Magnetic Lymphocytes as Cellular Carriers for Nanoparticle Delivery Across the Blood–Brain Barrier in Glioblastoma

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Glioblastoma (GBM) is the most aggressive primary tumor of the central nervous system (CNS), with a 5-year survival rate below 5%. Its treatment is strongly limited by the blood–brain barrier (BBB), which restricts the entry of most therapeutic agents into the brain, including temozolomide, which reaches only ~20% CNS penetration [1] .
In this context, magnetic nanoparticles (MNPs) have been explored as multifunctional platforms for drug delivery, imaging, and magnetic hyperthermia. However, their clinical application is hindered by rapid immune clearance and poor ability to cross biological barriers. To address these limitations, CD4+ T lymphocytes have been investigated as cellular carriers due to their intrinsic capacity to traverse the BBB and migrate toward inflamed neural tissue [2] .
In this work, CD4+ T cells were functionalized with magnetic nanoparticles to generate magnetic lymphocytes. These cells retained key biological properties relevant for CNS delivery, including viability and migratory potential. The resulting hybrid system combines the natural BBB-crossing ability of T cells with the magnetic responsiveness of nanoparticles, enabling external magnetic guidance and improved targeting potential.
Overall, these results support the feasibility of using T cell–based magnetic nanoparticle carriers as a promising strategy to enhance delivery systems across the BBB for GBM applications.

Keywords:
Glioblastoma, magnetic nanoparticles, lymphocytes, blood-brain barrier

References:

[1] S. E. Combs, S. Heeger, R. Haselmann, L. Edler, J. Debus, and D. Schulz-Ertner. BMC Cancer, vol. 6, no. 1, p. 133, May 2006.
[2] M.Ayer, M.Schuster, I.Gruber, C.Blatti, E.Kaba, G.Enzmann, O.Burri, R.Guiet, A.Seitz, B.Engelhardt, H.-A.Klok. Adv. Healthcare Mater. 10, 2001375. 2021.

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