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due to a PRELP-mediated transcriptional upregulation of components of the MHC class I APM components TAP1, TAP2 and TAPBP as determined by qPCR and promoter assay in PRELP transfectants versus mock controls. Furthermore, MHC class I surface expression was even more pronounced upon BGN co-transfection with PRELP. PRELP overexpression was able to inhibit the proliferation of the B16F10 cells. Bioinformatics analyses demonstrated a positive correlation of PRELP with HLA-A , -B and -C alleles in human melanoma.

Conclusions Our findings demonstrated that overexpression of PRELP correlates with higher MHC class I expression and inhibits cell proliferation. For the first time, co-transfections of the two proteoglycans PRELP and BGN had a synergistic effect on upregulating MHC class I expression. Therefore, PRELP can serve as a novel therapeutic strategy that deserves further investigation.

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REFERENCES

1. Subbarayan K, Leisz S, Wickenhauser C, Bethmann D, Massa C, Steven A, Seliger B. Biglycan-mediated upregulation of MHC class I expression in HER-2/neu-transformed cells. *Oncoimmunology* 2018;**7**:e1373233.
2. Xu L, Shen SS, Hoshida Y, Subramanian A, Ross K, Brunet JP, Wagner SN, Ramaswamy S, Mesirov JP, Hynes RO. Gene expression changes in an animal melanoma model correlate with aggressiveness of human melanoma metastases. *Molecular Cancer Research* 2008;**6**:760-769.

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869 ANTI-LUNX TARGETING THERAPY FOR LUNG CANCER

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Background The identification of novel therapeutic targets in lung cancer for the generation of targeted drugs is an urgent challenge. Lung-specific X (LunX) is a member of the palate, lung, and nasal epithelium clone (PLUNC) protein family. Some reports have suggested that the human PLUNC gene (also named LUNX) might be a potential marker for NSCLC, and PLUNC mRNA has been identified in peripheral blood and mediastinal lymph nodes from NSCLC patients.It is unclear whether LunX expression is associated with the pathological type and pathological severity in lung cancer patients. The utility of LunX as a potential therapeutic target in NSCLC is uncertain.

Methods Clinically, 80% of lung cancers are non-small-cell lung cancers (NSCLCs). Here, we analyzed 158 NSCLC samples and detected LunX expression.

Results It showed that the expression of LunX were elevated in 90% (108/150) lung cancers by IHC staining, which accompanied with significantly lower rate of postsurgery survival. Further evaluation of LunX expression in invasive tumor cells in subclavicular lymph nodes, draining lymph nodes, hydrothorax of lung cancer patients, turned out that LunX is highly expressed in invasive lung cancer cells. These data indicated that LunX overexpresses in lung cancer and associates with tumorigenesis and tumor progression.

Mechanistically, we discovered that LunX bound to 14-3-3 protein and facilitated their activation by maintaining these proteins in a dephosphorylated state, thereby contributing to the activation of pathways downstream of 14-3-3 protein, such as the Erk1/2 and JNK pathways. Thus, LunX promoted tumor growth and metastasis.

Furthermore, we generated a therapeutic antibody specific for lung cancer, which not only inhibited lung cancer growth and reduced Ki67 staining and angiogenesis in xenograft model of subcutaneously transplanted tumor, but also blocked tumor metastasis and invasion, improved the survival of these mice. We also detected that antibody treatment induces LunX antigen-antibody complex endocytosis and the degradation of LunX protein.

Conclusions Our study suggests that LunX is a novel therapeutic target in lung cancer and that the LunX-targeted therapeutic antibody may have considerable clinical benefit.

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870 INVESTIGATING SEXUAL DIMORPHISM IN THE TUMOR IMMUNE MICROENVIRONMENT OF NON-MUSCLE INVASIVE BLADDER CANCER

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Background While the incidence of non-muscle invasive bladder cancer (NMIBC) is four times higher in men than women, female patients display earlier recurrence than their male counterparts following treatment with Bacillus Calmette-Guerin (BCG) immunotherapy.[1] While patient sex (biological differences) and gender (social/behavioral differences) have long been associated with NMIBC incidence and clinical outcome, these factors remain the most understudied phenotypes in biomarker and treatment design.[2] We hypothesized that sexual dimorphism in the pre-existing tumor immune microenvironment (TIME) may contribute to the poor clinical outcomes observed in female NMIBC patients.

Methods To test this hypothesis, we interrogated the expression patterns of genes associated with specific immune cell populations and immune checkpoint pathways using tumor transcriptome profiles from n=460 NMIBC patients (357 males and 103 females). Based on this interrogation, we utilized multiplex immunofluorescence to selectively evaluate the density and spatial distribution of CD79a+ (B), CD163+ (M2-like tumor associated macrophages), and PD-L1+ (programmed death ligand 1) cells in an independent cohort of 510 NMIBC tumors collected from n=390 patients (305 males and 85 females).

Results We observed significantly higher expression of immune checkpoints genes CTLA4, PDCD1, TIGIT, LAG3 and ICOS in tumors from female patients. Importantly, transcript levels of the B cell recruiting chemokine CXCL13 and the B cell surface molecule CD40 were significantly increased in tumors from female patients. Multiplex immunofluorescence revealed that CD163+ cells were significantly higher in epithelial and stromal compartments of high-grade tumors ($p = 0.0011$, $p = 0.00034$, respectively) from female patients compared to males. While no sex-associated differences were observed in the density of CD79a+ B cells, this population was found to be significantly increased in the epithelial and stromal compartments ($p = 6.9e\text{-}9$, $9.4e\text{-}10$, respectively) of high-grade tumors compared to low-grade tumors. PD-L1 expression was significantly higher in the epithelial compartment of high-grade tumors from female