Supplementary Information

Use of surface-modified porous silicon nanoparticles to deliver temozolomide with enhanced pharmacokinetic and therapeutic efficacy for intracranial glioblastoma in mice

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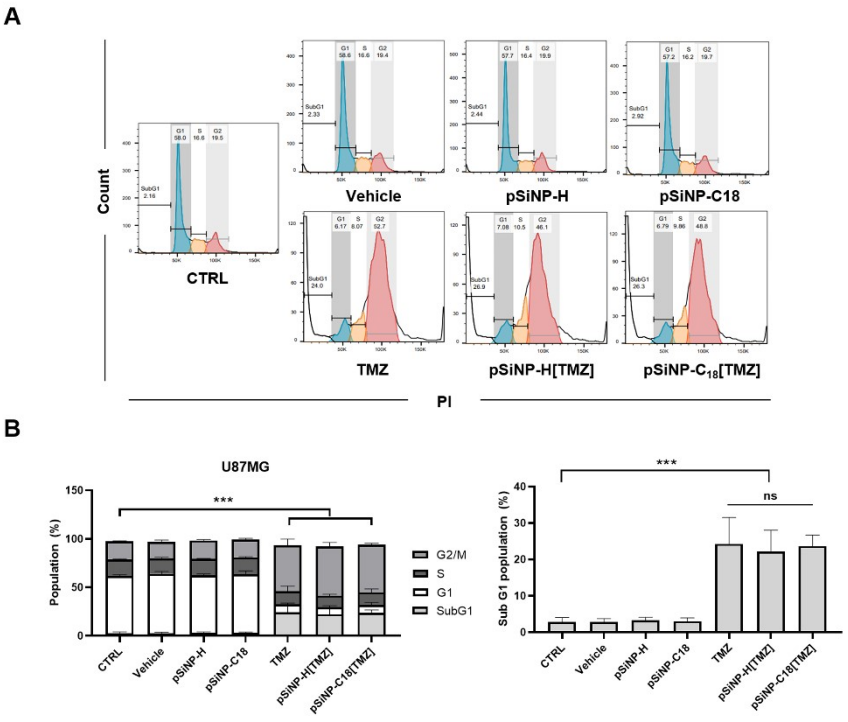
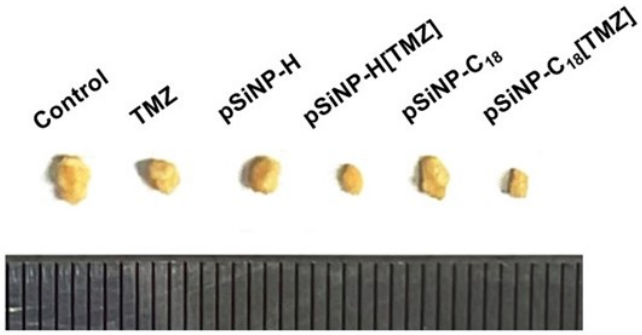
Glioblastoma (GBM) is one of the most common and fatal primary brain tumors, with a 5-year survival rate of 7.2%. The standard treatment for GBM involves surgical resection followed by chemoradiotherapy and temozolomide (TMZ) is currently the only approved chemotherapeutic agent for the treatment of GBM. However, hydrolytic instability and insufficient drug accumulation are major challenges that limit the effectiveness of TMZ chemotherapy. To overcome these limitations, we have developed a drug delivery platform utilizing porous silicon nanoparticles (pSiNPs) to improve the stability and blood brain barrier penetration of TMZ. The pSiNPs are synthesized via electrochemical etching and functionalized with octadecane. The octadecyl-modified pSiNPs (pSiNP-C_{18}) demonstrates the superiority of loading efficiency, *in vivo* stability, and brain accumulation of TMZ. Treatment of intracranial tumor-bearing mice with TMZ-loaded pSiNP-C_{18} results in a decreased tumor burden and a corresponding increase in survival compared with an equivalent free-drug dosing. Furthermore, the mice treated with TMZ-loaded nanoparticles do not exhibit *in vivo* toxicity, thus underscoring the preclinical potential of the pSiNP-based platform for the delivery of therapeutic agents to gliomas.

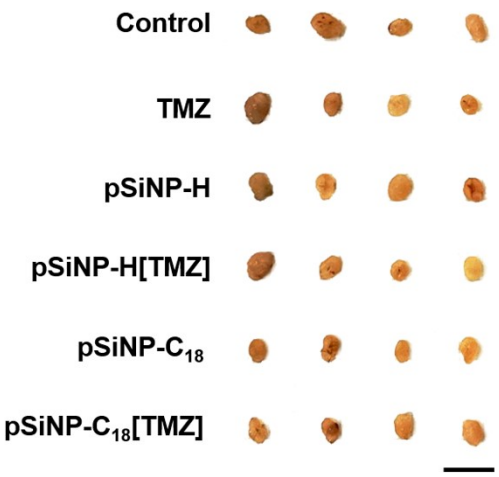
Supplementary Information



Supplementary figure 1. Cell cycle analysis of U87MG cells. U87MG cells treated with 100 μM of TMZ, TMZ-loaded pSiNPs at an equivalent dose, or their respective vehicles for 72 h. The cells were harvested, stained with propidium iodide (PI), and analyzed by flow cytometry. (A) Representative cytograms reporting the percentage of cells in each cell cycle phase (sub G1, G1, S, G2/M). (B) Quantification of the population in Sub-G1, G1, S, G2/M phases. The data are presented as the mean ± standard deviation of three independent experiments. ***P<0.001, ns: not significant



Supplementary Figure 2. Representative photography images of brain tumors isolated from U87MG tumor-bearing mice following five administrations of the drugs. U87MG cells were implanted into nude mice via subcutaneous injection of 1×10^6 cells per animal. Twelve days after glioblastoma cell injection, the mice received intravenous treatment with normal saline (control), TMZ (3 mg kg^{-1}), pSiNP-H, pSiNP[TMZ], pSiNP-C_{18}, or pSiNP-C_{18}[TMZ] (equivalent to a dose of 3 mg kg^{-1} of TMZ) every other day for 10 days.



Supplementary Figure 3. Representative images of inguinal lymph nodes excised from tumor-bearing mice after five rounds of drug administration. U87MG cells were implanted into BALB/c nude mice via stereotactic injection of 1×10^6 cells per animal. Twelve days after glioblastoma cell injection, the mice received intravenous treatment with normal saline (control), TMZ (3 mg kg^{-1}), pSiNP-H, pSiNP[TMZ], pSiNP-C_{18}, or pSiNP-C_{18}[TMZ] (equivalent to a dose of 3 mg kg^{-1} of TMZ) every other day for 10 days.