

論 文 要 旨

Reduction of MLH1 and PMS2 confers temozolomide resistance and is associated with recurrence of glioblastoma

MLH1発現抑制とそれに伴うPMS2の発現低下が
神経膠芽腫のTMZ耐性獲得に寄与する

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Although there is a relationship between DNA repair deficiency and temozolomide (TMZ) resistance in glioblastoma (GBM), it remains unclear which molecule is associated with GBM recurrence. We isolated three TMZ-resistant human GBM cell lines and examined the expression of O₆-methylguanine-DNA methyltransferase (MGMT) and mismatch repair (MMR) components. We used immunohistochemical analysis to compare MutL homolog 1 (MLH1), postmeiotic segregation increased 2 (PMS2) and MGMT expression in primary and recurrent GBM specimens obtained from GBM patients during TMZ treatment. We found a reduction in MLH1 expression and a subsequent reduction in PMS2 protein levels in TMZ-resistant cells. Furthermore, MLH1 or PMS2 knockdown conferred TMZ resistance. In recurrent GBM tumours, the expression of MLH1 and PMS2 was reduced when compared to primary tumours.