D609

In a study Kalluri et al. examined the role of anti-oxidative stress on the expression of GADD45B in glioma stem like cells (GSC). They show that patient derived GSCs have high survival in the absence of exogenous growth factors. Addition of D609 (Tricyclodecan-9-yl-xanthogenate), a known anti-oxidative compound, to GSCs reduced the cellular ATP content with significant effects observed when GSCs were cultured in growth factor free medium. D609 exposure also resulted in a decrease in the protein and an increase in mRNA of GADD45β with a concomitant decline in the survival of cells. However, under similar conditions the phosphorylation of p38 MAP kinase (stress activated MAP kinase), a downstream target of GADD45β, was significantly enhanced in response to D609. Therefore it appears that GADD45β might play a role in glioma stem cell survival and that p38 MAP kinase may not be directly activated by GADD45β. Together these observations suggest that anti-oxidative compounds like D609 can target GADD45β which may be one strategy to curtail the growth of glioma stem like cells ¹⁾.

They examined the effect of chronic D609 treatment on GSCs cultured in complete medium containing growth factors. The results show that chronic exposure of GSCs to D609 decreased the ATP content and reduced the expression of GADD45 β protein. Furthermore, cyclin D1 content and the phosphorylation of retinoblastoma protein also diminished, resulting in the arrest of cells in G1 phase of cell cycle after D609 treatment. In addition, the expression of Olig2, a protein responsible for the progression of glioblastoma was reduced by D609. Together these results indicate that chronic D609 treatment can inhibit the growth of glioma cells by arresting cells in G1 phase of cell cycle and/or reducing Olig2 expression ²⁾.

This could represent a new molecular approach in glioma biology not only for its ability in modulating cell metabolism, glioma growth and motility, but also for its inhibitory effect on crucial molecules involved in cancer progression ³⁾.

1)

Kalluri HS, Kuo JS, Dempsey RJ. Effect of D609 on the expression of GADD45β protein: Potential inhibitory role in the growth of glioblastoma cancer stem like cells. Eur J Pharmacol. 2016 Nov 15;791:510-517. doi: 10.1016/j.ejphar.2016.09.026. Epub 2016 Sep 20. PubMed PMID: 27658347.

Kalluri HSG, Kuo JS, Dempsey RJ. Chronic D609 treatment interferes with cell cycle and targets the expression of Olig2 in Glioma Stem like Cells. Eur J Pharmacol. 2017 Aug 10. pii: S0014-2999(17)30505-8. doi: 10.1016/j.ejphar.2017.08.001. [Epub ahead of print] PubMed PMID: 28802717.

Mercurio L, Cecchetti S, Ricci A, Pacella A, Cigliana G, Bozzuto G, Podo F, Iorio E, Carpinelli G. Phosphatidylcholine-specific phospholipase C inhibition down- regulates CXCR4 expression and interferes with proliferation, invasion and glycolysis in glioma cells. PLoS One. 2017 Apr 19;12(4):e0176108. doi: 10.1371/journal.pone.0176108. eCollection 2017. PubMed PMID: 28423060; PubMed Central PMCID: PMC5397108.

From: https://neurosurgerywiki.com/wiki/ - **Neurosurgery Wiki**

Permanent link: https://neurosurgerywiki.com/wiki/doku.php?id=d609

Last update: 2024/06/07 02:55



1/2

https://neurosurgerywiki.com/wiki/