

## **Role of BTLA and HVEM in Non-Small Cell Lung Carcinoma**

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Non-Small Cell Lung Cancer (NSCLC) stands as the predominant form of lung cancer, representing approximately 85% of diagnosed cases. Within the intricate network of immune regulation, the B and T lymphocyte attenuator (BTLA) emerges as a important inhibitory receptor modulating immune responses. Its interaction with the herpes virus entry mediator (HVEM) maintain immune homeostasis. Understanding the interplay between BTLA and HVEM holds promise for developing novel immunotherapeutic strategies for NSCLC.

The primary objective of this study was to assess the diagnostic and prognostic significance of BTLA and HVEM in NSCLC. The study employed the ddPCR method for mRNA expression analysis and immunohistochemistry (IHC) for protein expression assessment of BTLA and HVEM in surgically resected NSCLC tissues alongside adjacent tissues.

The expression analysis revealed aberrant levels of BTLA and HVEM mRNA in tumor samples, with significant differences observed between NSCLC subtypes. The correlation analysis showed association between BTLA and HVEM mRNA levels and NSCLC grade and stage. Additionally, the positive correlation was detected between mRNA expression of BTLA and HVEM. Further IHC staining detected BTLA protein on tumor-infiltrating lymphocytes in the majority of patients, while HVEM-positive tumor cells were observed in all samples, with 85% of cases exhibiting double-positive BTLA+HVEM+ expression.

In summary, our findings highlight dysregulated expression of both BTLA and HVEM at mRNA and protein levels in NSCLC, suggesting a potential involvement of the BTLA-HVEM pathway in immunosuppression within the NSCLC microenvironment. This underscores the importance of further research into targeted immunotherapeutic interventions focusing on this intricate regulatory axis.

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