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Serum biomarkers in cancer patients treated with checkpoint inhibitors

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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 tumors suppress the anti-tumor immune response. Therapeutic cancer vaccines are designed to generate an antigen-specific tumor response in cancer. To further augment the immune response, combination therapies of therapeutic vaccines with checkpoint inhibitors such as ipilimumab are currently tested in clinical studies. Ipilimumab is an antibody that blocks the immune checkpoint cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4). However, treatment with ipilimumab is associated with immune-related adverse events (irAEs). We investigated AAB profiles in cancer patients treated with therapeutic vaccines, ipilumumab, and combination therapy. Serum samples from cancer patients treated with therapeutic vaccines and/or ipiliumab therapy were tested for the presence of serum autoantibodies. Candidate antigens comprise immune-related and cancer signaling pathway proteins, autoimmune disease antigens and tumor-associated antigens. Samples were collected prior to treatment (T0 samples), at three and six month. In total, 87 AABs were found significantly different in patients with irAEs and those without irAEs. AABs associated with irAEs were also associated with overall survival. Analysis of pathways revealed that AABs predicting irAEs target cancer, cell cycle, cell adhesion and apoptosis pathways. We also found elevated levels of AABs in patients who do not experience irAEs. These AABs target proteins involved in inflammatory, adaptive and cellular immune response pathways or represent autoimmune disease antigens. Further studies in larger sample sets are needed to confirm these findings.

Biography

Peter Schulz-Knappe is working as MD and Cell Biologist by training. He is a Board Member of biotech companies and serves as CSO since 1997. His scientific passion for the last 25 years has been in the discovery, validation and development of protein biomarkers from blood. His main research topics are: proteomics, peptidomics, biomarkers, autoantibodies, protein microarrays, IVD-development. He has published and co-authored over 100 peer reviewed papers. In addition, he is inventor of > 20 patents and patent families on peptides, biomarkers, and analytical procedures.

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