MB-25 SUPPRESSION OF LEPTOMENINGEAL DISSEMINATION OF MEDULLOBLASTOMA BY PANOBINOSTAT, A HISTONE DEACETYLASE INHIBITOR

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Medulloblastoma (MB) with leptomeningeal dissemination (seeding) is associated with significant morbidity and poor prognosis. Novel therapeutic approaches are required because the prognosis of the patients with disseminated MB is dismal despite intensified therapies. The cause and cellular mechanism of MB seeding may be related to epigenetic changes. Therefore, we focused on the therapeutic effect of a histone deacetylase (HDAC) inhibitor, panobinostat for MB dissemination in vitro and in vivo. After treatment of panobinostat to 3 human MB cell lines, changes in the cell viability, proliferation, apoptosis, and cell cycle were assessed. After treatment of panobinostat, MB cell viability and proliferation were decreased. G2 arrest in cell cycle and increased apoptosis were noted. Cell migration and adhesion assays showed significantly decreased migration and adhesion capacity of tumor cells with panobinostat. We observed decreased expression of ID3, a key molecule regulating MB dissemination, and increased neuronal differentiation markers such as NeuroD1 and synaptophysin. To determine the therapeutic efficacy of panobinostat in vivo, a MB mouse model with leptomeningeal dissemination was used. Bioluminescence imaging revealed that panobinostat treatment effectively decreased dissemination of MB cells to the spinal subarachnoid space. The median survival of drug-treated mice was significantly increased compared with the control. Taken together, we suggest that the HDAC inhibitor, panobinostat can be a potential therapeutic agent for the treatment of MB with leptomeningeal dissemination.