GPR171, a prognostic marker of improved survival in cervix cancer – A Deep South Consortium in Oncology (DSCO) project.

Tanvi Joshi, MD[1]; Elisabeth A. Murphy, PhD[2]; Sagar Chokshi, DO[1]; Kevin J Lee, PhD[1]; Sharon Wu, PhD[2]; Matthew Oberley[2]; Britt K Erickson, MD[3]; Charles A Leath, MD, MSPH[4]; Bunja J Rungruang, MD[5]; Rodney P Rocconi, MD[6]; Nathaniel Jones, MD[1]; Jennifer Scalici, MD[7]

[1] USA Health Mitchell Cancer Institute; [2] Caris Life Sciences; [3] University of Minnesota; [4] University of Alabama at Birmingham; [5] Medical College of Georgia at Augusta University; [6] University of Mississippi Medical Center Cancer Center and Research Institute; [7] Winship Cancer Institute, Emory University

SGO ANNUAL MEETING ON WOMEN'S CANCER SEATTLE, WA • 2025

Background

- Women of poorer socioeconomic status are more likely to develop cervix cancer.
- Molecular markers of chronic stress have been shown to have an effect on tumor immunity.
- The tumor immune microenvironment can contribute to T-cell dysfunction.
- GPR171 is a G-protein coupled-receptor that plays a role in tumor immunity.
- The role of GPR171 in the immune landscape of cervix cancer has not been studied.

Methods

- Whole transcriptomic RNA sequencing of 3,371 samples were queried by Caris Life Sciences.
- Overall survival (OS) was calculated from tissue collection or first cycle of pembrolizumab (α-PD-1) to last contact.
- Hazard ratio (HR) was calculated by Cox proportional hazards model and p-values by log-rank test.
- DNA damage and tumor immune markers were analyzed in commercially available tumor microarrays by IHC.

Results

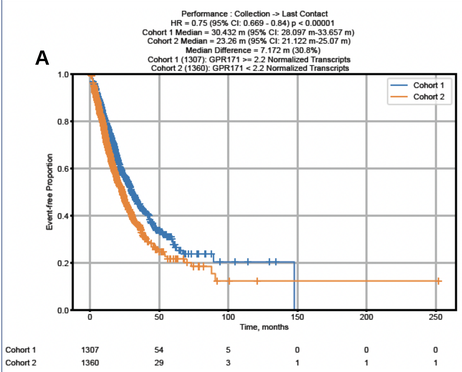

Figure 1. A) Caris database analysis based on mean GPR171 reveals better survival in GPR171-high expressing patients. B) Histogram analysis of GPR171 expression among samples analyzed.

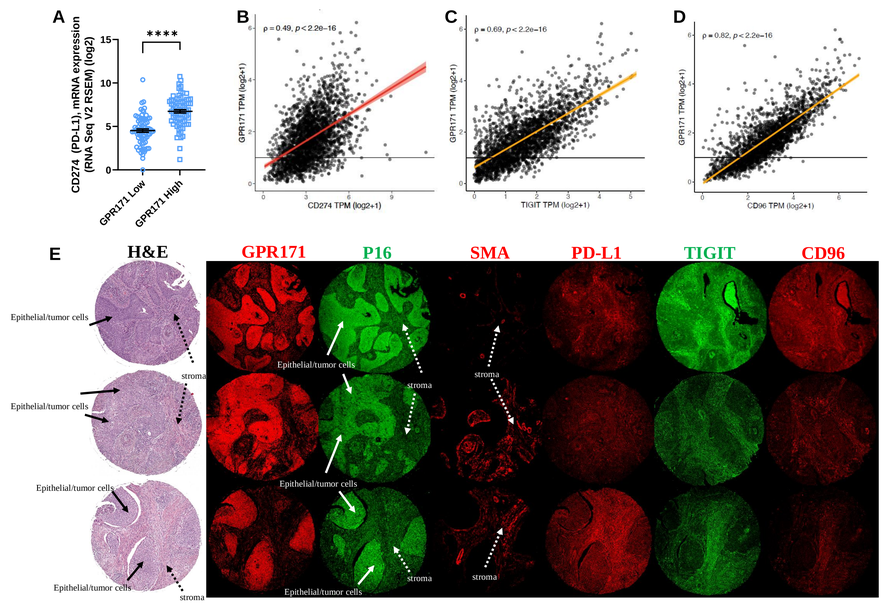

Figure 2. GPR171 and PD-L1 mRNA expression show a significant, positive correlation as observed across **A**) TCGA, and **B**) Caris database. GPR171 correlation to other immune markers in the Caris database showed positive correlation with TIGIT (**C**) and CD96 (**D**). **E**) Tissue microarray analysis revealed expression of GPR171 in P16 positive epithelial cells compared to immune markers PD-L1, TIGIT, and CD96 expression in stroma as confirmed by smooth muscle actin staining (SMA).

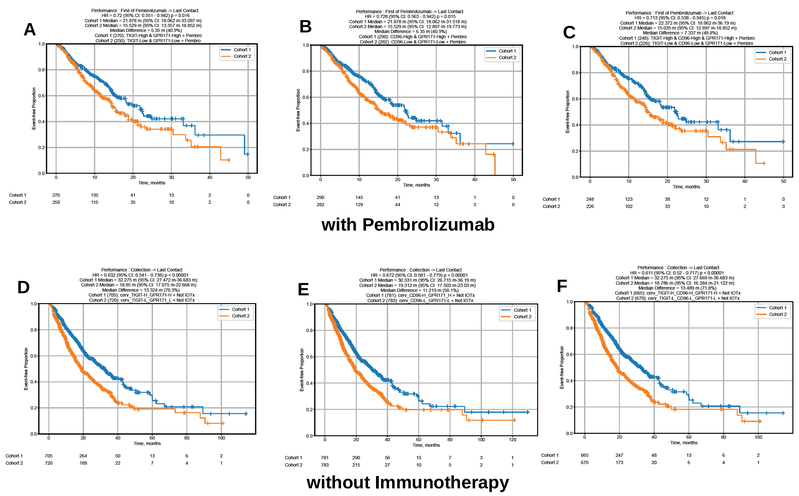

Figure 5. **A**) GPR171-High+TIGIT-High, **B**) GPR171-High+CD96-High, and **C**) GPR171-High+TIGIT-High+CD96-High show improved overall survival with the use of pembrolizumab compared to low expression of each. **D**) GPR171-High+TIGIT-High, **E**) GPR171-High+CD96-High, and **F**) GPR171-High+TIGIT-High+CD96-High show improved overall survival that is more significant with the use of non-IO treatment when compared to low expression and to the use of pembrolizumab.

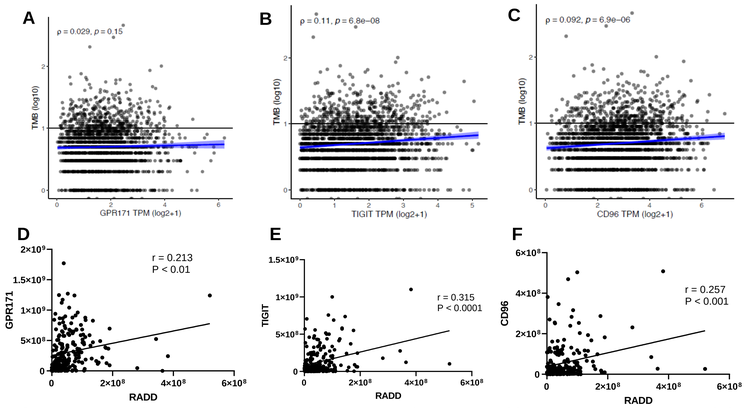

Figure 3. DNA damage as measured by TMB and RADD. Neither GPR171 (**A**), TIGIT (**B**), or CD96 (**C**) were associated with DNA damage as measured by TMB in the Caris database. However, (**D**) GPR171, (**E**) TIGIT and (**E**) CD96 were significantly positively associated with DNA damage as measured by RADD in the tissue microarray.

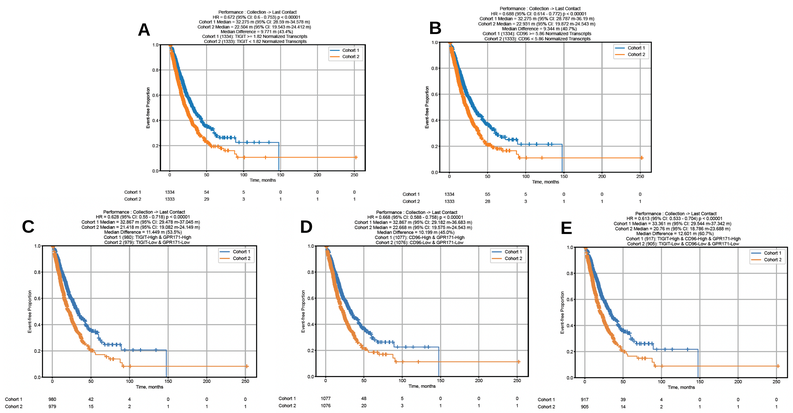

Figure 4. **A**) Analysis based on mean TIGIT expression. **B**) Analysis based on mean CD96 expression. **C**) Co-expression of GPR171-High and TIGIT-High expression correlates to an improvement in overall survival. **D**) Co-expression of GPR171-High with CD96-High also correlates to improved overall survival. **E**) Co-expression of GPR171-High, TIGIT-High, and CD96-High has the largest improvement in overall survival.

Conclusions

- GPR171 is a prognostic indicator of improved survival.
- GPR171 is shown to be expressed on p16+ epithelial tumor cells in contrast to other markers of tumor immunity.
- Co-expression of GPR171 with other tumor immune markers (CD96 and TIGIT) portends further improved survival.
- Patients with the best survival rate exhibited high co-expression of GPR171, CD96, and TIGIT without the use of pembrolizumab.