



SITC 2017

November 8-12

NATIONAL HARBOR
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Society for Immunotherapy of Cancer

November 8-12 • NATIONAL HARBOR, MD

SITC
2017

The transcription factor Myb enhances CD8⁺ T cell stemness and polyfunctionality to promote curative antitumor immunity

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National Cancer Institute

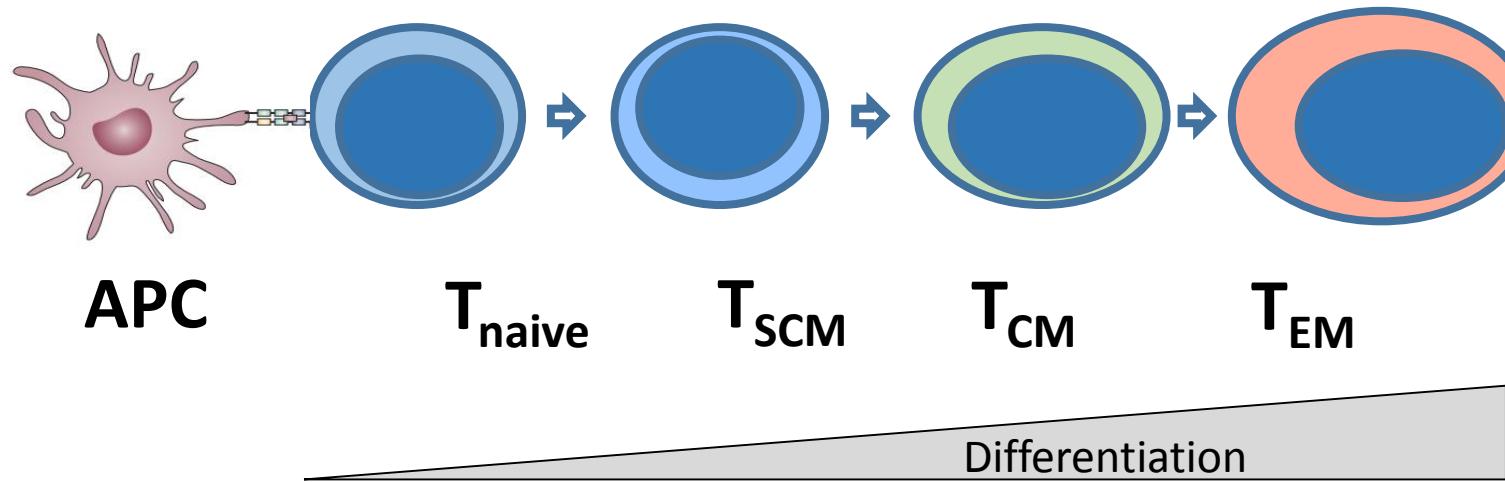


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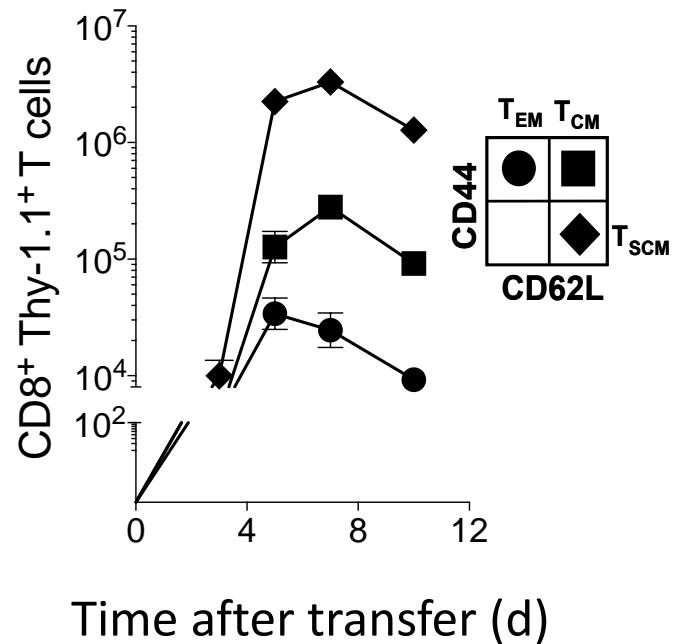


Progressive model of T cell differentiation

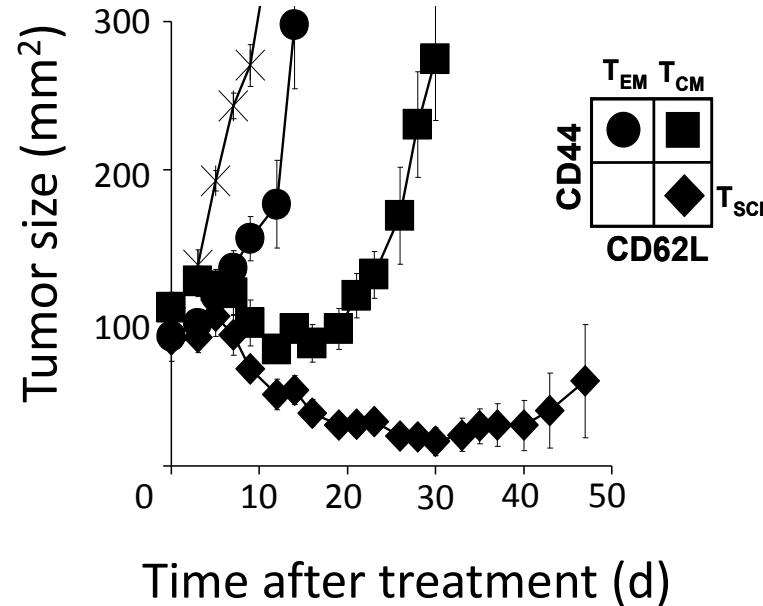


Less differentiated cells mediate enhanced antitumor responses

Adoptive transfer of antigen specific CD8⁺ T cells

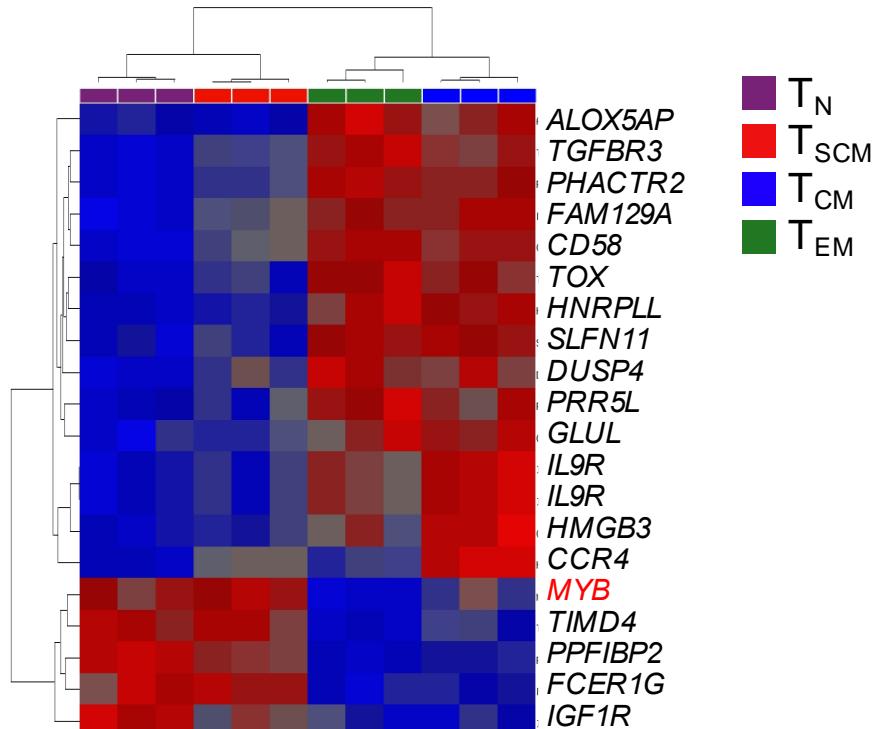


B16 melanoma tumor model

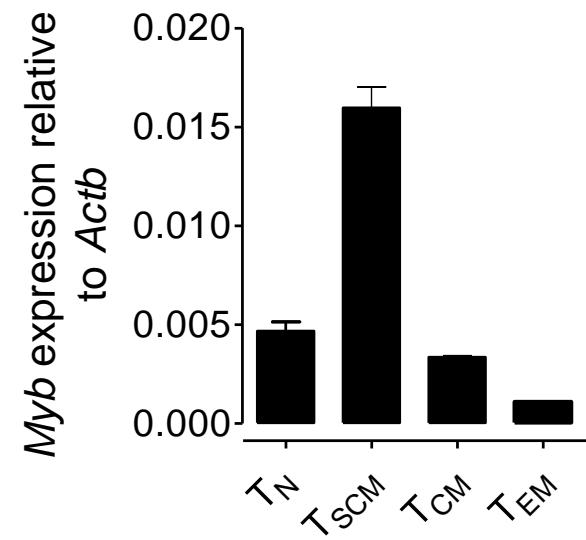


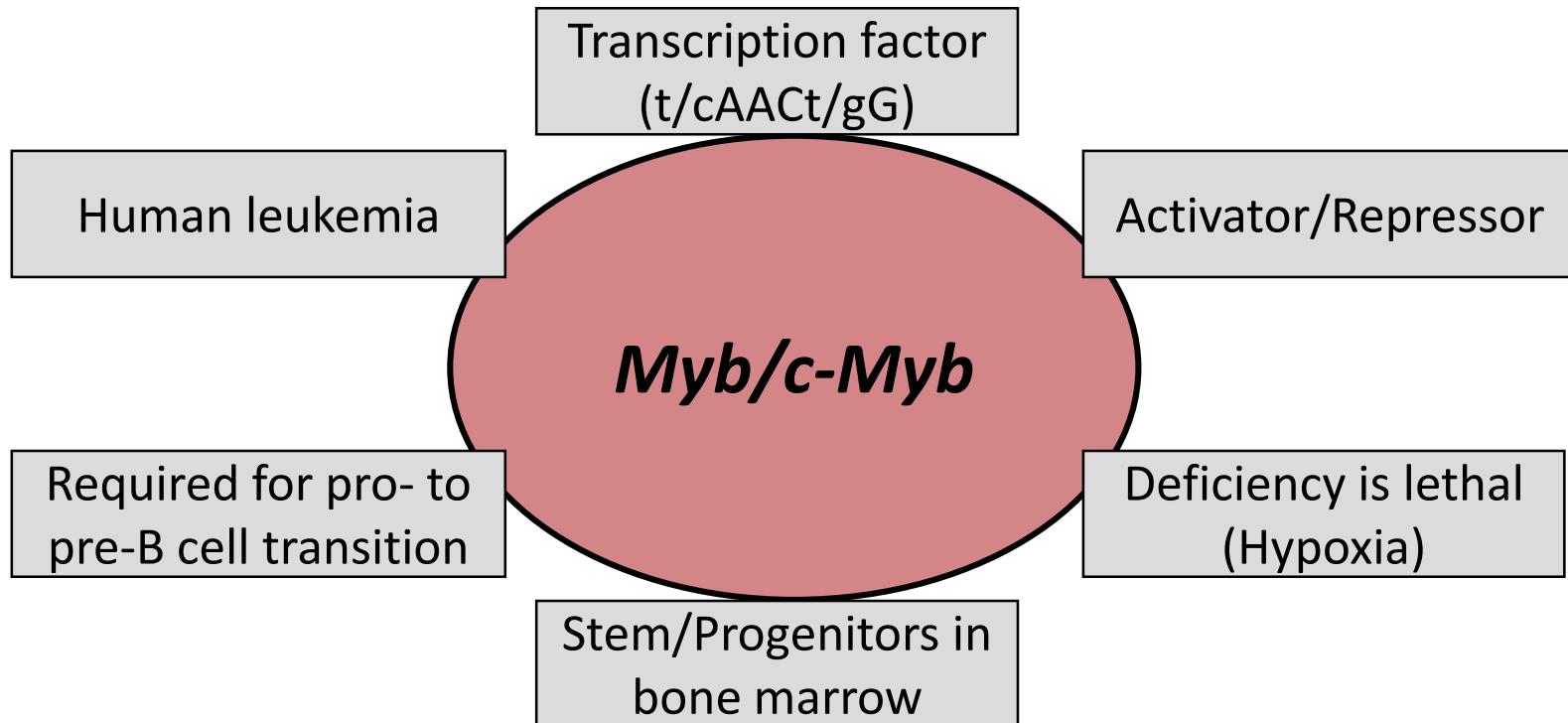
Gattinoni *et. al*, Nat. Med. 2011

Myb is highly expressed in T_{SCM} cells, but downregulated with progressive T cell differentiation

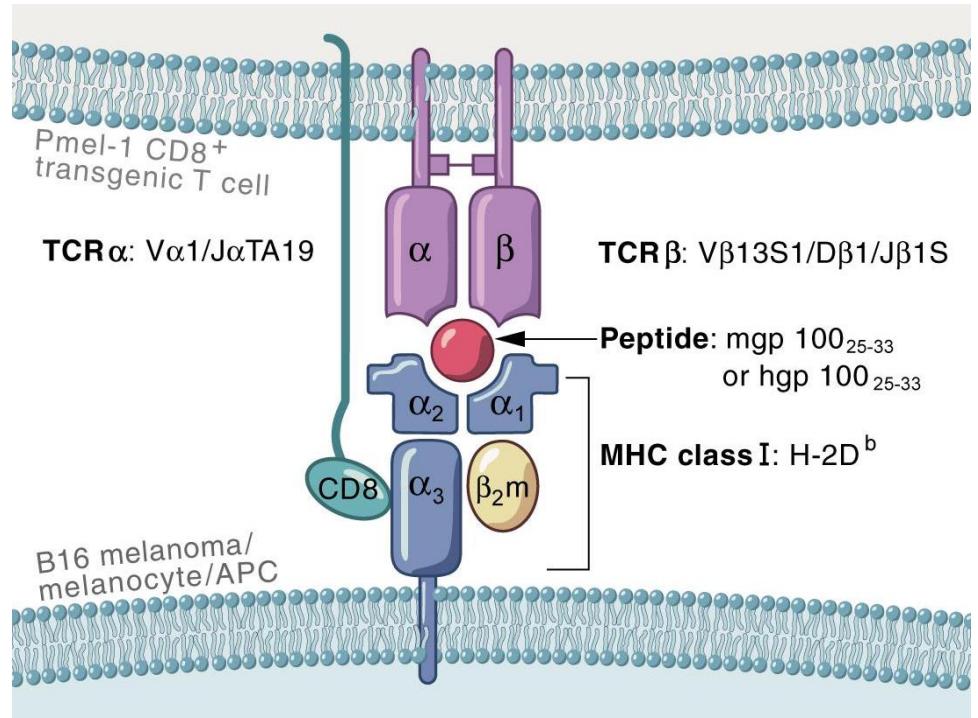


Gattinoni *et. al*, Nat. Med. 2011

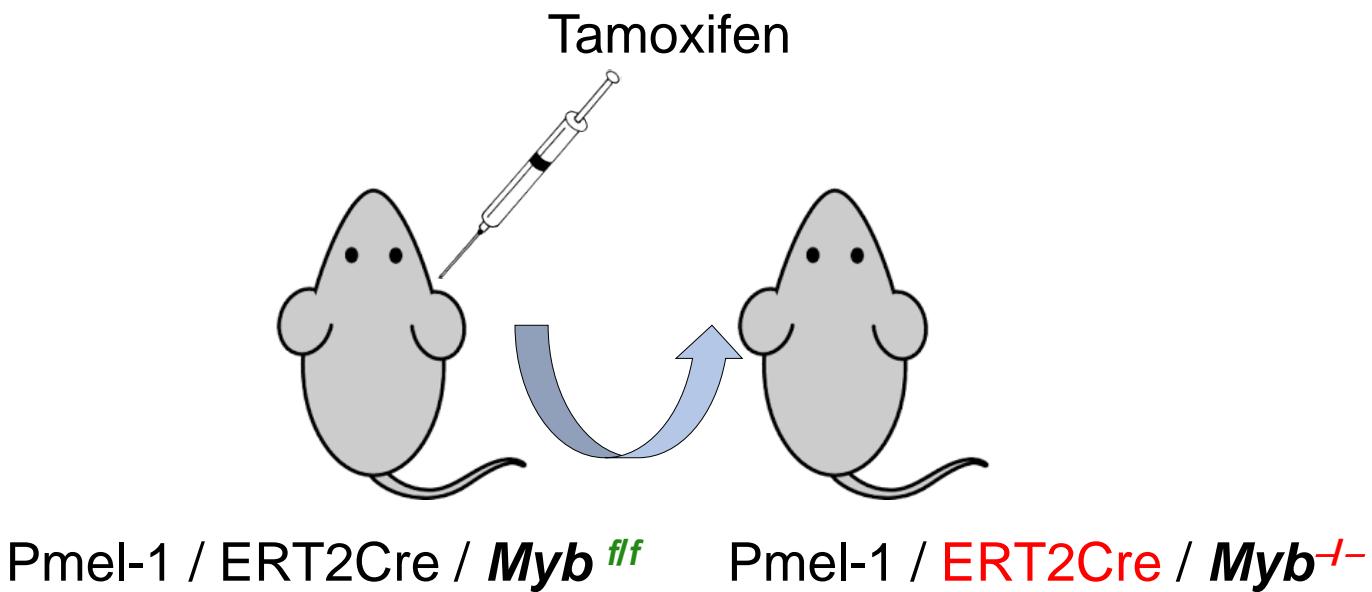




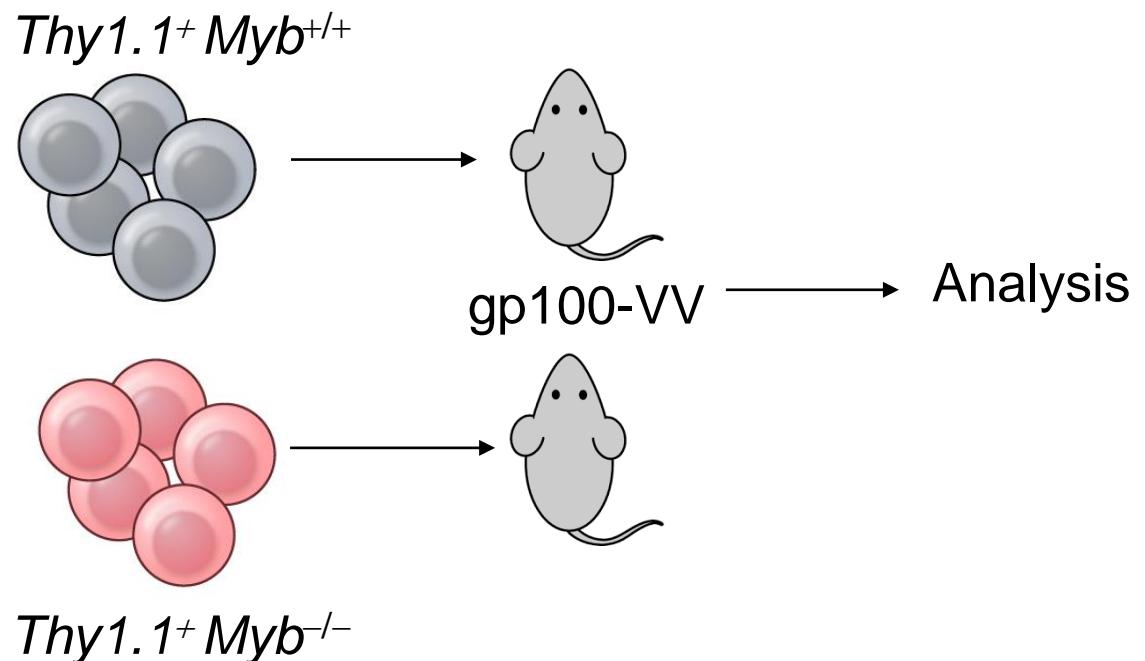
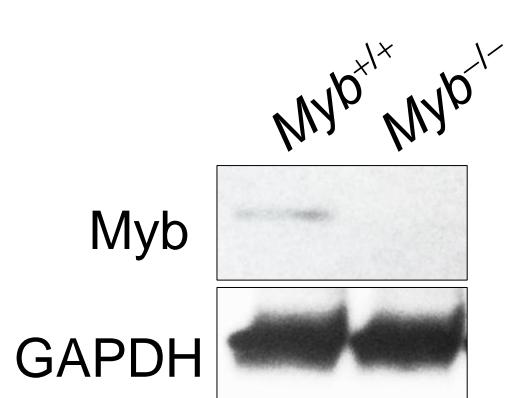
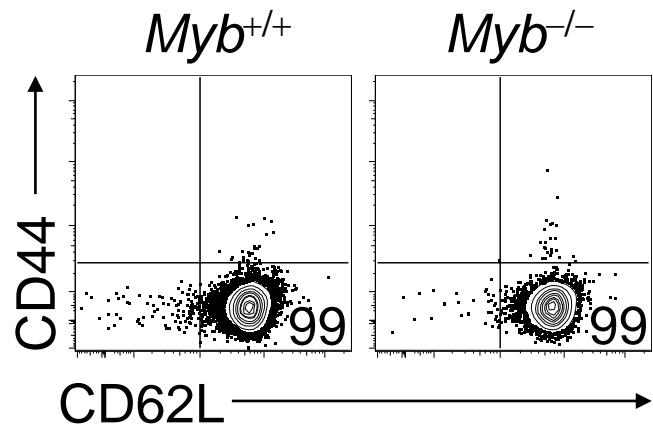
Model system: Pmel-1 gp100-specific TCR



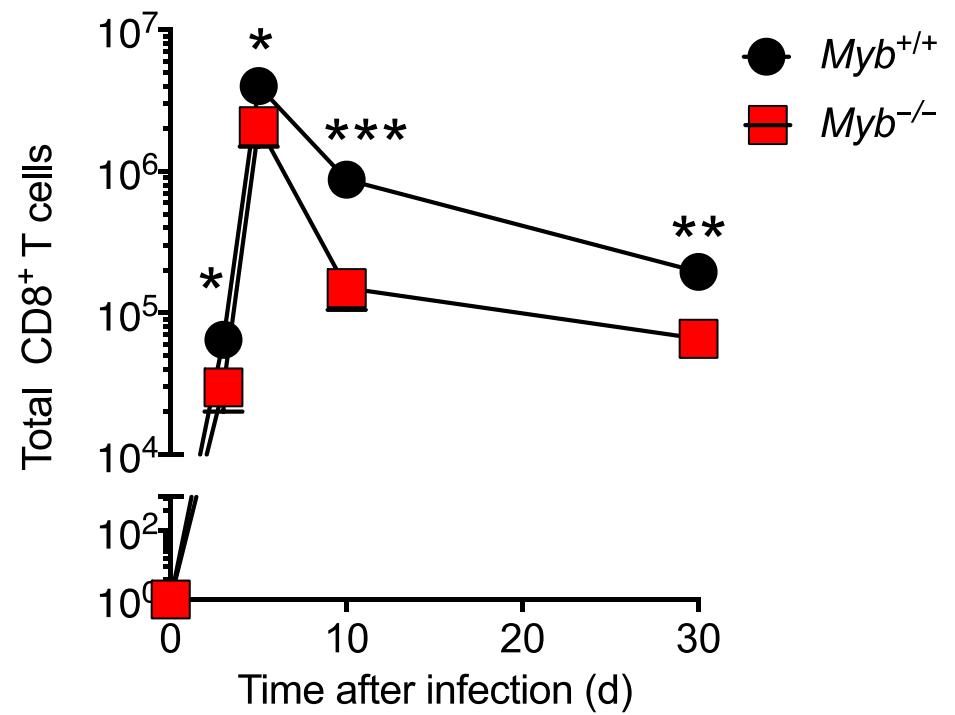
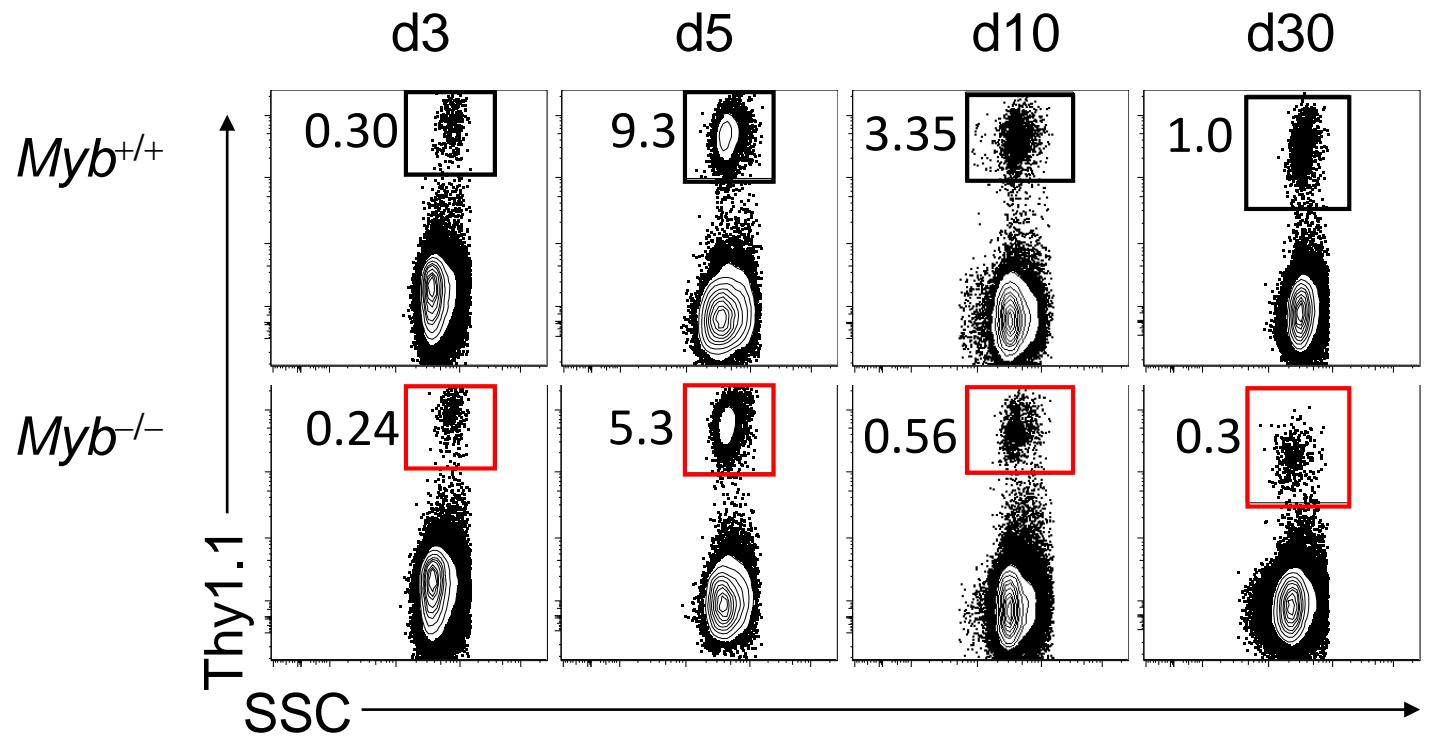
Overwijk et al. J. Exp. Med. 2003



Evaluating CD8⁺ T cell immuno-competence in *Myb*^{-/-}

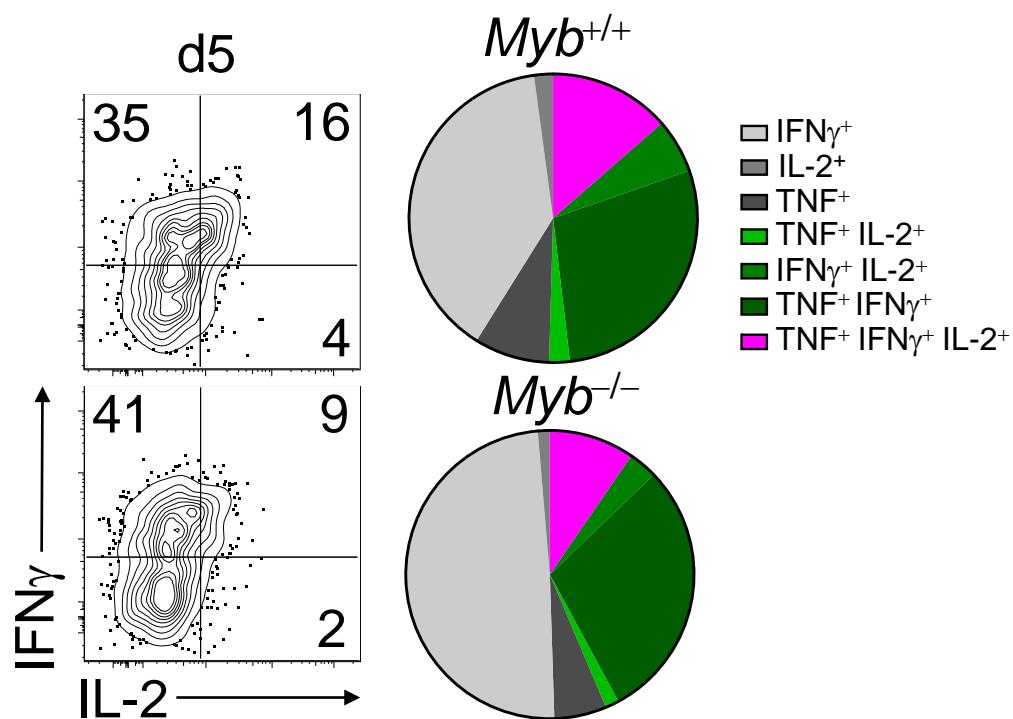
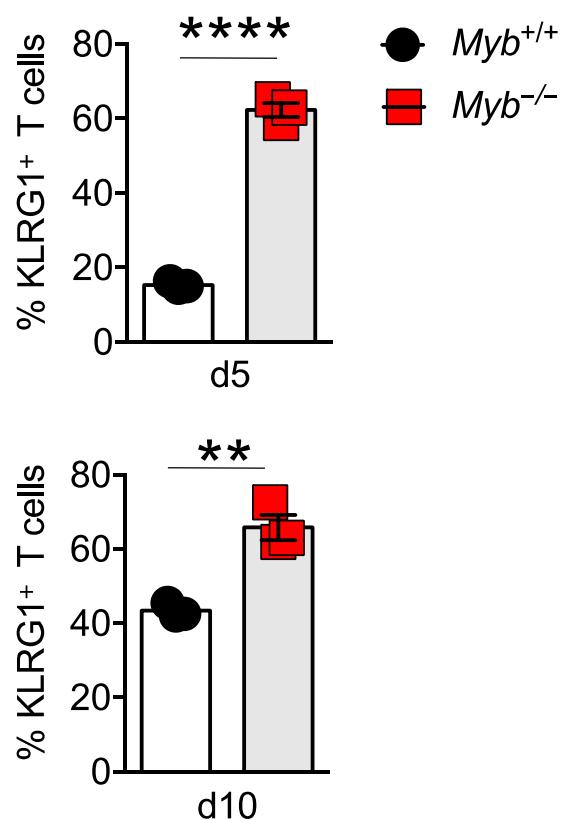
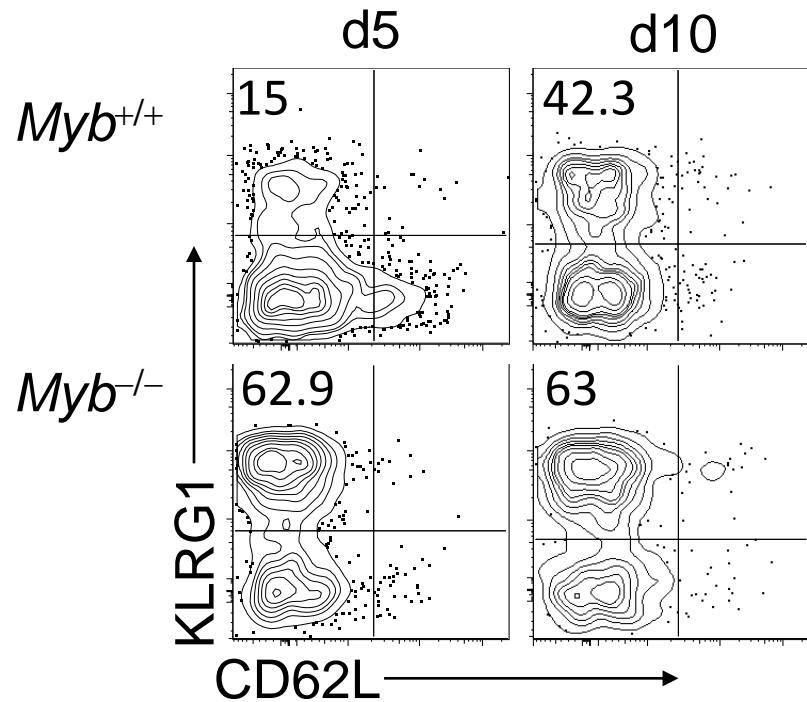


Myb is required for the effective generation and maintenance of CD8⁺ T cells

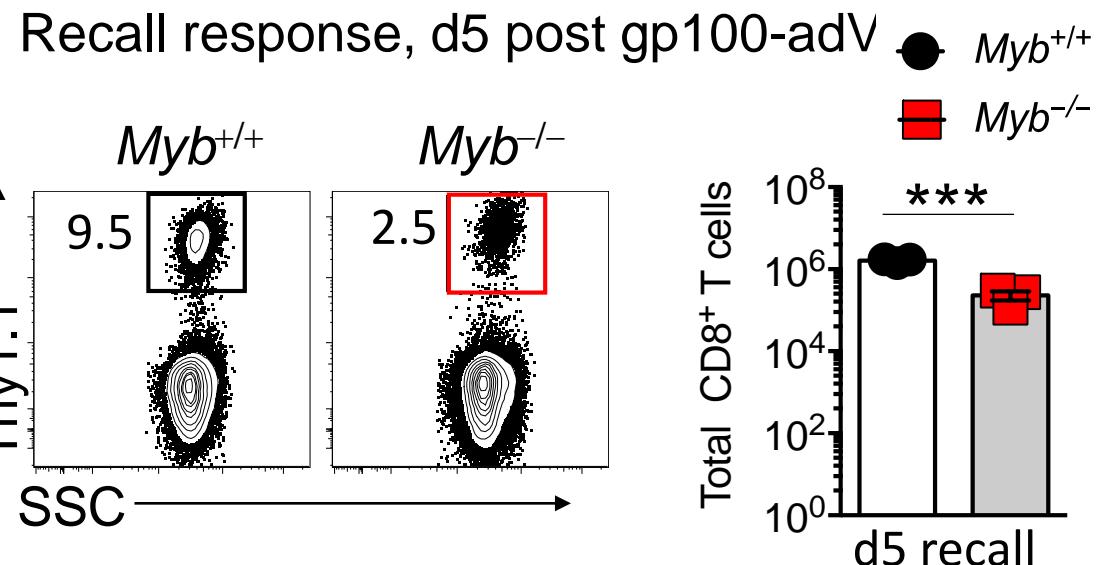
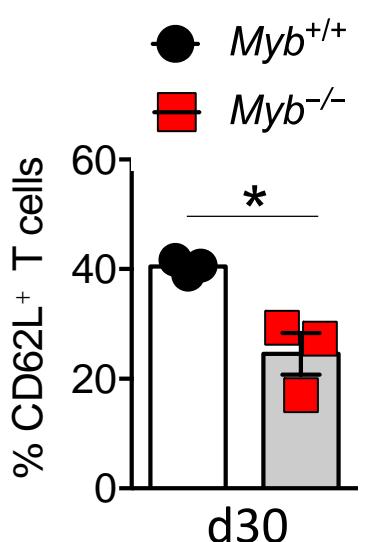
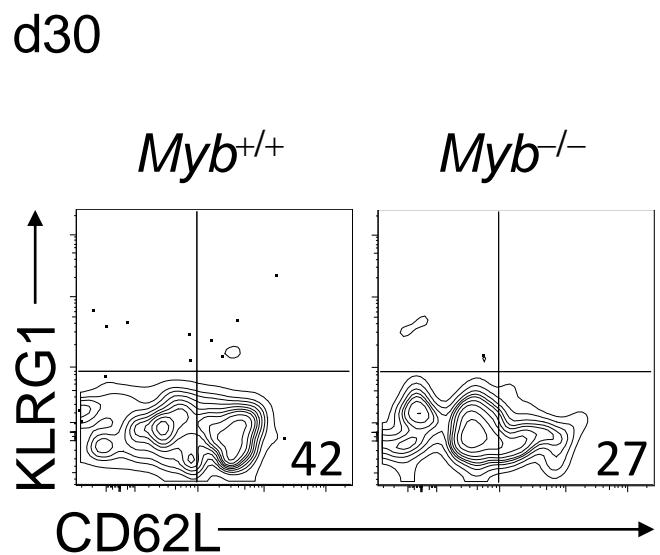


Gautam S et. al, unpublished

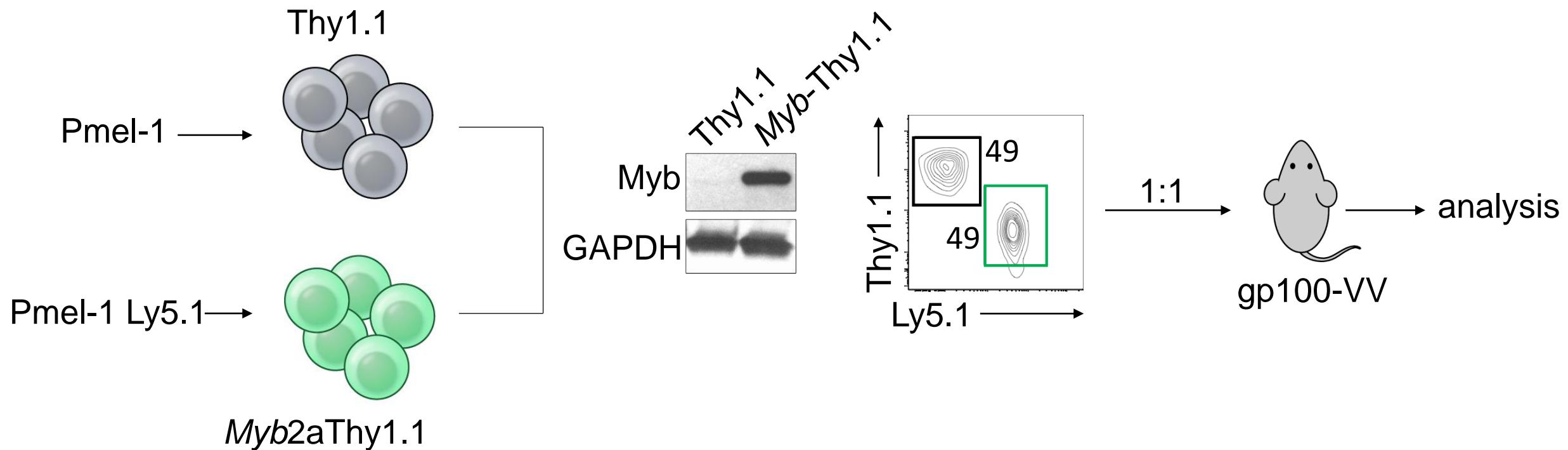
Myb^{-/-} CD8⁺ T cells preferentially undergo terminal effector differentiation



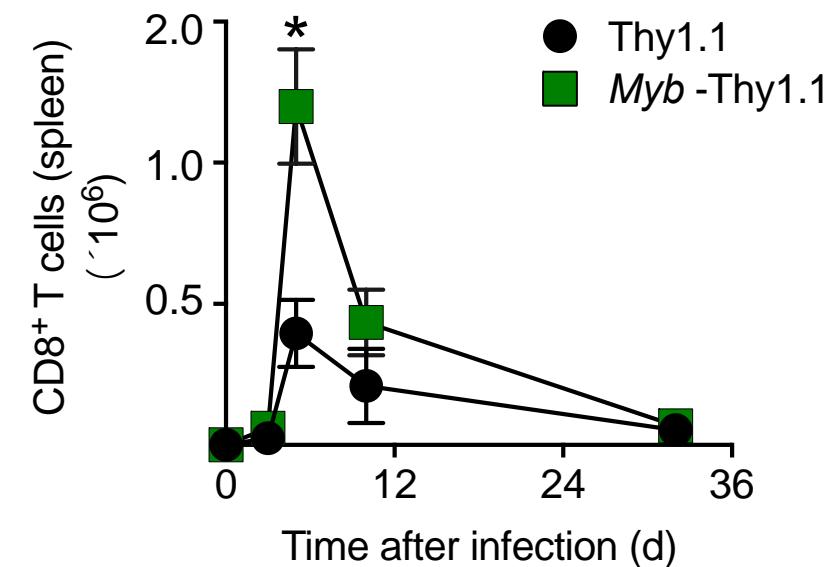
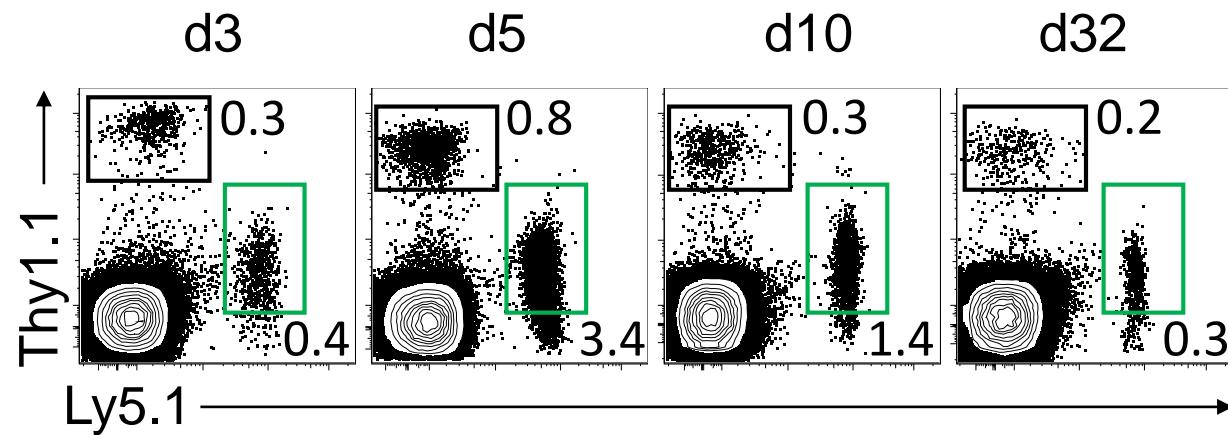
Myb^{-/-} impairs generation of memory CD8⁺ T cells



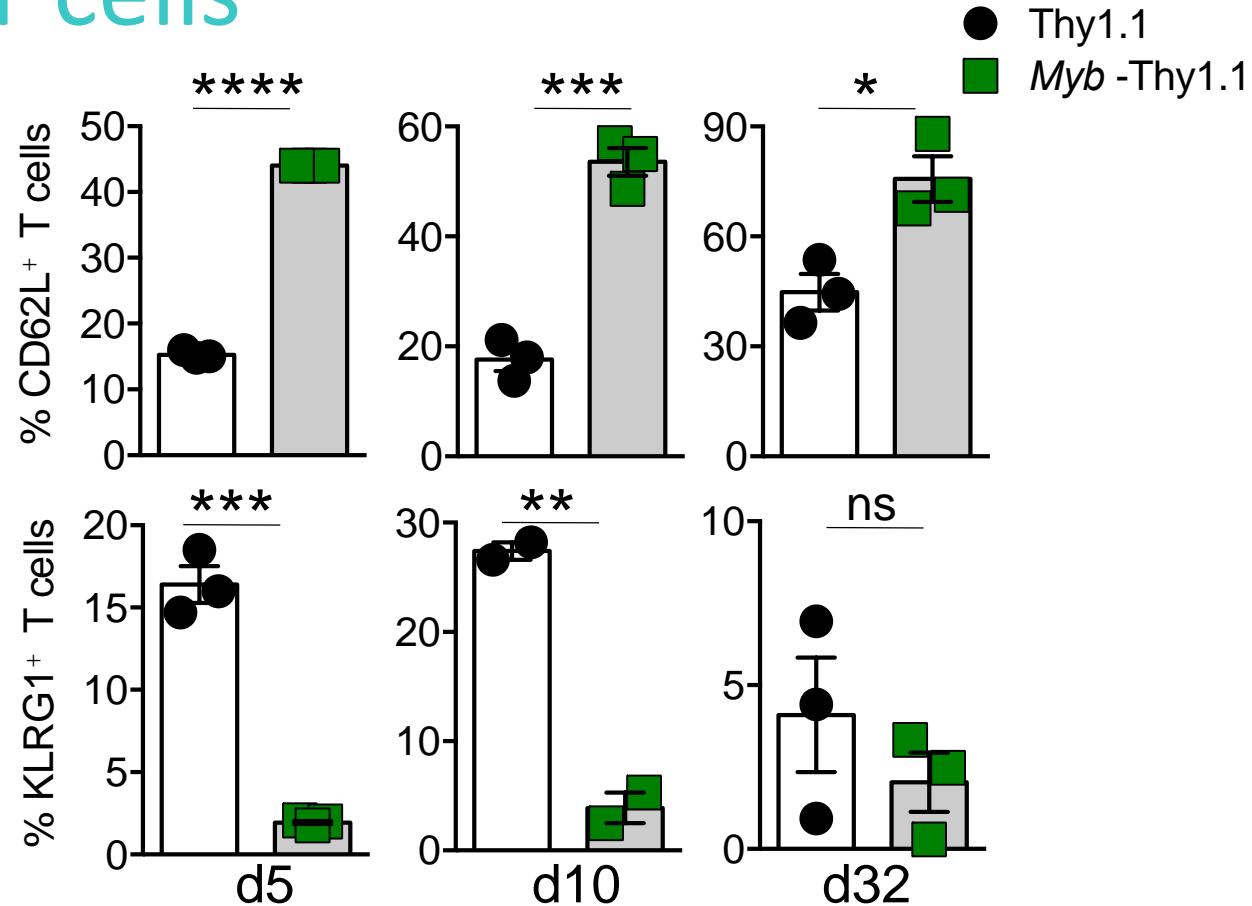
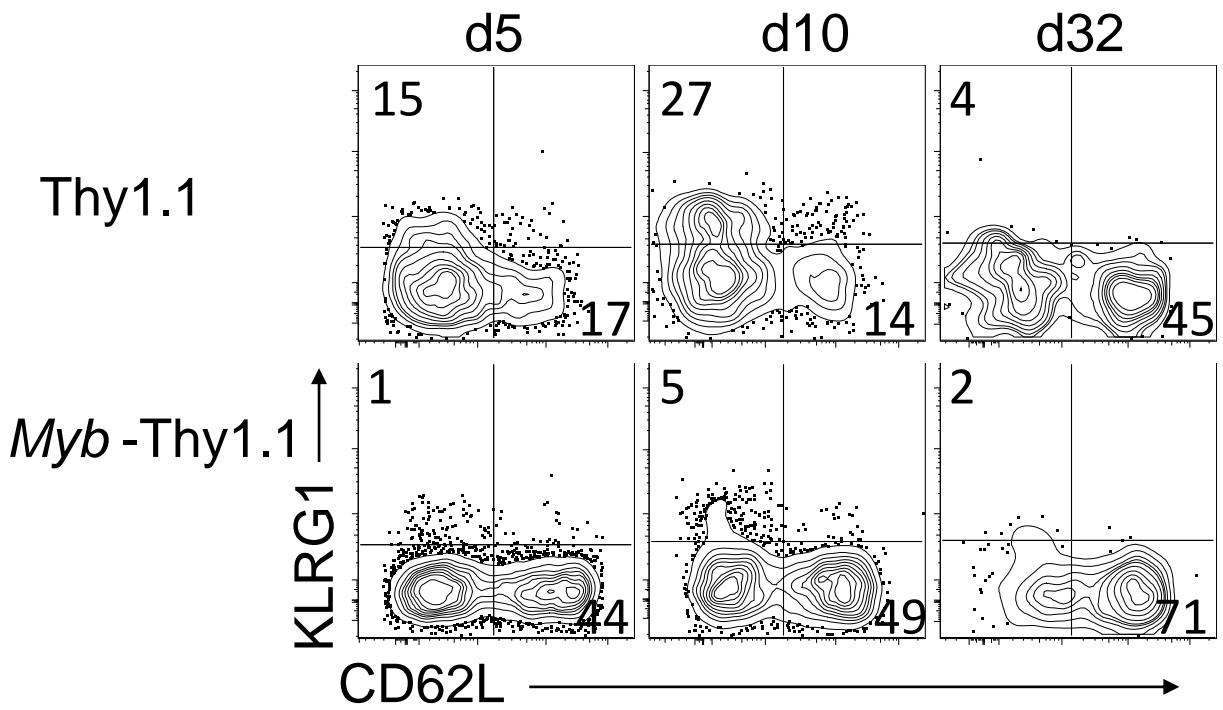
Evaluating CD8⁺ T cell immune responses in *Myb* overexpression



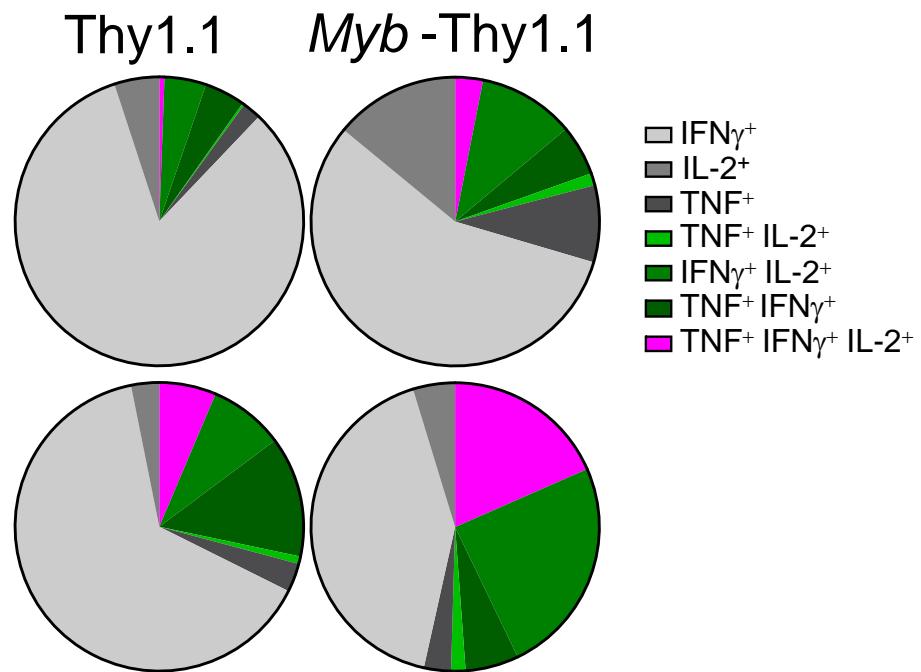
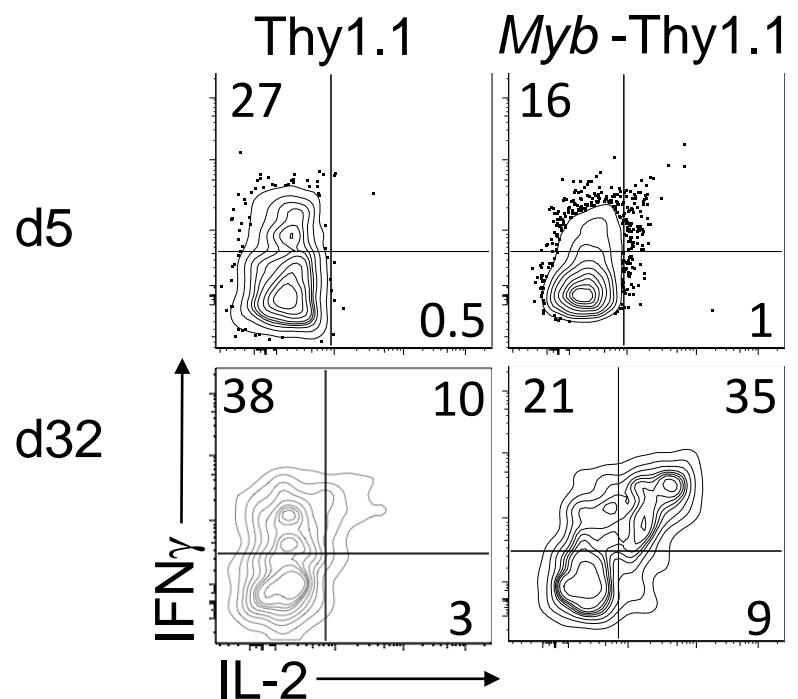
Myb overexpression promotes CD8⁺ T cell accumulation



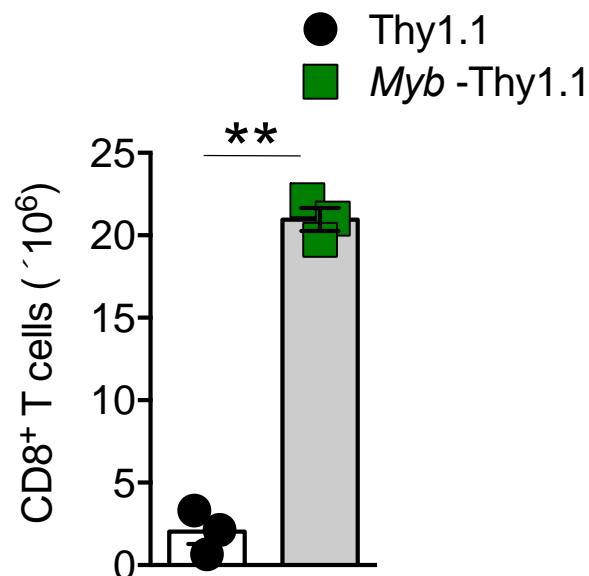
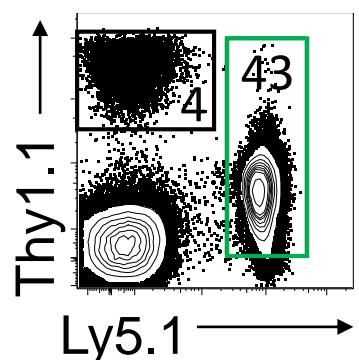
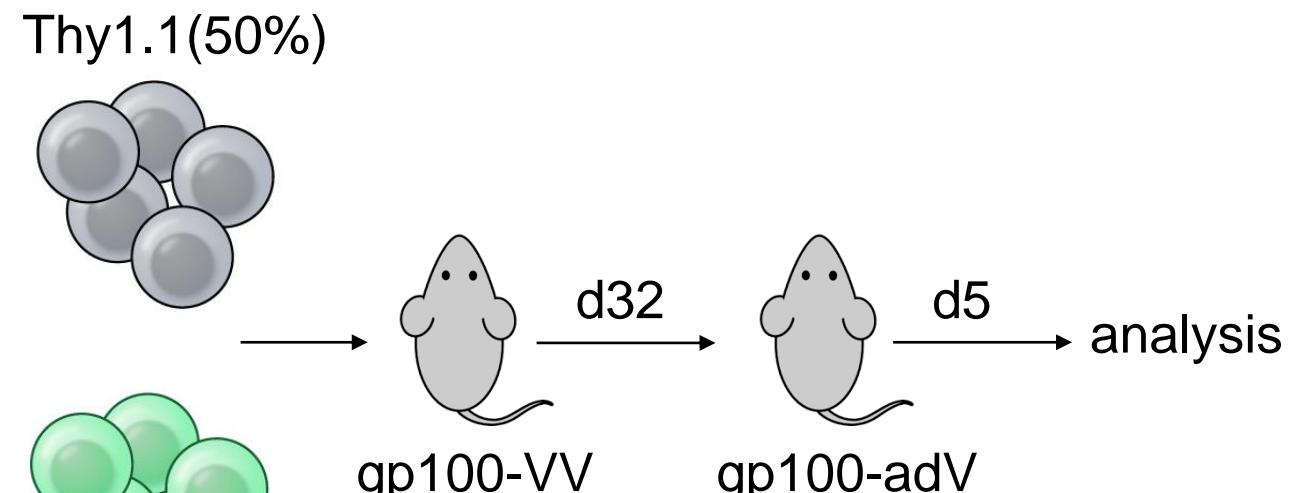
Myb overexpression enhances the generation of CD62L⁺ CD8⁺ T cells



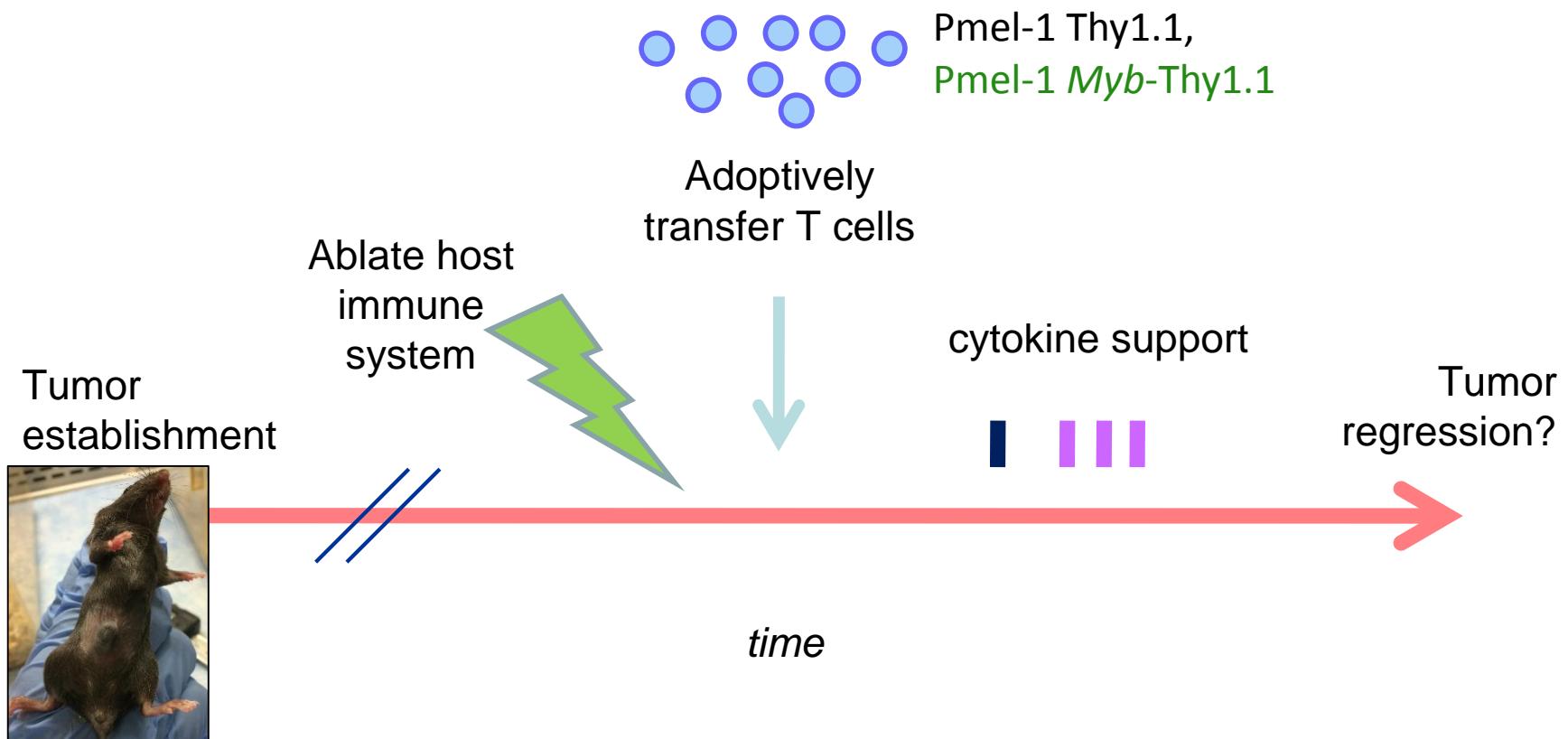
Myb overexpressing CD8⁺ T cells are polyfunctional



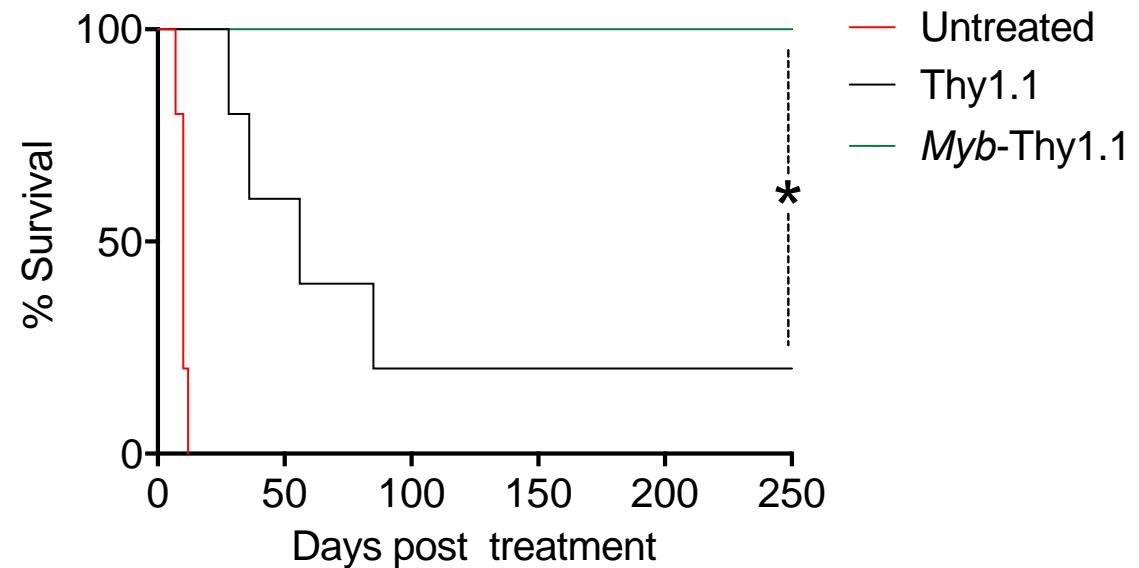
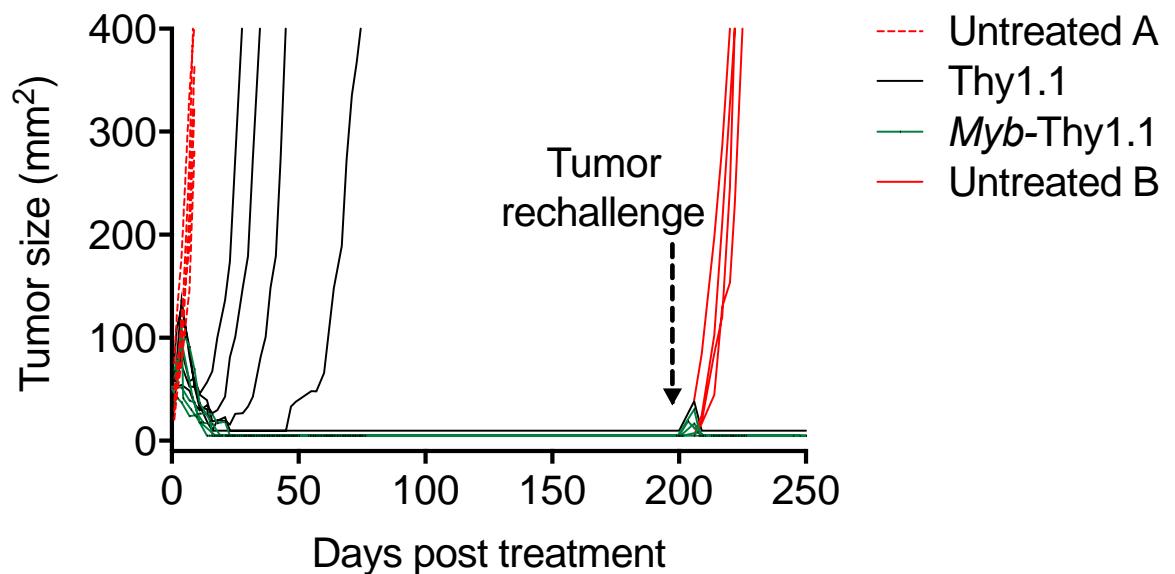
Myb overexpression enhances CD8⁺ T cell recall responses



Pmel-1 B16 melanoma mouse model



Myb overexpression promotes curative antitumor immunity



Take Home Messages

- *Myb* deficient CD8⁺ T cells demonstrate a decrease in total cell number and frequency. Furthermore, they preferentially generate short-lived effectors.
- *Myb* overexpressing cells expand more and retain a less-differentiated phenotype.
- *Myb* overexpression promotes stemness, memory formation, polyfunctionality, and therefore an enhanced therapeutic efficacy of CD8⁺ T cells.

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