Single cell RNA sequencing analysis of human glioblastoma stem-like cell cultures and xenograft tumors

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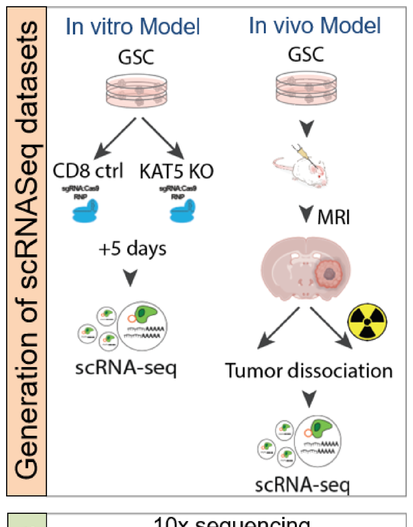
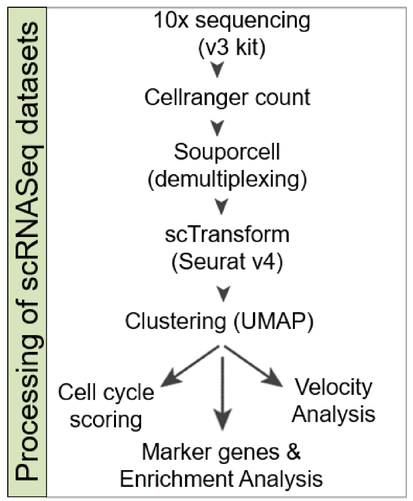
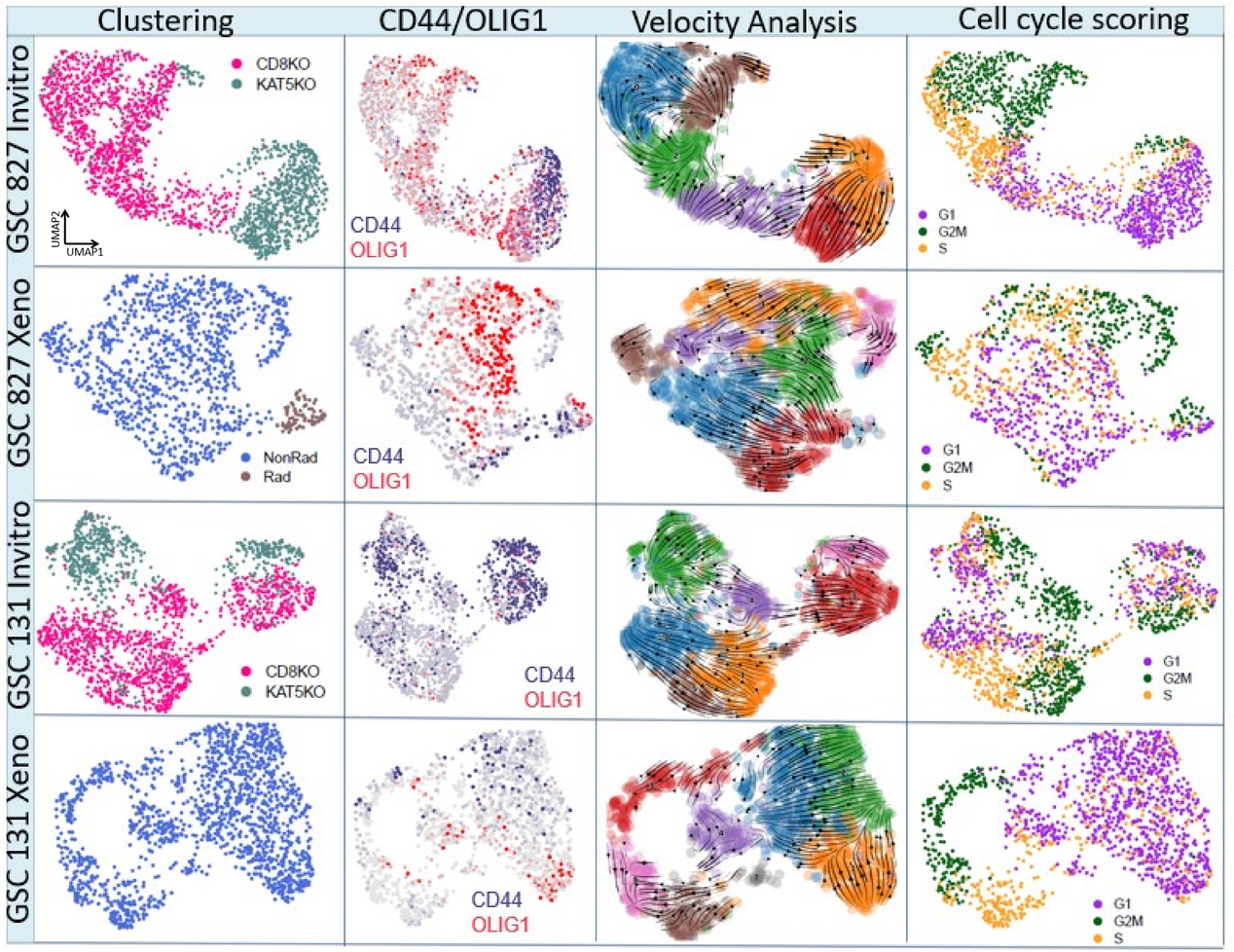
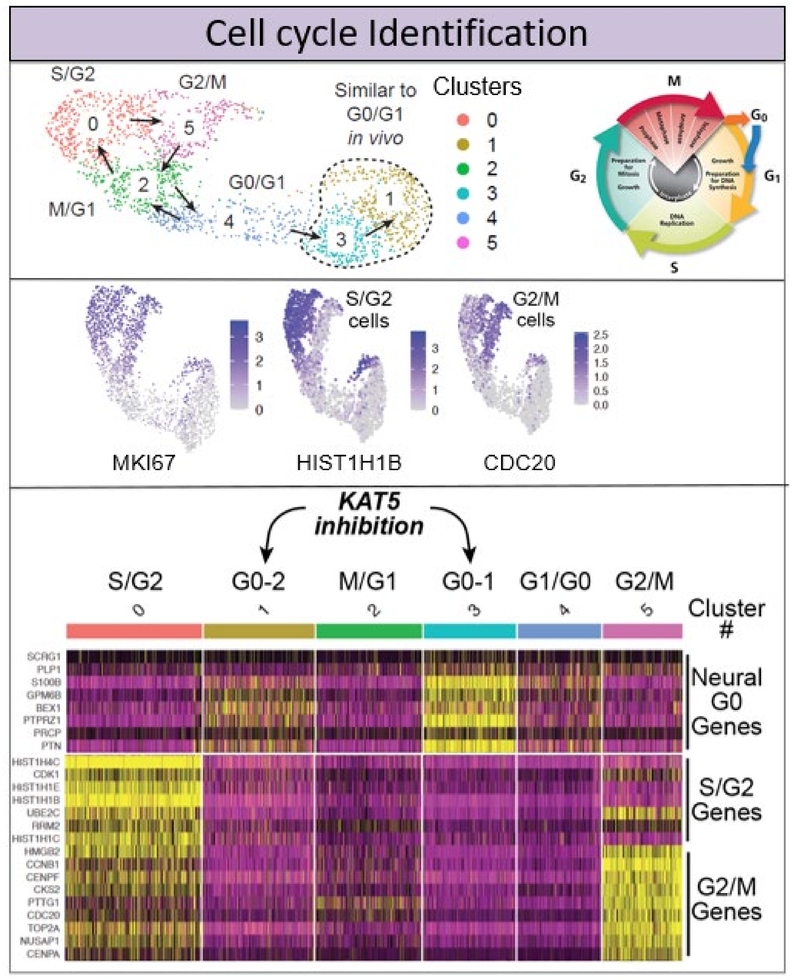
Abstract: Single cell RNA-seq (scRNA-seq) studies for glioma have yielded critical insight into intratumoral heterogeneity and developmental gene expression patterns for primary gliomas. One key conclusion from these studies is that each tumor represents a complex, yet maligned, neuro-developmental ecosystem, harboring diverse cell types, which presumably contribute to tumor growth and homeostasis in specific ways (e.g., vascular mimicry, immune evasion, recreating NSC niches, neural injury responses, etc.). Here, to better understand experimental models of human glioblastoma (GB), we performed single cell RNA-seq analysis of human GB stem-like cells (GSCs) of distinct tumor subtypes (mesenchymal and proneural) during their *in vitro* culture in serum-free conditions and also during tumor formation in immunocompromised mice. This analysis revealed surprising differences between *in vitro* and *in vivo* grown GSCs. Among our results, we find that *in vivo* mesenchymal GSCs are capable of transitioning to proneural-like states, while proneural GSCs are capable of transitioning to mesenchymal states. We characterize cycling cells based on expression of and G2/M and S phase makers, estimate RNA velocity, and examine different developmental trajectories arising *in vitro* and *in vivo*. We also compare and discuss different analysis pipelines for scRNA-seq data.









References

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