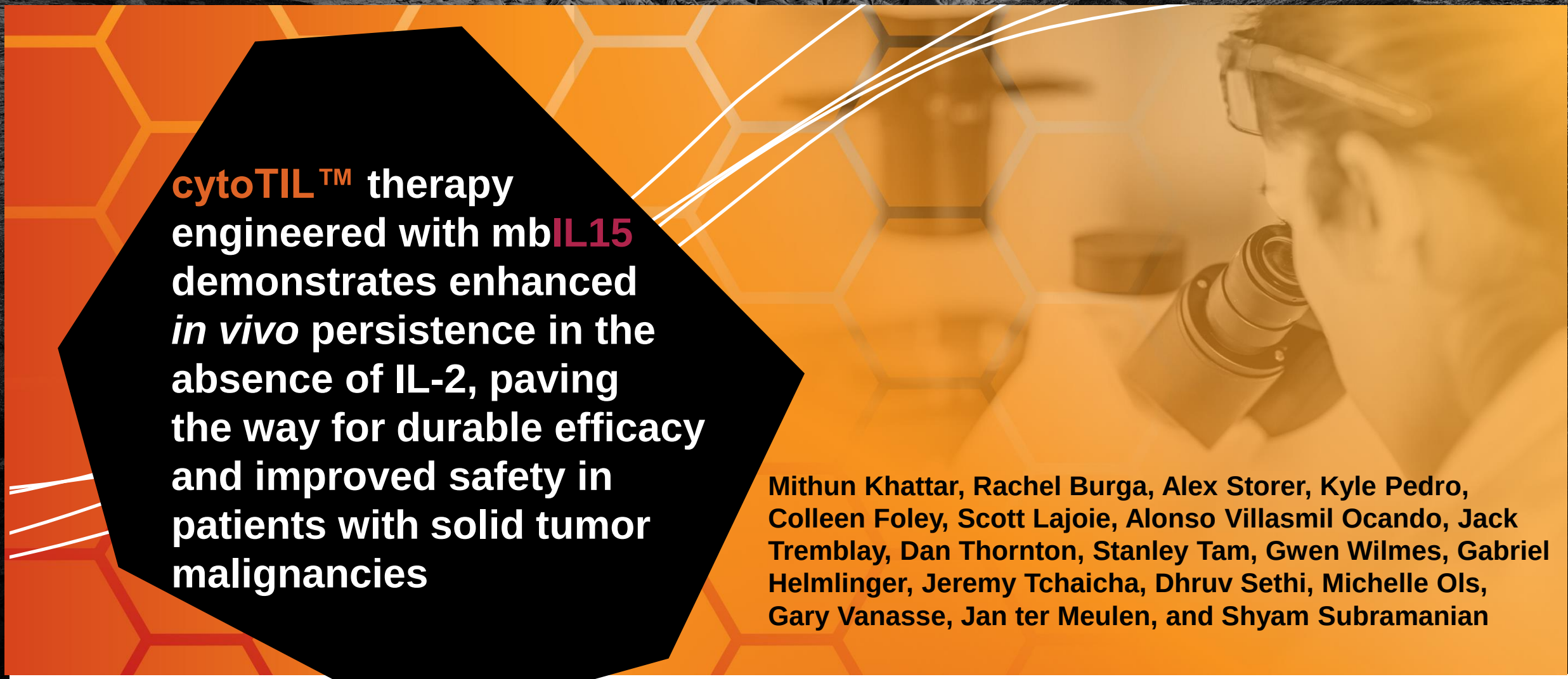
cytoTIL™ therapy engineered with mbIL15 demonstrates enhanced *in vivo* persistence in the absence of IL-2, paving the way for durable efficacy and improved safety in patients with solid tumor malignancies



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OBSIDIAN THERAPEUTICS

Pioneering engineered cell & gene therapies

mb = membrane-bound

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Un-engineered TILs have shown promising clinical results in solid tumors, but **systemic IL2 AE's** limit patient eligibility

Benefits of TIL Therapy

- Recognize multiple tumor antigens without an engineered binder (polyclonal)
- Targets intracellular tumor antigens
- Traffics into solid tumors

→ On track to be 1st cell therapy approved for solid tumors

- Positive interim Ph2 data
  - Lifileucel in Melanoma: 3% CR, 36.4% ORR
  - LN-145 in Cervical Cancer: 11% CR, 44% ORR

Challenges

IL2 therapy is highly toxic:

- TIL therapy in combination with systemic IL2 is associated with a high degree of Grade 3/4 AEs including cardiac & pulmonary.
- Risk of capillary leak syndrome and multi-organ dysfunction
  - Can be severe and result in death
- Black Box Warning* requires hospitalization and availability of ICU
- Limited to patients with normal cardiac and pulmonary functions

AE = Adverse Event | *Proleukin (aldesleukin) package insert

cytoTIL15: A **regulated interleukin-15 engineered TIL** therapy to drive potent and durable anti-tumor responses

Benefits of TIL-endogenous mbIL15 vs. systemic IL2

- Drive antigen-independent **TIL expansion & persistence**
- Drive **adjacent NK cell expansion** & activity
- Drive phenotype towards **CD8+** and **memory** T-cells
- **Unlike IL2**, suppresses activation-induced cell death, doesn't affect Tregs or cause capillary leak syndrome-associated toxicity
- IL15 expression of cytoTIL15 controlled by acetazolamide (ACZ), via **cytoDRIVE® technology**

cytoTIL15 engineering results in an improved TIL product, demonstrating **antitumor potency without need for IL2**

cytoTIL15 demonstrate enhanced persistence and improved phenotype while maintaining potency

Engineering

Successful **transduction** & IL15 expression

Persistence

Demonstrated superior persistence *in vitro* & *in vivo* **without IL2**

Phenotype

Exhibit desired phenotype, skewing toward **CD8+** T-cells

Potency

Maintains anti-tumor reactivity with potential for **lower cell dose** vs. conventional TILs

cytoTIL15 manufacturing process uses **novel engineered feeders** for REP expansion with **no exogenous cytokines**

Tumor Biopsy

Reduced source tissue requirement

Pre-REP Expansion

Reduced duration

High success rate

mbIL15 Engineering

Efficient retroviral vector **transduction**

REP Expansion

No IL2 required for TIL expansion

Engineered feeder cell co-stimulation

Infusion to Patient

Cryopreserved drug product

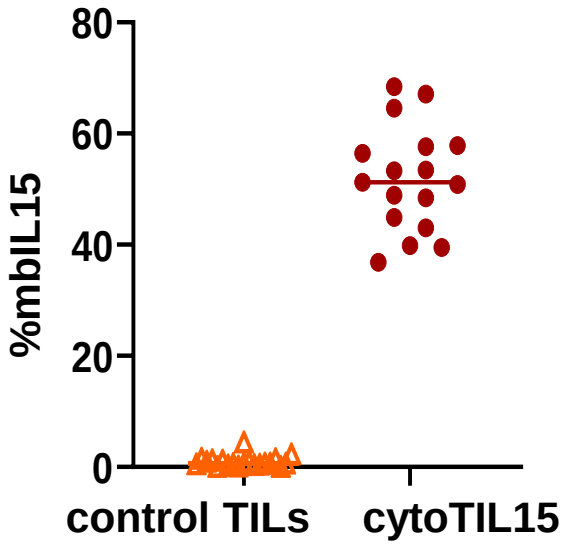
Reduced duration from biopsy

Automated and closed processing from end to end

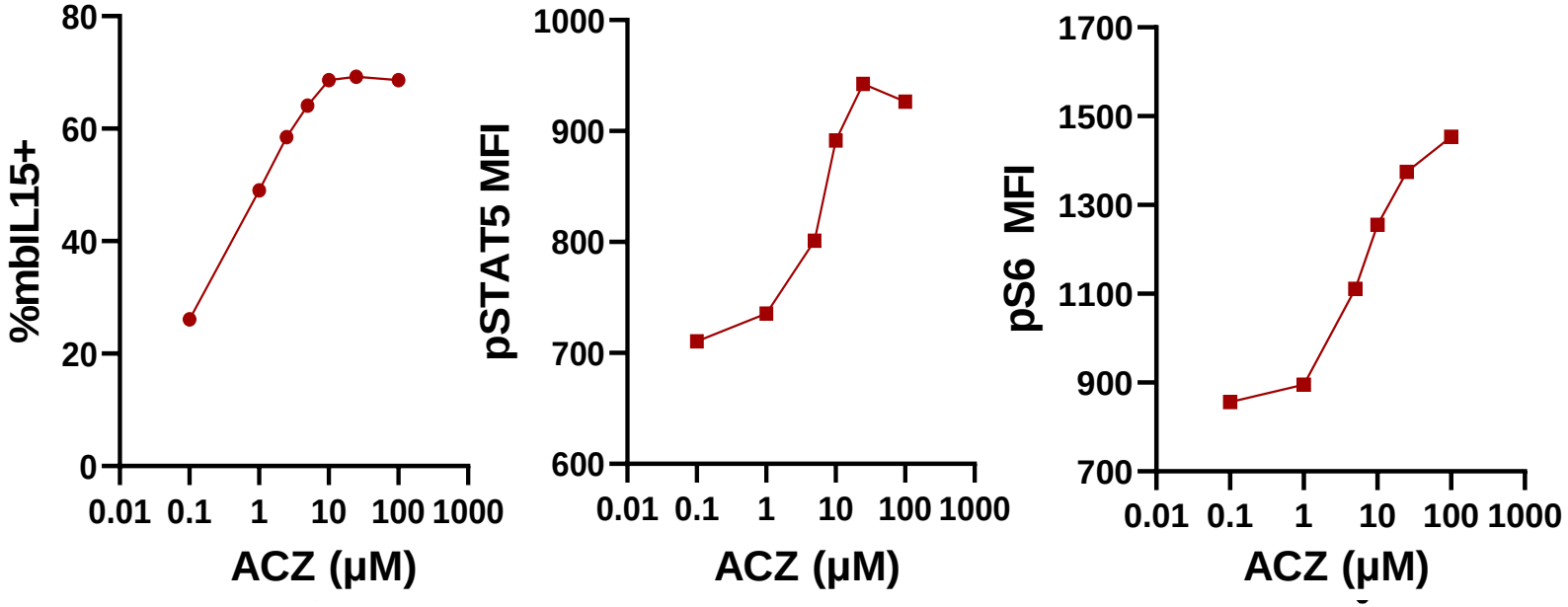
REP = Rapid Expansion Protocol

cytoTIL15 is engineered to express membrane-bound IL15 (mbIL15), regulated by ACZ in a dose-dependent fashion

IL15 expression Post-REP

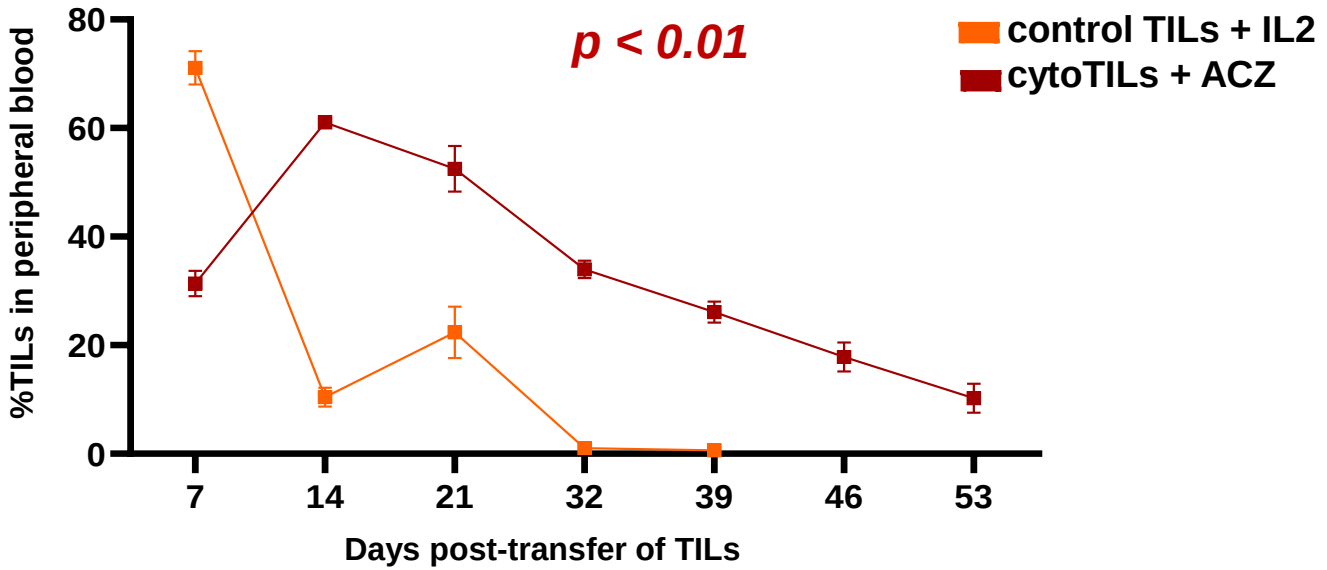


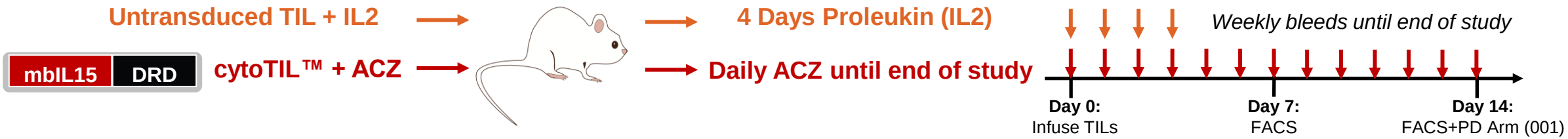
Regulation of IL15 expression, pSTAT5 & pS6 signaling by ACZ



- *Graph on the left shows membrane IL15 expression on TILs at the end of the REP.*
- *Graphs in the right panel show membrane IL15 expression, pSTAT5 and pS6 levels on cytoTIL15 cultured overnight with different concentrations of ACZ as marked.*

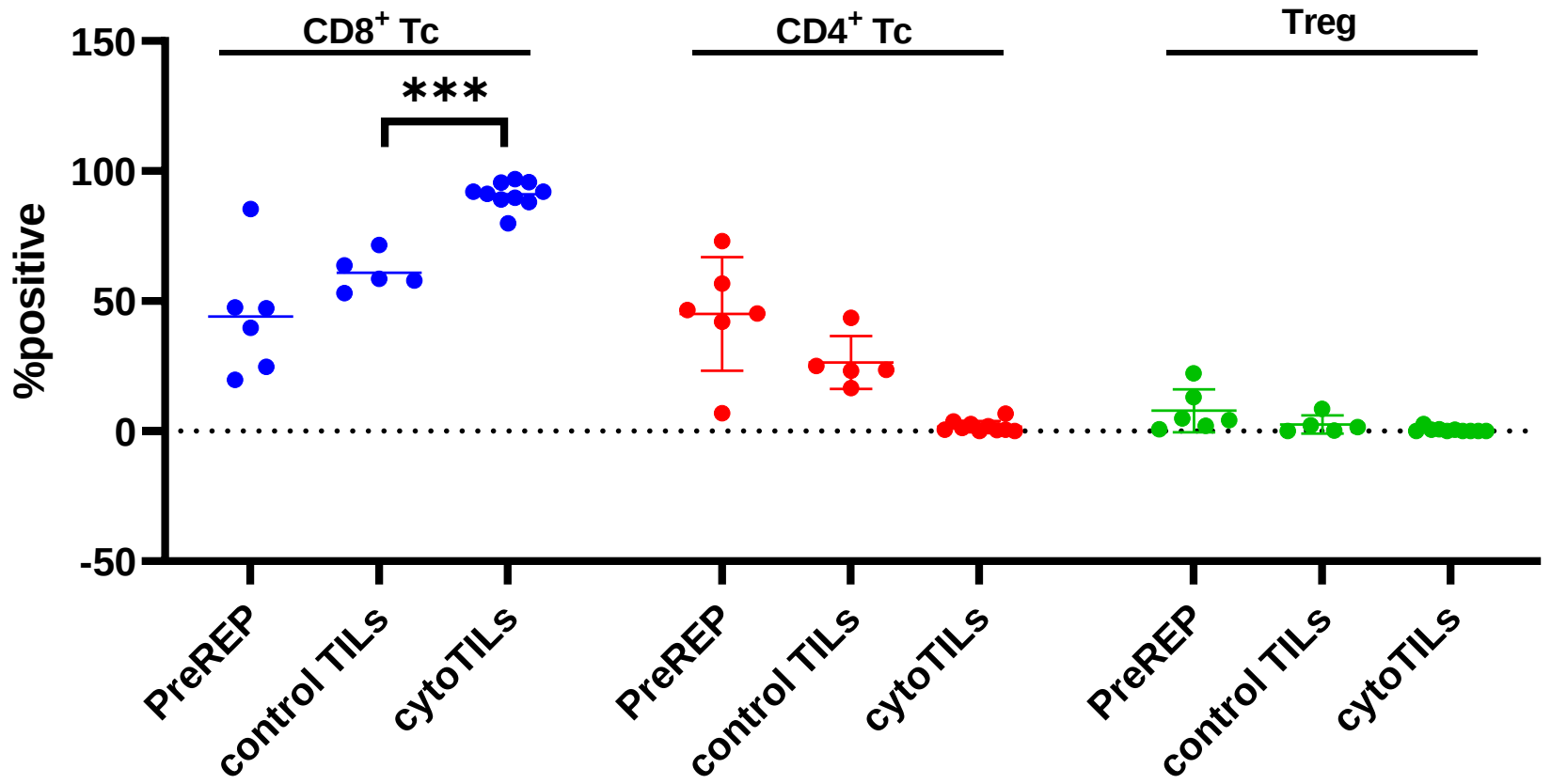
cytoTIL15 demonstrate **enhanced persistence** *in vivo*





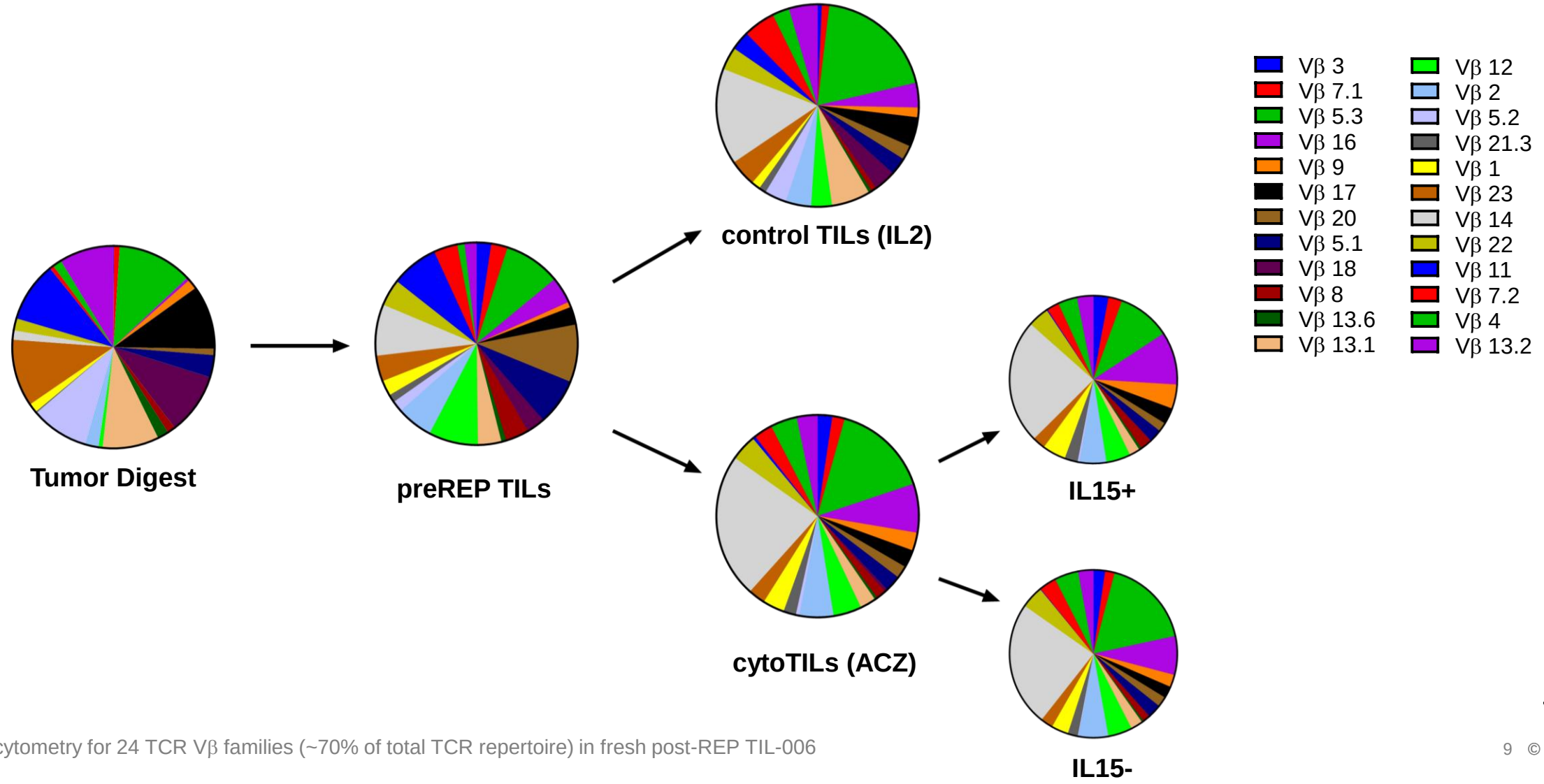
Curve comparisons performed between treatment groups with AUC summary metrics from Day 7 to endpoint (Day 39/Day42) using Mann-Whitney two-sided tests

cytoTIL15 have **higher CD8 T cell** frequencies compared to control TILs, indicating **better potency**



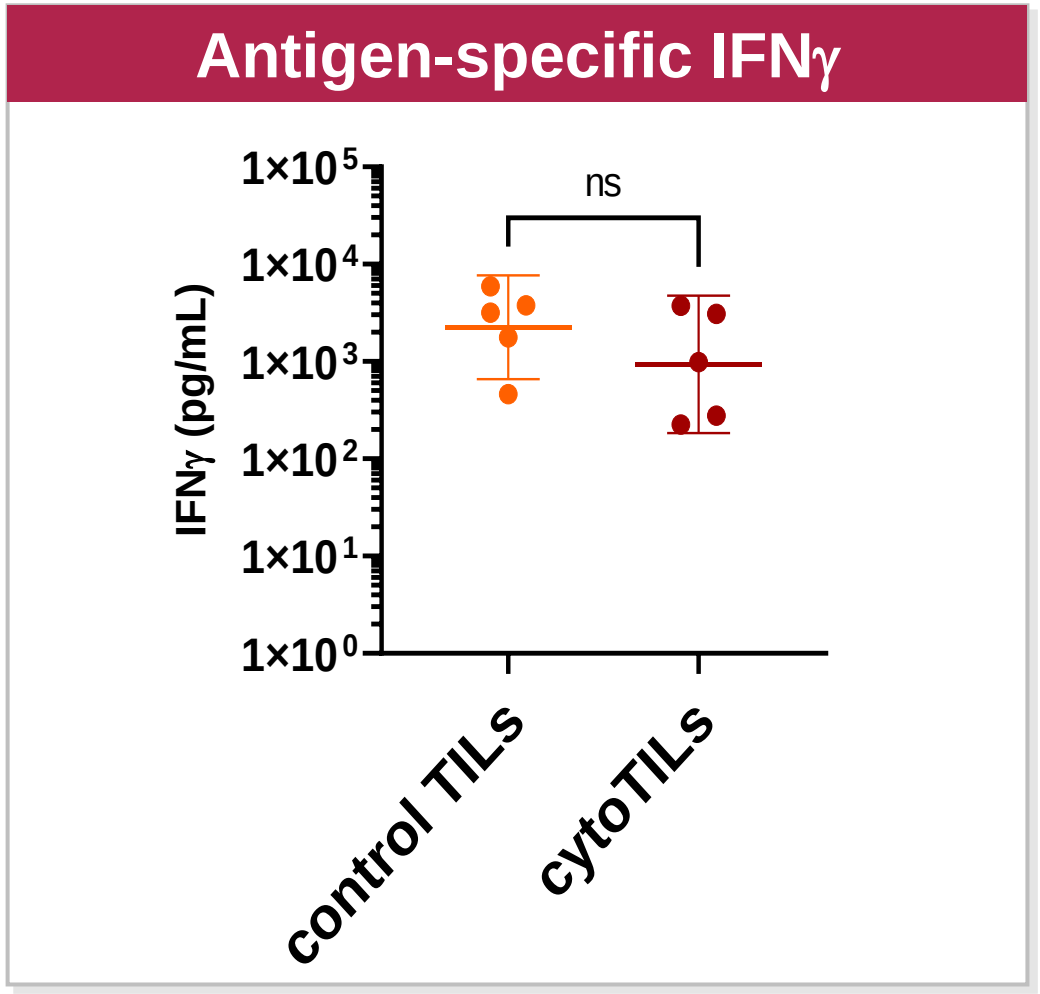
*** P<0.0005

cytoTIL15 maintain TCRVβ **diversity** through the manufacturing process



Flow cytometry for 24 TCR Vβ families (~70% of total TCR repertoire) in fresh post-REP TIL-006

cytoTIL15 maintain reactivity to HLA-matched tumor cell lines



ns: not significant *(P>0.05)*

cytoTIL15: engineered to make TILs more effective for more patients

- Engineered with mbIL15
- Eliminates toxic IL2 regimen
- Drives improved potency & persistence
- IL15 expression controlled by acetazolamide (ACZ), via cytoDRIVE® technology

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