Phosphodiesterase-4 Inhibition and Brain Tumor Growth

We appreciate the interest of Drs. Roessler et al. in our work on PDE4A1 and rolipram in brain tumors. Consistent with the data described in their letter, we previously published that rolipram inhibits the in vivo growth of intracranial xenografts of Daoy medulloblastoma cells in nude mice (1). In these studies, we found that systemic administration of 5 mg/kg/d of rolipram inhibited Daoy xenograft growth by 58% over a 7-week treatment period. Based on these data we also suggested that rolipram might have efficacy in the treatment of patients with medulloblastoma.

Drs. Roessler et al. make an excellent point regarding the potential for rolipram and cyclic AMP (cAMP) elevation to promote the growth of some tumors. This could clearly be an issue in the treatment of tumors derived from lineages whose growth is stimulated by cAMP. For example, cAMP stimulates the proliferation of Schwann cells (2) and therefore it might be anticipated that rolipram might stimulate the growth of tumors derived from this lineage. cAMP, however, is known to inhibit the proliferation of astrocytes (3) and to promote their differentiation (4). Further, it has previously been established that cAMP levels are inversely correlated with brain tumor grade (5, 6). Finally, rolipram has also been shown to inhibit the growth of the human glioblastoma cell line A-172 (7). Thus, although we agree that the results with U-138MG suggest that caution is necessary, we anticipate that cAMP elevation will have utility in the treatment of malignant brain tumors, including astrocytomas.

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Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

References

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