

SITC 2021 Poster # 304

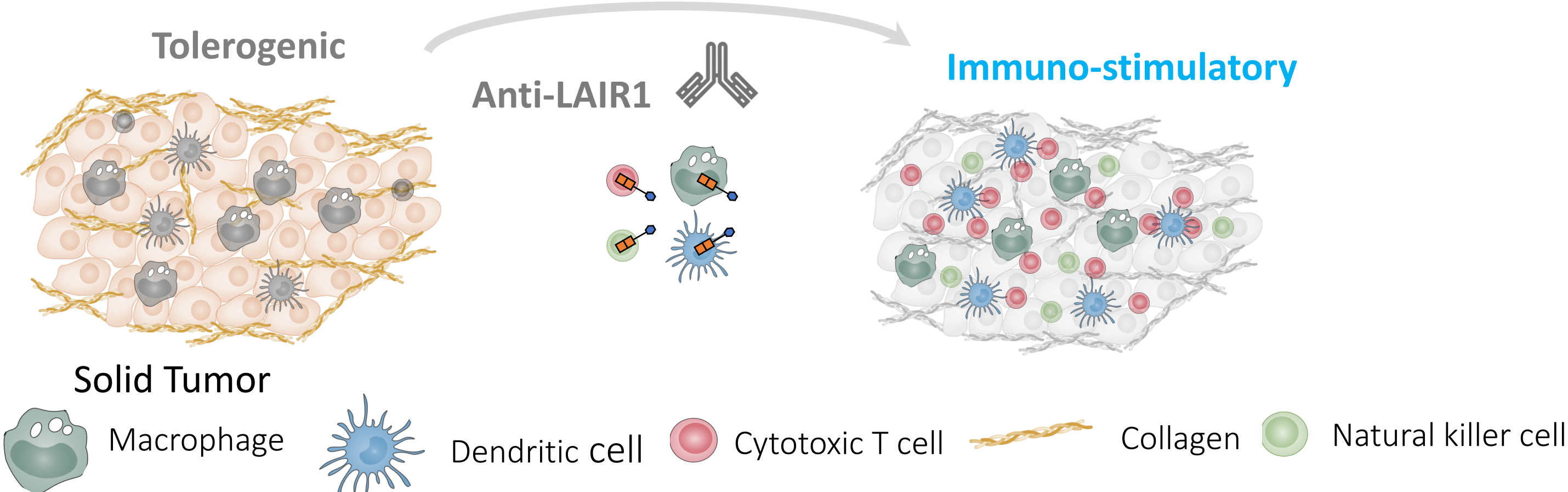
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## Background and rationale

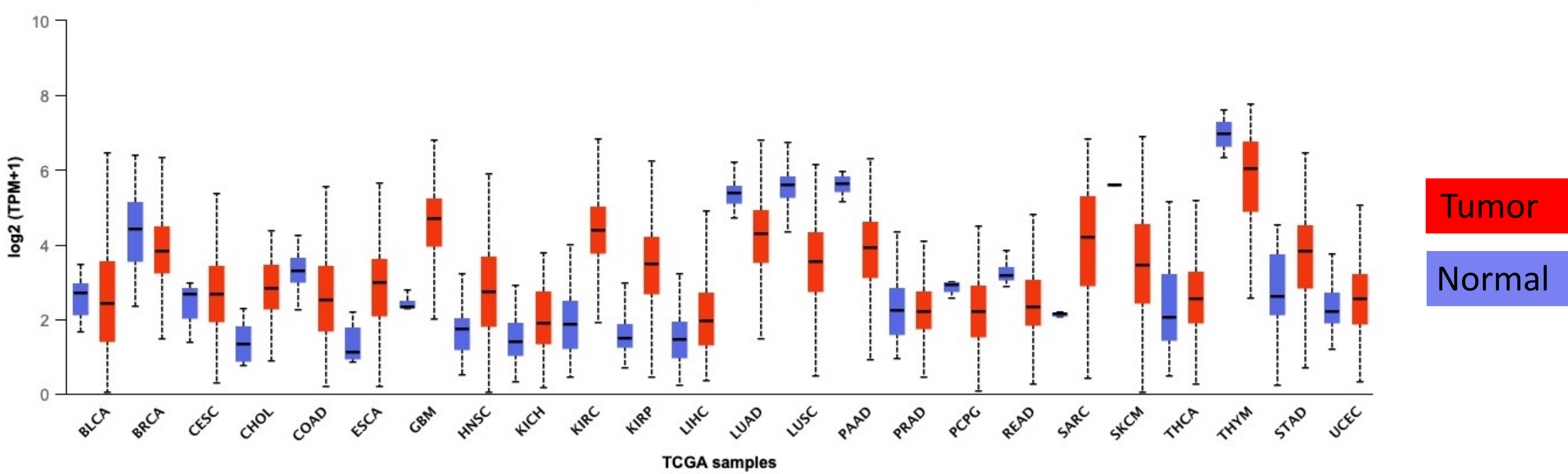
The Leukocyte Associated Immunoglobulin-like Receptor 1 (LAIR1) is an immune inhibitory transmembrane glycoprotein expressed on lymphocytes and myeloid cells. The known ligands for LAIR1 are proteins containing collagen-like domains including collagen, complement component 1q (C1q), and stromal protein Colec12. Myeloid-derived suppressor cells (MDSC), tumor associated macrophages (TAMs), as well as collagens, are important contributors of the immune-suppressive tumor microenvironment, and LAIR1 expression is negatively correlated with patient survival in many solid tumors. These findings prompt us to investigate LAIR1 as a novel immuno-oncology target in collagen-rich tumors. Utilizing LAIR1 antagonist antibodies, we aim to mobilize anti-tumor immunity by changing the collagen-induced tolerogenic state of the immune cells into proinflammatory.

## Mechanism of action

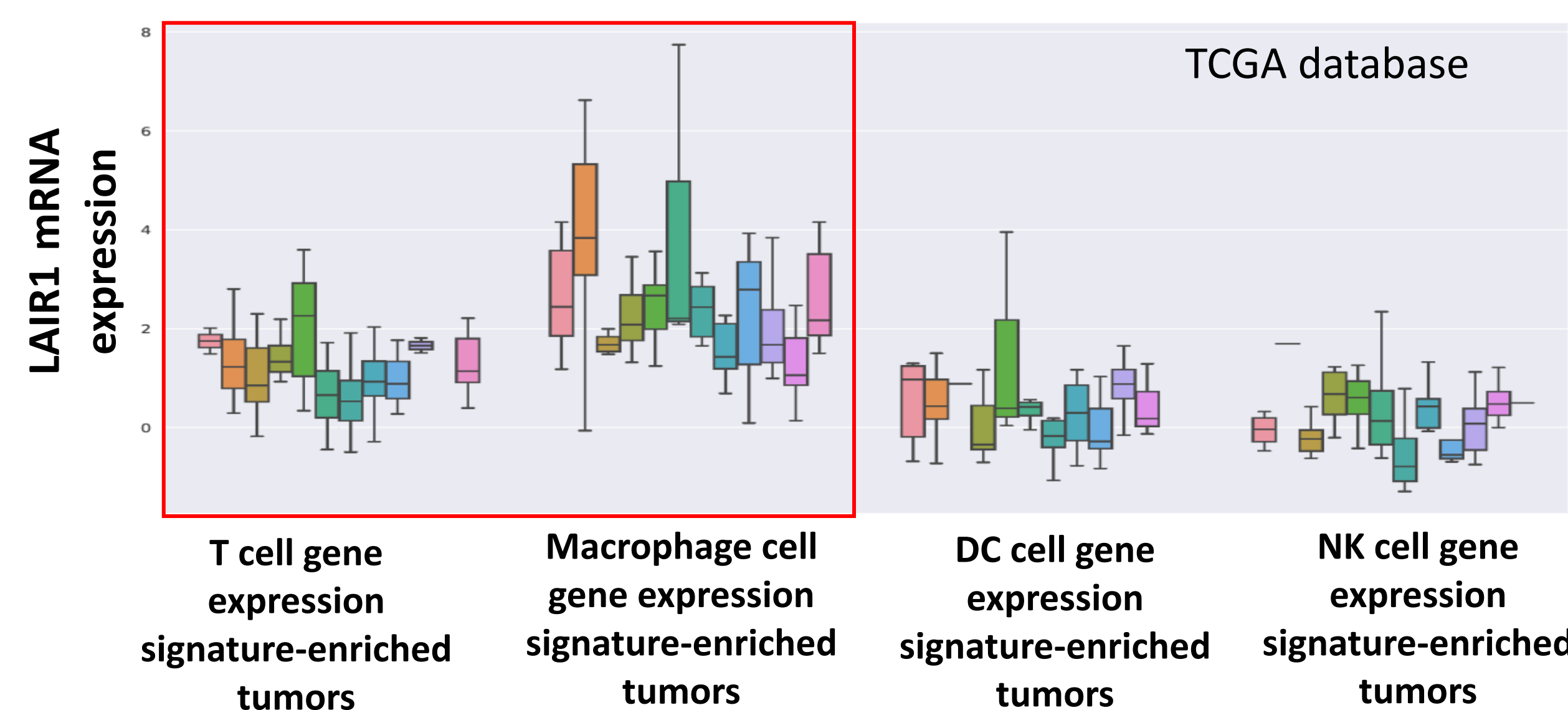


## LAIR1 expression up-regulated in some cancers

Expression of LAIR1 across TCGA cancers (with tumor and normal samples)

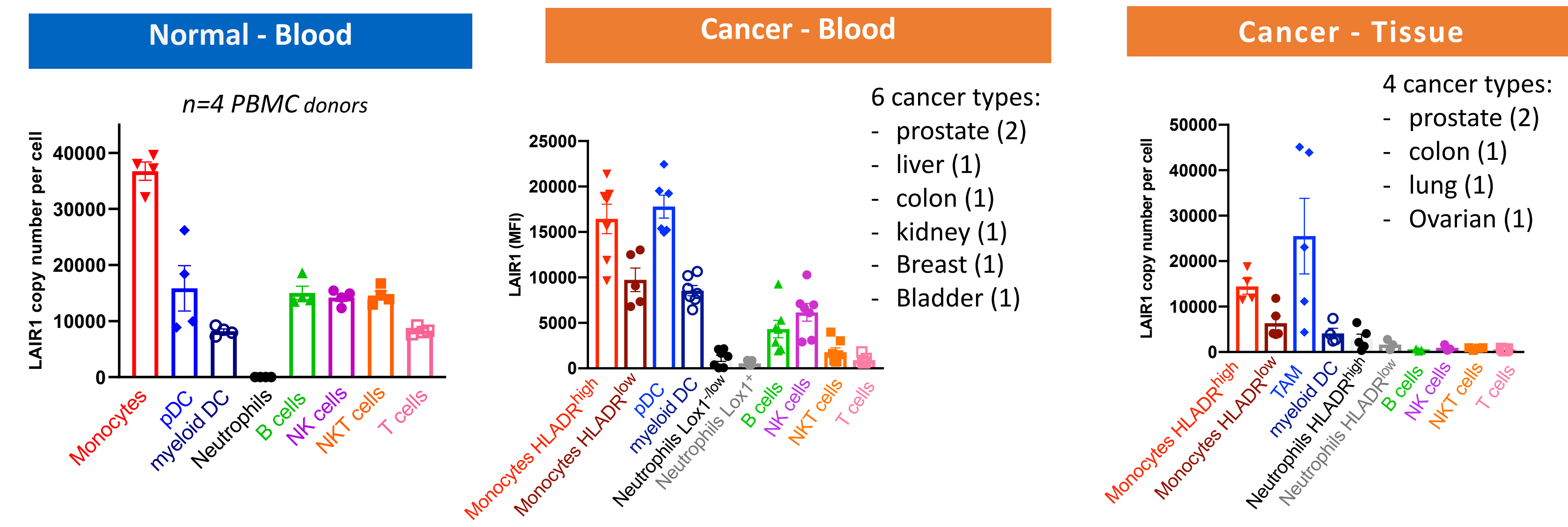


## High LAIR1 expression in certain T cell and macrophage signature enriched tumors



Cancer type 1  
Cancer type 2  
Cancer type 3  
Cancer type 4  
Cancer type 5  
Cancer type 6  
Cancer type 7  
Cancer type 8  
Cancer type 9  
Cancer type 10  
Cancer type 11  
Cancer type 12

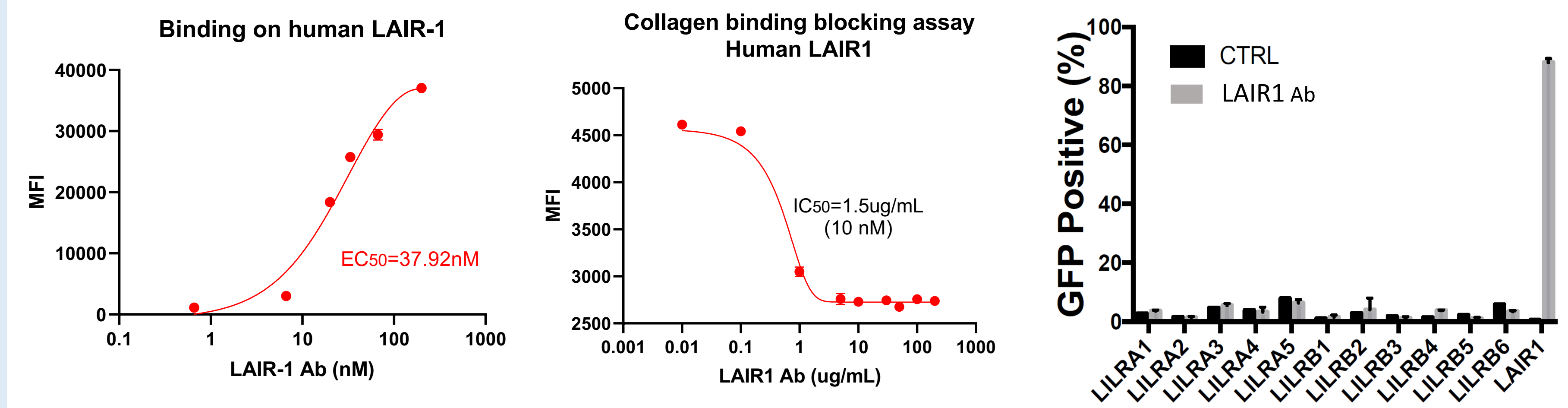
## LAIR1 is highly expressed on myeloid cells in peripheral blood and solid tumors



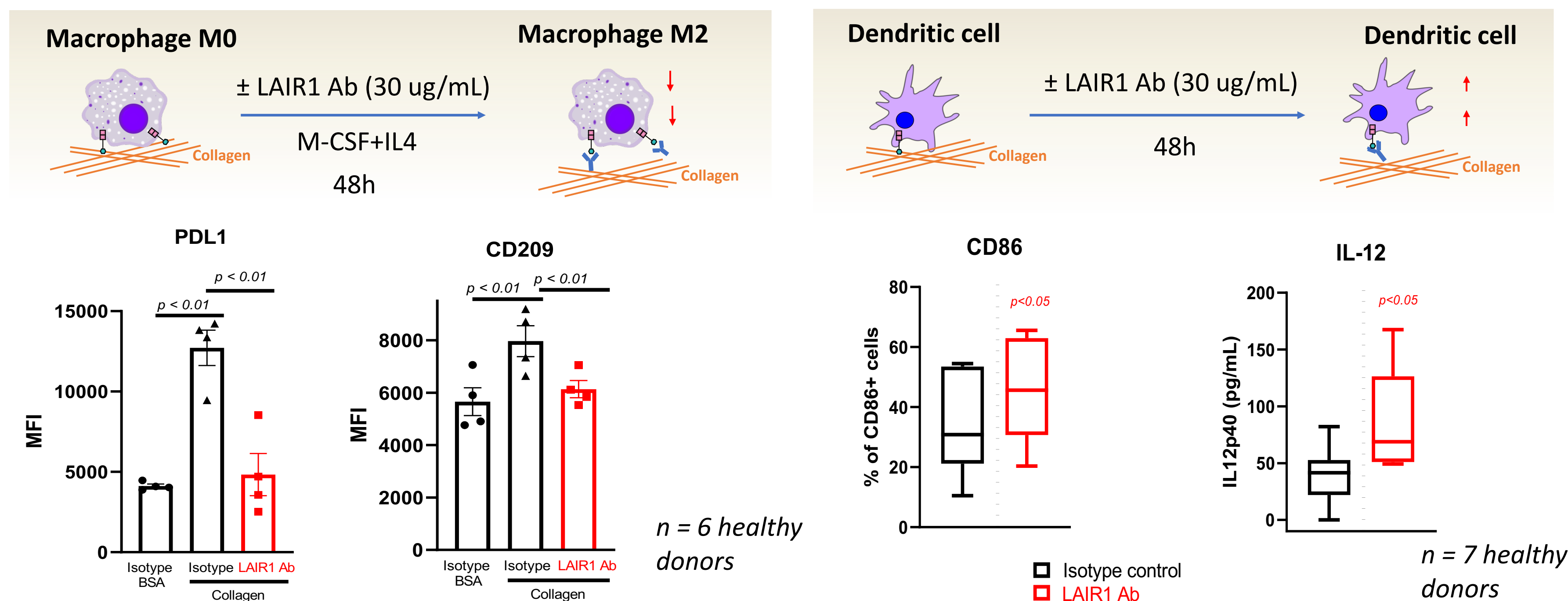
## Characteristics of Proof-of-Concept LAIR1 Blocking Antibody

- Humanized IgG4\_S228P with high affinity ( $K_D=0.6$  nM, Octet) to human LAIR1
- No binding to GPVI (Glycoprotein VI), a receptor for collagen expressed on platelets

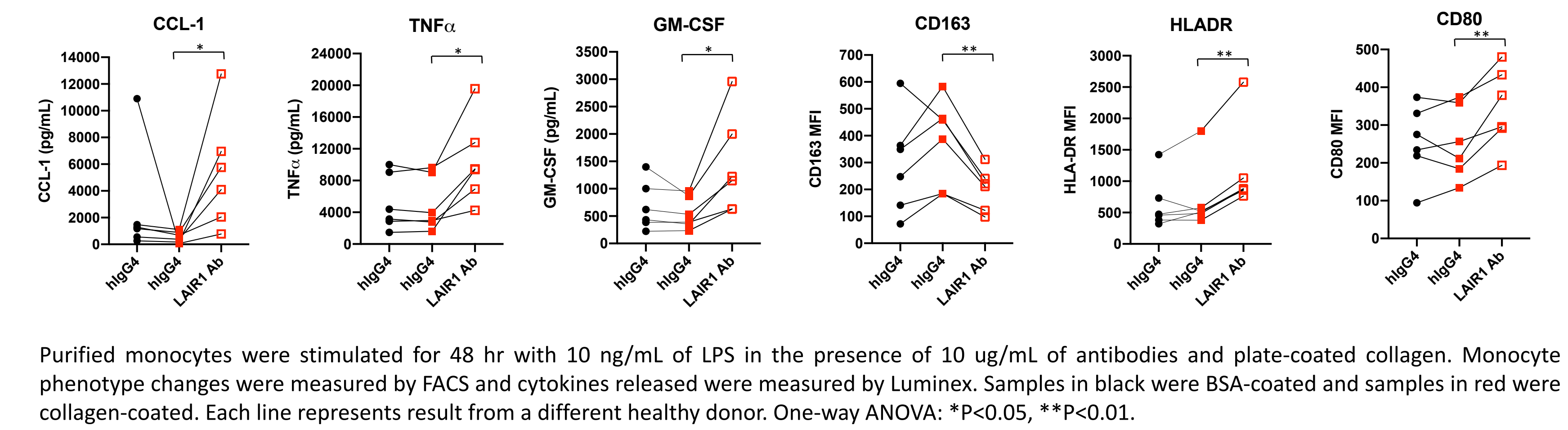
High affinity binding to human LAIR1      Blocks Collagen binding to LAIR1      No binding to other family members



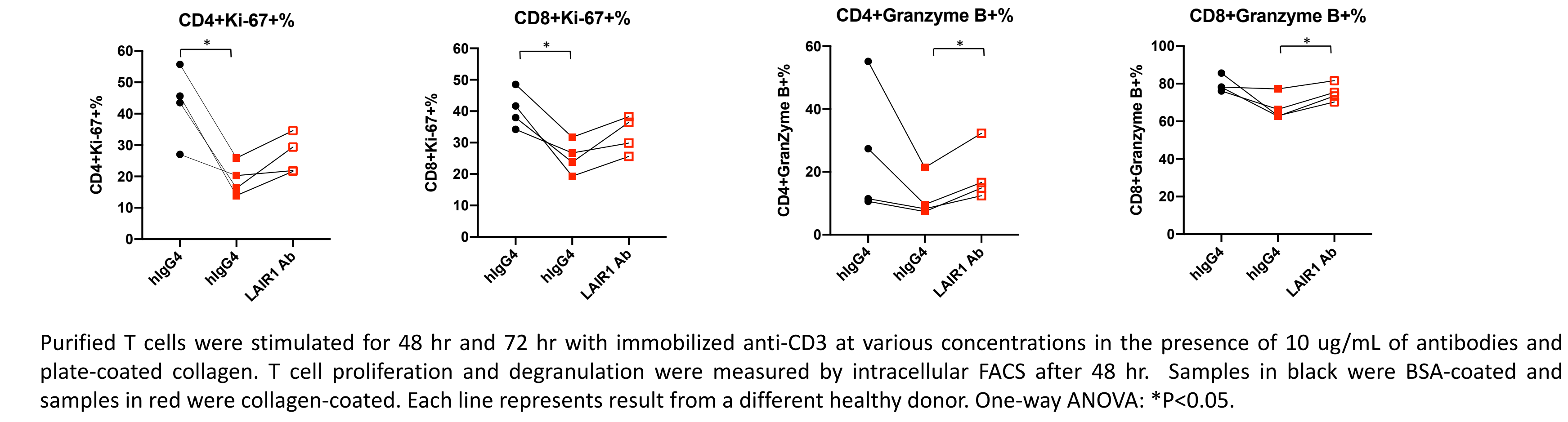
## LAIR1 blocking Ab attenuates collagen-mediated immunosuppressive phenotype of myeloid cells



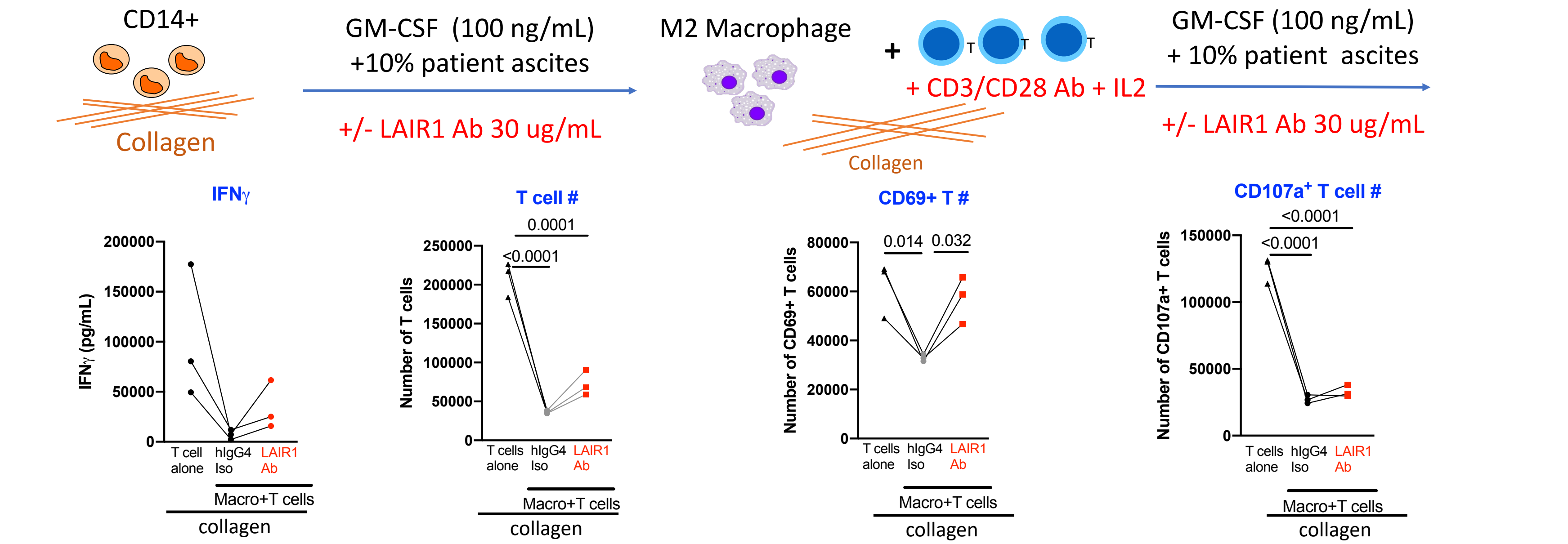
## LAIR1 blocking Ab reverses collagen-mediated monocyte tolerogenic effect



## LAIR1 blocking Ab enhances T cell proliferation and degranulation in collagen-suppressed T cells



## LAIR1 blockade reverses collagen-mediated T cell suppression in autologous macrophage/T cell co-culture



## Summary

- LAIR1 mRNA expression is associated with macrophage and certain T cell infiltration in many solid tumor types from TCGA (The Cancer Genome Atlas).
- LAIR1 is highly expressed on myeloid cells in peripheral blood and solid tumors by flow cytometry.
- POC humanized IgG4 (S228P) anti-LAIR1 antibody displays high affinity, specificity and potent antagonistic activity.
- LAIR1 blockade attenuates collagen-mediated immunosuppressive phenotype of myeloid cells.
- LAIR1 blockade reverses collagen-mediated monocyte tolerogenic effect.
- LAIR1 blockade enhances T cell activation and proliferation in collagen-suppressed T cells and in macrophage/T cell co-culture.