



ADVANCING CAR-T CELL THERAPY UTILIZING *IN SITU* TRANSDUCTION

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Introduction

While CAR-T cell therapy shows great promise in hematological malignancies, its implication is not without drawbacks. Amongst them are:

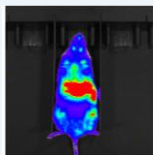
1. Lengthy manufacture time – at least 10 days from harvest to infusion
2. Costly - ~375K per patient
3. Personalized therapy – inconsistencies in production

Our goal:

Develop lentiviral vectors that specifically target endogenous T cells to redirect their activity against tumor antigens.

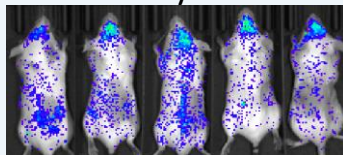
Targeting the virus specifically to T cells

Envelope: VSVG-LUC

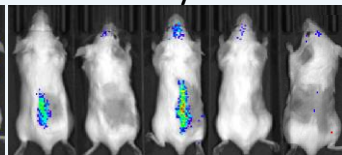


α CD3-LUC

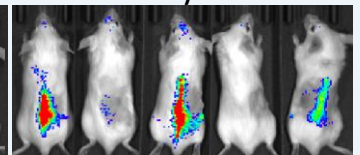
Day 3



Day 5



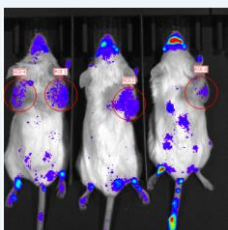
Day 6



While using a VSVG enveloped virus, carrying the luciferase gene, resulted in high percentage of *in situ* transduction, it was not specifically targeting T cells (left). When using an envelope directed specifically to CD3 T cells, luciferase signal in lymphatic organs is detected indicating transduction of T cells (right).

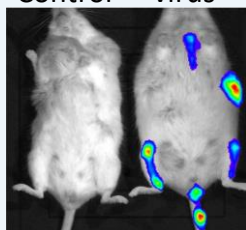
In situ transduction of CAR in different animal models

CD19CAR-LUC



4D5CAR-LUC

Control virus



A mouse lymphoma model (A20) transduced *in situ* with a virus carrying the CD19 CAR (left) and a humanized HER2 mouse model transduced with a virus carrying the 4D5 (α HER2) CAR (right). In both models we can detect luciferase signal indicating CAR transduction. In the lymphoma model the signal is located in the tumor area while in the humanized HER2 model a signal is detected in the lymphatic organs.

***In situ* transduction of T cell with CAR can be the future of CAR-T cell therapy by resolving major issues in current manufacturing process**

Future plans:

- Improving *in situ* transduction percentage and specificity by envelop modifications
- Directing the *in situ* transduced lymphocytes to the tumor site.