



MARKET CHALLENGES

Cancer cells endowed with self-renewal, differentiation and tumor-initiating properties have been isolated from many malignancies, including brain neoplasms. In the brain, they have been most frequently reported in glioblastoma, the most common and malignant primary brain tumor in adults. This malignant glioma remains without successful treatment, all patients relapsing despite aggressive multimodal therapies. Targeting glioma-initiating cells constitutes one of the main therapeutic challenges to significantly improve anti-cancer treatments.



INNOVATIVE SOLUTIONS

Pr Chneiweiss and his team demonstrated that the exposure of Glioma Stem Cells (GSC) to Gamma-Hydroxybutyric acid (GHB) inhibits their self-renewal potential. In particular, GHB administration triggers decrease of Nanog protein levels, the delocalization of this stemness marker from the nucleus and a decrease in cell proliferation. Under this non stem-like state, the cells lose their tumorigenicity and might become more vulnerable to standard therapies.



SUGGESTED APPLICATIONS

Treatment of adult or pediatric glioblastomas, in combination with standard chemotherapy or radiotherapy.

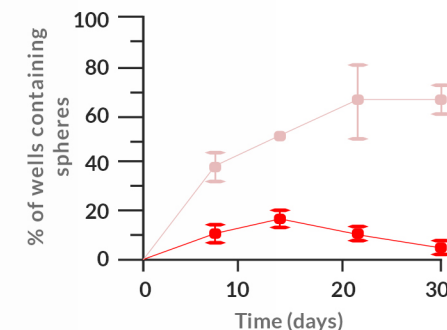
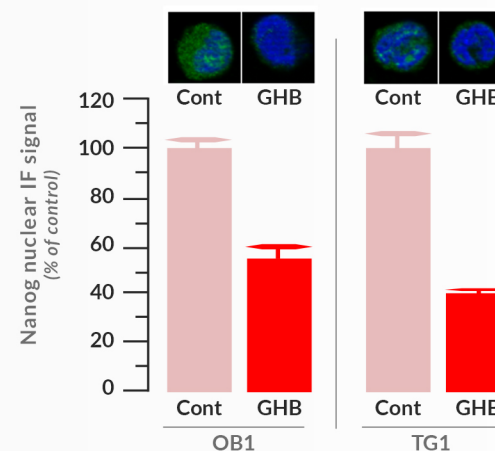
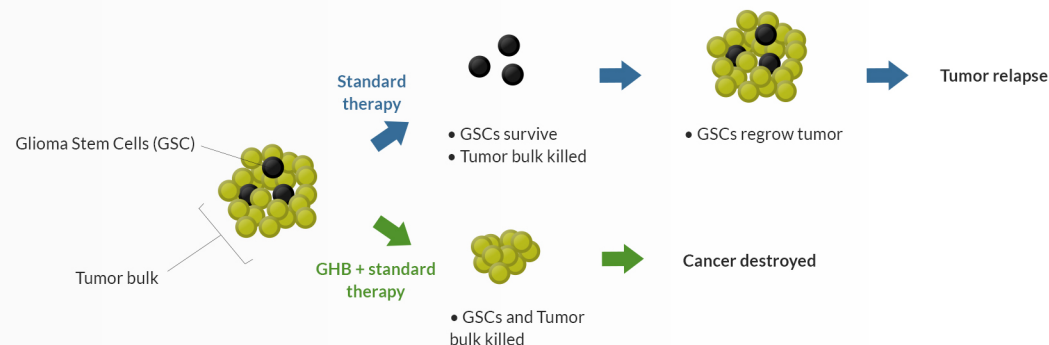


DEVELOPMENT STATUS

GHB has been administered to patient-derived GSC in ex vivo experiments. GHB inhibitory effects were observed on GSC derived from distinct malignant gliomas of adult and pediatric patients, each bearing different genetic alterations.

The team dissected mechanism of action of GHB: it acts via a non-canonical pathway, by inhibiting TET methylcytosine dioxygenases that oxidize 5-methylcytosine (5-mC) into 5-hydroxymethylcytosine (5-hmC).

These epigenetic marks regulate in turn the transcription of the genes involved in stemness maintenance. Preclinical studies in mice bearing orthotopic xenografts are now being planned.



COMPETITIVE ADVANTAGES

- Targets GSC and contributes to eliminate tumors recurrence
- Effective for resistant cancers in combination with other treatments
- GHB is able to cross the blood-brain-barrier
- The compound has already been used in human clinic