Targeting the cell cycle of medulloblastoma (MB) cancer cells

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Abstract

Medulloblastoma (MB) is the most prevalent malignant tumor of the central nervous system in children. Patients with MB are categorized into high-risk and standard-risk groups based on clinical and histological criteria. The standard treatment approach includes surgical resection aimed at maximal tumor removal, followed by radiotherapy and chemotherapy. Common chemotherapeutic agents used in this regimen include cisplatin, vincristine, cyclophosphamide, and carboplatin. The cell cycle in medulloblastoma (MB) cells is characterized by significant dysregulation, contributing to the aggressive nature of this pediatric brain tumor.

This study focuses on analyzing the cell fate of SHH-driven MB cell lines (ONS76, DAOY, and UW228) and Group 3 MB cells (MB03). We investigated cell doubling times, determined cell size prior to division, and evaluated the response of SHH-driven DAOY cells to various doses of standard chemotherapy agents. The goal was to identify differences in cell cycle progression and its disruption due to chemotherapy, aiming to uncover potential therapeutic targets that could improve MB treatment.

Our findings characterize the response of MB cell lines to chemotherapeutic drugs, observing expected outcomes such as cell death during interphase with cisplatin and during mitosis with vincristine. However, we also identified heterogeneous cell fates, which may contribute to drug resistance. Additionally, we established an experimental setup using the G1 FUCCI system to monitor MB cell progression through the G1 phase of the cell cycle. This system will be further employed to assess differences in cell cycle timing across MB cells with varying genetic backgrounds. Understanding MB cell cycle dynamics can lead to developing therapeutic strategies targeting specific phases of the cell cycle to develop more effective treatments against MB.

Key words: Medulloblastoma, DAOY cells, cisplatin, vincristine, cell fate, cell cycle, mitosis