Purpose: Palmar and plantar squamous cell carcinoma (SCC) tumor tissue, and the effects of the extracellular matrix (ECM) on cancer progression have been extensively described. Our study aims to determine if levels of ECM remodeling contribute to metastatic HNSCC. This study aims to determine if HNSCC cells affect the production of these remodeling agents, and how the ECM participates in the activation of mechanotransduction for metastatic phenotype.

Experimental design: Our laboratory has previously generated mouse HNSCC cell line models from primary human cancers and used them to study tumor progression. We have also performed syngeneic tumor implantation in the nude mouse skin pad to study tumor-stromal interactions in the tumor microenvironment in vivo. In this study, we aimed to examine the role of ECM remodeling in the development of metastatic tumors to determine if ECM remodeling can be altered to inhibit metastatic progression.

Methodology: We performed western blot analysis to determine levels of extracellular matrix proteins in metastatic and non-metastatic HNSCC cell lines. We also performed RNAseq analysis to determine mRNA expression levels of ECM remodeling genes. We then compared the expression levels of ECM remodeling genes in metastatic and non-metastatic HNSCC cell lines to determine if there are any significant differences.

Results: In this study, we found that metastatic HNSCC cells exhibit increased expression of ECM remodeling genes compared to non-metastatic HNSCC cells. Additionally, we found that metastatic HNSCC cells have increased migration and invasion rates compared to non-metastatic HNSCC cells. These results suggest that ECM remodeling plays a critical role in the development of metastatic tumors.

Conclusion: ECM remodeling plays a critical role in the development of metastatic tumors. Understanding the mechanisms of ECM remodeling and how it affects metastatic tumor progression could lead to new therapeutic strategies for the treatment of HNSCC.

Hypothesis

SCC cells upregulate laminins and integrin expression to facilitate metastasis.

Methodology

- Syngeneic lines derived from both metastatic and non-metastatic tumors to study both cell autonomous activity and tumor-stromal interactions
- Transwell and scratch assays to assess invasion and migration in vitro
- Evaluate metastatic burden in vivo by subcutaneous and orthotopic tumor transplants
- Transcriptome analysis with RNAseq
- Assess protein expression of PI3K, TGFβ-Smad, and ECM-integrin signaling pathway members by immunoblotting, IF, and IHC

Summary

- Metastatic HNSCC cells have elevated levels of laminins, laminin-binding integrins, and ECM remodeling proteins
- Metastatic HNSCC cells have heightened TGFβ-Smad pathway activity
- Metastatic HNSCC cells have heightened TGFβ-dependent motility

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