Discovery of phospho-peptide neoantigen tumor targets (PTTs) and identification of novel T cell receptors (TCRs) targeting phospho-MLL for adoptive cell therapy

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AgenTus Therapeutics: differentiated cell therapy

Precision Receptors

- T-Rx™ Mammalian Display - Direct selection for function
- Targets optimal balance between activity and specificity

Novel Targets

- Proprietary target discovery and validation platforms
- Proprietary Phosphopeptide Tumor Targets (PTTs)

Allogeneic Format

- Allogeneic approach; "Off-the-shelf"
- Scalable, shorter diagnosis to treatment interval

Phosphopeptide Tumor Targets (PTTs) are unique immunogenic cancer neo-antigens

Nature of change

- Mutations
- Deregulated Expression
- Deregulated Signaling

Consequence for Proteins

- EML-4-ALK
- Bin-Abi
- KRAS
- WT-1
- Telomerase Survivin
- Cancer-Testis Antigens
- Embryonic Antigens
- Post-Translational Modifications (phosphorylation, glycosylation, etc.)

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We identified the first fully-human phosphopeptide-specific TCR

Primary T-cell expansion platform

- Autologous antigenic cells pulsed with phosphopeptides
- T-Rx™ display platform

State-of-the-art ligandome technology identifies PTTs from patient samples

Resected Human Tissue

- (tumor/normal)

Tissue Lysis

- Immunoaffinity Purification

STAGE Tip Sample Cleanup

HPLC-ESI-MS/MS

- Analysis and Manual Validation

IMAC Phosphopeptide Enrichment

10-200 Phosphopeptides present

- +1/100 cognate cell

Primary human T cells expressing the AGENT 04002 TCR kill AML cells presenting the cognate PTT

Summary

- AGENT 04002 is targeting a novel class of neoantigens: phosphopeptide tumor targets (PTTs)
- State-of-the-art, sensitive ligandome platform method identifies phosphopeptide neoantigens from primary tumor samples
- Using optimized protocols for identification of natural TCRs from TCM cells, we have identified the first fully-human phosphopeptide-specific TCR targeting MLL
- The anti-MLL TCR AGENT 04002 targets HLA-B*0702 bound to the EPRiP/PSHSM phosphopeptide
- AGENT 04002 is potent in vitro, specific and efficiently controls tumor growth in vivo