Medical Xpress

SNAP reverses chemotherapy resistance in human tumor cells through downregulation of MGMT

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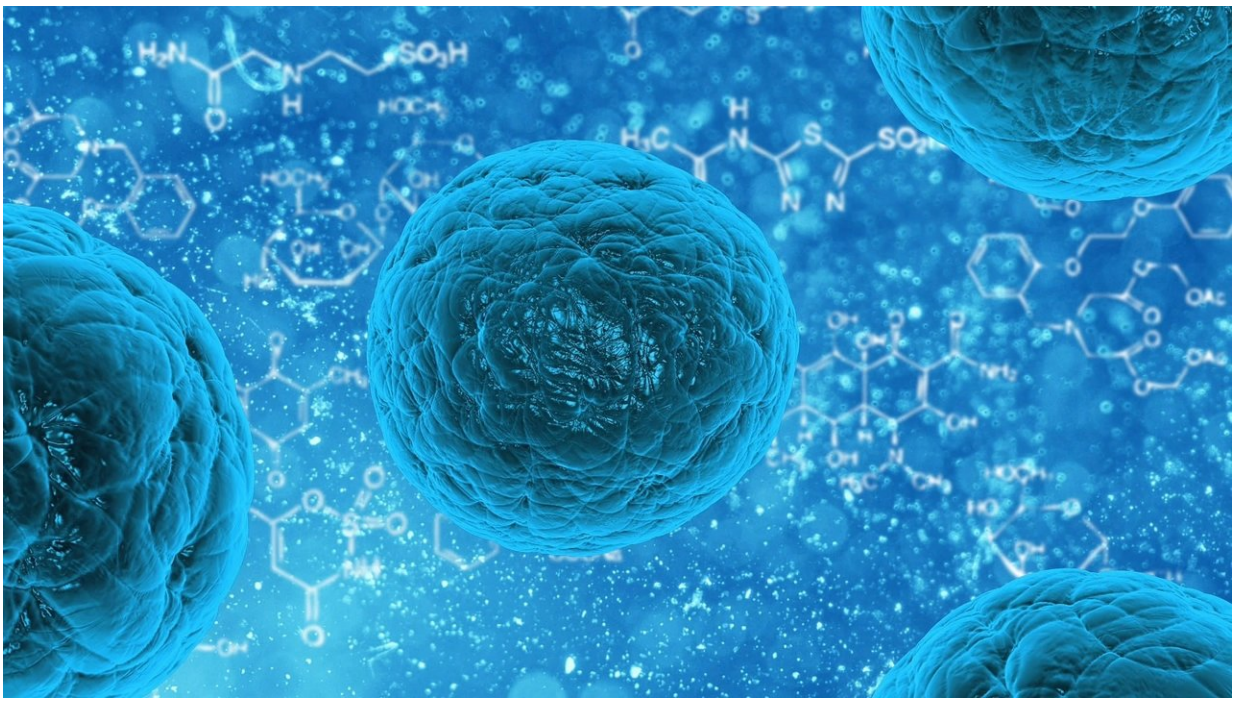

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Glioblastoma multiforme, or GBM, is the most frequently occurring and gravest primary tumor of the central nervous system in adults. Poor survival rates among patients with GBM are associated with the development of resistance to chemotherapy drug temozolomide (TMZ).

A recent study in *The FASEB Journal* sheds light on a potential strategy to overcome TMZ resistance in GBM cells.

The researchers established two lines of human TMZ-sensitive GBM cells and two lines of TMZ-resistant GBM cells. The TMZ-sensitive and TMZ-resistant cells were then exposed to a nitric oxide donor called SNAP (S-nitroso-N-acetylpenicillamine) to assess cell growth and proliferation.

The researchers observed that exposure to SNAP halted cell proliferation in the TMZ-resistant cells, thereby demonstrating a re-sensitization to TMZ. The study further revealed that SNAP overcomes TMZ resistance by decreasing the protein stability of MGMT, a DNA repair enzyme that leads to TMZ resistance.

The researchers also tested the drug treatment in vivo using orthotopic tumor grafts in a group of mice. The study demonstrated the same effect of SNAP on the TMZ-resistant GBM cells in vivo.

"Downregulation of MGMT expression could be an attractive strategy for overcoming TMZ resistance in GBM treatment," said Dueng-Yuan Hueng, MD, Ph.D., associate professor and chief of the division of brain tumors at the Department of Neurological Surgery, Tri-Service General Hospital, National Defense Medical Center, in Taipei, Taiwan. "We hope these findings will have implications for the treatment of glioblastoma in the future."

"Even when the biochemical basis of tumor drug resistance is known, finding a circumvention is typically challenging. This study is most encouraging, especially given the clinical severity of GBM," said Thoru Pederson, Ph.D., Editor-in-Chief of *The FASEB Journal*.