

IL7R TME expression correlates with immunotherapy response and is associated with T-cell stemness and decreased apoptosis

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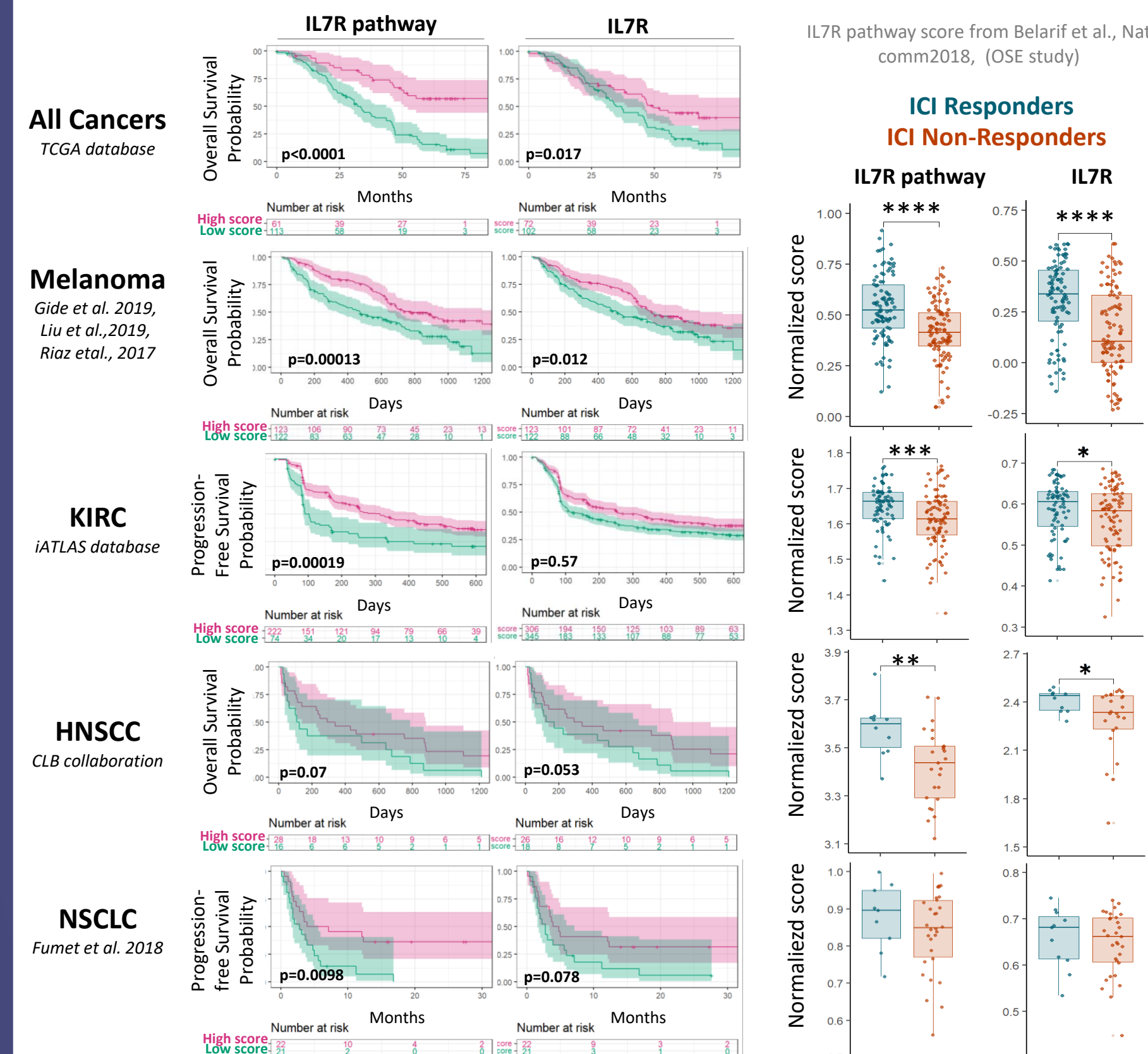
Immune checkpoint inhibitor (ICI) therapy can reinvigorate exhausted Tcells by inducing a proliferative burst of PD1+TCF7+ stem-like Tcells, but they rapidly undergo exhaustion and death, limiting efficacy of ICI therapy.

IL7 cytokine is promising to promote long-term survival and homeostatic proliferation of T cells. IL7R , IL-7 engagement pathway and its biological effect to reactivate cancer-specific Tumor infiltrated Lymphocytes (TILs) remains unknown. We studied gene expression of the IL7/IL7R pathway on bulk RNAseq (n=1 036 samples) and on single cell RNAseq (n=39 samples) in multiple datasets of anti-PD1/PDL1 responder and non-responder patients and also evaluated the effect of anti-PD1 fused IL-7 mutein (BICKI®IL7v) *in vitro* and *ex vivo* to reactivate exhausted human Tcells.

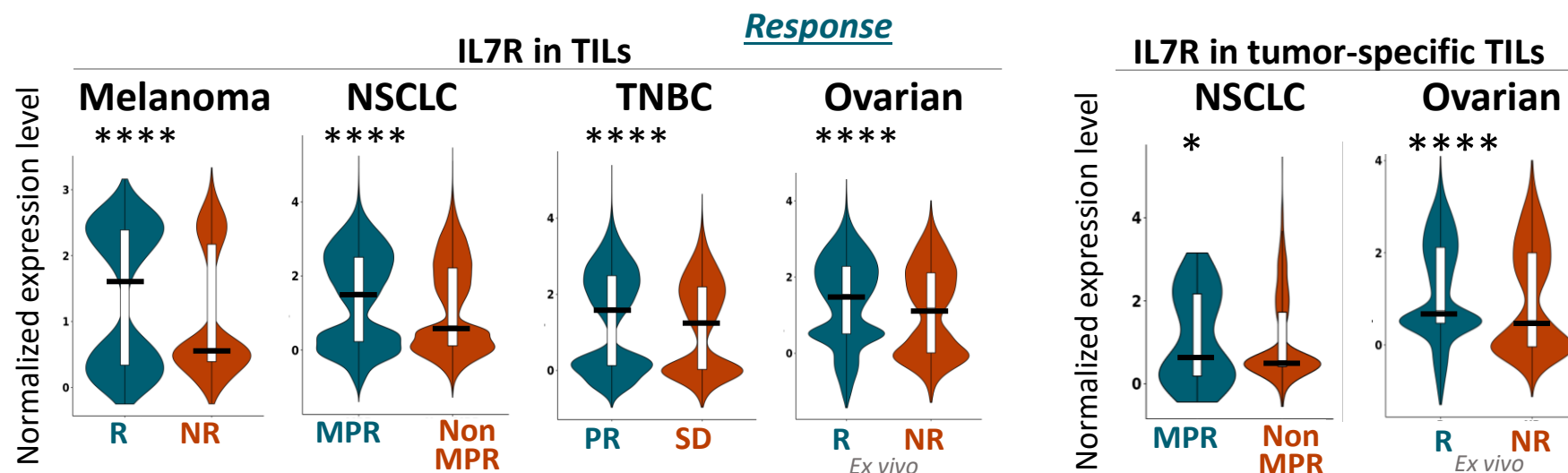
Introduction

1/ IL7R & IL7R engagement in TILS are associated with better survival and response to ICI

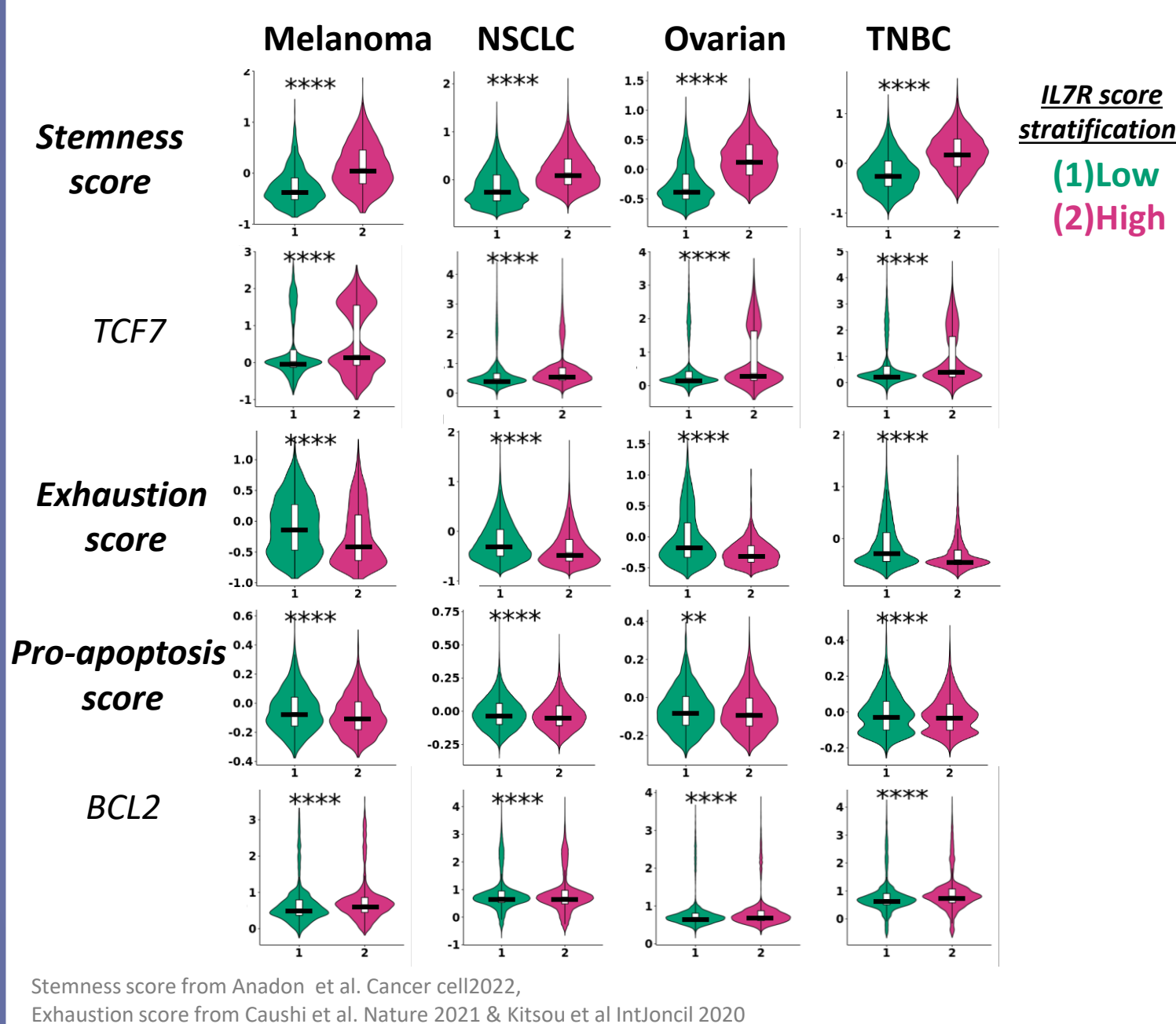
In Bulk RNAseq : IL7R pathway or IL7R high score expression prior therapy is correlated with significant higher OS and PFS and with Response to ICI (anti PD-(L)1/CTLA-4)



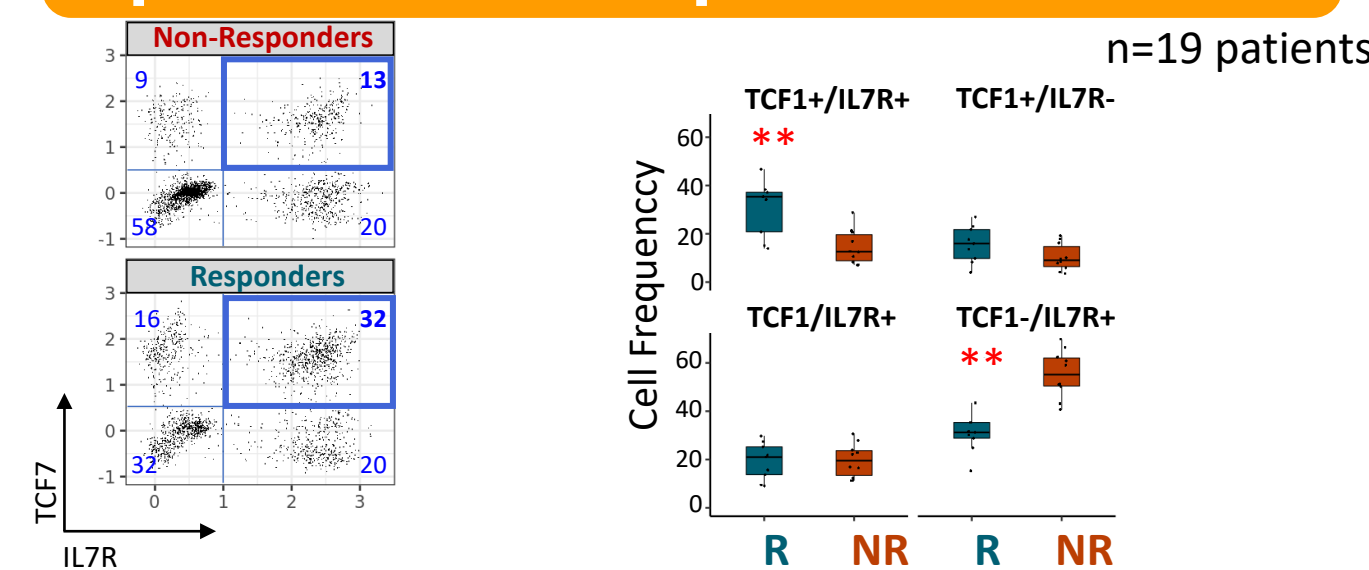
In scRNAseq of tumor TILs and tumor specific TILs : IL7R expression level significantly associated with ICI Response



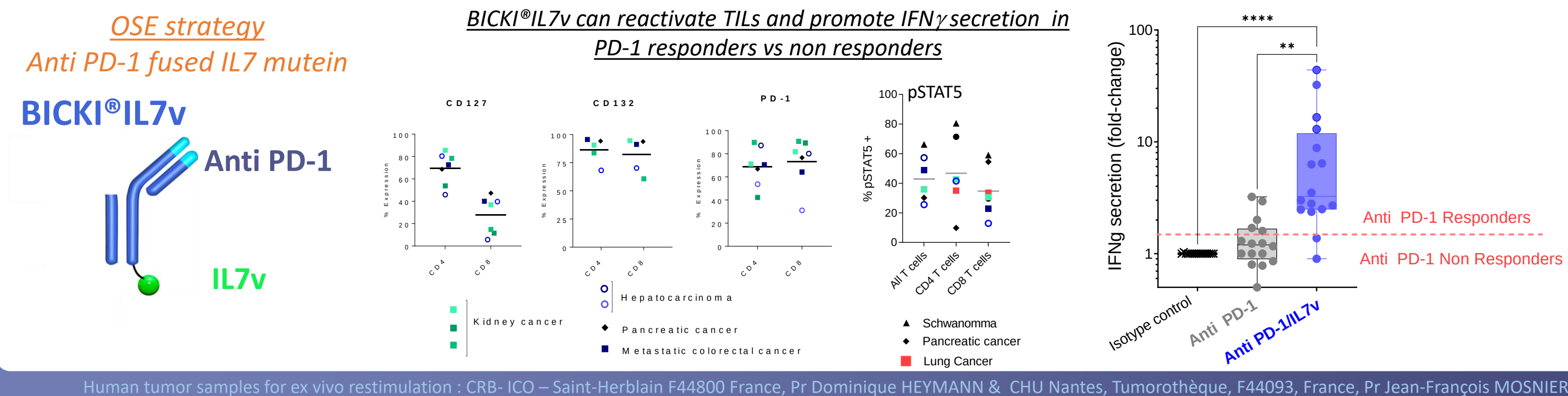
2/ TILs IL7R + are associated with stemness and survival phenotype



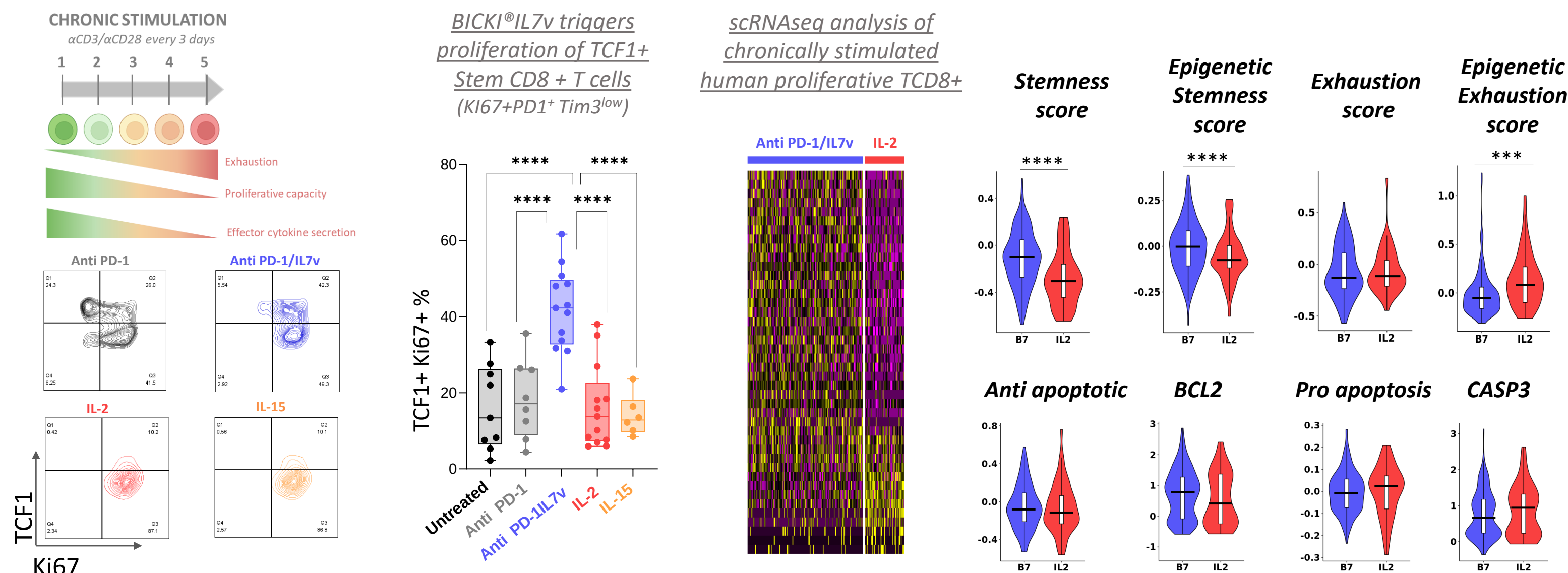
3/ Coexpression of TCF7 and IL7R is predictive to ICI response in Melanoma



4/ IL7 fused to an antagonist anti-PD1 (BICKI®IL-7v) mAb synergistically reinvigorate TILs



5/ IL7 promotes proliferation and long-term survival of stem-like Tcells (TCF7+Tcells)



Conclusion

- IL7R/IL7R pathway expression in TILs and tumor-specific T cell clonotypes are predictive of long-term ICI clinical response.
- Redirecting IL7 on PD1+Tcells provides stemness, proliferative and survival signals to tumor-specific Tcells capable to induce durable response
- **POSTER #1366** Preclinical efficacy of Anti-PD-1/IL-7v bispecific antibody