate that abatacept binding CD80/CD86 may provoke a negative reverse signal to B cells to further regulate B cells activation.

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THU0042 CANCER IMMUNOTHERAPY ARRAY: A NOVEL SCREENING TOOL FOR IMMUNE SYSTEM PROFILING IN CANCER IMMUNOTHERAPY BRIDGING AUTOIMMUNITY AND CANCER

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Background: Recent FDA-approved checkpoint inhibitors targeting the cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4) and programmed death 1 (PD-1)/PD-L1 pathway represent milestones in the field of cancer immunotherapy. In general, cancer immunotherapy works only in a subset of patients, but some patients experience prolonged responses. Cancer immunotherapy can cause severe immune-related adverse events (irAE) in patients, who are increasingly seen by rheumatologists. We propose that that autoantibody profiling will reveal novel B-cell associated mechanisms of therapy response and side effects. This may yield minimally-invasive biomarkers to identify patients at risk to develop iRAE and monitor cancer patients over the course of their life under immunotherapy

Objectives: We have developed a novel Cancer Immunotherapy Array, which includes a combination of antigens important in autoimmune diseases, anti-tumour immunity, and oncogenes and tested the array in patient sera from a diverse set of cancer immunotherapy trials.

Methods: The Cancer Immunotherapy Array consists of a bead-based multiplex array using minimal patient serum samples incubated with antigen-coated, color-coded Luminex beads. Run in microtiter plate format, the Array permits quantification of the autoantibody reactivity in thousands of serum samples towards approximately 900 human protein antigens in each sample. Magnetic beads are employed to enable automated pipetting and washing steps.[1] We selected human protein antigens from groups A) tumor-associated antigens (TAA), B) autoimmune disease antigens, C) cytokines, and D) cancer signalling pathway proteins

Results: In total, over 2000 serum samples from diverse cancer indications plus hundreds of samples from autoimmune diseases such as RA, SLE, Sjogren's disease and healthy controls were screened with the Cancer Immunotherapy Array. As key findings we report autoantibody panels which can differentiate patients with irAEs and those without irAEs. Also, but less prominent, individual autoantibodies are associated with overall survival. Autoantibodies that target antigens involved in cancer signalling pathways are associated with irAEs. Also, patients with increased levels of a distinct autoantibody against an inflammatory cytokine do not develop irAEs across multiple tumours.

Conclusions: The Cancer Immunotherapy Array is a high throughput array suitable for the analysis of thousands of cancer patient serum samples. Its first application presents novel autoantibody signatures for therapy-related toxicities (irAEs) as well as response. These signatures have the potential to serve as useful tools that will broaden our understanding of the mechanisms of therapy response and irAE occurrence.

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THU0043 AUTOANTIBODY PROFILING IN PROSTVAC AND IPILIMUMAB TREATED PROSTATE CANCER PATIENTS REVEALS POTENTIAL BIOMARKERS OF IMMUNE-RELATED ADVERSE EVENTS

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Background: Autoantibodies (AAB) targeting self-antigens can be found in two clinically and immunologically opposing diseases, autoimmune diseases and cancer. While in autoimmune diseases, the immune system is hyperactivated against self-antigens, many tumours suppress the anti-tumour immune response. The therapeutic cancer vaccines PSA-Tricom (Prostvac) is designed to generate an antigen-specific tumour response in metastatic castration-resistant prostate cancer (mCRPC), which is in phase 3 testing. To further augment the immune response, combination therapies of Prostvac with ipilimumab are currently tested in clinical studies. Ipilimumab is an antibody that blocks the immune checkpoint molecule cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4). However, treatment with ipilimumab is associated with immune-related adverse events (irAEs).[1]

Objectives: Since there are no biomarkers for predicting irAEs, we aimed to investigate AAB profiles as biomarkers associated with irAE in mCRPC patients treated with prostvac and ipilumumab combination therapy.

Methods: Serum samples from 24 mCRPC patients treated with prostvac and ipiliumab therapy were tested for the presence of serum autoantibodies against 842 preselected antigens. Candidate antigens comprise immune-related and cancer signalling pathway proteins, autoimmune disease antigens, and tumor-associated antigens (TAA). Samples were collected prior to treatment (T0 samples), at 3 and 6 month. IrAEs included rash, elevated aminotransferases, neutropenia, diarrhoea, colitis and endocrine irAEs. Overall survival was also captured and correlated with AABs. Autoantibody levels were measured by Luminex FlexMap3D bead based multiplex protein arrays[2] and data were analysed by significance analysis of microarrays (SAM), Partial least squares regression (PLS) and Pearson's correlation.

Results: In total, 87 AABs were found that were significantly different in patients with irAEs and those without irAEs (SAM |d|>2.5; Pearson's correlation |3|>0.35). PLS analysis revealed that AABs associated with irAEs were also associated with overall survival. Gene ontology analysis of pathways, molecular function and cellular localization revealed that AABs predicting irAEs target cancer, cell cycle, cell adhesion and apoptotic pathways. We also found elevated levels of AABs in patients who do not experience irAEs. Interestingly, these 40 AABs target proteins that are involved in inflammatory, adaptive and cellular immune response pathways or are autoimmune disease antigens.

Conclusions: AABs that target antigens involved in cancer signalling pathways are associated with irAEs following prostvac plus checkpoint inhibitor combination therapy. In contrast, AABs targeting immune response pathways were found in patients who do not develop iRAEs and may counteract the action of inflammatory molecules. Similarly, anti-cytokine AABs have been found in autoimmune diseases, were they appear to counteract the pathological effects of cytokines.[3] Further studies in larger sample sets are needed to confirm these findings.

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