**Background** Despite unprecedented clinical success of CAR T cell therapy against B cell malignancies, its widespread application is limited by lengthy (~4 weeks) and labor intensive ex vivo manufacturing procedures that result in (i) extremely high cost, (ii) delays to infuse CAR T cells to patients with rapidly progressing disease, and (iii) more exhausted T cell phenotypes that limits their in vivo engraftment and persistence. There is a clear scientific and medical need for approaches that increases the accessibility and affordability CAR T cell therapy, extends remission and increase the efficacy beyond liquid tumors.

**Methods** We prepared macroporous scaffolds from calcium-crosslinked alginate. Macroporosity is built into scaffolds through mild cryogelation. The pores not only enhance mass transfer of nutrients but also provide an interface for homogeneous distribution of T cells and contact with viral particles. anti-CD3 and anti-CD28 was conjugated while IL-2 was physically encapsulated onto the scaffold to facilitate activation and expansion of T cells. These scaffolds can be seeded with human peripheral blood mononuclear cells and CAR-encoding retroviral particles and implnated in the subcutaneous space (figure 1).

**Results** Scaffold generated CAR-T cells enter the bloodstream and control distal tumor growth in multiple mouse xenograft models of lymphoma, pancreatic adenocarcinoma, ovarian cancer showing greater expansion and persistence than conventional CAR-T cells. Scaffold generated CAR T cells had 30 fold higher absolute counts in blood and outperformed iv infusion in a rechallege model of lymphoma (figure 2).

**Conclusions** These scaffolds represent a platform technology that promises to transform CAR-T cell therapy by fast-tracking manufacture, extending remission and potentially reducing the complexity and resources needed for provision of this type of therapy. It is a platform technology that can be adapted to reprogram other immune cells or to deliver immunomodulatory factors to support cell function synergistically. Beyond its potential for cancer therapy, the this technology might inspire new treatments harnessing the capacity for reprogramming and release of therapeutic cells.1

**REFERENCE**
Abstract 225 Figure 2  (A) Experimental timeline of the lymphoma xenograft model in NSG mice engrafted and rechallenged with FFLuc-labeled CD19+ human Daudi tumor cells. (B) In vivo tumor bioluminescence imaging of NSG mice treated with scaffold, conventional CAR-T cells or control non-tranduced (NT) cells. (C) Survival of mice is shown as Kaplan-Meier curves. Six mice per treatment group are shown.

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