



Tumor and Stromal AXL Expression Regulate Ovarian Cancer Metastasis

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Objectives

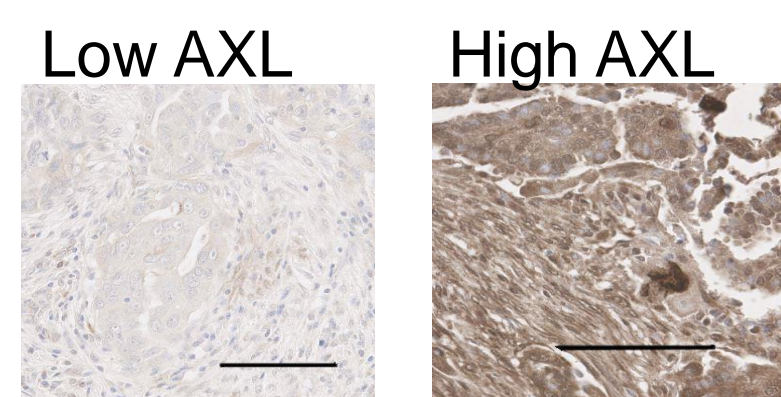
- To evaluate if high AXL expression in metastatic ovarian cancer tumors correlates with survival outcomes.
- To understand the role of tumor and stromal AXL in the key steps of tumor metastasis.

Methods

- HGSOC samples were collected from primary and metastatic tumor sites.
- AXL expression was measured using immunohistochemistry in a tissue microarray
 - 121 samples, 85 matched samples
- Attachment assays and invasion assays were performed
- Mesothelial clearance assays were performed using primary human omentum-cultured mesothelial cells (HPMC)
- Fibroblasts were obtained from patient derived normal omentum
- AVB-500 was supplied by Aravive Biologics

Results

Figure 1: High AXL Expression in Metastatic Tumors is Associated with Decreased PFS & OS



| Multivariate overall survival analysis using a Cox proportional hazard model | | |
|--|--------------|-------------------------|
| Prognostic Factor | Hazard Ratio | 95% confidence interval |
| AXL – Metastasis | 1.805 | 1.034 - 3.145 |
| AXL – Primary | 1.111 | 0.615 - 2.008 |
| Age | 1.044 | 1.019 - 1.070 |
| Stage | 4.926 | 1.493 - 16.39 |
| Residual Disease | 1.531 | 0.911 - 2.571 |

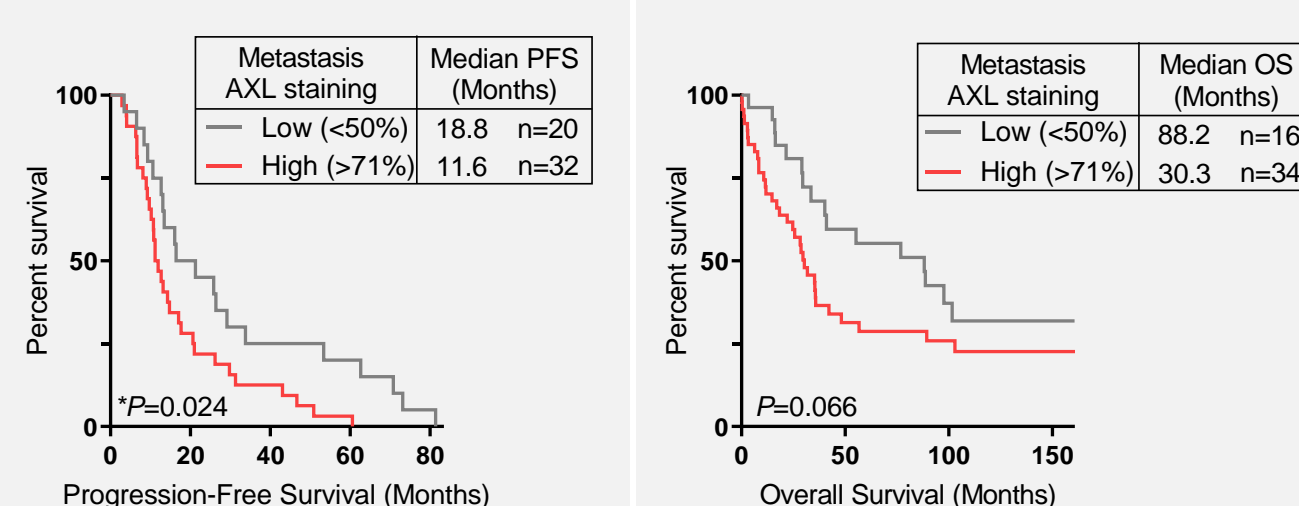


Figure 2: Genetic and Therapeutic Inhibition of AXL Decreases Attachment of Ovarian Cancer Cells

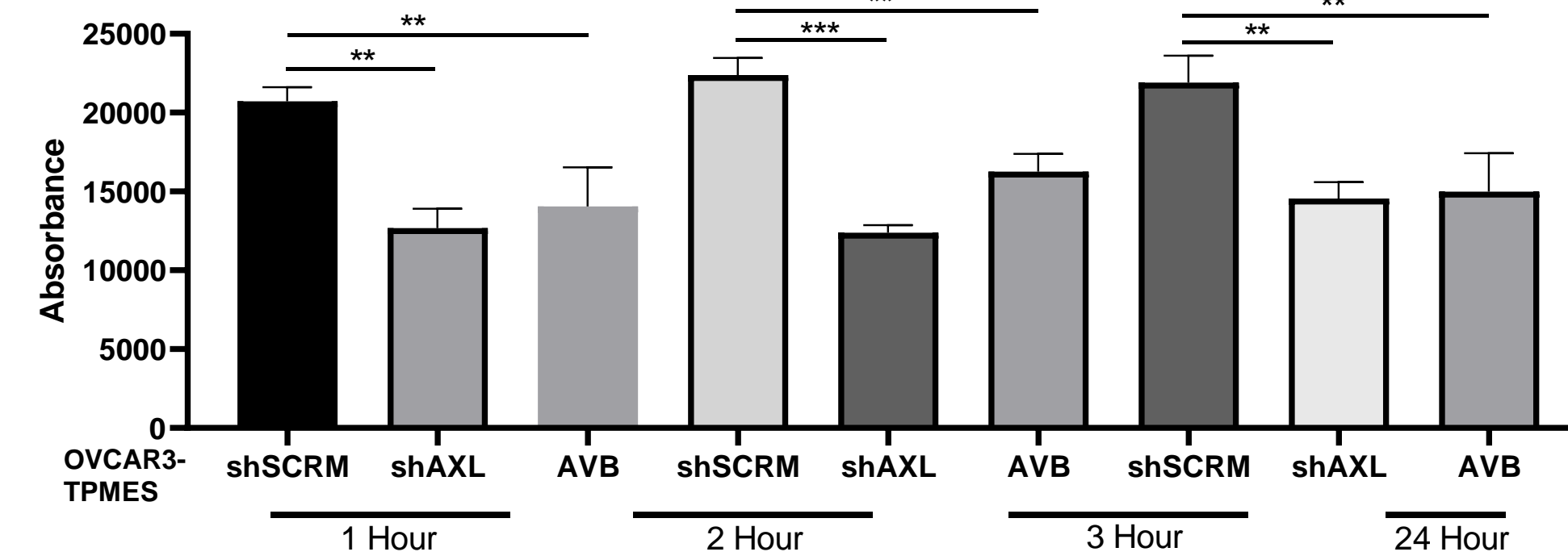


Figure 3: Genetic Inactivation of AXL in Tumor Cells Decreases Mesothelial Cell Clearance

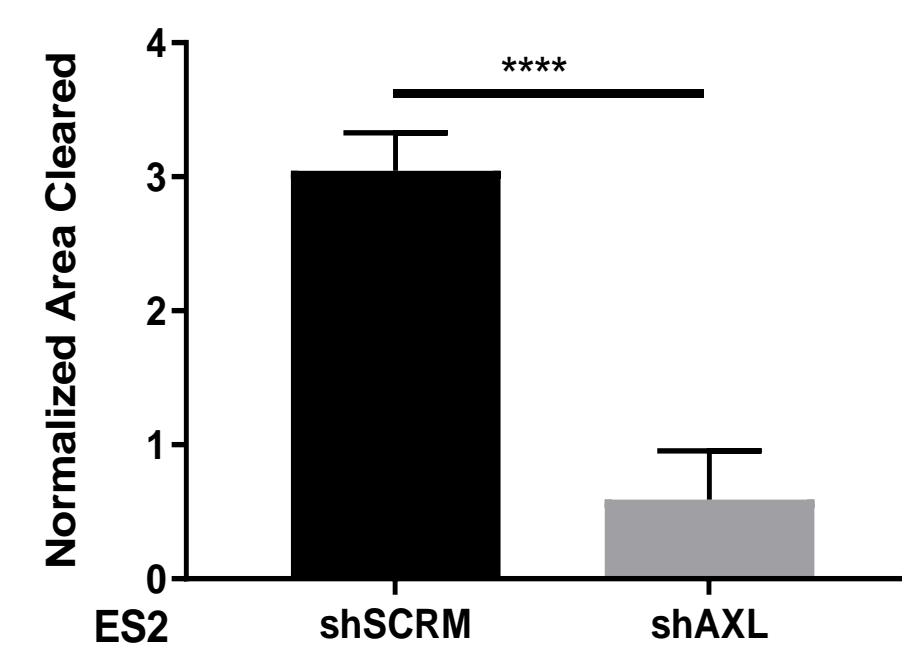
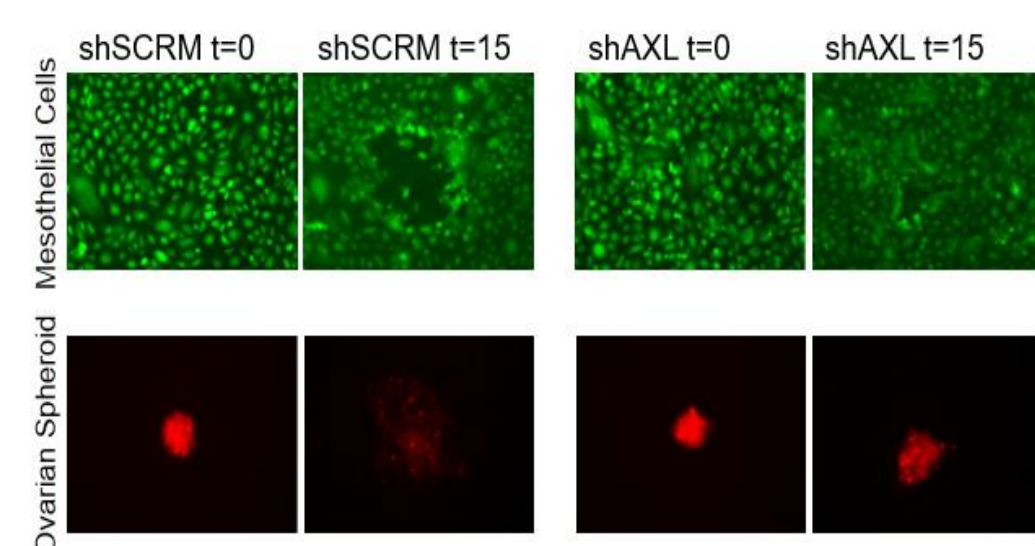
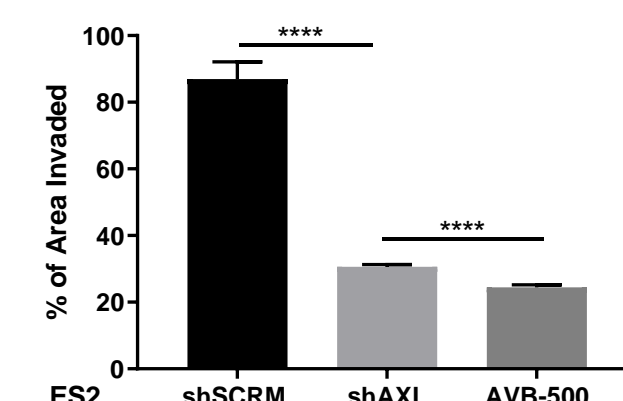
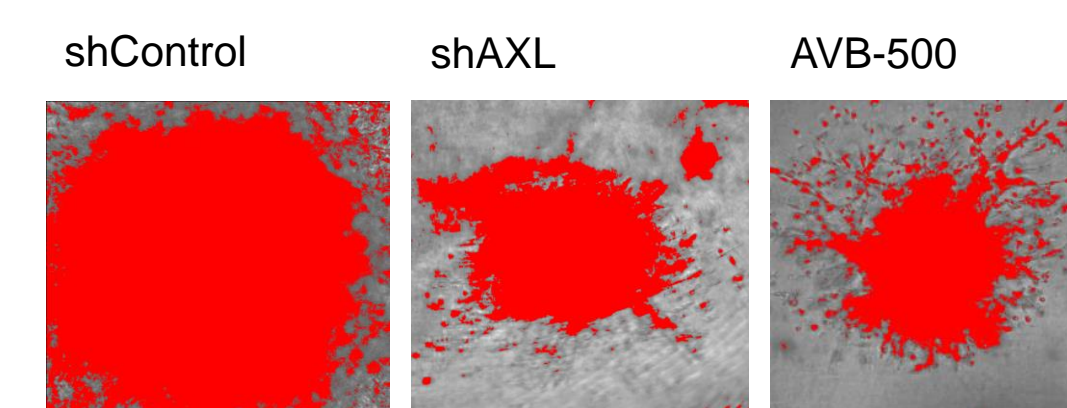
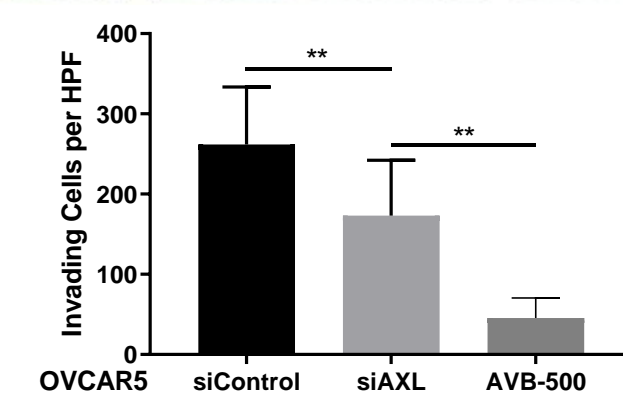
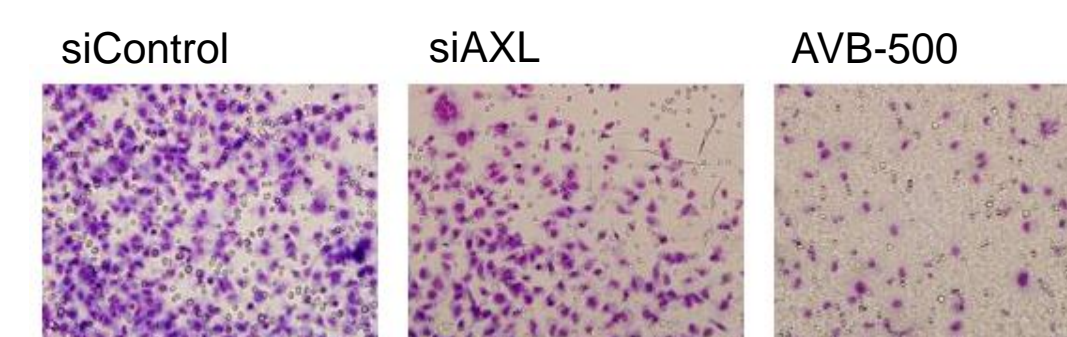


Figure 4: Genetic & Therapeutic Inhibition of AXL Decreases Tumor Cell Invasion



Results

Figure 5: Tumor Cell and Stromal Cell AXL Expression are Directly Correlated

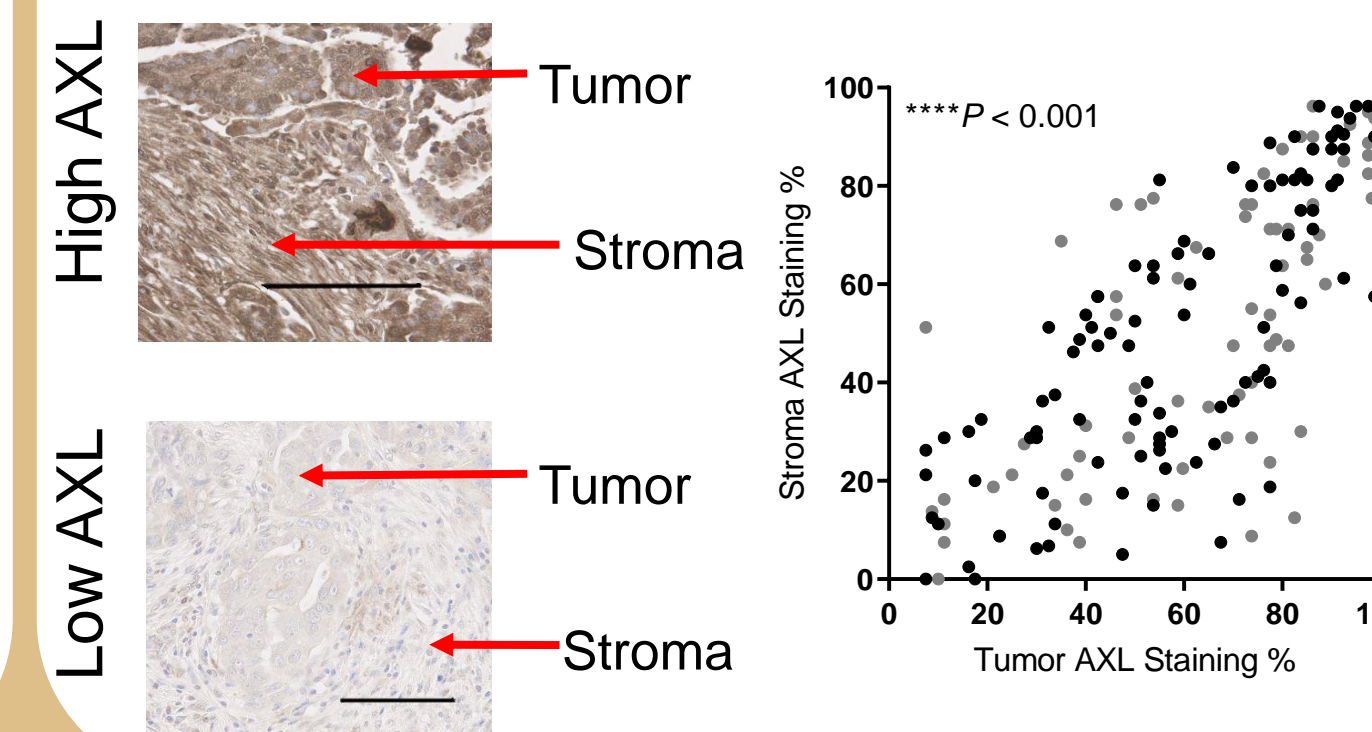


Figure 6: High AXL Expression in Tumor Stroma is Associated with Decrease OS

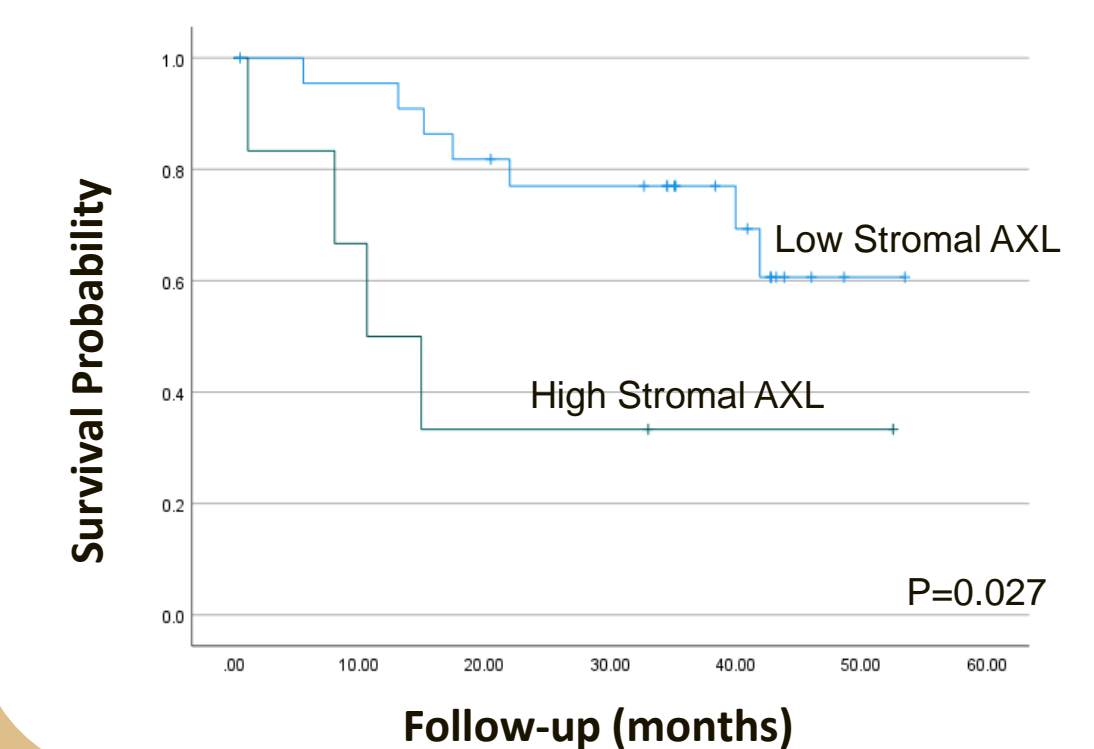


Figure 7: Genetic Inactivation of AXL in Mesothelial Cells Decreases Tumor Cell Clearance of HPMCs

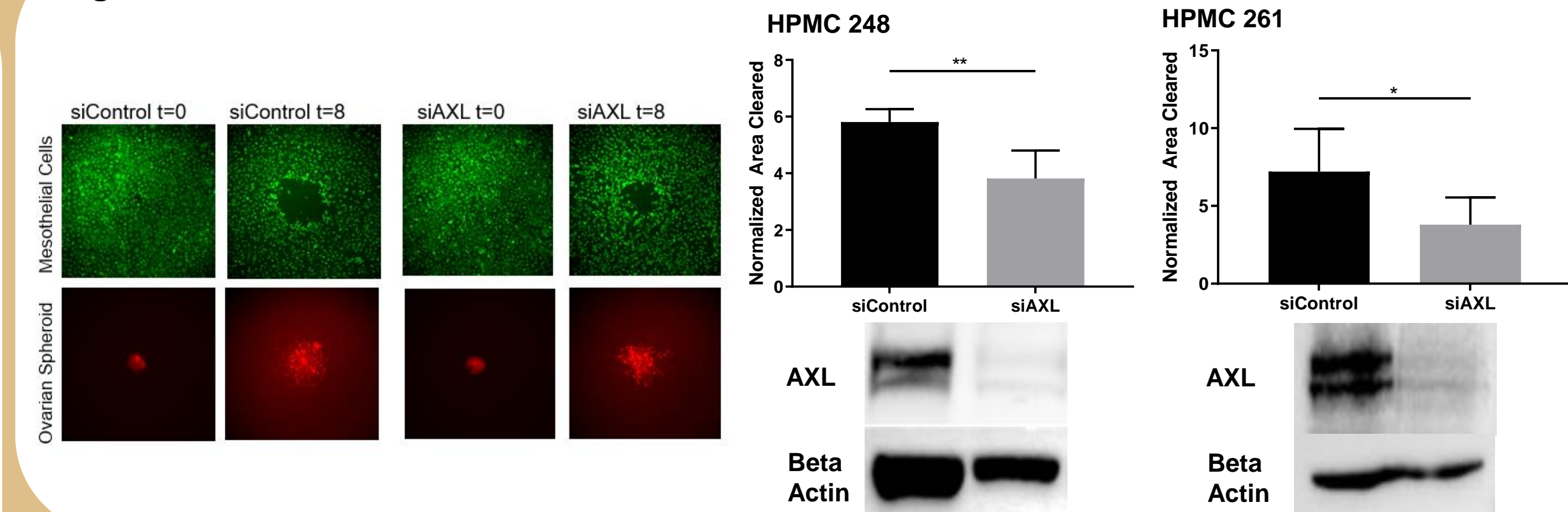
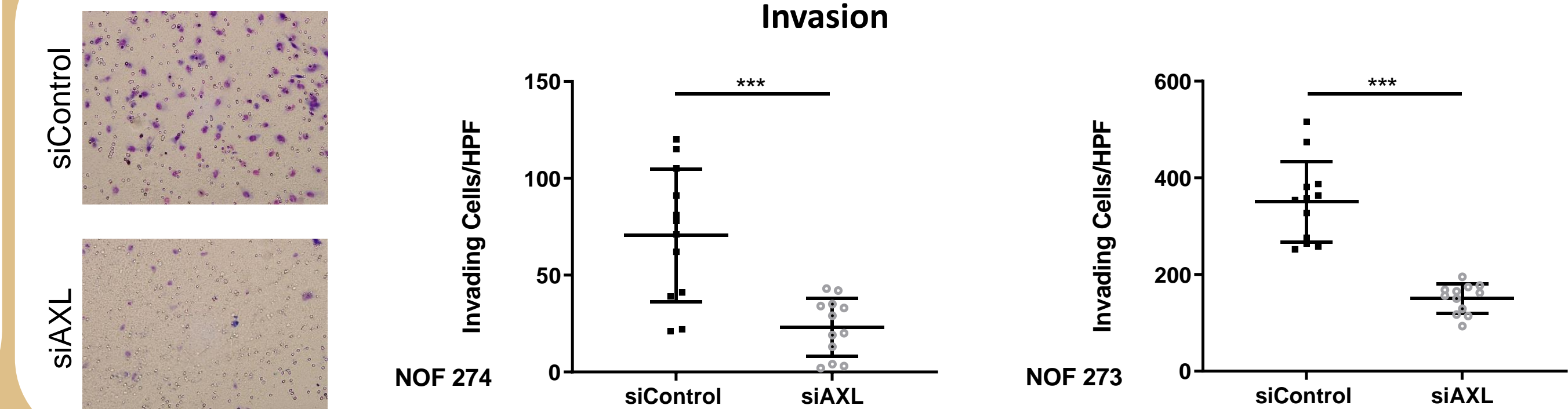


Figure 8: Genetic Inactivation of AXL in Normal Omental Fibroblasts (NOF) Decreases Tumor Cell Invasion



Conclusions

- High AXL expression in metastatic ovarian cancer tumors and associated stromal cells correlates with worse progression-free and overall survival
- AXL expression in ovarian tumor and stromal cells contributes to tumor cell attachment, clearance, and invasion and therapeutic inhibition of AXL can obstruct these key steps of metastasis
- Future studies are necessary to evaluate the use of AVB-500 in the maintenance setting of ovarian cancer

Acknowledgements

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