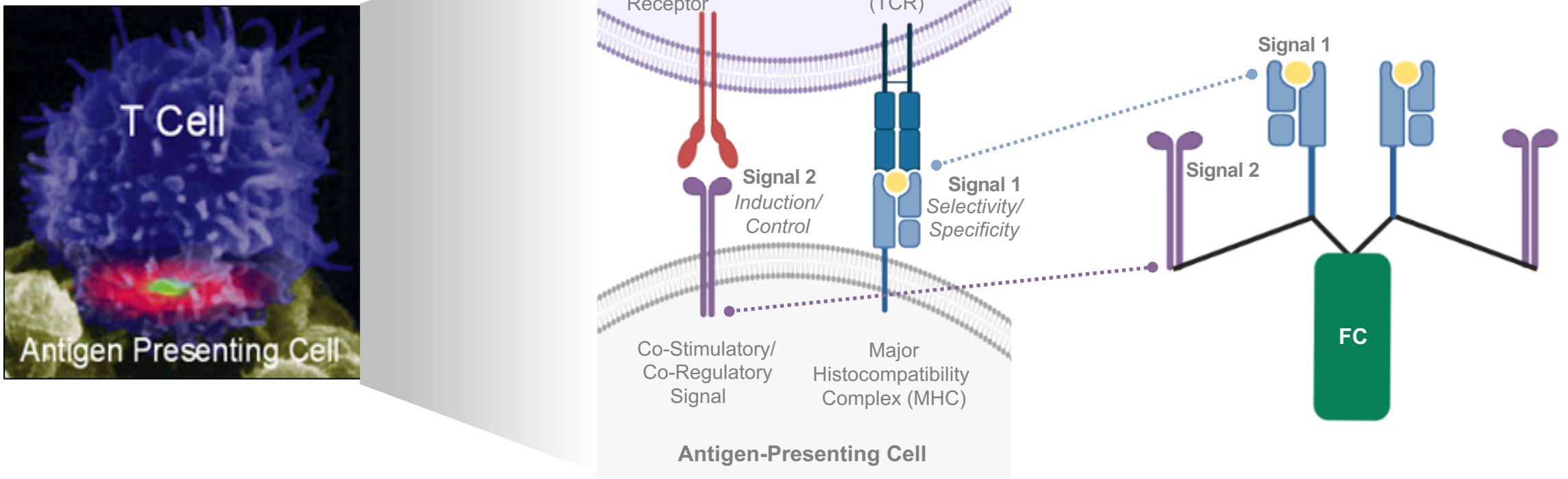
Cue Biopharma/Merck Collaboration

Immune Responses, On Cue™

Nasdaq: CUE | February 2020

Antigen-Specific Immune Tolerance Drug Development Summit | February 26, 2020

Emulating Nature's Cues to Selectively Modulate T Cells



Rationally engineered Immuno-STAT biologics selectively target and modulate the activity of disease-relevant T cells

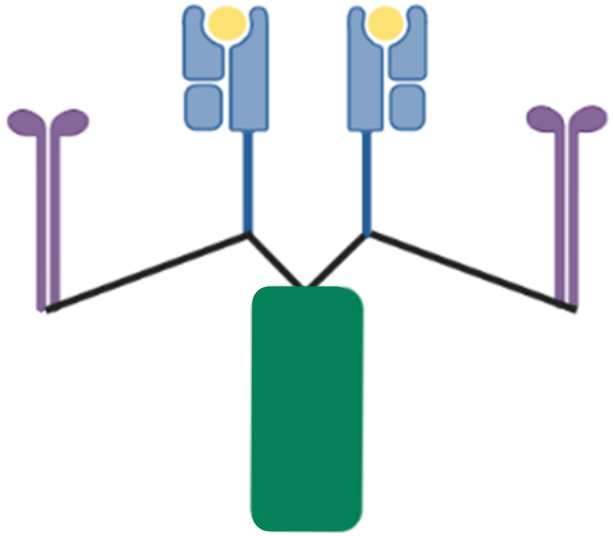
Immuno-STAT Modularity

MHC

Different HLA alleles (class I and II) to address global patient populations

Co-stim/Co-reg

Distinct biological signals, including cytokines; cell-surface receptors; and/or other targeting modalities (e.g. scFv etc)



Peptide

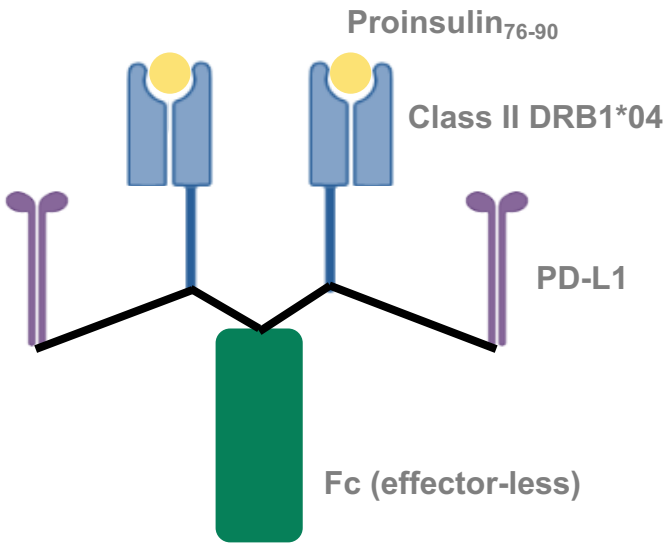
Peptide epitopes to target different diseases

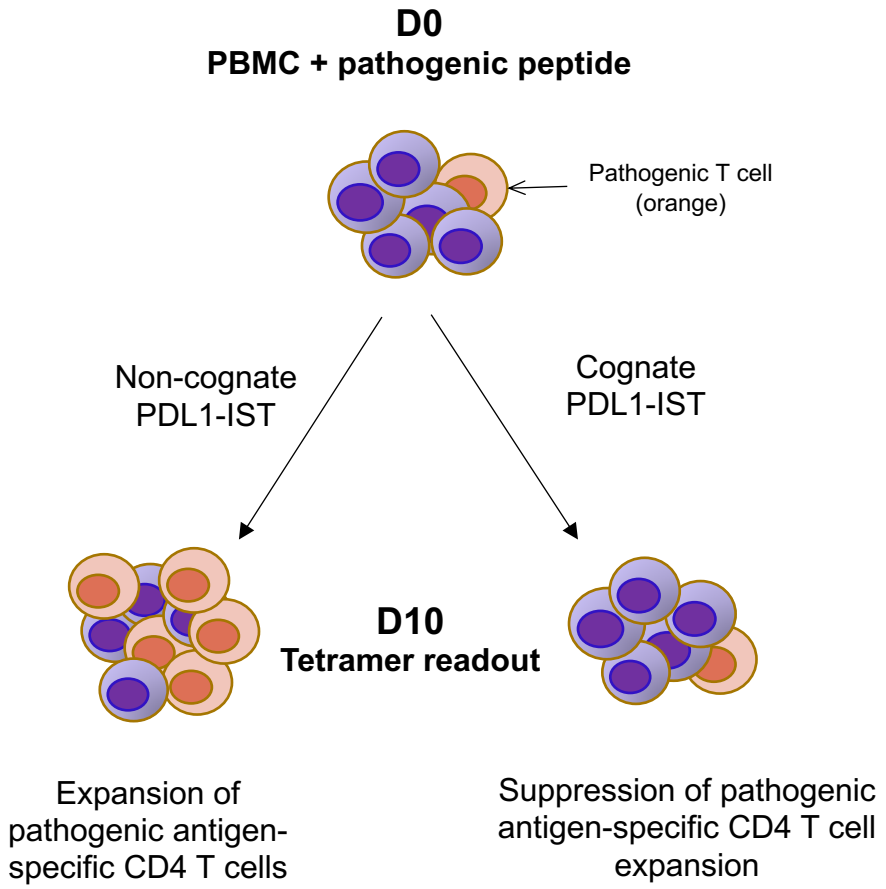
Fc Backbone

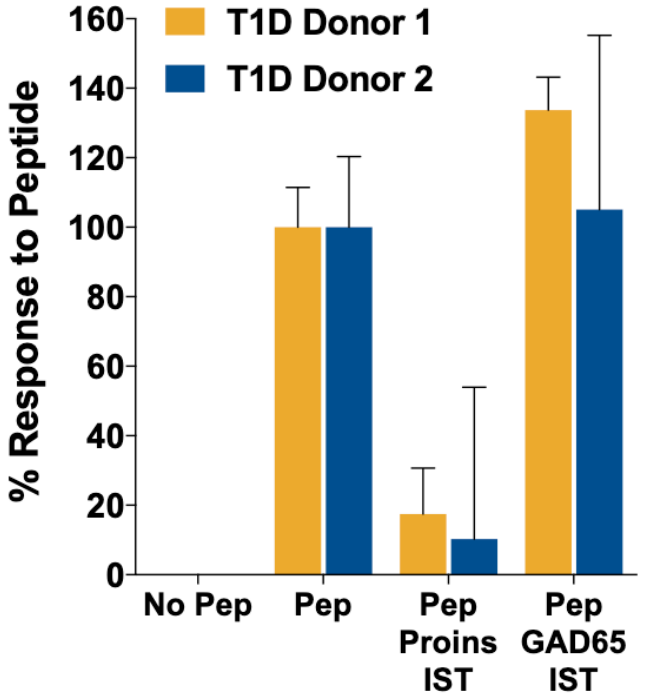
Fc engineering to dial in or dial out biological and effector functions

Combinatorial diversity presents potential to generate therapeutic molecules for a broad set of diseases and patient populations

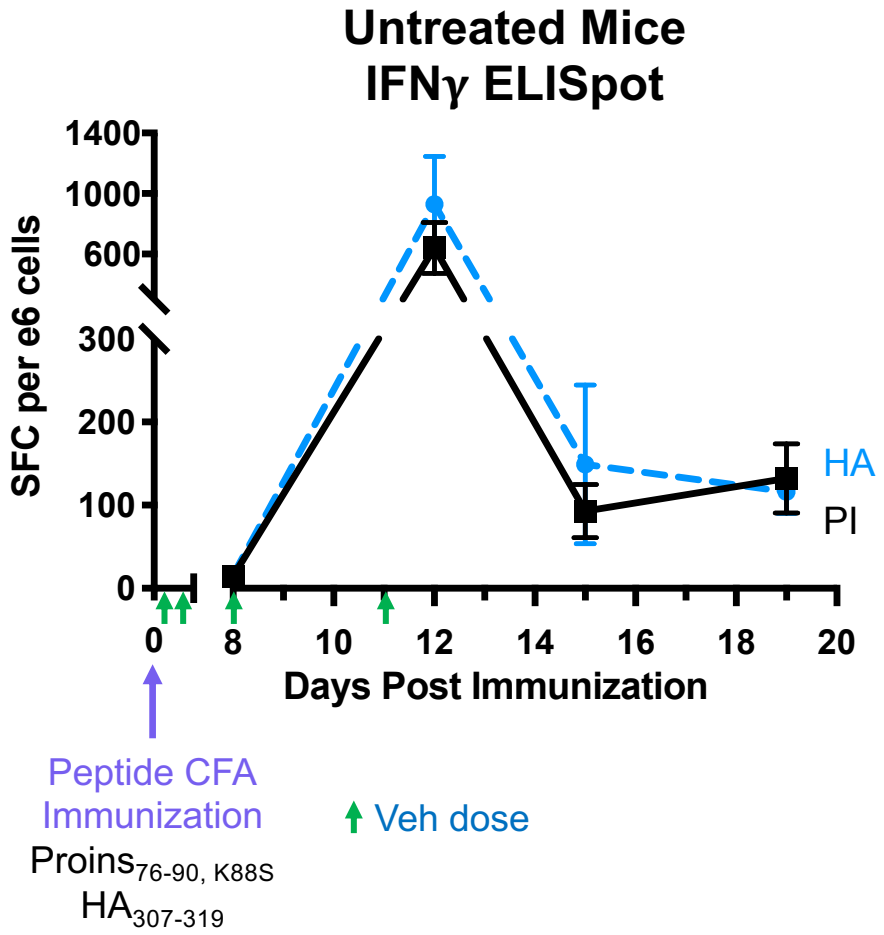
Proins$_{76\text{-}90,\ K88S}$/DR4-PDL1 Immuno-STAT (IST) Selectively Inhibits Antigen-Specific CD4^{+} T Cell Expansion from PBMCs of T1D Donors

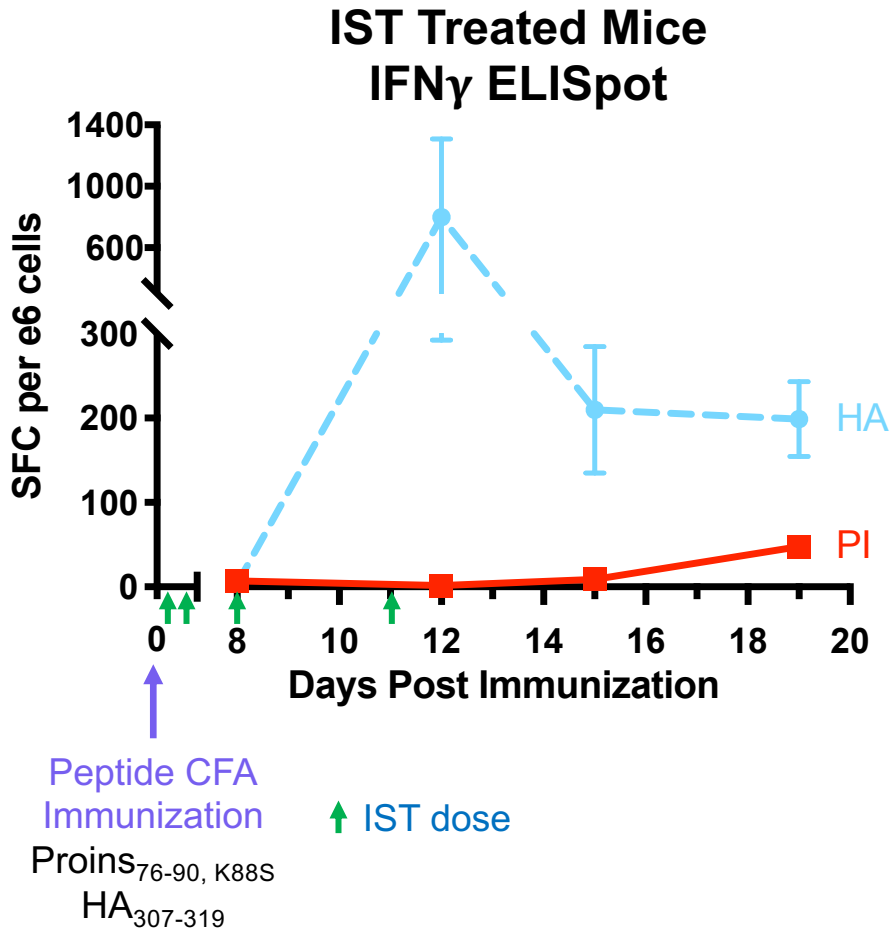






Early Intervention with Immuno-STAT Selectively Reduces the Number of Proinsulin (PI) Responsive CD4+ T Cells in Transgenic Mice

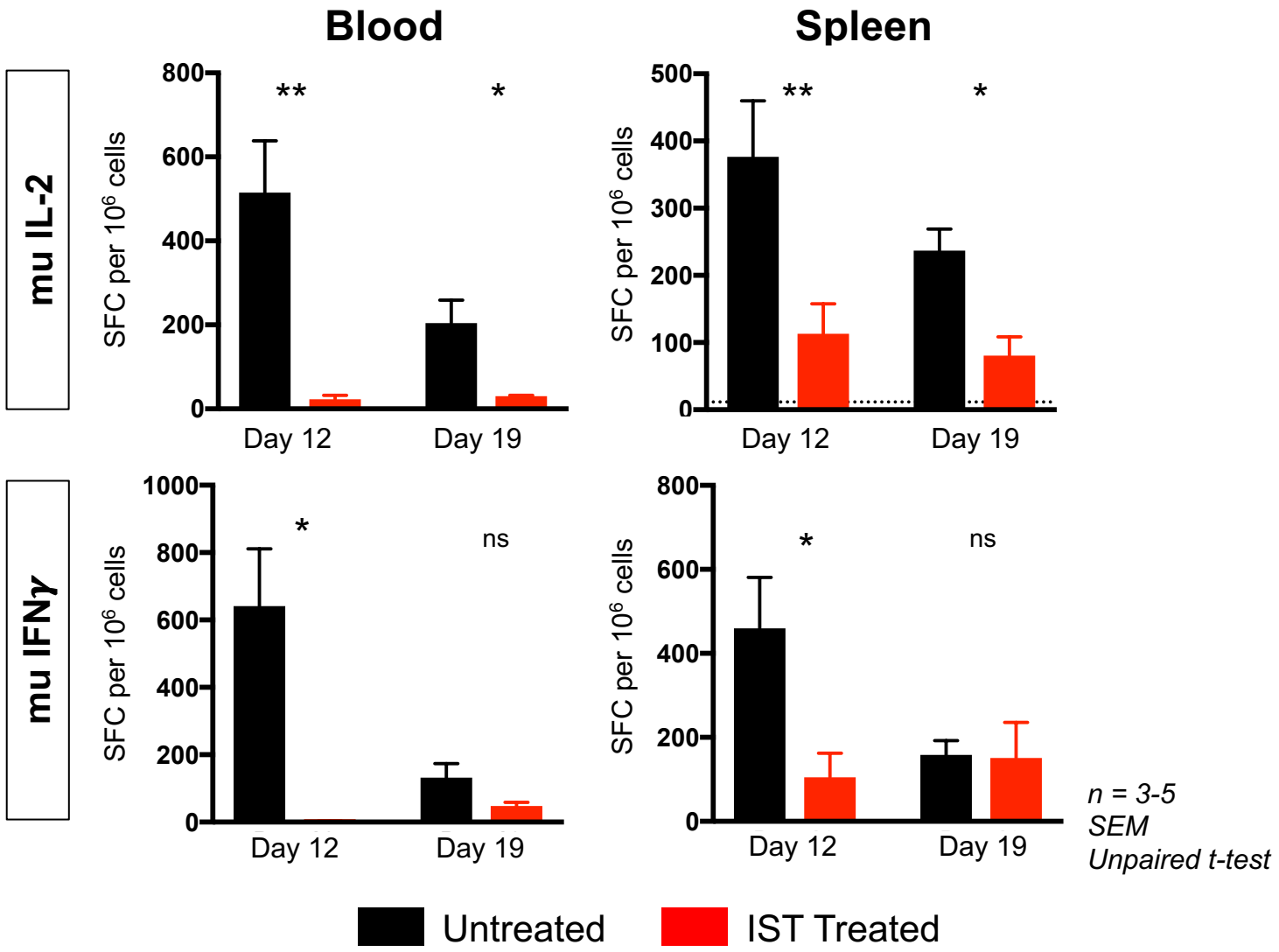




Treatment with Proins-DR4-PDL1 IST starting on Day 1 post immunization selectively suppresses expansion of PI-reactive cells without inhibiting expansion of HA-reactive cells

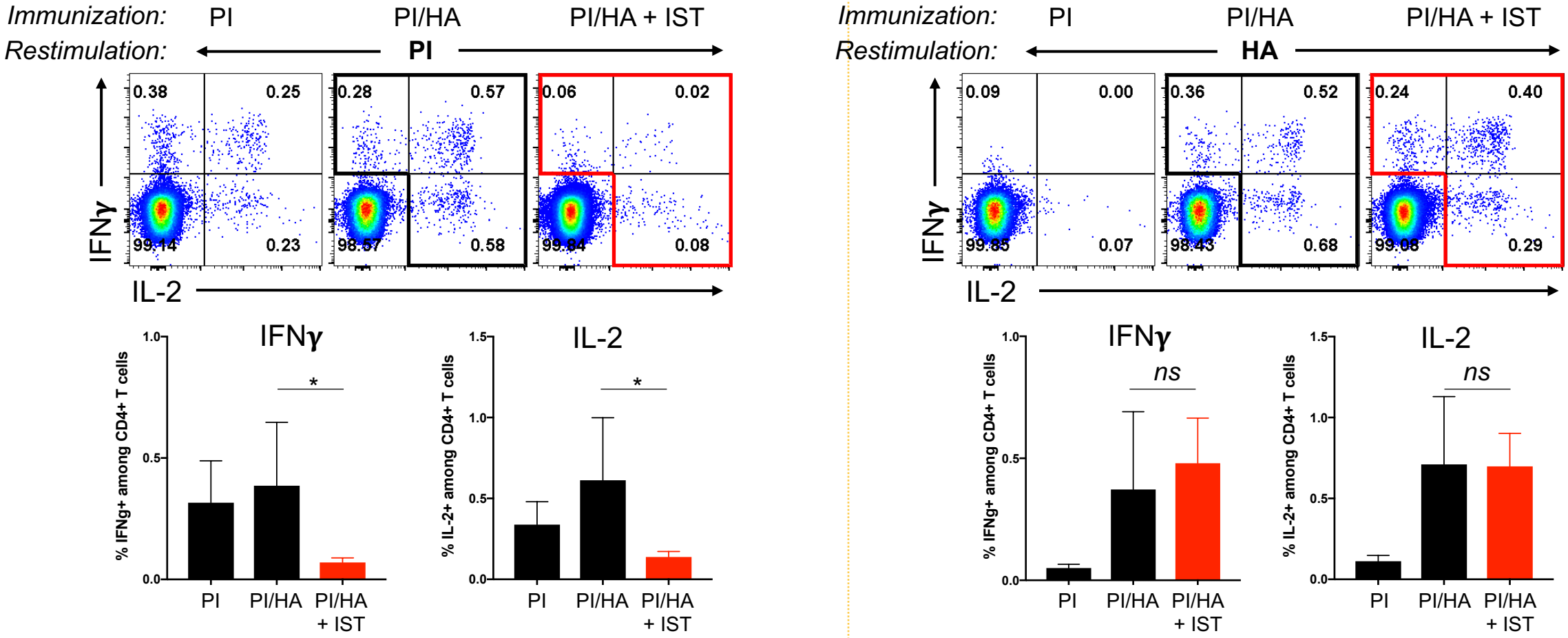
Significant Reduction in Proinsulin-Specific IL-2 & IFNγ Producing CD4+ T Cells in Blood and Spleen after Immuno-STAT Treatment

PI/HA Immunized DR4 Tg Mice
$PI_{76\text{-}90\ K88S}$ Peptide Stimulated



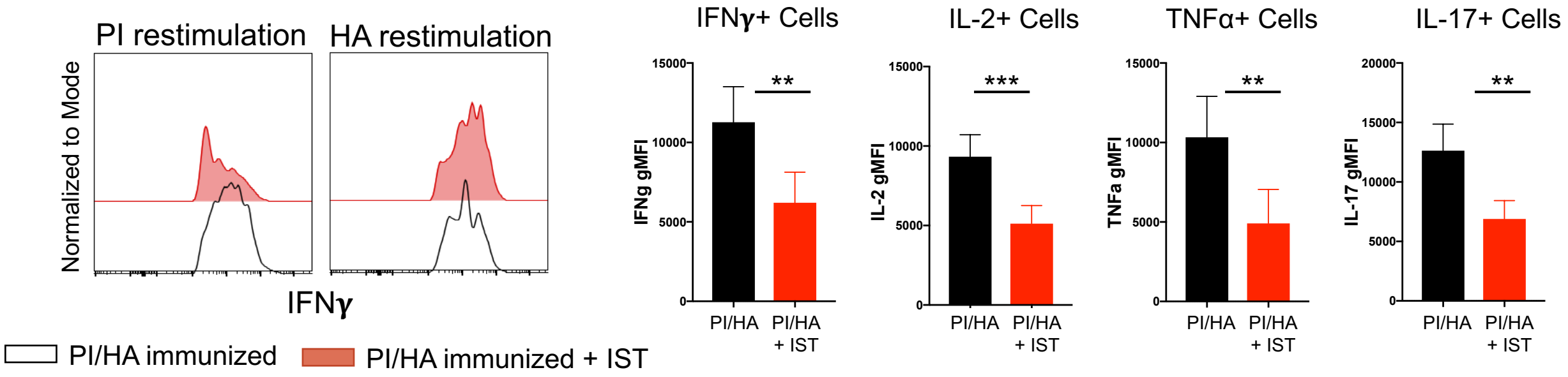
n = 3-5
SEM
Unpaired t-test

In Vivo Treatment with Proins$_{76\text{-}90,\ K88S}$/DR4-PDL1 Immuno-STAT Suppresses Cytokine Production by Proins (PI)-Specific CD4$^+$ T Cells



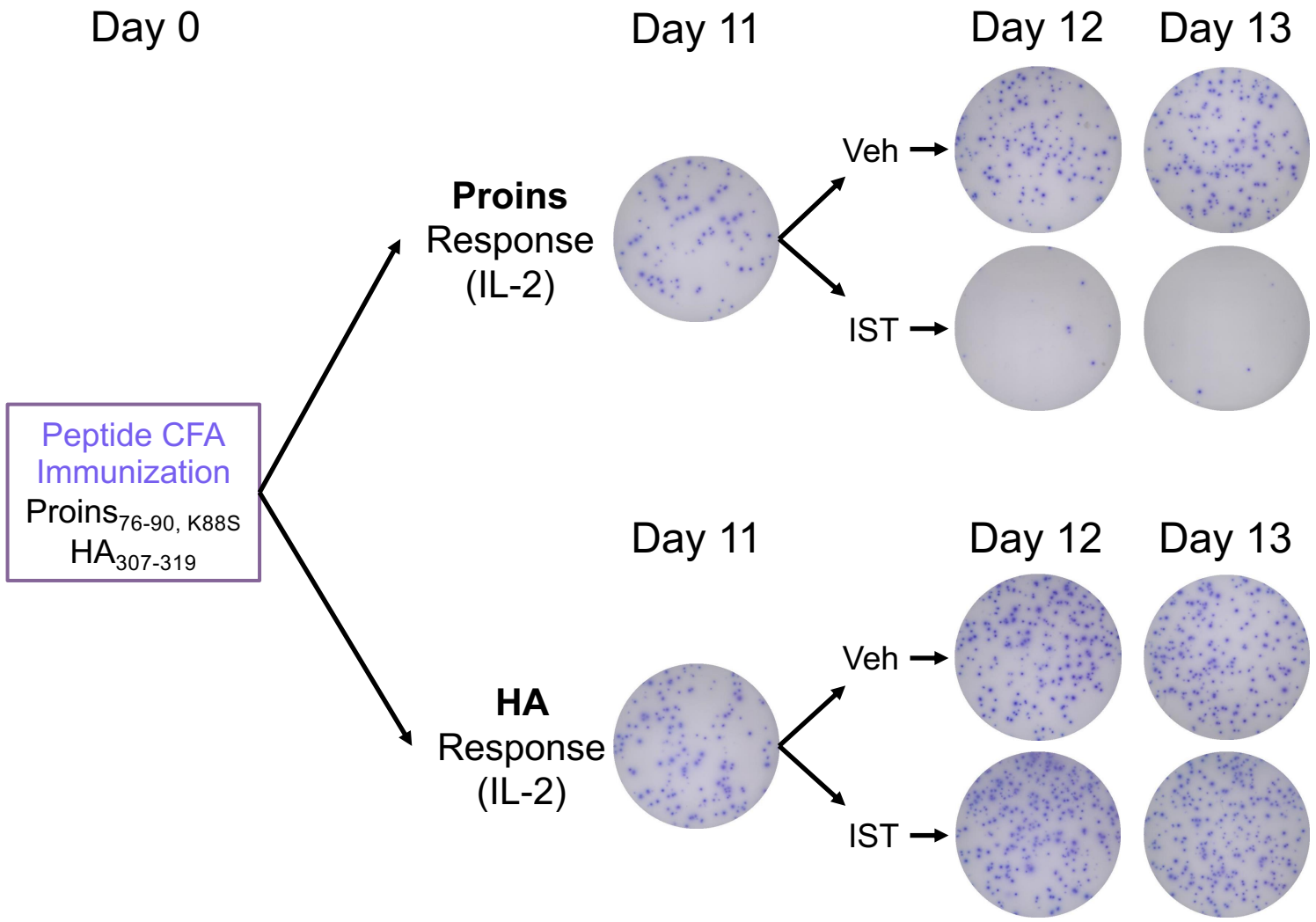
Treatment with ProIns-DR4-PDL1 IST suppresses cytokine production of PI-specific CD4$^+$ T cells (IL2, IFNγ, TNFα, IL-17) without affecting HA-reactive cells

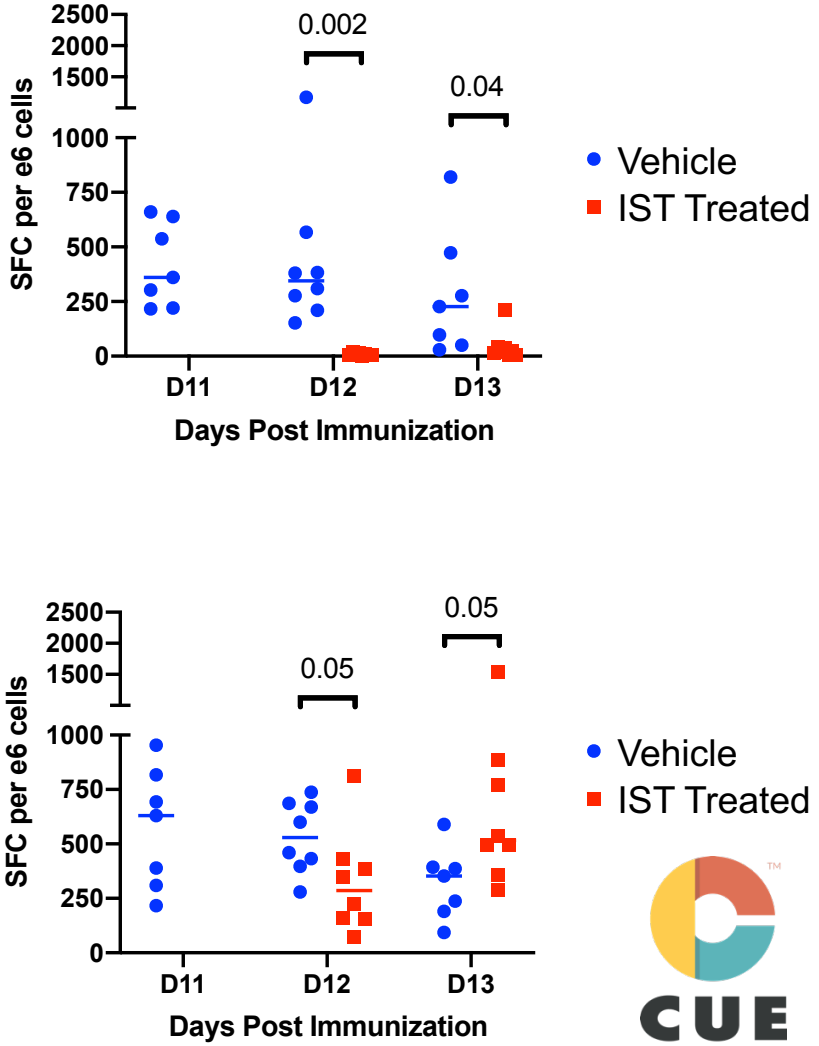
Proins (PI)-Specific CD4+ T Cells Produce Lower Levels of Cytokine Following Proins$_{76\text{-}90,\ K88S}$/DR4-PDL1 Immuno-STAT Treatment



Treatment with ProIns-DR4-PDL1 IST reduces the gMFI of cytokines produced by PI-specific cytokine+ CD4+ T cells without affecting HA-reactive cells

Late Intervention with Immuno-STAT Selectively Reduces the Number of Proins (PI) Responsive CD4+ T Cells In Vivo





Summary

- Successful generation of Immuno-STAT molecules comprised of Class II HLA molecules (DRB1*04) along with PD-L1 inhibitory ligand to selectively dampen autoreactive $CD4^+$ T cells
- Treatment with $Proins_{76\text{-}90,\ K88S}$/DR4-PDL1 Immuno-STAT significantly suppressed expansion of Proins-specific $CD4^+$ T cells both in vitro and in vivo
- The effect of $Proins_{76\text{-}90,\ K88S}$/DR4-PDL1 Immuno-STAT treatment was antigen specific as treatment did not result in a reduction of HA-specific $CD4^+$ T cells
- A single in vivo administration of $Proins_{76\text{-}90,\ K88S}$/DR4-PDL1 Immuno-STAT at the peak of immunization response significantly reduced the frequency of Proins-responsive T cells