γδ T cells in colorectal cancer represent an impaired phenotype with potential to regain effector functions

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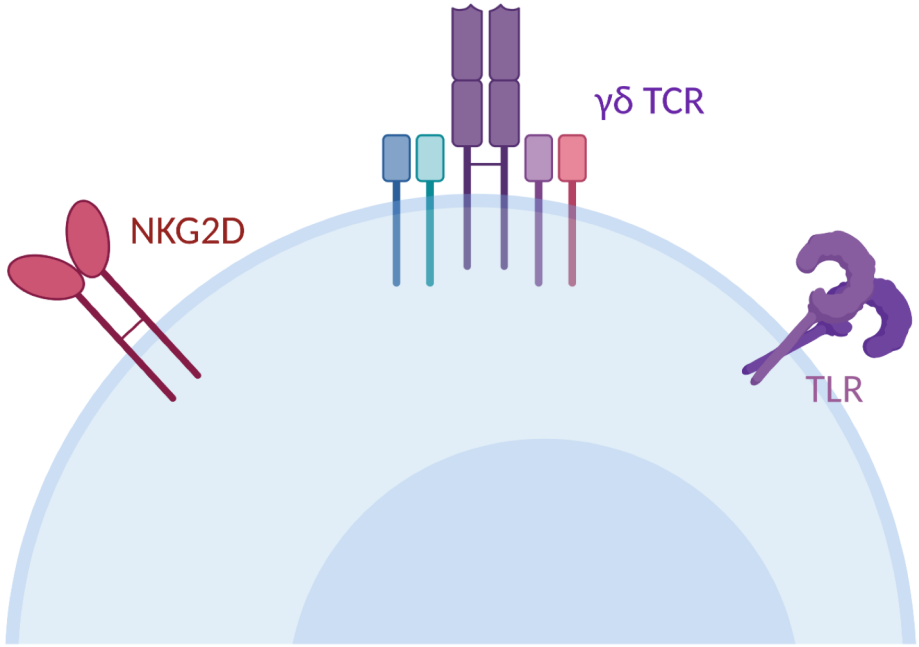
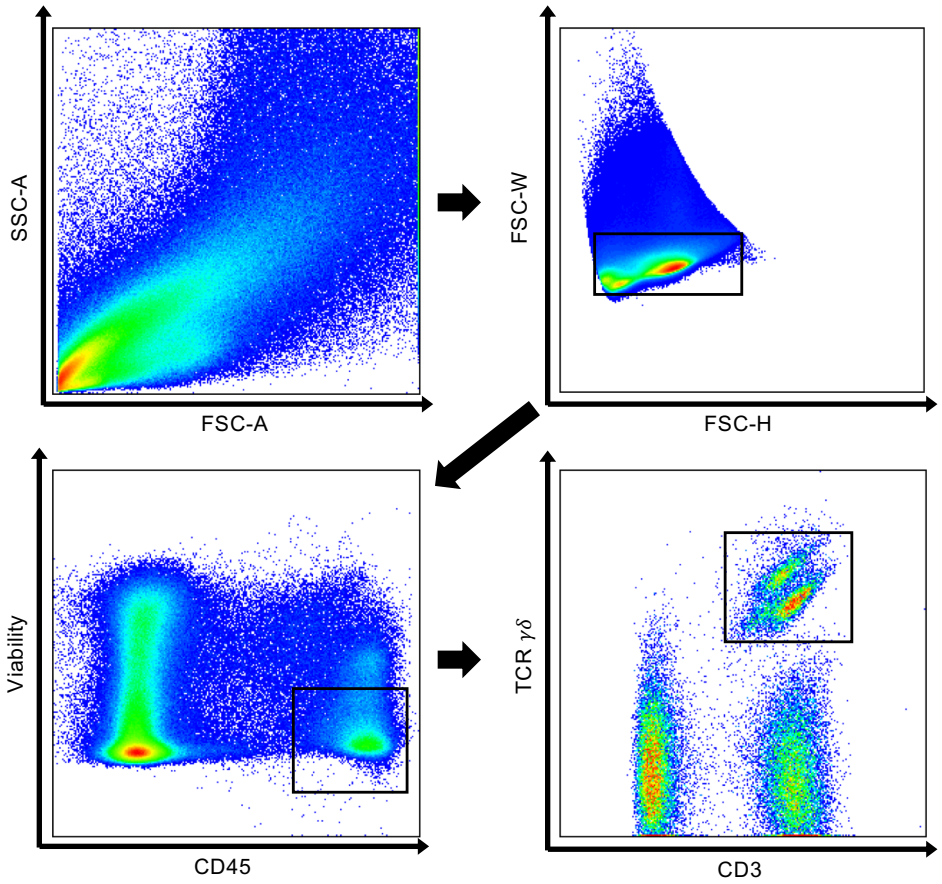
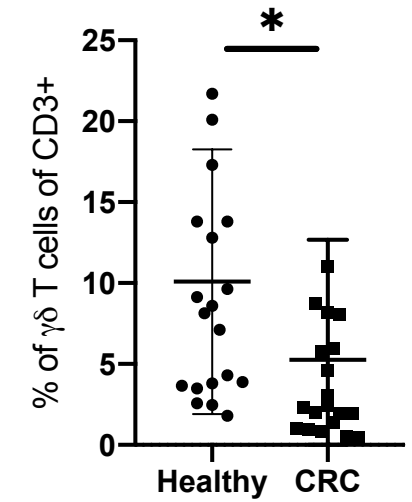
γδ T cells – on the edge of innate and adaptive immunity

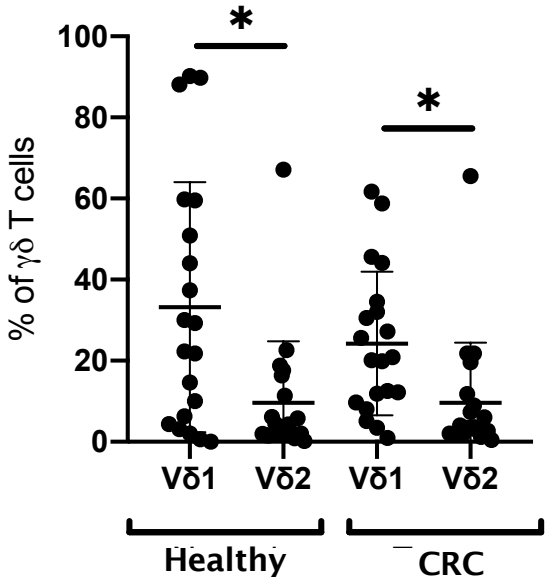


- recognize different metabolites
- do not depend on MHC antigen recognition
- rearrange TCR genes: junctional diversity+memory phenotype
- lyse tumor cells (granzyme B, perforin)
- induce apoptosis (FasL, TRAIL)
- potent cytotoxicity (TNF-α, IFN-γ)
- antigen presentation for αβ (conventional) T cells

γδ T cells are depleted in human CRC



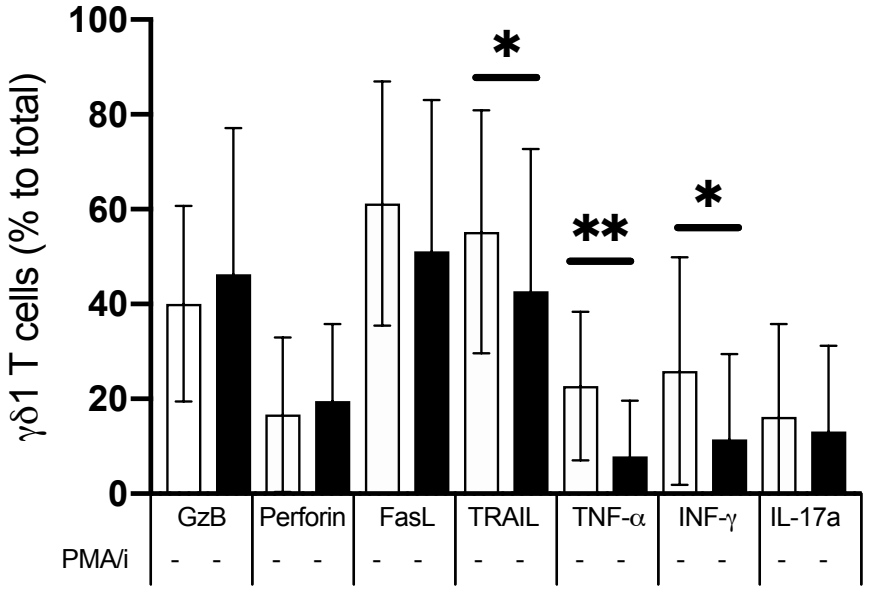


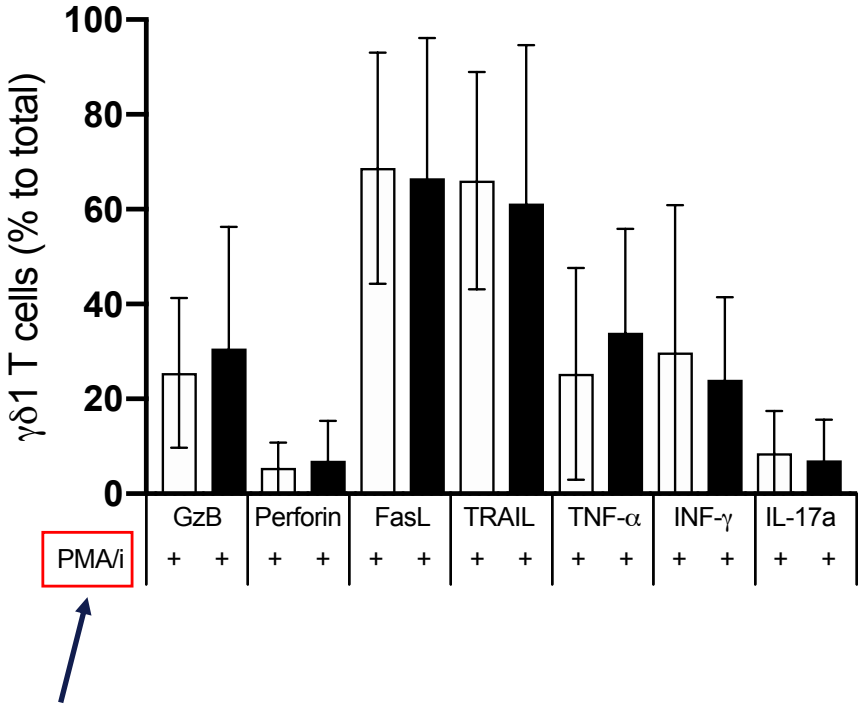


- 2 subsets identified = γδ1 and γδ2
- potentially more subsets

n=20

Impaired phenotype of γδ1 T cells in CRC can be restored





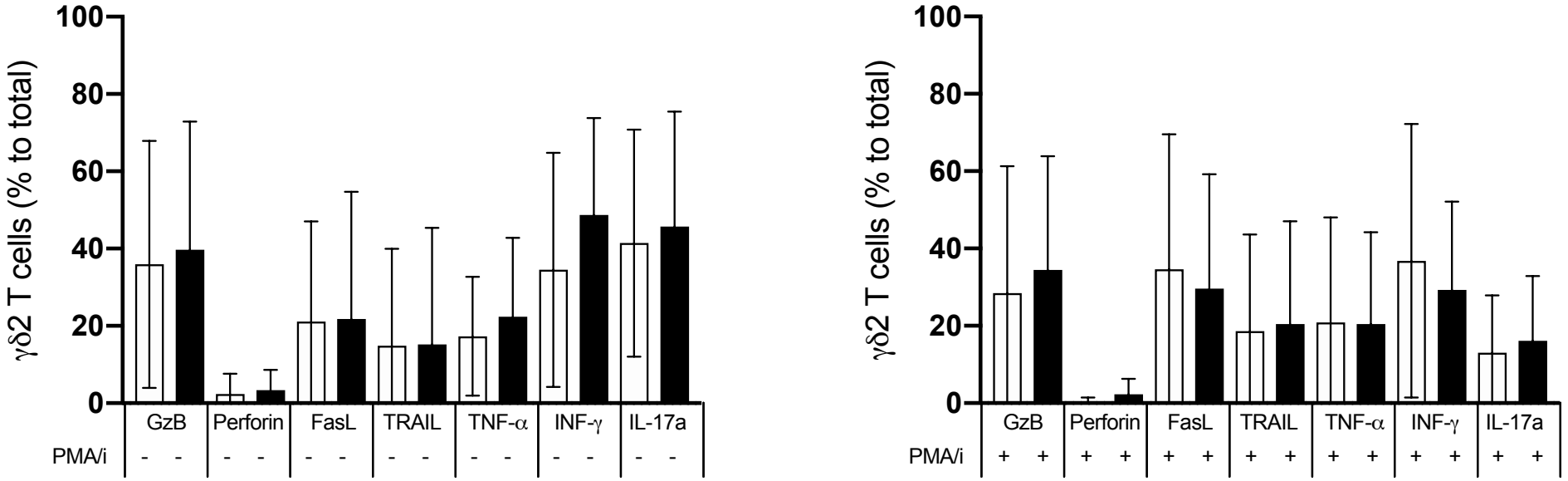
Healthy mucosa

Colorectal cancer

PMA+Ionomycin = stimulation

n=20

No significant differences between γδ2 T cell subtype in CRC vs healthy



Healthy mucosa

Colorectal cancer

n=20

Conclusion

- $\gamma\delta1^+$ T cell count is diminished in CRC vs healthy gut mucosa
- cytotoxic functions are impaired in $\gamma\delta1^+$ T cells but not in $\gamma\delta2^+$ T cells
- cytotoxicity of $\gamma\delta1^+$ T cells can be restored
- $\gamma\delta2^+$ T cells are distinct from $\gamma\delta1^+$ T cells – no surrogate marker

harness $\gamma\delta1^+$ T cells as a targets in colorectal cancer

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