



# CAR-T cell immunotherapy and nanotechnology: An integrated approach for cancer care

**\*Corresponding Author(s): Sachin Kumar Deshmukh**

Department of Oncologic Sciences, Mitchell Cancer  
Institute, University of South Alabama, 1660 SpringHill  
Avenue, USA  
Tel: 251-445-9872  
Email: skdeshmukh@health.southalabama.edu

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## Introduction

Overwhelming results of CAR-T cells cancer immunotherapy for the treatment of lymphoma have offered an excellent opportunity to explore the efficacy of CAR-T cell therapy in other malignancies. However, less exciting results derived from CAR-T cells treated solid tumors demand an urgent need to investigate the possible hurdles in the path of this therapy. CAR-T cell infiltration barriers and immunosuppressive tumor microenvironment efficiently influence the therapeutic outcomes. Nanotechnology-based approaches can be exploited to improve the efficacy of CAR-T cells as nanotechnology has proved highly efficient tools for cancer drug delivery. In this article, we have highlighted the specific areas of CAR-T cell therapy that needs atten-

tion and discussed the importance and benefits of CAR-T and nanotechnology combination approach. A better understanding of nano-immunotherapy would further help in the successful execution of CAR-T cell immunotherapy.

Cancer immunotherapy is one of the most exciting breakthroughs and promising advancement in the area of cancer research in recent years. In simple words, immunotherapy uses the body's own immune system or components of the immune system to fight cancer [1,2]. The immunotherapeutic strategy includes the use of vaccines, cytokines, T cell infusions and antibodies that bind to and inhibit the function of receptors ex-



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pressed by tumor cells. Chimeric Antigen Receptors (CARs) T cells are engineered immune cells that recognize an antigen on targeted tumor cells with the help of CARs expressed on these cells [3,4]. CAR-T cells are generated by manipulating T cells from a patient to cancer targeting cells, growing them in bulk in the laboratory and then administering them back into the patients. CAR-T cell immunotherapy has shown tremendous accomplishments in the treatment of liquid malignancy such as lymphoma, however, in the case of solid tumors, the expected success is still out of reach. Presence of tumor-infiltrating lymphocytes (TILs) indicates and predicts the antitumor immune response to immunotherapy. The tumors lacking TILs generally correlate with poor prognosis [5]. The efficacy of cancer immunotherapy largely depends on the activation and infiltration of immune cells including T cells into the Tumor Microenvironment (TME). However, transport barriers such as desmoplasia and immunosuppressive TME limits the therapeutic potential of T cells. Nanotechnology-based approaches which use nanomaterials, that accumulate at the tumor site due to the Enhanced Permeability and Retention (EPR) effect attributed to the leaky tumor vasculature. These approaches offer the opportunity to manage the transport barriers and immunosuppressive TME effectively. The efficacy and effectiveness of a combination strategy that involves immunotherapy and nanotechnology is being extensively explored and tested in the recent time.

The DNA-carrying polymeric nanoparticles demonstrated excellent efficacy in introducing CAR genes in T-cells and offer additional transfection strategy parallel to the lentiviral system [6]. In addition, DNA-carrying nanoparticles shown to favorably programmed T cell in circulation by incorporating leukemia-targeting CAR genes [6]. Cell surface-conjugated protein nanogels (NGs) were developed recently which were designed and tuned to release after T cell encounter and recognize the antigen. Comparing to systemic administration of free cytokine, NGs demonstrated a considerably higher expansion of T cells in the tumor. These NGs has been expected to improve the efficacy of CAR-T cell therapy [7]. Trafficking from blood and infiltration of CAR-T cells in TME is crucial for the effective immunotherapy that influences the therapeutic outcome of cancer. However, TME which nurture the immunosuppressive environment poses an additional challenge for the CAR-T cells to remain active. Adenosine, a recognized immunosuppressive molecule binds to CD4<sup>+</sup> and CD8<sup>+</sup> T cells A2a adenosine receptor (A2aR) and reduces their activities in TME. A2aR-specific small molecule antagonist SCH-58261 (SCH) holds the capacity to block the suppressive pathway in TME. CAR-T cells developed and tested in *in vitro* and *in vivo* studies to deliver the SCH-loaded cross-linked, multi lamellar liposomal vesicles within the TME to break the immune suppression [8]. This strategy has been suggested to improve the activity of CAR-T cells in the immunosuppressive TME.

Nanoparticles are in use for the cancer diagnosis, imaging, drug delivery and for the treatment of cancer. However, it has been realized recently that the nanoparticles based approaches can be utilized to improve the immunotherapeutic strategies. The nanoparticles based transfection approaches seems lucrative to generate or modify the CAR-T cells with enhanced activity for tumor clearance. Further, NPs can be handy tools to break the T cells transportation barriers and enhance their tumor clearing capacity in TME. Moreover, selective targeting of immunosuppressive cells by NPs can provide the additional boost to cancer-killing CAR-T cells which get exhausted in TME even if they cross the transportation barriers. Advancement in nanotechnology intervention, improved efficacy of CAR-T cell immunotherapeutic approaches and their merger hopefully will facilitate the translation of novel immunotherapies to manage the deadly disease efficiently and improve the clinical outcome for cancer patients.

## References

1. Yang Y. Cancer immunotherapy: harnessing the immune system to battle cancer. *J Clin Invest*. 2015; 125: 3335-3337.
2. van den Bulk J, Verdegaal EM, de Miranda NF. Cancer immunotherapy: broadening the scope of targetable tumours. *Open Biol*. 2018; 8.
3. Cheadle EJ, Gornall H, Baldan V, Hanson V, Hawkins RE, et al. CAR T cells: Driving the road from the laboratory to the clinic. *Immunol Rev*. 2014; 257: 91-106.
4. Srivastava S, Riddell SR. Engineering CAR-T cells: Design concepts. *Trends Immunol*. 2015; 36: 494-502.
5. Barnes TA, Amir E. HYPE or HOPE: the prognostic value of infiltrating immune cells in cancer. *Br J Cancer*. 2017 8;117: 451-460.
6. Smith TT, Stephan SB, Moffett HF et al. In situ programming of leukaemia-specific T cells using synthetic DNA nanocarriers. *Nat Nanotechnol*. 2017; 12: 813-820.
7. Tang L, Zheng Y, Melo MB et al. Enhancing T cell therapy through TCR-signaling-responsive nanoparticle drug delivery. *Nat Biotechnol*. 2018; 36: 707-716.
8. Siriwon N, Kim YJ, Siegler E, Chen X, Rohrs JA, et al. CAR-T Cells Surface-Engineered with Drug-Encapsulated Nanoparticles Can Ameliorate Intratumoral T-cell Hypofunction. *Cancer Immunol Res*. 2018; 6: 812-824.