Introduction

Non-small cell lung cancer (NSCLC) is a leading cause of cancer-related deaths, particularly due to its high propensity to metastasize. Our lab performed an in vivo screen and identified the transmembrane lysosomal protein TMEM106B, a novel driver of NSCLC metastasis. TMEM106B activates transcription factor EB (TFEB) and lysosomal exocytosis which releases cathepsins into the tumour microenvironment (TME) that promote metastasis. Beyond cathepsin release, the mechanism of how TMEM106B mechanistically alters cellular biology and the TME to promote metastasis remains unclear. TFEB is necessary for lysosomal exocytosis, autophagy, invasion in prostate cancer, and activates immune gene transcription. We hypothesize that 1) TMEM106B mediated TFEB activation upregulates autophagy to promote metastasis and 2) TMEM106B is dependent on TFEB to regulate lysosomal exocytosis and secretion in NSCLC, which alter the tumour immune microenvironment (TIME) to become pro-metastatic. It will be crucial to know how TMEM106B mechanistically alters cellular biology and the TIME as this will provide new therapeutic targets and strategies to limit NSCLC metastasis.

Results

- TMEM106B is necessary for NSCLC invasion and metastasis and affects immune signaling genes.
- TMEM106B enhances TFEB nuclear translocation and elevates TFEB target gene expression.
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- TMEM106B overexpression alters the TIME to be immunosuppressive.
- Autophagy flux measured by starving cells in HBSS +/- BafilomycinA1, affecting metastasis and alterations on TIME to affect metastasis.
- TMEM106B mediated alterations on TIME to affect metastasis.

Future Directions

- Perform qPCR immune gene screen and cytokine array to validate immune genes/signaling pathways regulated by TMEM106B as identified by microarray.
- Determine contribution of TFEB as a downstream target of TMEM106B mediated alterations on TIME to affect metastasis.

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