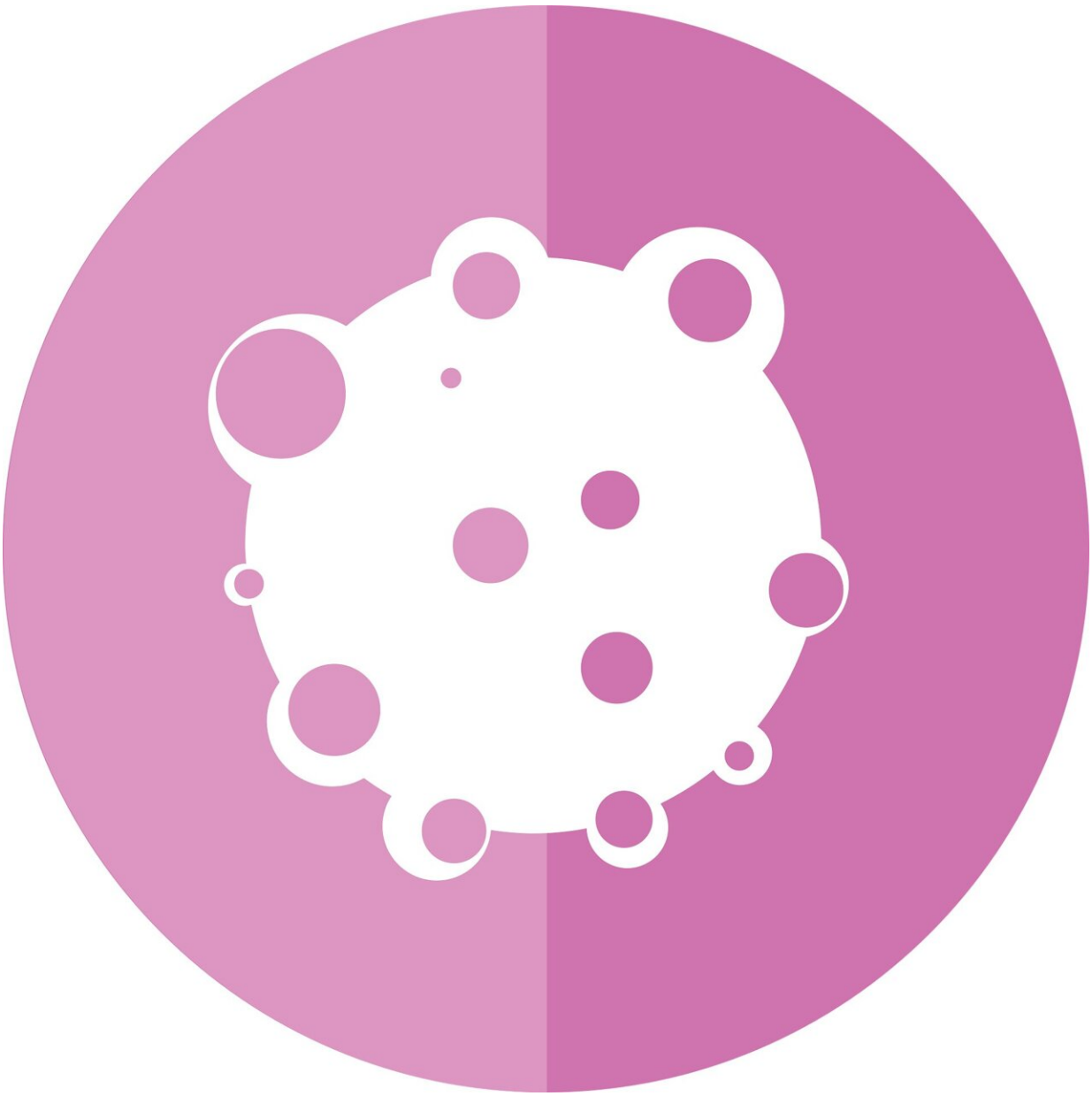
Editorial: GBP3-STING interaction in glioblastoma coordinates poor response to temozolomide

October 17 2023



Credit: Pixabay/CC0 Public Domain

A new editorial paper was published in *Oncotarget*, titled "GBP3-STING interaction in glioblastoma coordinates autophagy, anti-oxidative, and DNA repair programs in response to temozolomide."

In their recent editorial, researchers Jun Ma, Ziyu Wang, Clark C. Chen, and Ming Li from the University of Minnesota discussed the methylating agent, Temozolomide (TMZ). TMZ is the standard adjuvant chemotherapeutic drug for glioblastoma, which constitutes 17.7% of overall primary central nervous system tumors. The survival rate of this WHO Grade IV tumor has achieved a clinically significant prolongation of 2.5 months overall and an increase of 16.3% 2-year survival rate. However, one intractable challenge is the diverse reactions to temozolomide treatment.

"The acquired resistance to the standard adjutant radiochemotherapy including temozolomide has favored the recurrence of some glioblastoma cases and has kept the milestone from moving forward for more than 15 years," write the researchers.

Guanylate-binding proteins (GBPs) are a group of dynamin-related large (~65 kDa) GTPases expressed in response to interferon and mediate intracellular immunity. Consisting of 7 members in humans, little is known about the function of GBPs beyond their role in innate cellular immunity. After recent years of dedication to the GBP family, its role in glioblastoma's development and recurrence has drawn great attention.

"More recently, Li's lab did informatic analysis of clinically annotated

glioblastoma datasets, laboratory studies of protein-protein interaction, and functional characterization after depletion or exogenous expression," the authors say.

GBP family members such as GBP1, GBP2, GBP3, and GBP5 are highly elevated and play pro-tumor roles through multiple mechanisms in glioblastoma. Although other GBP family members did not show a prominent relationship with treatment resistance at the present stage, GBP3 showed significant up-regulation in response to temozolomide. Furthermore, it's revealed that high levels of GBP3 expression in glioblastoma was associated with a worsened survival after temozolomide treatment. Consistent with this observation, exogenous expression of GBP3 induced temozolomide resistance in independent patient-derived glioblastoma neurosphere lines, while GBP3 silencing conferred temozolomide sensitivity, both in vitro and in vivo.

"This sensitivity was associated with the accumulation of cytoplasmic DNA fragments, suggesting the involvement of Stimulator of interferon genes (STING)," conclude the researchers.

More information: Jun Ma et al, GBP3-STING interaction in glioblastoma coordinates autophagy, anti-oxidative, and DNA repair programs in response to temozolomide, *Oncotarget* (2023). DOI: 10.18632/oncotarget.28370

Provided by Impact Journals LLC