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Expression patterns of novel genomic markers in pulmonary versus extra-pulmonary small cell neuroend

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BACKGROUND

Extrapulmonary Neuroendocrine Carcinomas (EP-NECs) are a heterogeneous group of rare tumors with poor clinical outcomes. These patients have limited treatment options and they follow SCLC treatment. Although DLL3, SEZ6, and HEPACAM2 are novel markers for SCLC with several ongoing targeted therapy trials, there is not enough data to understand their role in EP-NECs.

METHODS

The Tempus Lens Platform was used to query the de-identified Tempus multimodal database to analyze a cohort of patients with a histological diagnosis of SCLC or extrapulmonary NEC with xT (DNA; 648 genes) xR (RNA; whole transcriptome) testing, and tumor purity of at least 30%. RNA-seq data were normalized and quantified as transcripts per million (TPM). Expression levels of DLL3, SEZ6, HEPACAM2, TACSTD2 (TROP2), BCL2L11, BBC3, BID, BCL2 (BH3), and CD276 (B7H3) were compared across subgroups of EP-NEC and SCLC patients. Wilcoxon rank-sum test was used for 2-groups; and Kruskal-Wallis test for 3+ groups comparisons and Spearman correlations for marker co-expression. Analyses were two-sided, with statistical significance evaluated at the 0.05 alpha level.

RESULTS

2242 SCLC vs 965 EP-NEC were compared. SCLC samples had significantly higher expression of DLL3, SEZ-6, HEPACAM2, and BCL2, while EP-NEC had higher TACSTD2,

BBC3, BID and CD276 expression (p <0.001). Among EP-NEC subgroups, small cell EP-NEC (EP-SC-NEC) had significantly higher DLL3, SEZ-6, HEPACAM2, and BCL2 expression and lower BID expression compared to large cell EP-NEC (EP-LC-NEC) (p <0.001). There were also differences among EP-NEC primary tumors, with higher SEZ-6 and HEPACAM2 but lower TACSTD2 and BID expression in gastrointestinal (GI), genitourinary (GU), breast, and gynecological (Gyn) EP-NEC compared to head and neck (H&N) EP-NEC. BCL2 expression was higher in breast and Gyn EP-NEC, while CD276 was higher in GU and H&N EP-NEC.

CONCLUSIONS

Although SCLC and EP-SC-NEC share profound histological and morphological similarities, our results highlight significant molecular variation between both groups. These unique genomic traits should inform clinical development of novel therapies and could impact therapeutic decisions for EP-NEC according to their morphological, cellular, and site of origin subtypes.

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