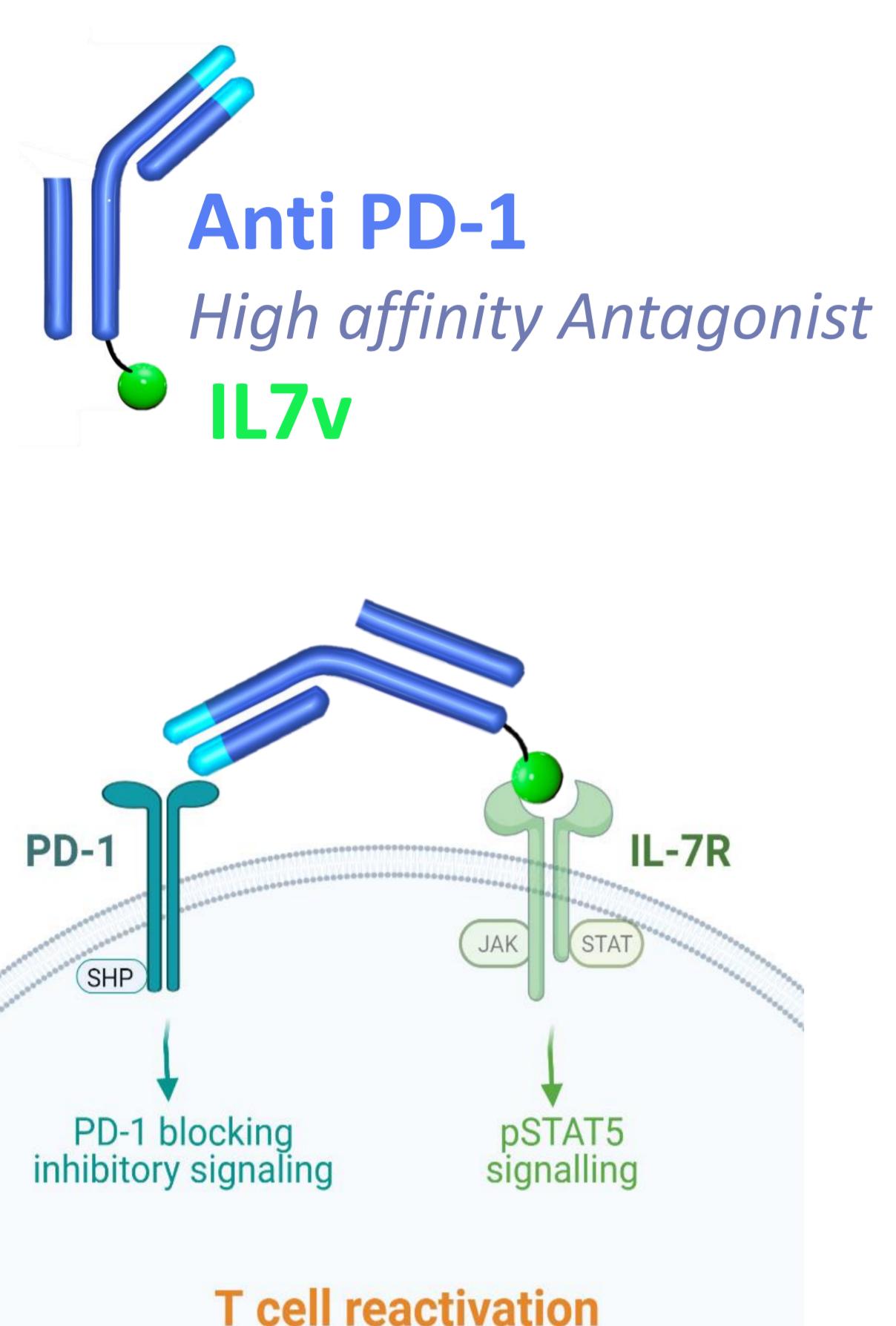


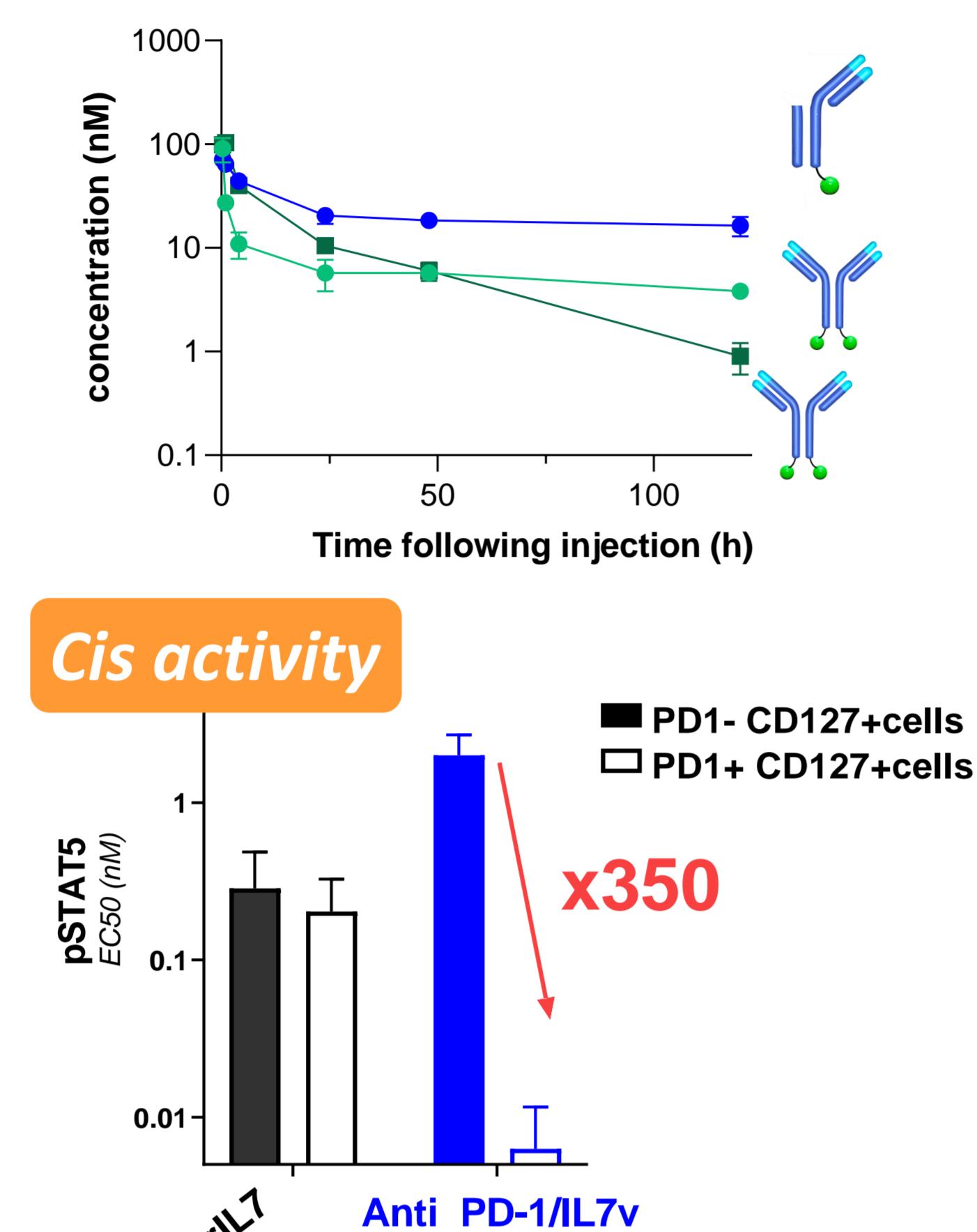
Anti-PD-1/IL-7v bispecific antibody (BICKI®IL7v) promotes TCF1+ stem like T cells expansion and long-lasting in vivo efficacy

Aurore Morello, Margaux Seit , Justine Durand, Isabelle Girault, G raldine Teppaz, Virginie Thopenier, C cile Batty, Sabrina Pengam, Emmanuelle Wilhelm, Ariane Desselle, Kevin Biteau, Julien Taurelle, Caroline Mary, Nicolas Poirier

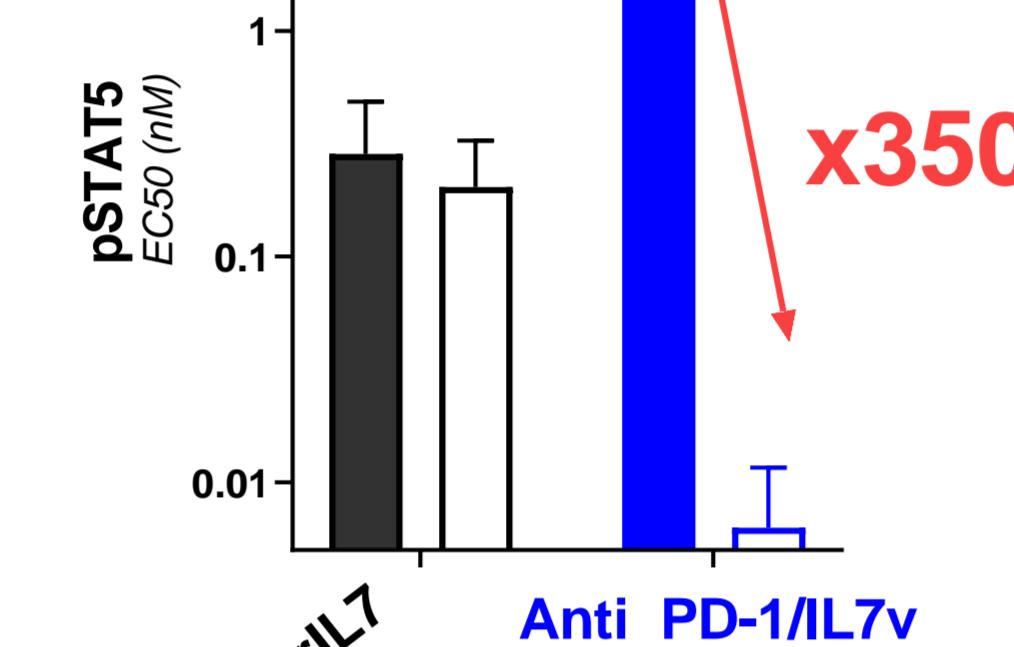
1/ BICKI®IL7 Optimized anti PD-1/IL7v immunocytokine design for selective cis-potentiation



Enhanced in vivo drug exposure

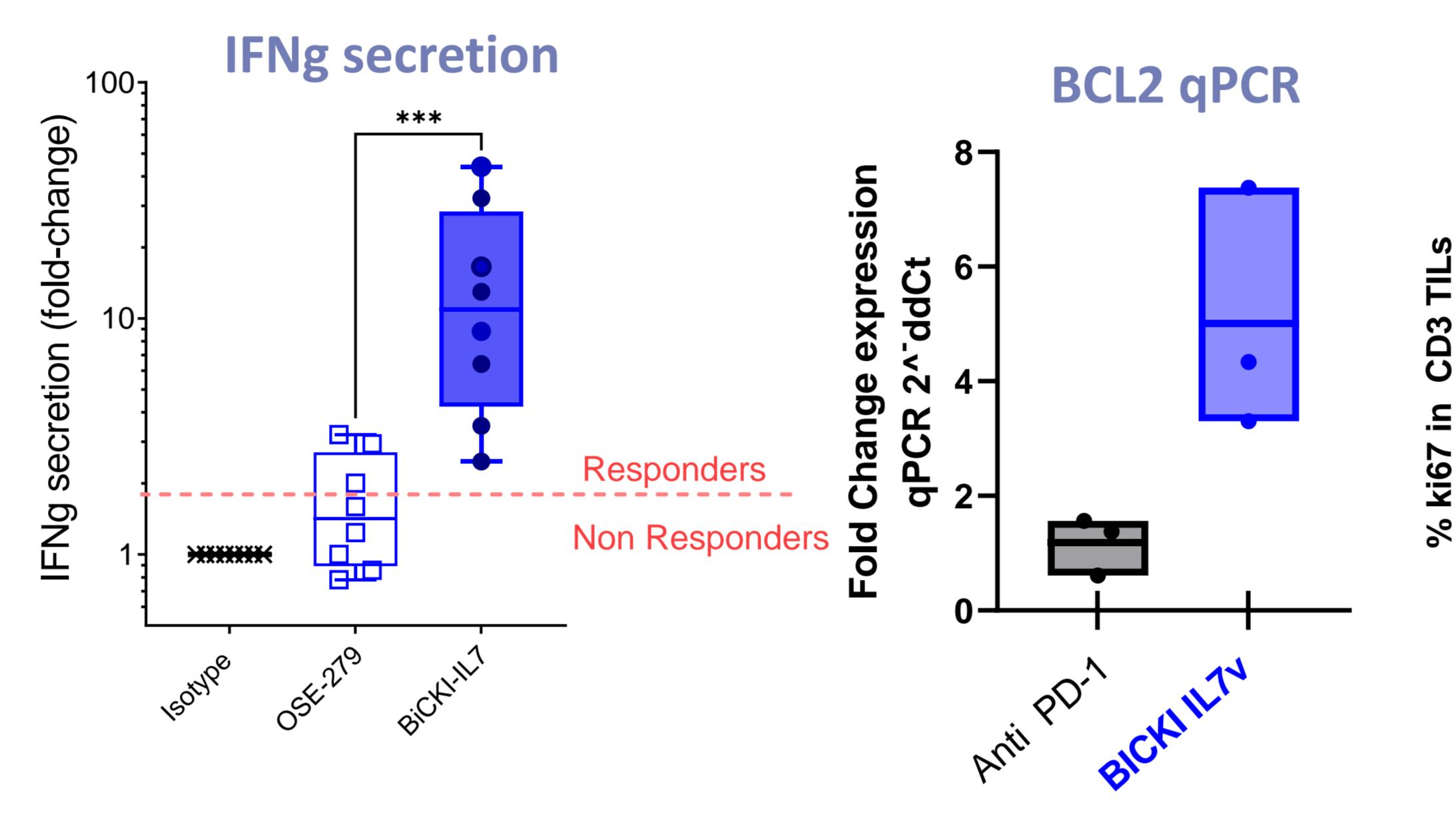


Cis activity

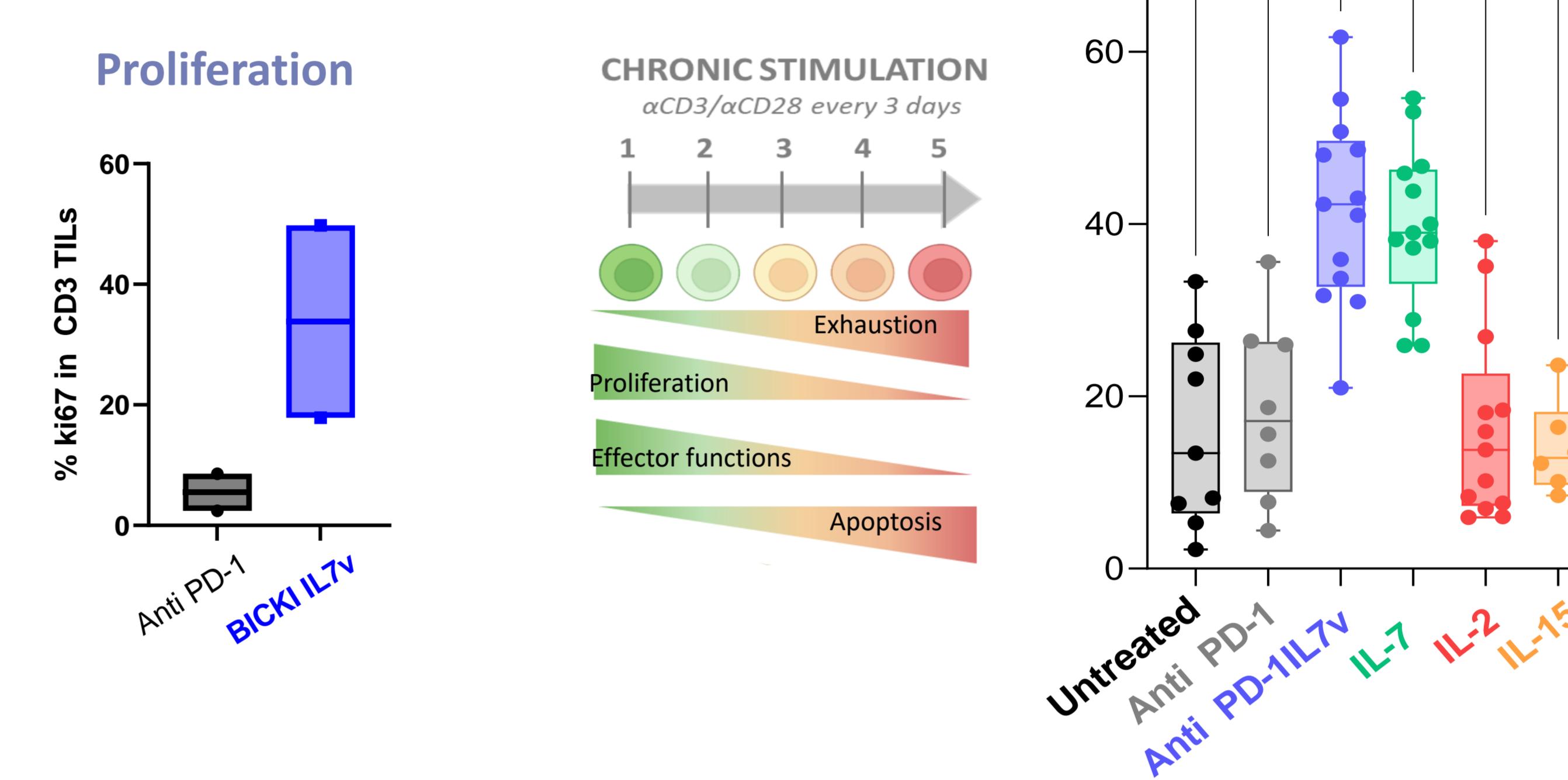


3/ BICKI®IL7v revives TILs & promotes long-term proliferation stem-like TCF1+ CD8 T cells

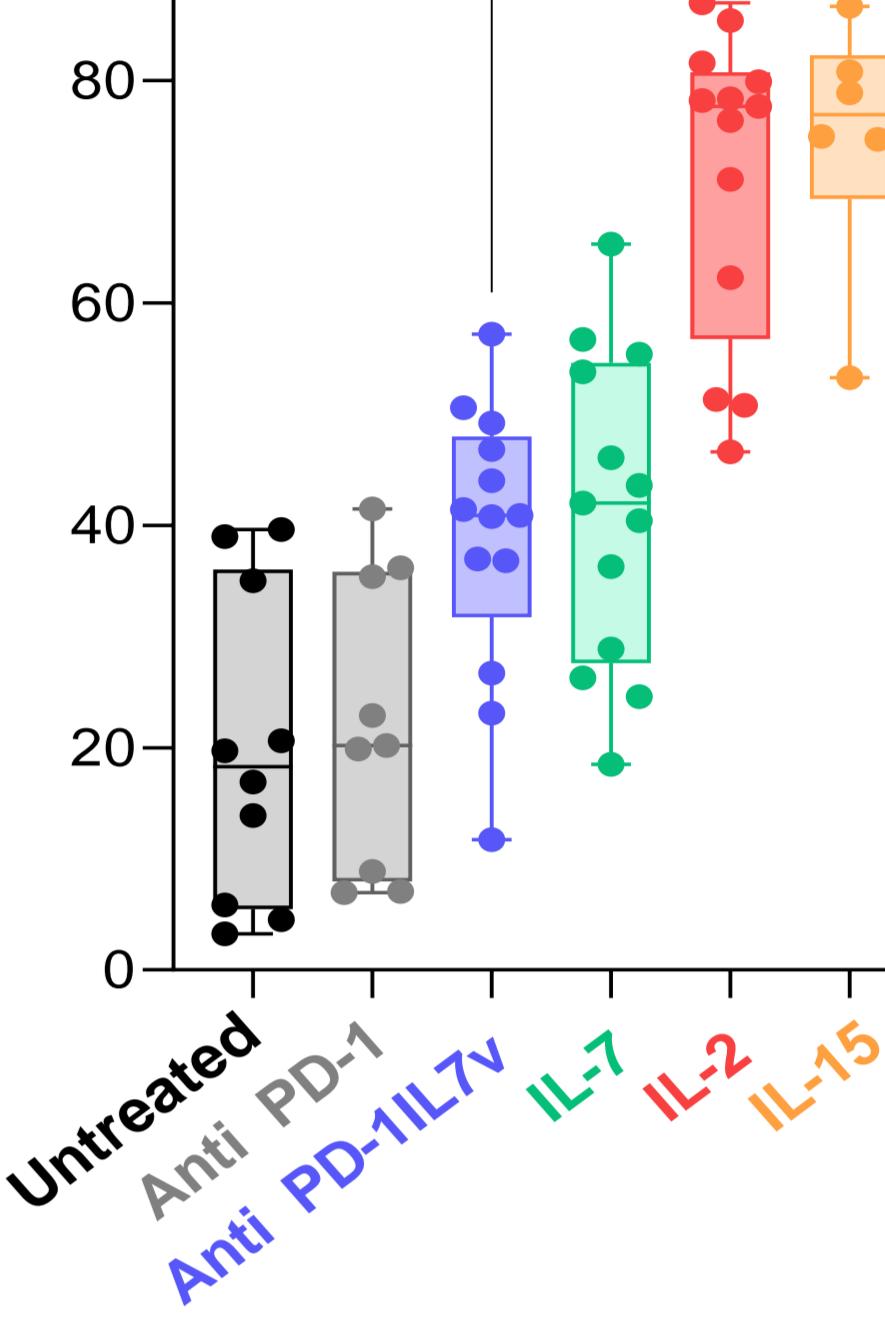
Enhanced IFNg secretion, proliferation & survival of human TILs



Proliferation Chronically stimulated T cells



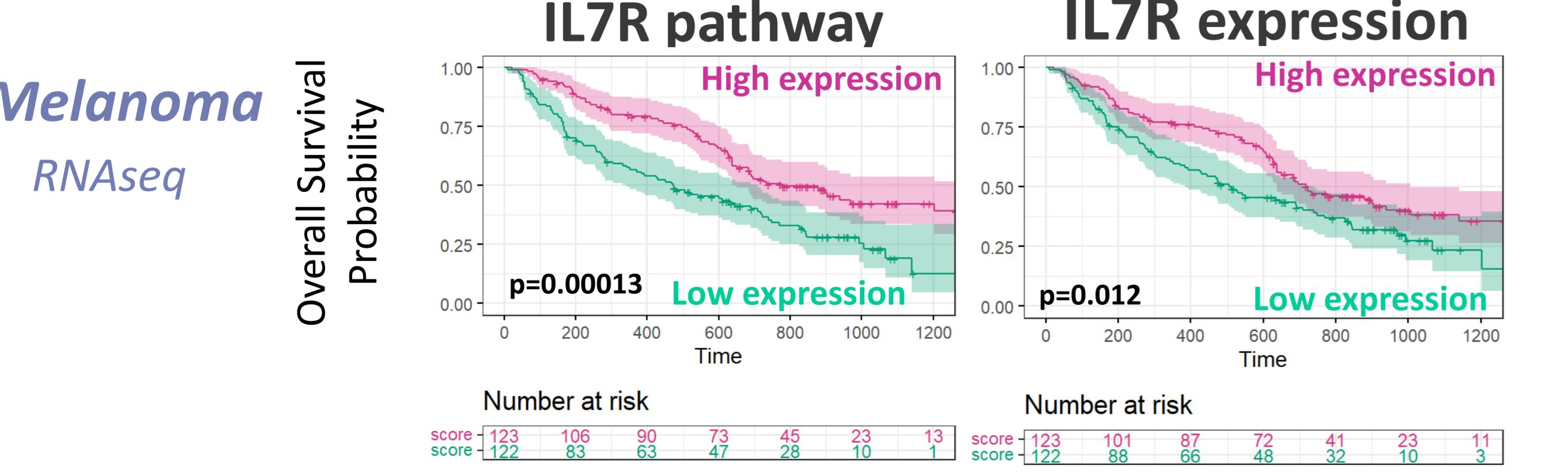
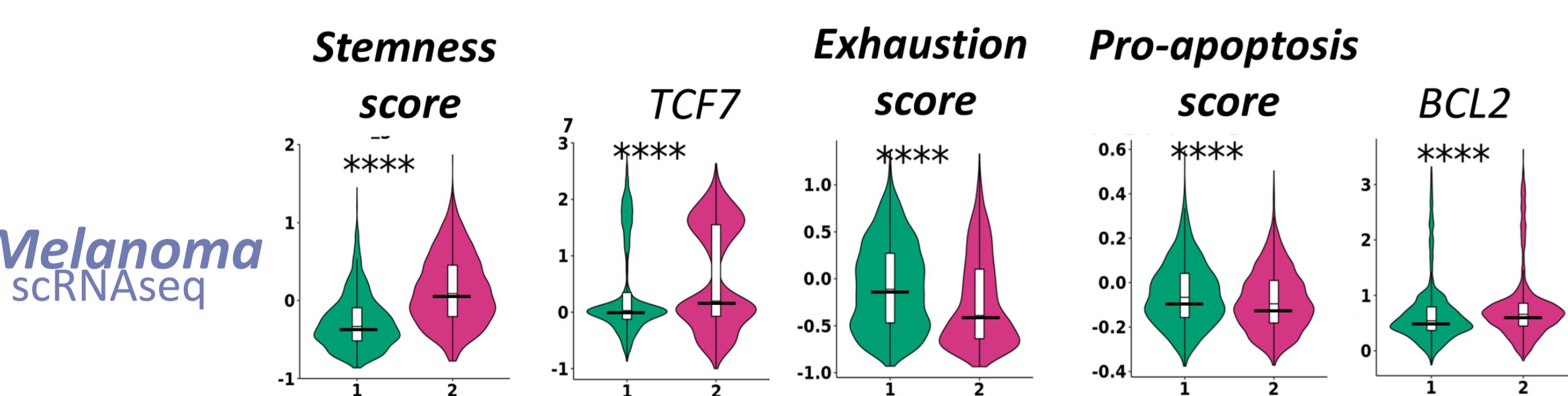
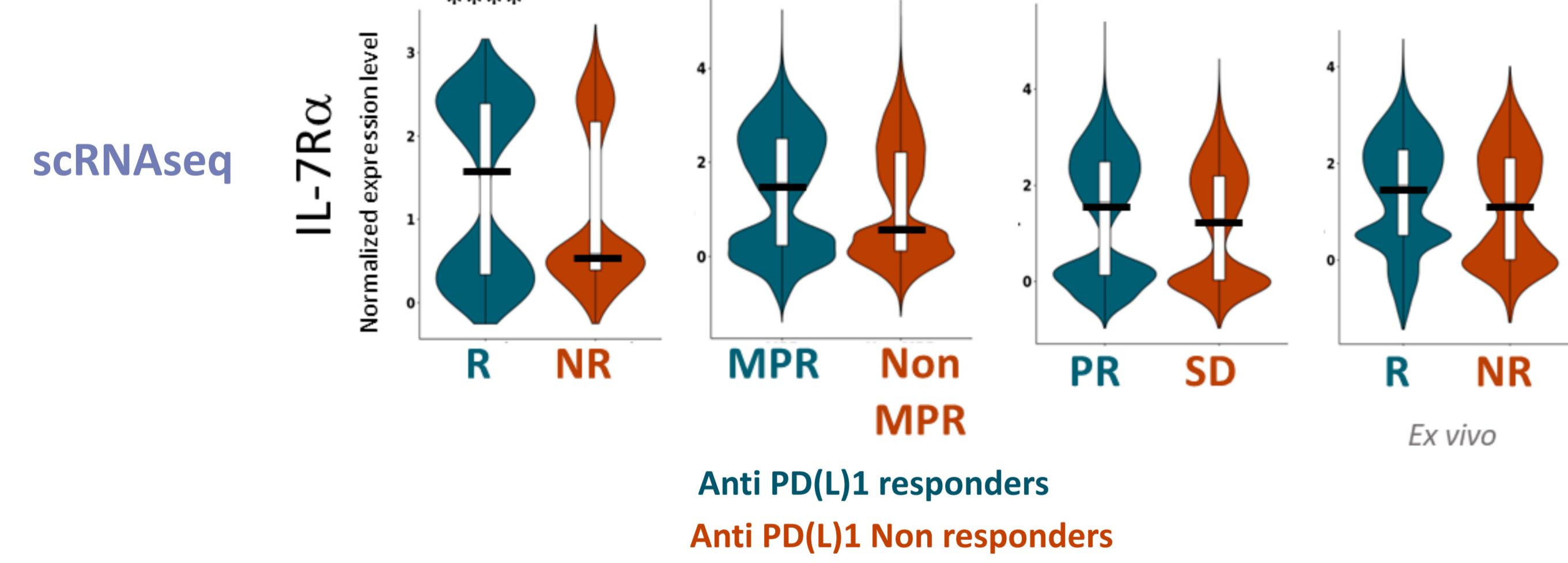
TCF-1- Ki67+



2/ Rationale for co-targeting PD-1 and IL-7 in TILs:

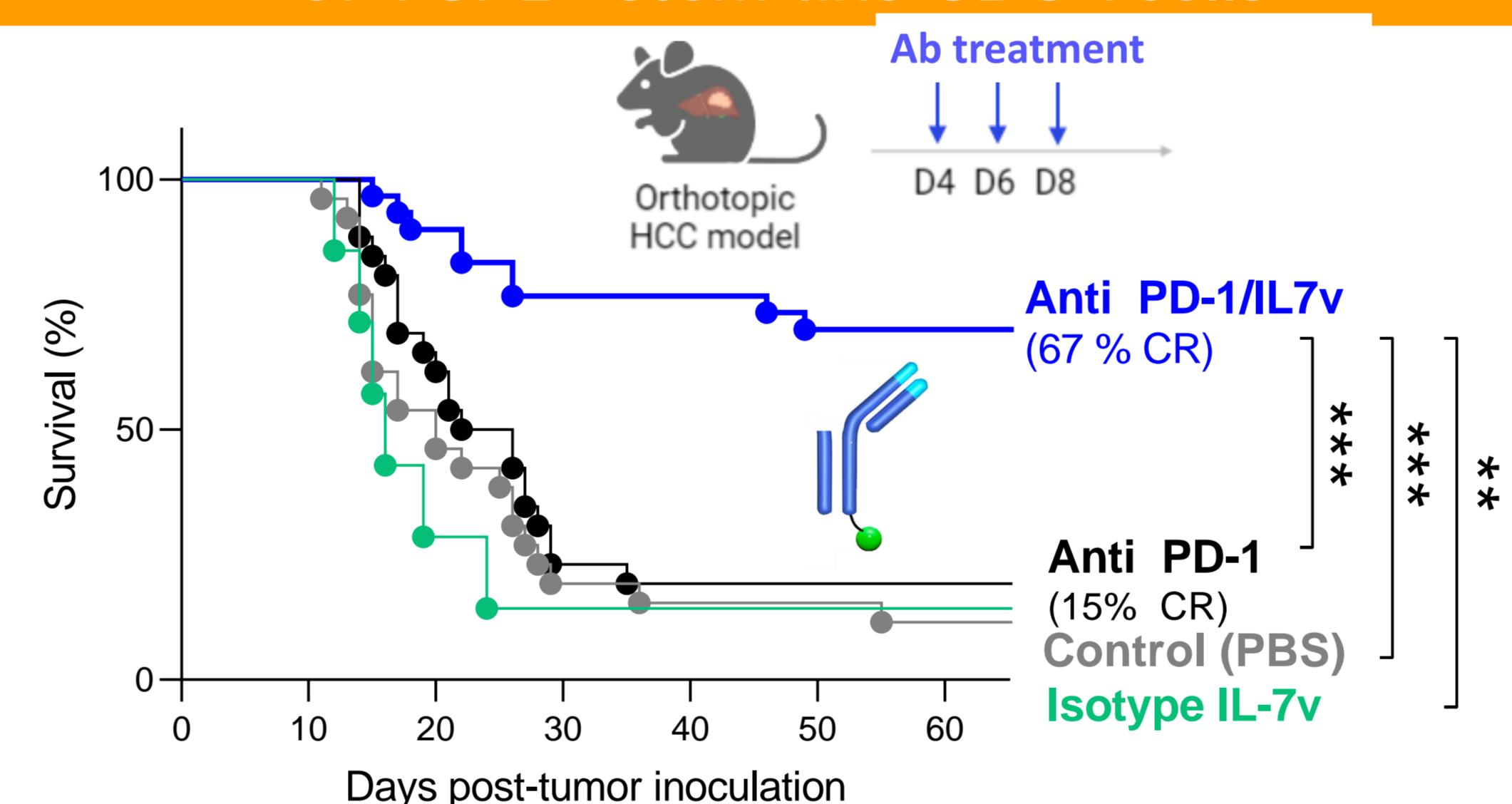
IL7R expression correlates with better ICI response/survival and T-cell stemness

Melanoma

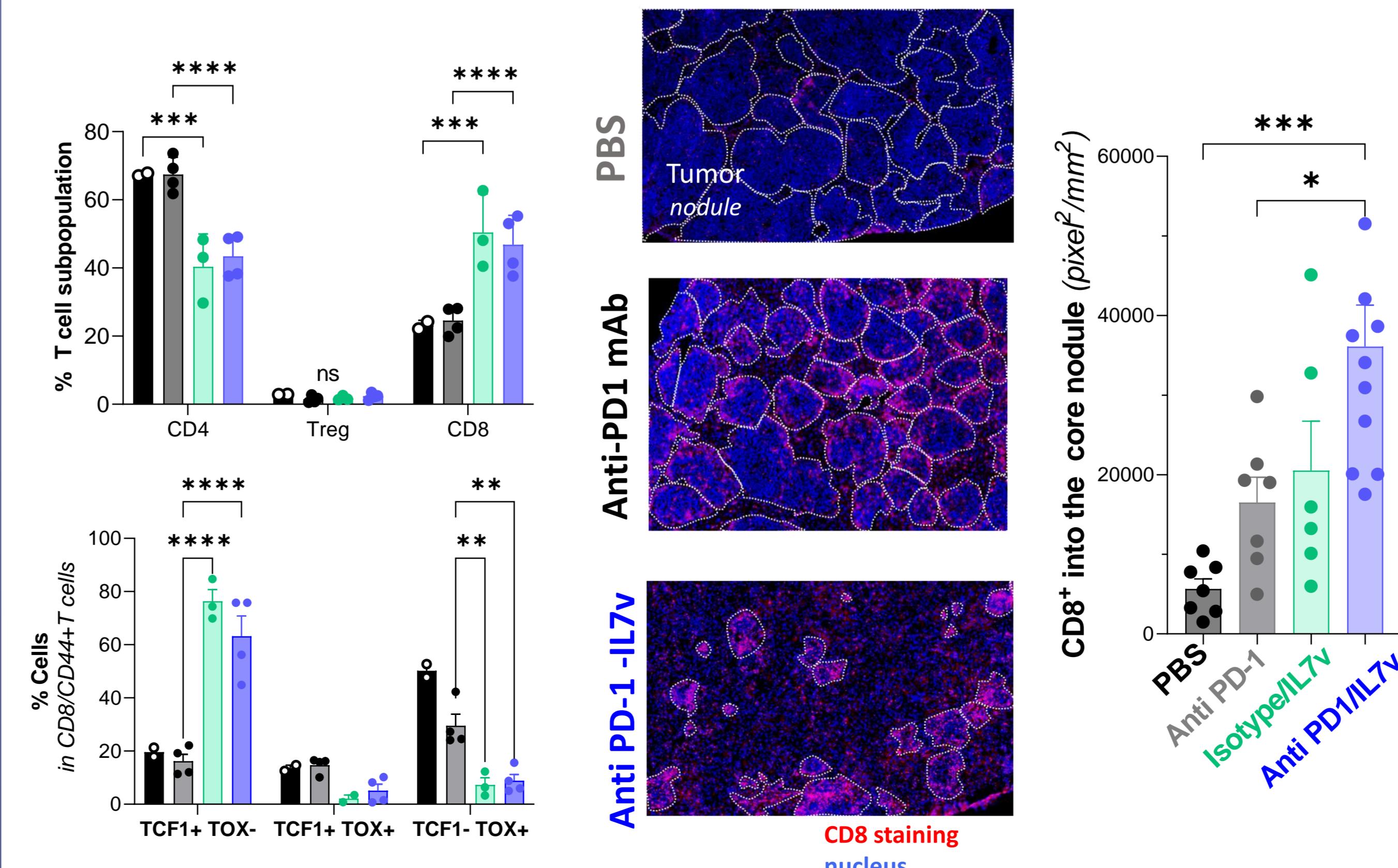


Sade-Feldman et al. 2018, Caushi et al. 2021, Zhang Y et al. 2021, Duraiswamy et al. 2021, Gide et al. 2019, Liu et al. 2019, Riaz et al., 2017

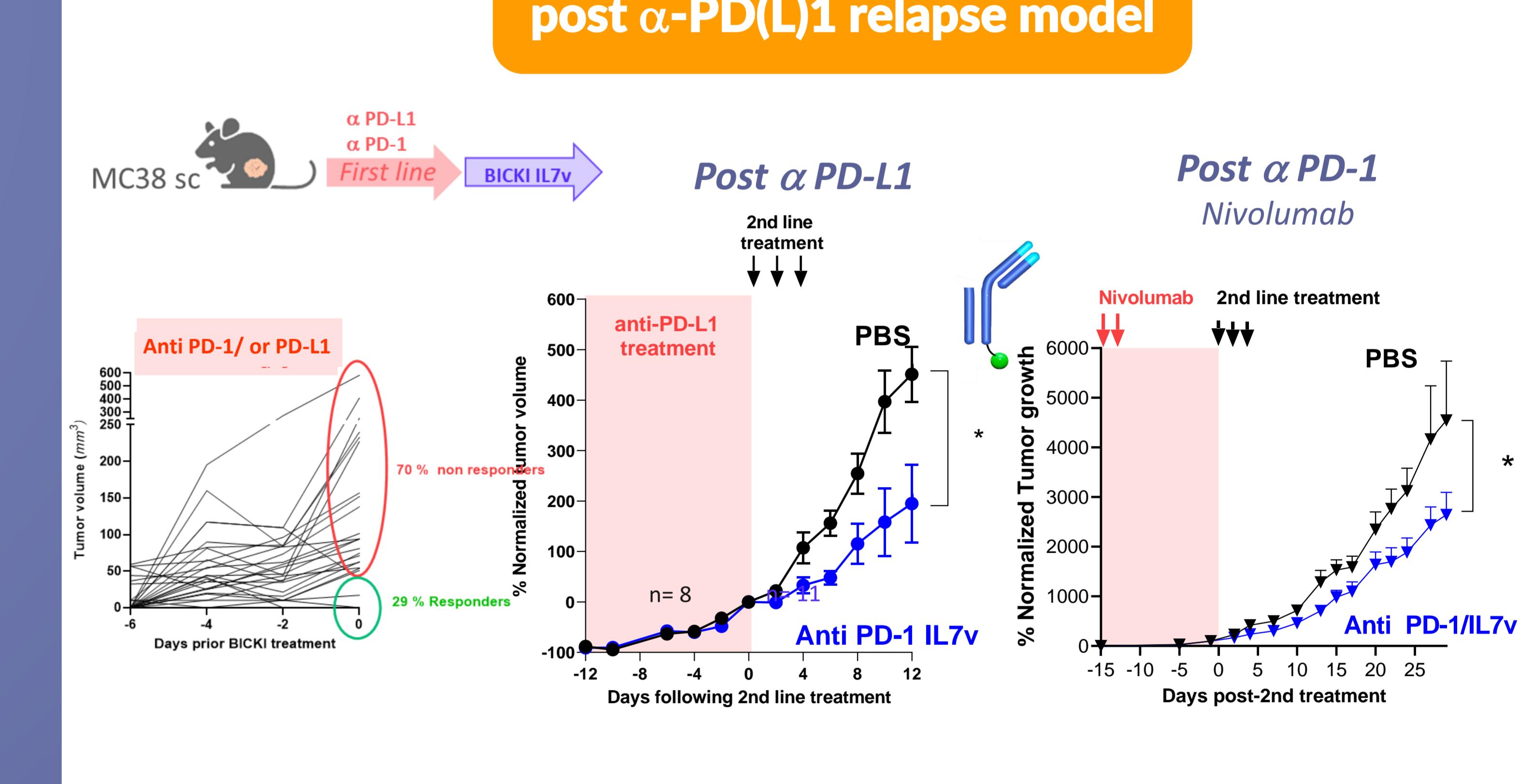
4/ Anti PD-1 IL7v monotherapy in vivo efficacy by promoting infiltration and proliferation of TCF1+ stem-like CD8 Tcells



Anti PD-1 IL7v overcomes T cell exclusion & induces high proliferation of stem-like T cells



5/ Anti PD-1/IL7v efficacy post  -PD(L)1 relapse model



Conclusion

To sustain a durable PD-1+ stem like CD8 T cell response

- Optimized molecule for Cis targeting activity
- Conserved high PD-1 binding and PD-1/PD-L1 antagonist activity
- Allows a selective delivery of IL-7 on PD-1+ cells
- Promotes proliferation of PD-1+ CD127+ TCF1+ stemness T cells
- Significant *in vivo* anti tumor efficacy
- in PD-1 sensitive, resistant syngeneic and humanized models
- In vivo* efficacy post  -PD-1 or  -PD-L1 refractory tumor