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Nano-optogenetic engineering of CAR T-cells for precision immunotherapy with enhanced safety

Chimeric antigen receptor (CAR) T cell-based immunotherapy approved by FDA shows promising curative potential in patients with CD19-positive hematological immunotherapy. CAR T-cell therapy, nevertheless, lacks precise control over the location and duration of the anti-tumor immune response, and therefore, is fraught with devastating side effects in some patients. Herein, we present the design of light-switchable CAR (designated “LiCAR”) T-cells that enable photo-tunable activation of therapeutic T cells to induce CD19-positive tumor cell killing both in vitro and in vivo. When coupled with imaging-guided, surgically removable upconversion nanoplates (UCNPs) that have enhanced near infrared (NIR)-to-blue upconversion luminescence as miniature deep tissue transducers, LiCAR T-cells enable precise spatiotemporal control over T cell-mediated anti-tumor therapeutic activity with greatly mitigated side effects. This remotely controllable nano-optogenetic device will not only provide a unique tool for interrogating CAR-mediated anti-tumor immunity, but also set the stage for developing smart immunotherapy to deliver personalized anti-cancer therapy.