**CT Antigens are Frequently Expressed in Non-Inflamed Tumors**

**INTRODUCTION**

Cancer testis antigens (CTA) are tumor antigens that have a highly tissue restricted expression in germ cells but are often expressed in diverse malignancies. With their highly immunogenic expression limited to tumor cells, CTAs have become a prime target for cancer vaccinations and T-cell based therapy with chimeric T-cell receptors.

In this study, we investigated the association of two CTAs (NY-ESO-1 and LAGE-1A) with the immune microenvironment of real-world clinical tumors spanning multiple histologies. NY-ESO-1 & LAGE-1A are the two most common vaccine/CAR-T/IO therapy trial targets totaling 132 for NY-ESO-1 and 62 for LAGE-1A. Furthermore, we describe the association of CTAs with traditional biomarkers of immunotherapy such as PD-L1 immunohistochemistry (IHC) and tumor mutational burden (TMB), with inflammatory status and cell proliferation status with confirmatory studies performed on a large TCGA pan-cancer cohort of >11,000 tumors.

**METHODS**

Unsupervised clustering was performed on gene-expression data of 395 immune transcripts from 1323 FFPE tumors representing >30 histologies to reveal three inflammatory tumor phenotypes (Inflamed, Borderline, Non-Inflamed) and three distinct gene groups (CTA, inflammatory and other immune genes). Test for proportions was performed using Pearson’s chi-squared test to describe association of NY-ESO-1 and LAGE-1A with PD-L1 IHC, TMB, inflammation and cell-proliferation.

A retrospective cohort (n=242) of NSCLC, melanoma and renal cell carcinoma patients with immune checkpoint inhibition (ICI) treated tumors was utilized to perform overall survival (Kaplan-Meier curves) and response to ICI therapy for CTA tumors. Survival analysis was confirmed against the Pan-Cancer TCGA cohort (n=11,001).

**CONCLUSION**

- This study presents an in-depth analysis of the immune landscape of CTA positive tumors across multiple histologies.
- CTA bearing tumors not only have unique immune profiles but also have significant associations with biologically relevant emerging biomarkers such as inflammatory signature, TMB and cell proliferation.
- In addition to serving as a target for vaccine and cell-based IO therapy, patients with NY-ESO-1 positive tumors may have improved response rates to ICI therapy.

**REFERENCES**

1. https://clinicaltrials.gov/ October 2019