Background

- Lymph node metastases is the primary determinant of stage, recurrence risk, and survival in head and neck squamous cell carcinoma (HNSCC).
- The underlying mechanisms driving lymph node spread are unknown.
- One proposed mechanism is the migration of "tumor initiating cells" or TICs from the primary site to the lymph node metastatic niche.
- Microenvironment microarrays are a novel platform for evaluating which growth factors and extracellular matrix proteins lead to cell adhesion, survival and TIC marker expression.
- The Wnt pathway is intimately involved in niche interactions and migration through the non-canonical planar cell polarity pathway.

Microenvironment Microarrays (MEMAs)

- HNSCC cell lines UMSCC-10A, 10B, 22A, and 22B were incubated on microarrays for 5 days and stained with TIC marker CD44.

Wnt 5a Validation

In Vitro

- HNSCC cell lines UMSCC-10A, 10B, 22A, and 22B were incubated on microarrays for 5 days and stained with TIC marker CD44.

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<tr>
<th>Wnt5a</th>
<th>Wnt10b</th>
<th>SDF1α</th>
<th>EGF</th>
<th>Jagged2</th>
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Table 1. Proteins leading to increased CD44 expression in MEMA screen in both primary (A) and lymph node (B) lines.

Wnt 5a Validation

Patient Samples

- MEMAs can yield interesting targets involved in microenvironment niche interactions.
- Inhibition of niche proteins may lead to more effective therapy.
- Non-canonical Wnt5a ligand is overexpressed in HNSCC lymph nodes.
- Non-canonical Jnk inhibitor SP600125 inhibits migration and tumorigenicity indicating this pathway may be a good target for future preclinical studies.
- Ongoing in vitro assays will clarify the interaction between Wnt5a and Jnk pathways and the role of Wnt5a in migration.

Conclusions

Future Directions