Celyad Oncology

Allogeneic Non Gene-Edited shRNA Platform

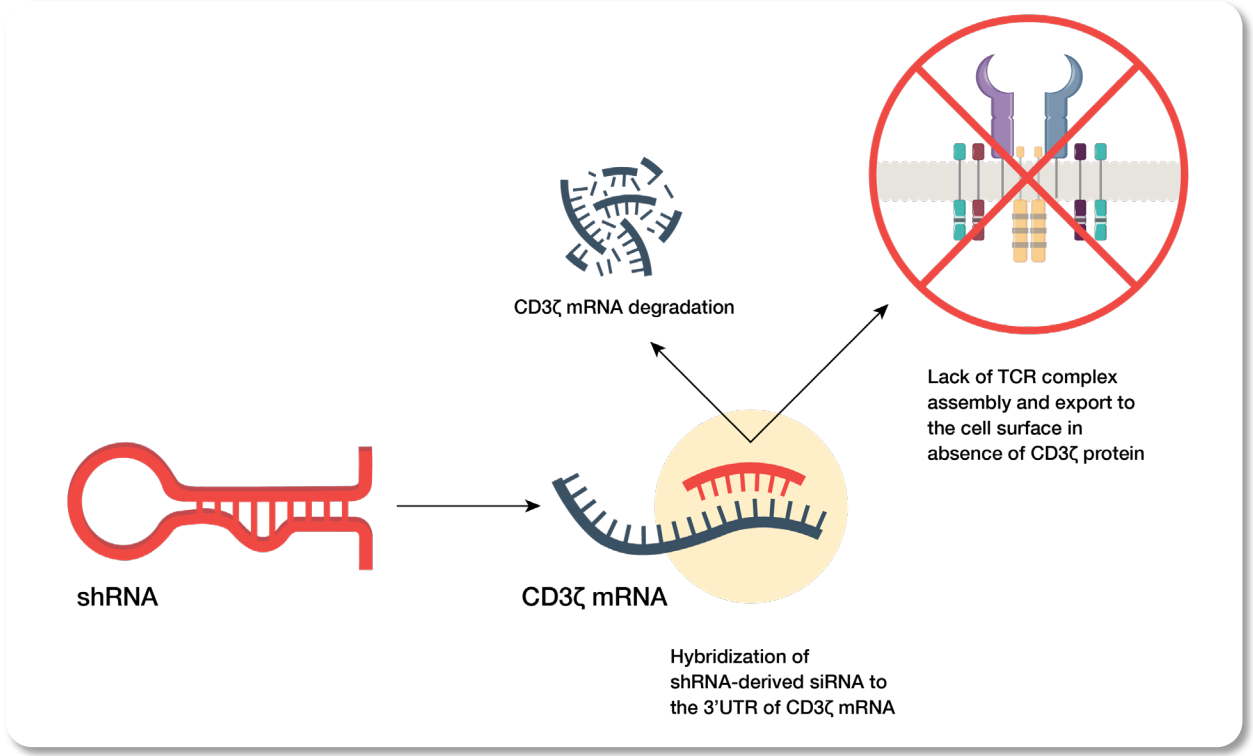
The ability to control gene expression and optimize function of CAR T cells is essential in order to expand application of CAR T therapies to a wider range of cancers

Short hairpin RNA (shRNA) is a small piece of RNA that can decrease gene expression, effectively turning genes off

- No modification of the T cell genome which avoids potential safety issues of gene editing – and particularly multiple gene edits
- Level of shRNA mediated gene knockdown (KD) can be titrated accordingly to need
- Ability to knockdown multiple targets simultaneously
- All in One vector approach employs a single vector for all elements of the therapy
- Minimized cell manipulation results in a shorter manufacturing process - single step enrichment

A number of gene-editing techniques have been used to modify CAR T cells

- Acts at the DNA level by cutting the genome to permanently eliminate TCR expression
- Demonstrating the absence of off target editing is a regulatory challenge
- All or nothing gene knockout
- Editing multiple genes requires multiple steps (additional complexity when combined with a CAR)
- Multiple GMP grade tailor made reagents required and longer manufacturing times



shRNA *in vivo* data demonstrate:

- Protection of GvHD using shRNA knockdown similar to CRISPR-Cas9 knockout
- Persistence of allogeneic T cells produced with shRNA technology is superior to cells engineered with CRISPR-Cas9