Deciphering Glioblastoma Multiforme Mechanisms Using an HRASV12-Expressing Transgenic Zebrafish Model and Microglia Interactions

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Glioblastoma multiforme (GBM) is one of the most aggressive and prevalent malignant primary brain tumors, accounting for 50.1% of all gliomas and 16% of all primary brain tumors. In the United States, the incidence of GBM ranges from 0.59 to 3.69 cases per 100,000 people annually. Despite extensive research, GBM remains associated with poor survival rates, a median overall survival of 14.6 months and a 5-year survival rate of below 6%. One of the main challenges in GBM treatment is its late-stage diagnosis, due to the limited understanding of its early developmental stages. To address this gap, we developed an HRASV12-expressing transgenic zebrafish larvae model and a co-culture system to investigate GBM progression and invasiveness. The zebrafish model was established by microinjecting a plasmid containing the oncogenic HRASV12 gene into single-cell stage embryos, allowing for in vivo modeling of early tumorigenesis. Using this model, we performed qPCR and western blot analysis to compare gene expression patterns and protein abundances associated with GBM development. Simultaneously, we established a co-culture system combining microglia and GBM cells to study their interactions and effects on key signaling pathways. This approach enabled us to identify molecular mechanisms that drive GBM progression and provided insights into how microglia influence tumor behavior. Our findings highlight potential therapeutic targets and emphasize the importance of early intervention strategies to improve GBM prognosis. The integration of the zebrafish model with microglia-GBM co-culture offers a powerful platform for exploring novel treatment approaches and understanding the complex cellular interactions underlying GBM pathophysiology.

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