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## IN VIVO EXPANSION OF ENDOGENOUS ANTIGEN-SPECIFIC CD8<sup>+</sup> T CELLS USING ARTIFICIAL T-CELL STIMULATING MICROPARTICLES

Natalie Livingston\*, John Hickey, Hajin Sim, Hai-Quan Mao, Jonathan Schneck. *Johns Hopkins University, Baltimore, MD, USA*

**Background** T cell-based immunotherapies such as chimeric antigen receptor T cell therapy (CAR T), have seen some clinical success; however, these therapies are still currently limited to a select few cancer types and have price tags that further limit accessibility for patients. Here, we create a novel biomaterials-based platform for the *in vivo* activation of naïve, antigen-specific T cells, removing the need for expensive and lengthy *ex vivo* expansion steps.

**Methods** Thiol-modified HA is cross-linked with PEDGA in the presence of thiol-modified signals 1 (here, KbOVA) and 2 (anti CD28).<sup>1</sup> The cross-linked gel is passed through a mesh to form microparticles (MPs) (figure 1A). MPs are mixed with naïve B6 CD8<sup>+</sup> T cells and injected subcutaneously into mice. Eight days after injection, target cells expressing OVA antigen are injected i.v. On day 9, mice are sacrificed and analyzed for enrichment of antigen-specific cells and killing of target cells. MPs were also tested therapeutic tumor model, in which MC-38 OVA tumor cells were injected on day 0 and naïve OT I CD8s plus MPs were injected on day 6.

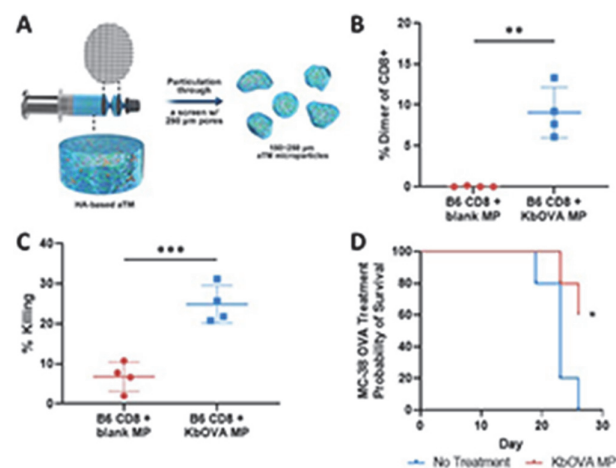
**Results** Nine days after co-injecting naïve B6 CD8<sup>+</sup> T cells with KbOVA MPs, we can detect a significant enrichment of OVA-specific T cells via flow cytometry (figure 1B). Cells expanded *in vivo* showed significant and robust killing of target splenocytes (figure 1C). In the MC-38 OVA cancer treatment model, injection of naïve OT I CD8<sup>+</sup> T cells with OVA MPs increased survival compared with naïve OT I CD8<sup>+</sup> cells injected with blank MPs (figure 1D).

**Conclusions** We have developed an injectable, LN-mimicking MP platform that incorporates T-cell activation signals and critical ECM cues of the LN. These MPs are capable of expanding antigen-specific T cells from a fully endogenous B6 repertoire, and these cells are able to robustly kill target splenocytes as well as reduce tumor growth and extend survival in a therapeutic cancer model. Developing a system for the *in vivo* activation of antigen-specific T cells reduces both cost of T cell-based therapies as well as the time to treatment for patients.

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### REFERENCE

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**Abstract 256 Figure 1** (A) Schematic of the preparation of T cell-stimulating MPs. (B) Enrichment of OVA-specific T cells within the biomaterial site 9 days after injection. (C) *In vivo* killing of OVA-pulsed splenocytes after 9 days of *in vivo* expansion of OVA-specific T cells. (D) Survival plot after mice are injected with MC-38 OVA tumor cells on day 0 and naïve OT I CD8s plus MPs on day 6.

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