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**TITLE**  
RNA-modified T cell as a platform to deliver immunomodulatory agents to brain tumors.

**HYPOTHESIS:**  
RNA-modified T cells can deliver immunomodulatory molecules directly to brain tumor microenvironment.

**BACKGROUND/AIMS:**  
Cancer immunotherapy using immunomodulatory agents can potentially meet clear and urgent need for effective therapeutics for invasive malignant brain tumors. Cytokines such as granulocyte macrophage colony-stimulating factor (GM-CSF) have been applied as an adjuvant in cancer immunotherapy in attempt to potentiate anti-tumor immunity and overcome the robust immunosuppressive tumor microenvironment. Although this approach has proven efficacy, systemically delivered immunomodulatory agents to brain tumors have limited access to the central nervous system (CNS) due to the blood brain barrier (BBB). Furthermore, it may require high dose regimens to reach therapeutic concentrations at the tumor site, increasing the risk of systemic side effects and induction of potentially counterproductive immune responses.

**METHODS:**  
Using mRNA electroporation (EP) approach, we evaluated GM-CSF secretion *in vitro* and *in vivo* following intravenous injection of GM-CSF RNA-modified T cells. In addition, we further tested anti-tumor efficacy of GM-CSF RNA modified T cells in a murine brain tumor model.

**RESULTS & CONCLUSIONS**  
Murine and human activated T cells can be modified to secrete GM-CSF protein *in vitro*, while retaining effector T cell functions. Moreover, our results demonstrated the capacity for GM-CSF RNA-modified T cell to deliver enhanced cytokine concentrations to intracranial tumors *in vivo*. Finally, we demonstrated that GM-CSF RNA-modified T cell potentiated antigen-specific T cell expansion and prolonged overall survival in a murine brain tumor model.  
**CONCLUSIONS:** Our findings suggest that activated RNA-modified T cells cross the BBB, and can be used as an effective cellular vehicle to deliver therapeutic molecules effectively to invasive brain tumors.