Boosting Therapeutic Response By Outsmarting Tumor

In the past 2 decades, there have been major advances in the treatment of cancer. The use of immunotherapy is also been widely employed for cancer treatment. Previous clinical trials suggest that immunotherapy with immune checkpoint inhibitors appears to shrink tumours in a number of patients across a wider range of tumour types.

Recent studies suggest that up to 85 percent of patients don't benefit from

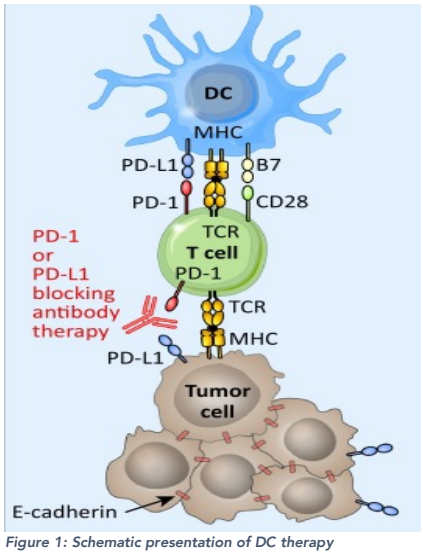

Figure 1: Schematic presentation of DC therapy administered with Checkpoint inhibitor.

checkpoint inhibitors. New research published in Nature 2019 has uncovered a mechanism thought to explain why some cancers don't respond to widely used anti-PD-1 and PD-L1 drugs. Dr. Khelif and his colleagues from Georgetown Lombardi Comprehensive Cancer Center, USA demonstrated that "If the immune cells are not in the appropriately activated state, treatment with anti-PD-1 drives these T cells into a dysfunctional, non-reprogrammable state, thereby inducing resistance to further immune therapy." Furthermore, tumors expressing low mutation rate or are immunologically quiet are immune to checkpoint inhibitor treatment.

The use of combination therapies can overcome such resistance to immunotherapy. More than 50 clinical trials are still running that employ the use of combination-based immunotherapy. Among these trials, several findings have explored the mechanism

where activation of T cells using DC based immunotherapy (based on a patient's specific tumor) can lead the way to reduce tumor load and to enhance PD-1 inhibitors activity. The use of DC based therapy prior or in conjugation with anti-PD-1 therapy can improve the patient survival rate significantly.

DC therapy aims to induce an in vivo adaptive immune response against set of antigens expressed onto the patient tumor tissue. This implies leveraging specific functions of dendritic cells in order to trigger T-helper cell responses

to support production of antibody and induce cytotoxic effector T-cells (Figure 1).

DC based therapy aims to deliver unequivocal clinical benefit for cancer patients by maximizing the induction of a T-cell response with optimal amplitude, specificity and effector profile. They also ensure that these activated T-cells can reach the tumor site and perform their function without any restraint.

The future of cancer treatment involves combining DC based therapy with drugs that target the dominant immunosuppressive pathway in a given tumor promises to unlock the true power of cancer vaccines and potentially offer long-term protection from disease relapse (Figure 2).

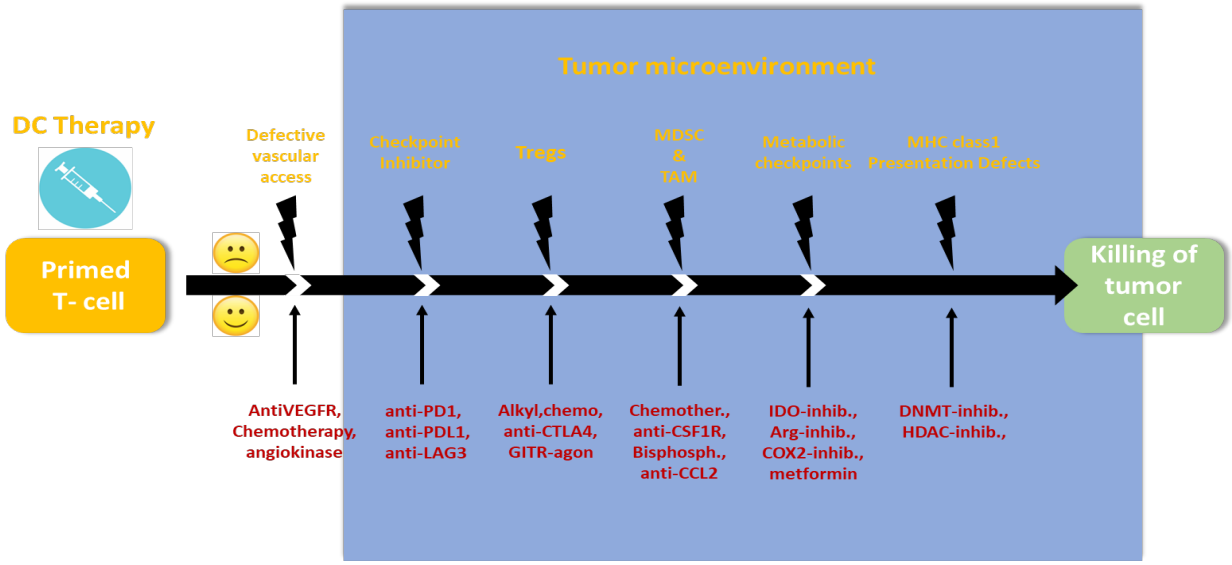

Figure 2: The multiple obstacles to effective anti-tumor immune responses following successful priming of tumor antigen-specific T-cells by a vaccine. Each obstacle offers opportunities for therapeutic intervention in order to increase vaccine efficacy.