

OVOL2 Inhibits the Formation of Micropapillary Features in Lung Adenocarcinoma Regulated by Lactation of Histone H3K18

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INTRODUCTION

- Micropapillary pattern in lung adenocarcinoma (LUAD) is a highly aggressive histological subtype prone to metastasis and recurrence, but its driving mechanisms remain poorly understood.
- Genomic profiling shows minimal DNA-level divergence between micropapillary (MP) and acinar components. Instead, transcriptomic differences are prominent, particularly in EMT, cell migration, anti-anoikis, and glycolysis.

METHODS

- Validate OVOL2 expression across expanded clinical cohorts and evaluate its correlation with metastasis and survival.
- Assess the effects of OVOL2 knockout on invasion, EMT, anti-anoikis, and metastasis using cell line models, zebrafish, and mouse xenografts.
- Quantify glycolytic changes, map H3K18la genomic distribution via CUT&Tag sequencing, and confirm transcriptional activation of target genes.
- Evaluate the efficacy of glycolytic inhibition (2-DG) in rescuing MP phenotypes *in vitro* and *in vivo*.

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Figure 1. Downregulation of OVOL2 as a Key Transcriptomic Feature in Micropapillary LUAD.

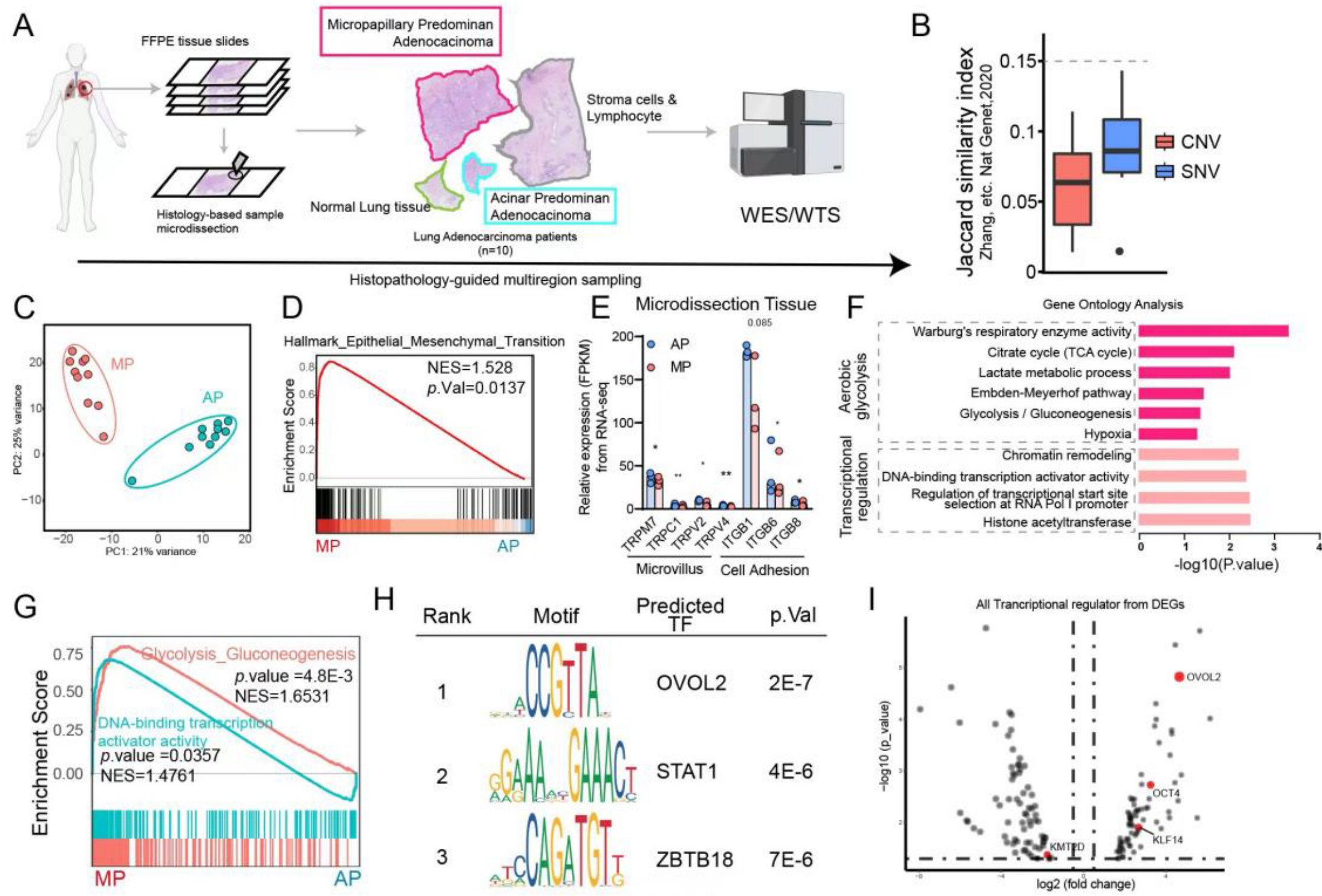


Figure 2. Clinical Significance and Prognostic Value of OVOL2 Downregulation in LUAD.

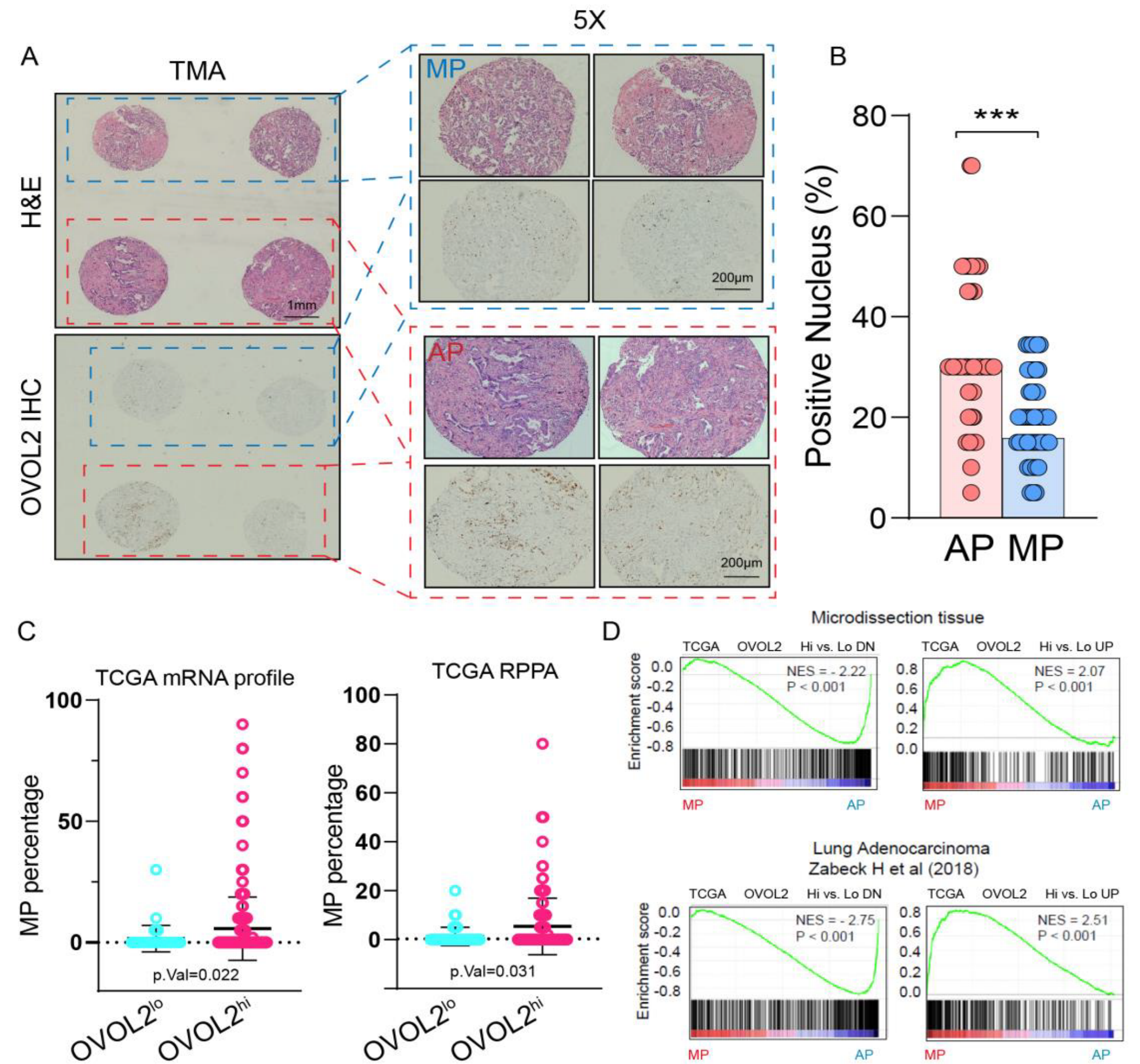


Figure 3. Depletion of OVOL2 Promotes Aggressive Phenotypes and Metastatic Potential.

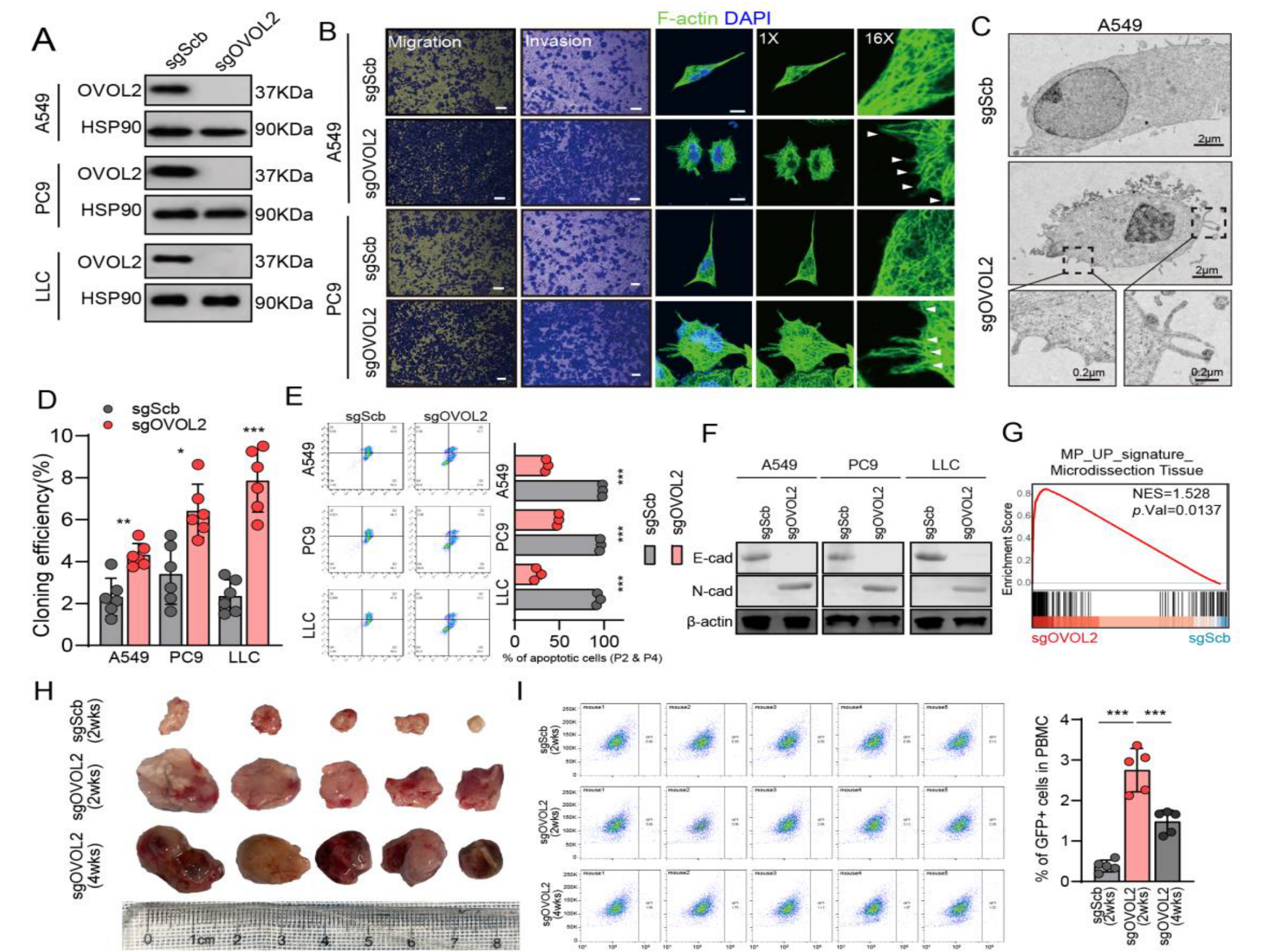


Figure 4. OVOL2 Represses Glycolytic Reprogramming and Lactate Accumulation.

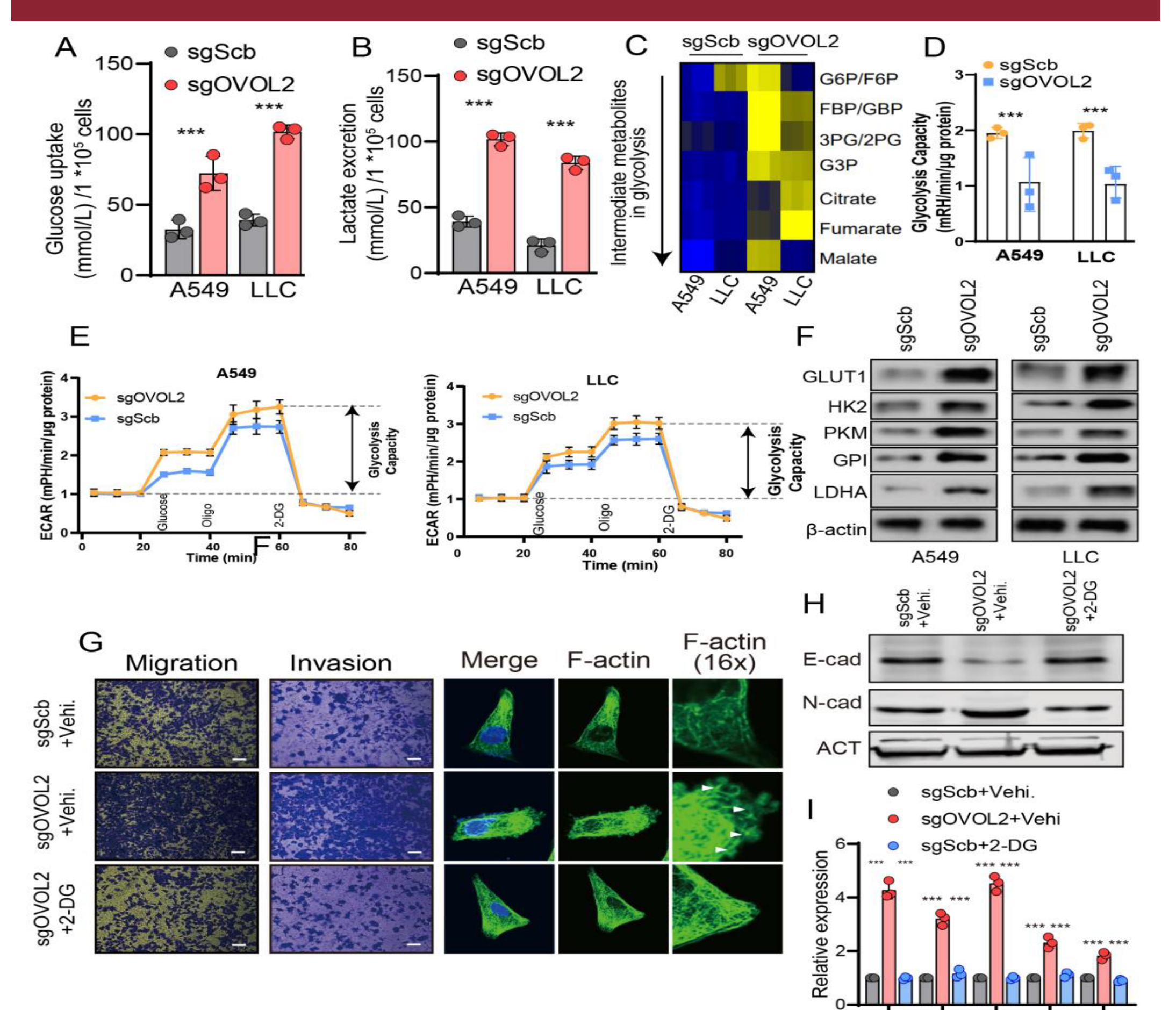
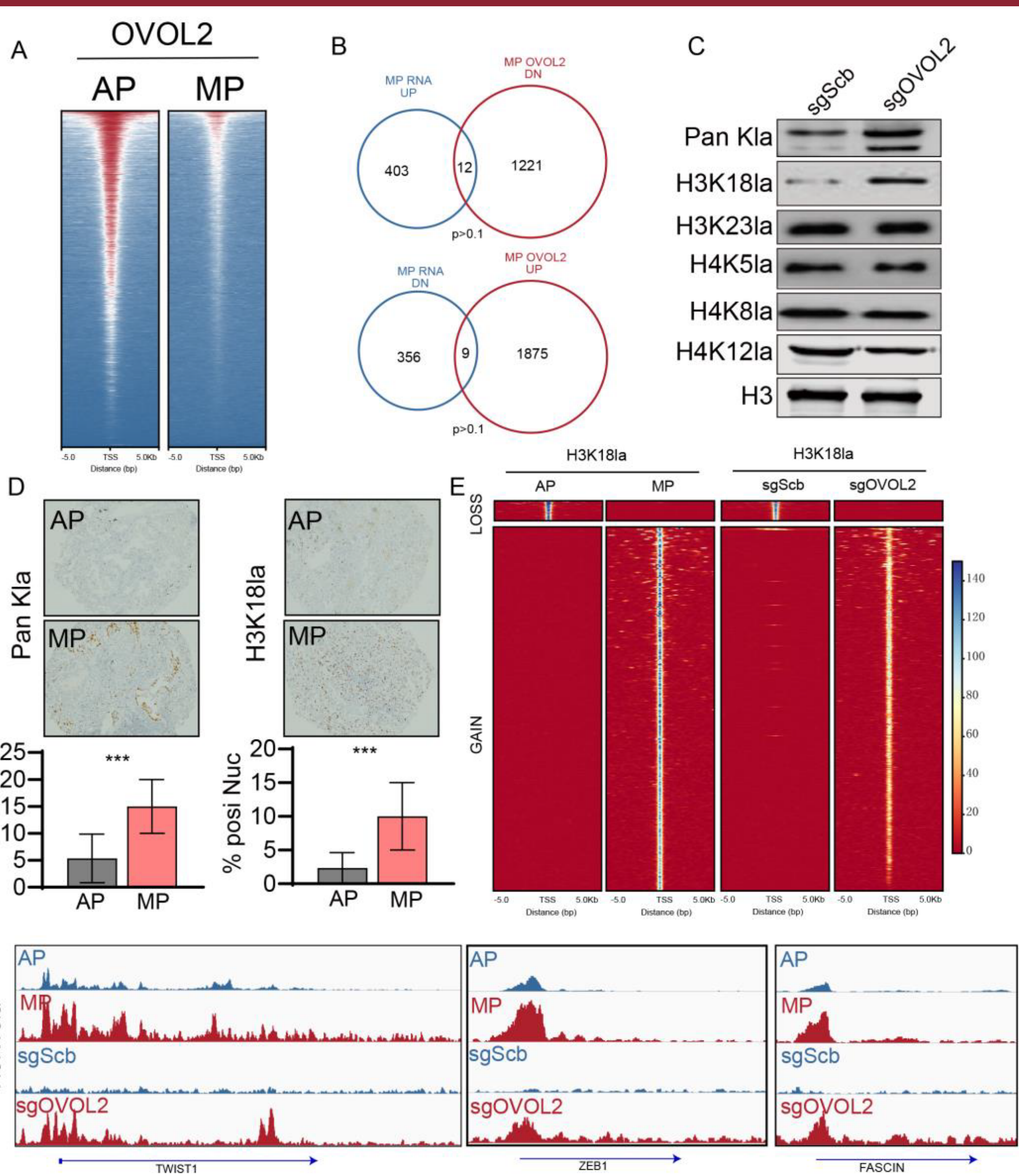


Figure 5. H3K18 Lactylation Mediates Epigenetic and Transcriptional Activation of Invasive Programs.



CONCLUSION

Clarifying how OVOL2 downregulation drives the formation of highly invasive micropapillary features in lung adenocarcinoma by suppressing glycolysis and lactate accumulation, thereby attenuating histone H3K18 lactylation (H3K18la)-mediated transcriptional activation of target genes.