Pre-treatment IgG autoantibodies associated with favorable Ipilimumab outcomes in melanoma include testis antigens and proteins linked to neurodegeneration.

**Baseline Serum IgG Autoantibodies Associated with Favorable Clinical Outcomes to Ipilimumab**

Outlier pre-existing autoantibody repertoire of stable disease (SD) n=11 and partial response (PR) n=10 following anti-CTLA4 immunotherapy for malignant melanoma. Outliers are for >1.5 z-score targets with a minimum >2x average signal increase in responders and >2 responders with z-scores >1.2 response across the population. Sorted by number of z-score responses then largest average increase.

**Baseline Serum IgG Autoantibodies in Patients with Progressive Disease Following Ipilimumab**

Correspondence for those autoantibodies most associated with improved outcomes following anti-CTLA4 immunotherapy for malignant melanoma. Sorted by response-associated targets as outlined above.

**Methods**


**Data Collection and Analysis**

All data collected for this study was previously reported using samples collected with approval of the NYU Institutional Review Board at the NYU Perlmutter Cancer Center. Targets identified included those with 20-50% enrichment as compared to 5-10% background. Targets were filtered based on number of responses, fold change, and enrichment scores. The analysis was performed on sera from patients with baseline IgG autoantibody (IgG) signals to neoantigen peptides than their wild-type counterpart peptides (unknown). The relevance of these identities was confirmed by sensitivity analysis and validation of statistical significance.

**Results**

In this small pilot study, there were baseline IgG autoantibodies in patient sera that differentiated patients destined for “good outcome” (POD) rather than “poor outcome” (SD / PR) following anti-CTLA4 checkpoint blockade (anti-CTLA4). The authors performed a correlation analysis on baseline IgG autoantibody targets, and identified enrichment in proteins related to neurodegeneration. These proteins included known testis antigens, as well as proteins associated with amyotrophic lateral sclerosis, frontotemporal dementia, Parkinson’s, and Alzheimer’s.

**Conclusion**

The identification of these baseline IgG autoantibodies may provide insight into the mechanisms of therapeutic response and resistance to anti-CTLA4 therapy in melanoma patients. Further studies are needed to validate these findings in larger patient populations and to explore the potential role of these autoantibodies as biomarkers for predicting patient outcomes.

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**References**