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Cancer testis antigen and interleukin expression correlates with survival in small bowel neuroendocrine tumors

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BACKGROUND

Patients with small bowel neuroendocrine tumors (SBNETs) frequently present with metastatic disease, and unfortunately, the range and efficacy of available therapies is limited. Immunotherapeutic checkpoint inhibitors have demonstrated benefit in other malignancies and may also play a role in SBNETs, although relatively little is known about the immune infiltrate in these tumors. Toward a goal of developing novel immunomodulatory strategies, we sought to evaluate the tumor immune microenvironment of SBNETs utilizing Nanostring transcriptional profiling.

METHODS

Patients with SBNETs who underwent surgical resection at MD Anderson Cancer Center from 2003 to 2016 were retrospectively analyzed. Clinicopathologic data was collected, and patients were stratified by survival. Overall survival (OS) from date of resection was assessed using the Kaplan-Meier method, and p-values were calculated using the log-rank test. Multivariate (MV) analysis was performed using the Cox proportional hazards model. Transcription expression from bulk RNA was analyzed using the Nanostring PanCancer Immune Profiling Panel.

RESULTS

Patients with SBNETs who underwent surgical resection at MD Anderson Cancer Center from 2003 to 2016 were retrospectively analyzed. Clinicopathologic data was collected, and patients were stratified by survival. Overall survival (OS) from date of resection was assessed using the Kaplan-Meier method, and p-values were calculated using the log-rank test. Multivariate (MV) analysis was performed using the Cox proportional hazards model. Transcription expression from bulk RNA was analyzed using the Nanostring PanCancer Immune Profiling Panel.

CONCLUSIONS

High expression of CTA and IL signatures in resected SBNETs identified patients with improved survival agnostic of stage. While CTA expression across multiple tumor subtypes have been implicated in their immunogenicity and potential for therapeutic targeting, this is the first work to identify a clinically relevant signal in SBNET.

The concurrent increase of key cytokines (which are known to mediate anti-tumor activity) among CTA-high patients suggests an immune-mediated component to their improved survival. Further work is underway to elucidate the epigenetic mechanisms of CTA expression and silencing, with the goal of validating key CTAs such as PRAME and GAGE1 as predictive and therapeutic targets for immunologic intervention.

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