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Abstract

The Suppression of Medulloblastoma Cell Migration Using Clinically Significant Doses of Simvastatin through Mevalonate Pathway Targeting †

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Aims: Medulloblastoma (MBs), the most prevalent malignant paediatric brain tumour, exhibits distinct subgroups—Wingless (WNT), Sonic Hedgehog (SHH), Group 3 (G3), and Group 4 (G4)—and each is characterized by unique molecular signatures and clinical outcomes. Despite being the most aggressive, Group 3 (G3) and Group 4 (G4) remain the least understood. Current treatments, involving surgical resection, radiation, and chemotherapy, are associated with significant morbidity and adverse effects. This study aims to explore the potential of clinically significant doses of simvastatin, known for its ability to penetrate the blood-brain barrier, as a targeted and less toxic therapy for aggressive MBs.

Method: In-silico gene expression analysis assessed mevalonate pathway (MVP) enzyme expression in MBs, corroborated by immunocytochemistry and RT-PCR in SHH, G3, and G4 cells. The anti-cancer and anti-metastatic properties of low doses of simvastatin were investigated through both 2D and 3D cell culture methods.

Results: Our findings reveal that clinically significant doses of simvastatin effectively reduce the migration of MBs cells in both 2D and 3D in vitro cultures.

Conclusions: This study establishes simvastatin as a promising therapeutic candidate for mitigating MBs cell invasion, offering a potential avenue for the development of novel and less invasive treatment strategies for MBs tumours.

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