Results Results show > 4 log enrichment of tumor cells and average recovery of spiked CTC > 85% in the clinical relative range <100 cells per ml of whole blood (R2=0.929) with a throughput of 60 ml/hr. Isolated cells were confirmed to be cancer cells with imaging analysis and single cell genomic sequencing. The protocol was also validated with other cell line cells such as A549. The purity of the cells prepared by MARS are ideal for single cell genomics platforms.

Conclusions The fluidics of MARS is also replaceable and can be sterilized to minimize sample to sample contamination. The high molecular debris removal achieved by MARS is ideal for single cell genomics platforms, as is the first-to-market automated and integrated sample preparation and cell separation system designed to be a versatile tool for downstream cell analysis.

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12 DEVELOPMENT OF AN IN VITRO ASSAY TO ASSESS BISPECIFIC T CELL ENGAGER USING T CELLS FROM CD3E HUMANIZED MICE
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Background Bispecific T cell engagers (BiTE) is a fast-growing class of immunotherapies. They are bispecific antibody that bind to T cell-surface protein (for example, CD3e) and a specific tumor associate antigen (TAA) on tumor cells, by which to redirect T cells against tumor cells in a MHC-independent manner. A successful example in the clinical is Blinatumomab, a BiTE antibody against CD3/CD19 approved in 2014 to treat acute lymphoblastic leukemia. Currently, many CD3-based BiTE are in clinical trials, including BCMAXCD3, Her2xCD3, CEAxCD3, and PSMAXCD3. To evaluate the efficacy of BiTE in vitro, human peripheral blood monocyte cells (hPBMC) are commonly being used as a source of T cells to co-culture with tumor cells. The disadvantage of using hPBMC is donor-to-donor variability and the availability of the original donor if a study needs to be repeated.

Methods To overcome this, we proposed to replace hPBMC with T cells from human CD3e (hCD3) genetically engineered mouse models mice (GEMM) for in vitro coculture assay. T cells were isolated from hCD3 GEMM mice using negative selection mouse T cell isolation kit. Conventional tumor cell lines or luciferase-engineered patient-derived xenograft (PDX)-derived organoids (PDXO) expressing specific antigens are co-cultured with hCD3 T cells in 96-well plates in the presence of BiTE antibody.

Results We measured the killing of tumor cells using either flow cytometry or luciferase activity as readouts. To analyze tumor-reactivity of T cells to cancer cell line or organoids, IFN-gamma in the culture medium was measured and activation markers on T cells was assessed.

Conclusions Our data showed the feasibility of using humanized mice T cells as a replacement for hPBMCs to assess BiTE antibody in vitro. We are further validating the application of murine hCD3 T cells for in vivo models to test bispecific T cell engagers.

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13 USE OF ANTI-VIRAL T CELLS TO MODEL HLA-RESTRICTED ANTI-TUMOR CYTOTOXIC LYMPHOCYTE RESPONSES
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Background With the success of T cell checkpoint antagonists in treating cancer, we must better understand treatment response heterogeneity and develop more physiological preclinical models for evaluating the next wave of candidate therapeutics. Several hurdles limit the successful recapitulation of the cellular and molecular interactions between human T cells and tumor cells, not the least of which involves the challenge of access to – and ex vivo manipulation of – bona fide tumor antigen-specific T cells.

Methods In order to improve on our understanding of checkpoint therapy using human model antigens, we developed an antigen-specific T cell-mediated cytotoxicity model using antiviral human T cells co-cultured with a human tumor cell line expressing viral peptide epitopes.

Results We found that anti-viral T cells could be used to model cytotoxic HLA-restricted anti-tumor responses and these responses varied by donor according to peptide antigen density, antigen quality, T cell numbers, and time. By identifying sub-optimal conditions in a donor-specific fashion, we demonstrated enhanced cytolytic function of T cells in vitro when combined with multiple disparate anti-tumor modalities, including immune checkpoint blockade, growth factor blockade, and chemotherapy. This in vitro model was then successfully adapted to an in vivo tumor model system that demonstrated control of tumor growth in an antigen-dependent manner that was responsive to checkpoint blockade.

Conclusions These in vitro and in vivo systems represent a simple, yet elegant and robust platform for testing human T cell-directed immuno-oncology (IO) therapeutics and IO combinations.

Ethics Approval All animal experiments were conducted in a facility accredited by the Association for Assessment and Accreditation of Laboratory Animal Care in accordance with institutional animal care and use committee guidelines and after appropriate approvals.

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14 NOVEL CD3 EPSILON HUMANIZED N-TERMINAL EPITOPE MODEL FOR ASSESSMENT OF EFFICACY OF T-CELL ENGAGERS
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Background T-cell engagers have proved to be a promising therapeutic strategy in immunotherapy, for redirecting T cells activity against tumor cells. To facilitate the preclinical assessment of novel T-cell engagers and their translatability, we have developed an immunocompetent CD3 epsilon N-terminal epitope humanized mouse model.

Methods This model was developed to express the human epitope of the CD3 epsilon chain, which is recognized by approximately 70% of the T-cell engagers (clone SP34). The rest of the extracellular domain was kept from mouse origin to preserve the amino acids involved in the interaction with CD3 gamma and delta. Similarly, the transmembrane domains

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