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Bioinformatics Approaches Reveal the Pathogenesis of Rare Primary Brain Sarcomas

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Sarcoma is an extremely rare and aggressive cancer that arises in connective tissues and is frequently associated with genetic rearrangements. Primary sarcomas of the brain are exceedingly rare, and their pathogenesis remains poorly understood. In this study, we characterized the cellular and molecular features of primary brain sarcomas at single-cell resolution. We identified evidence suggesting a pericyte-related origin of tumor cells and defined three major tumor subtypes—MYC-related, immune-infiltrated, and neuronal. WT1 emerged as a potential distinguishing transcription factor. The tumor microenvironment was predominantly composed of diverse immune cell populations, with microglia showing marked heterogeneity and dynamic transitions across subtypes. To better understand these features, we compared tumors with the tumor-free subventricular zone, a neurogenic niche, which provided important context for the immune and stromal landscape. Finally, spatial profiling of primary and recurrent tumors revealed key differences in gene expression patterns. Collectively, these findings provide the first comprehensive view of the cellular complexity and molecular landscape of rare primary brain sarcomas, offering novel insights into their biology and potential therapeutic targets.