Stimulator of interferon genes (STING) activation triggers immune surveillance and inhibits tumor growth in glioblastoma

Soo Yeon Baek[a], Sanghee Lee[a,b]*

[a] Brain Science Institute, Korea Institute of Science and Technology, Seoul 02792, Republic of Korea
[b] Department of HY-KIST Bio-convergence, Hanyang University, Seoul 04763, Republic of Korea

E-mail: baeksoo@kist.re.kr

Glioblastoma multiforme (GBM) is one of the most malignant brain tumors. However, tumor heterogeneity, recurrence, and chemoresistance make it difficult to treat GBM. The lack of immune response in GBM limits the application of immunotherapy in clinical trials. To address the weak immune cell infiltration in GBM, we focused on innate immunity triggered by stimulator of interferon genes (STING)-mediated type I interferon response. Bioinformatics analysis of patients with GBM revealed that STING expression correlates with survival by modulating the immune landscape of tumor microenvironment (TME) in GBM. STING-mediated type I interferon response induced apoptosis in both STING-expressing and STING-deficient GBM through direct activation or microglial activation, respectively. The pharmacological activation of STING effectively inhibited tumor growth in patient-derived GBM cells and in vivo models by altering the immunophenotype of GBM. Furthermore, STING agonist inhibited temozolomide-resistant tumors in cells and mouse model. Therefore, we unveiled the bridge role of STING between innate immune activation in microglia and adaptive immune activation of TME in GBM and demonstrated its valuable therapeutic potential to overcome chemoresistance and treat brain tumors.

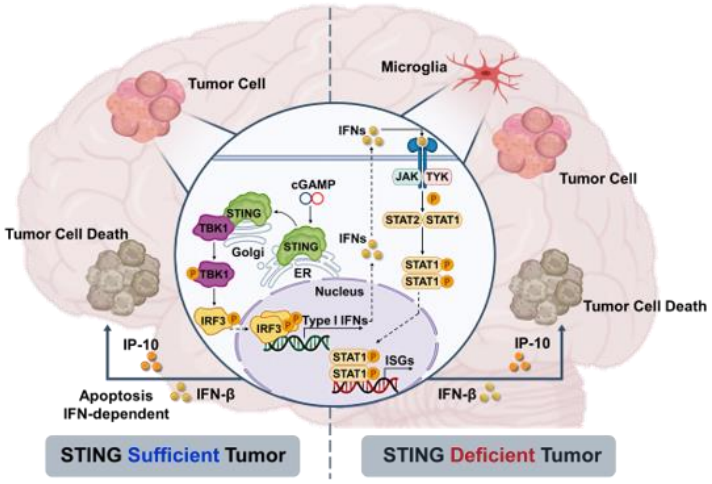

Figure 1. Schematic figure for the mechanism of STING agonist-induced cell death in glioblastoma.