

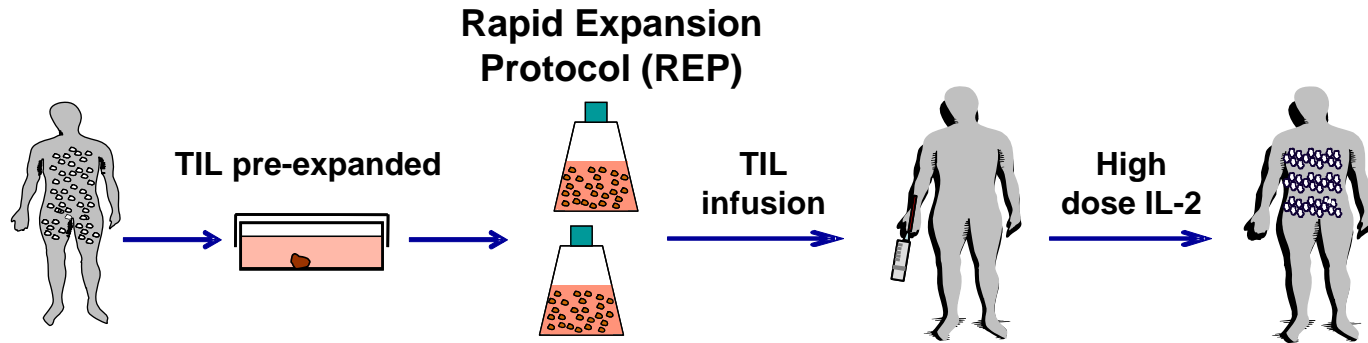
**CD28+ melanoma tumor-infiltrating
lymphocytes exhibit improved survival and
expansion capability following antigenic
re-stimulation**

Yufeng Li

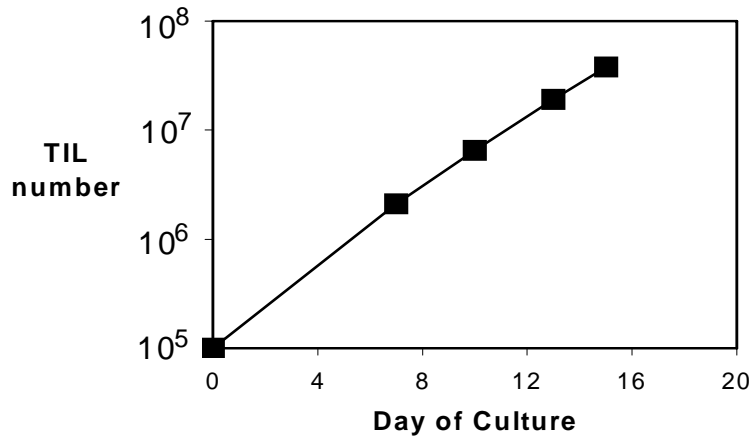
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Program of Immunology, UT-GSBS
The University of Texas**

Oct 31, 2008

Adoptive Cell Therapy (ACT): Current State-of-the-Art



Typical TIL REP



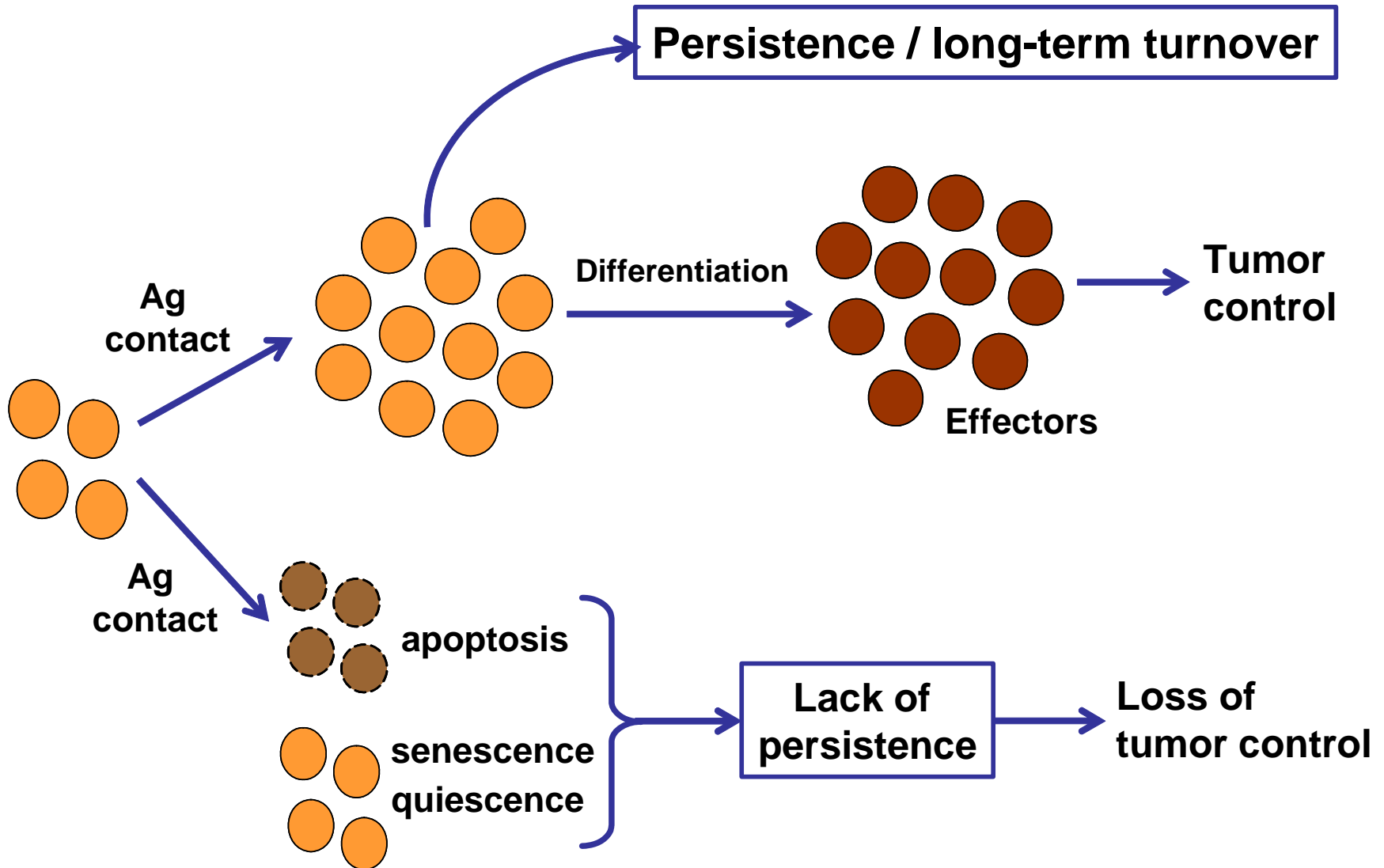
- anti-CD3 Ab + IL-2 + allogeneic feeders
- 500X to 1000X expansion
- 5 to 100 billion cells infused
- The more cells infused the better the CR

Key issues in ACT for melanoma:

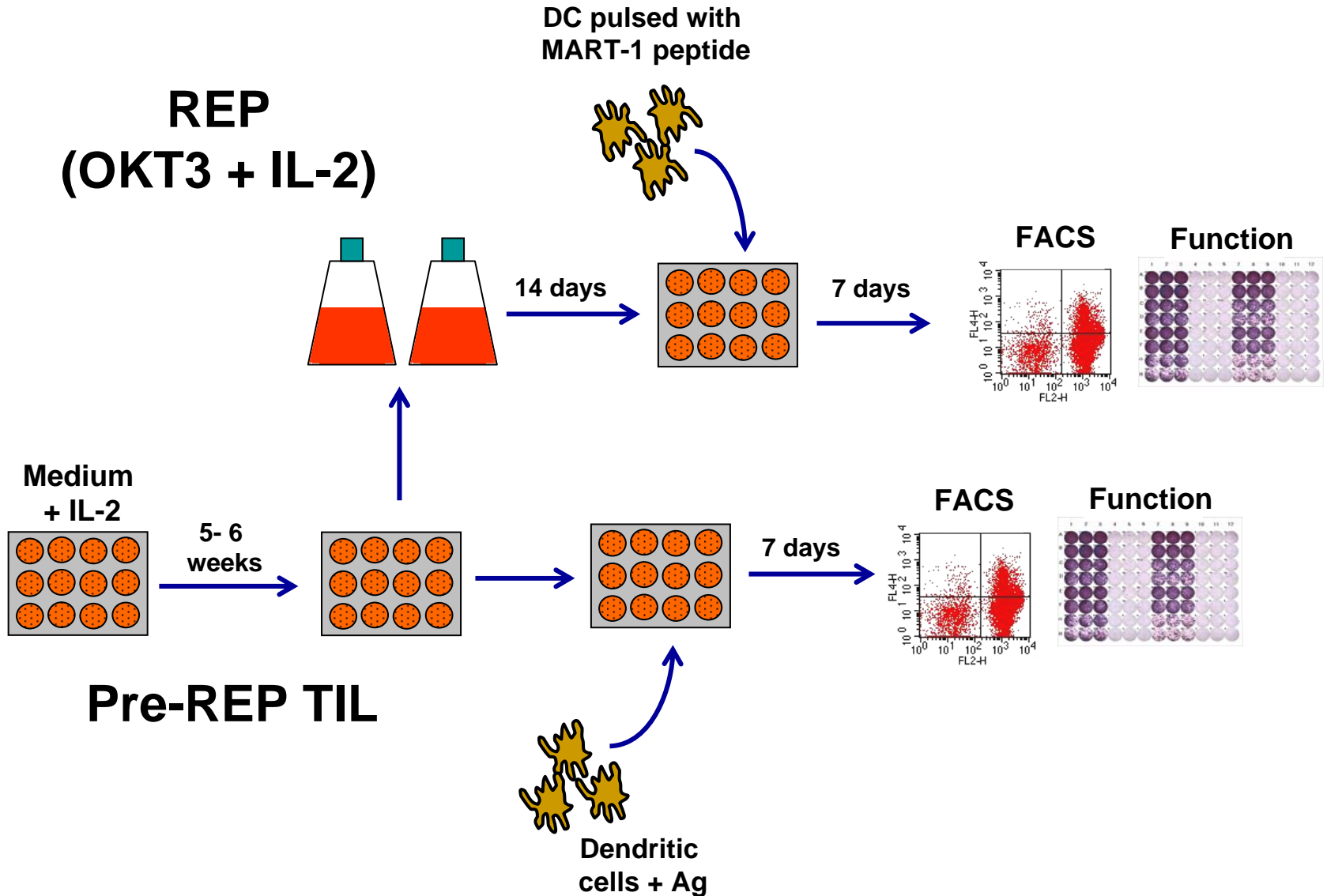
Long-term persistence of TIL associated with clinical responses (>3 months)

- **What markers / signaling pathways delineate TIL with a better propensity to survive *in vivo*?**
- **How do post-REP TIL respond to antigenic re-stimulation in addition to cytokine contact?**

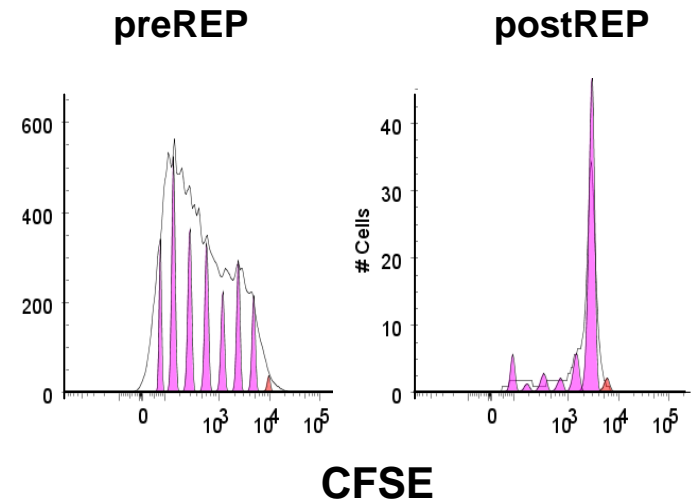
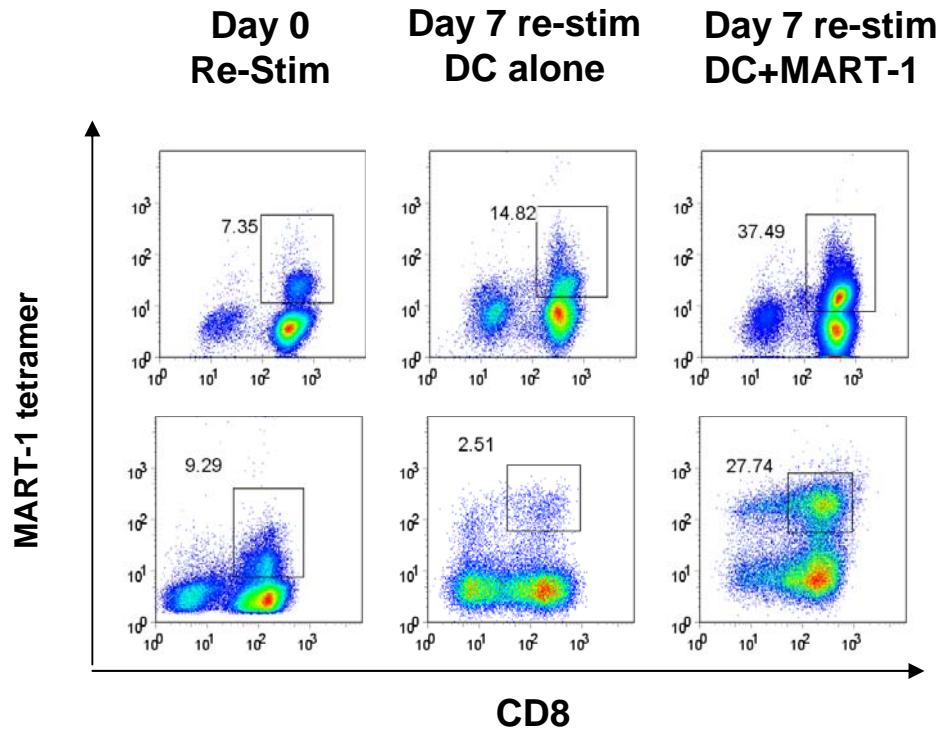
Possible fates of adoptively-transferred TIL



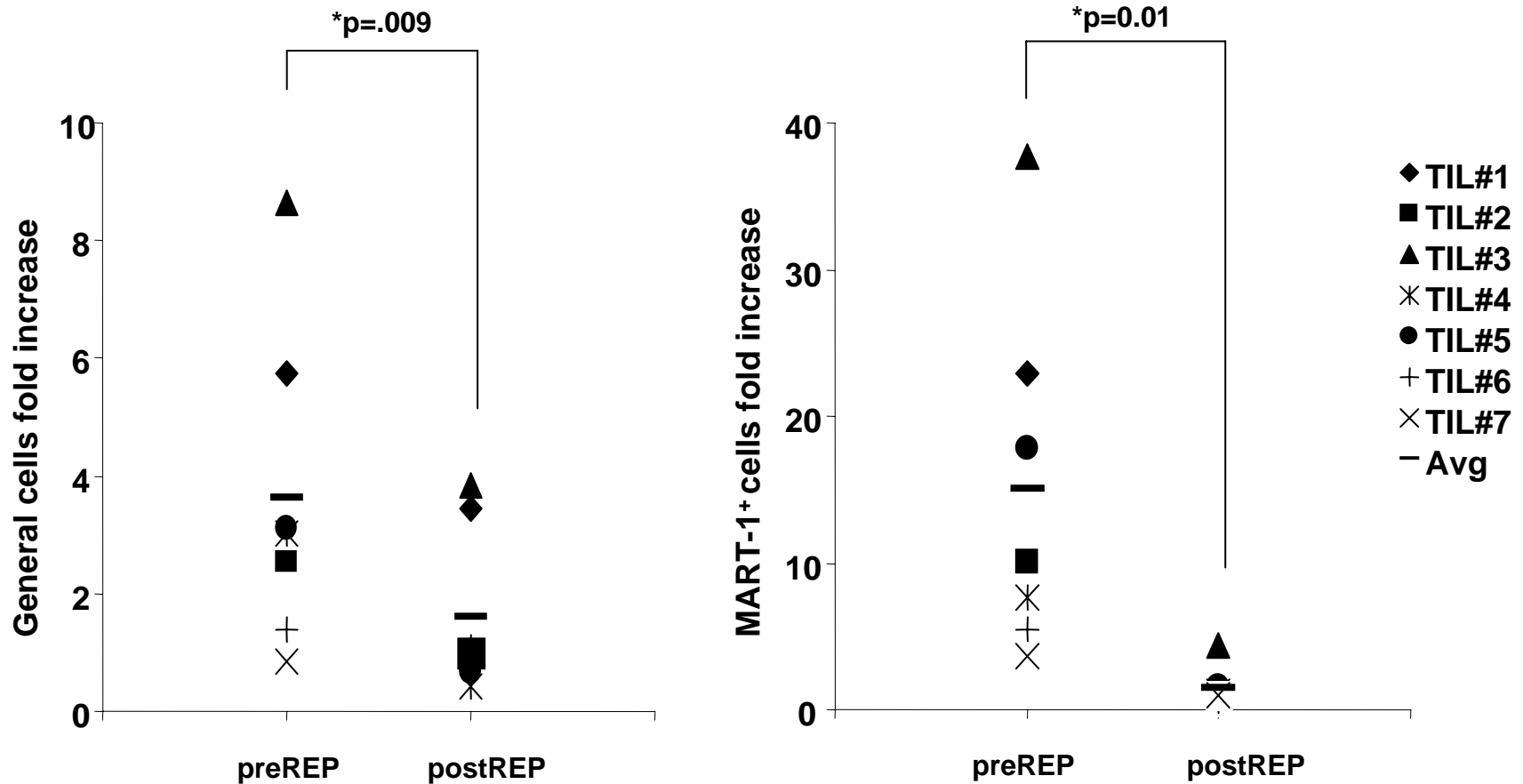
Experimental scheme



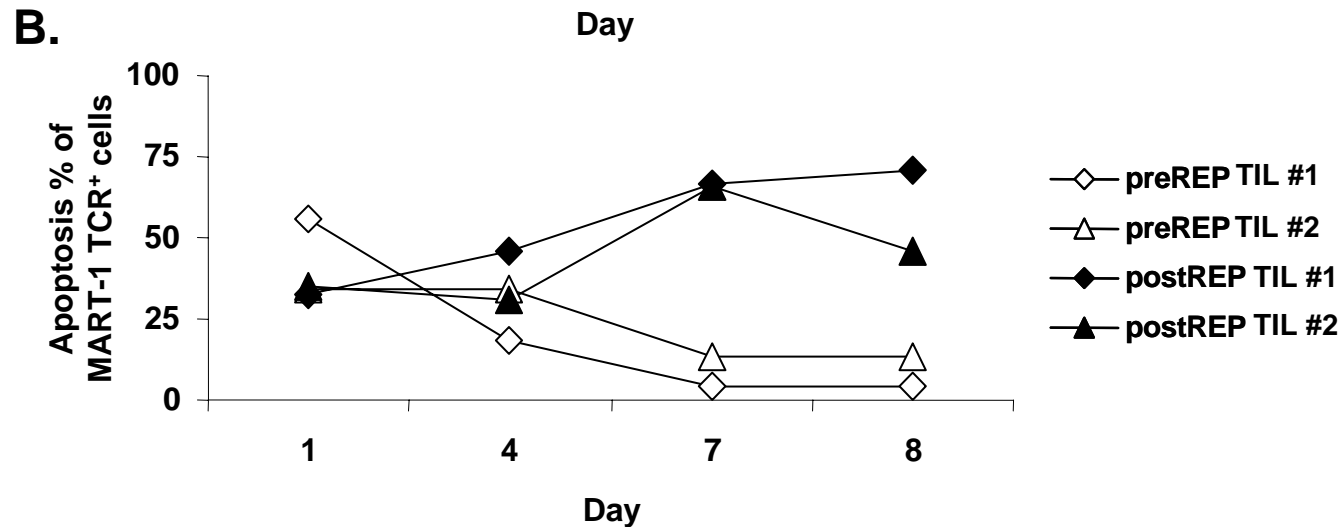
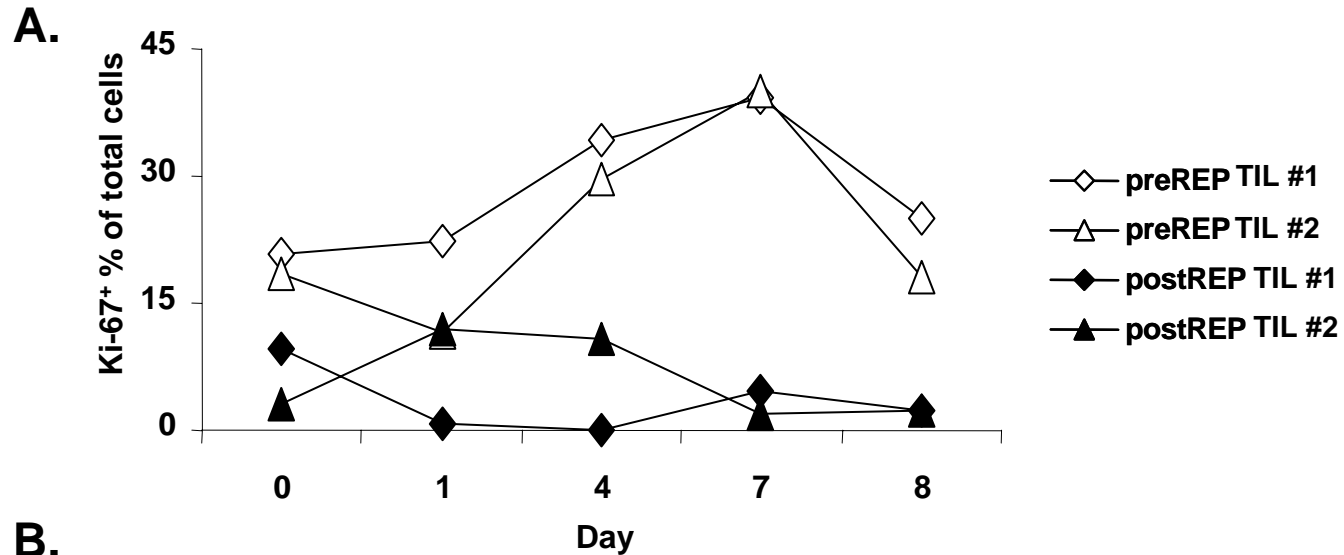
Post-REP MART-1-specific TIL are hypo-responsive to Ag re-stimulation



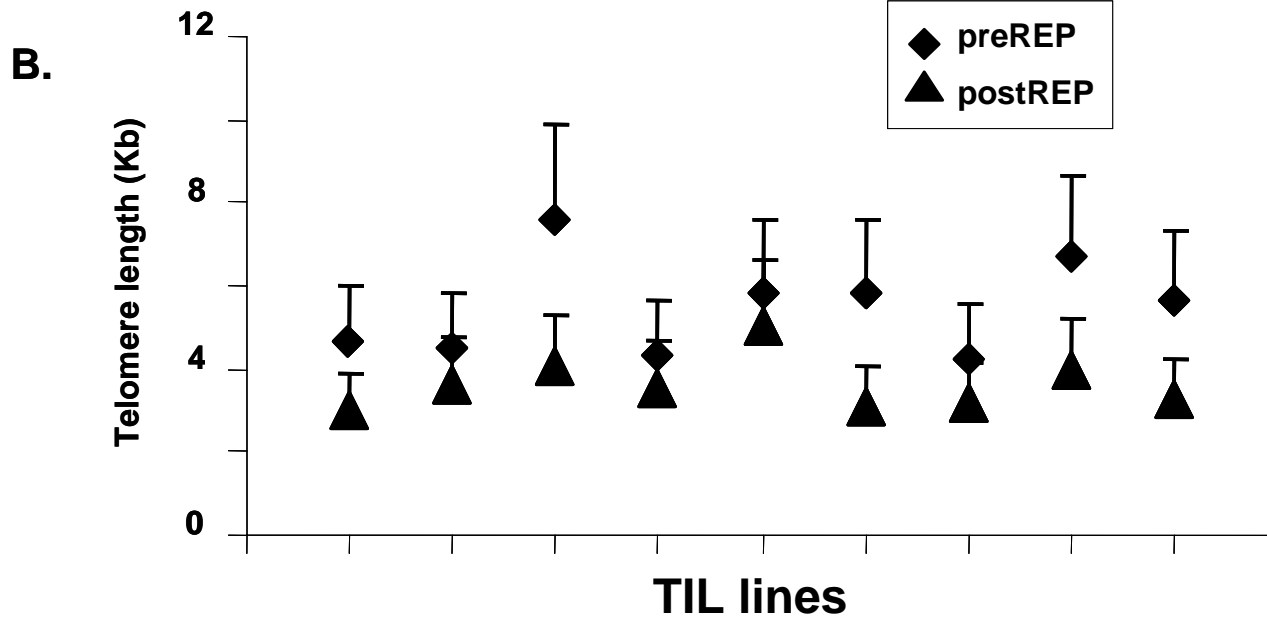
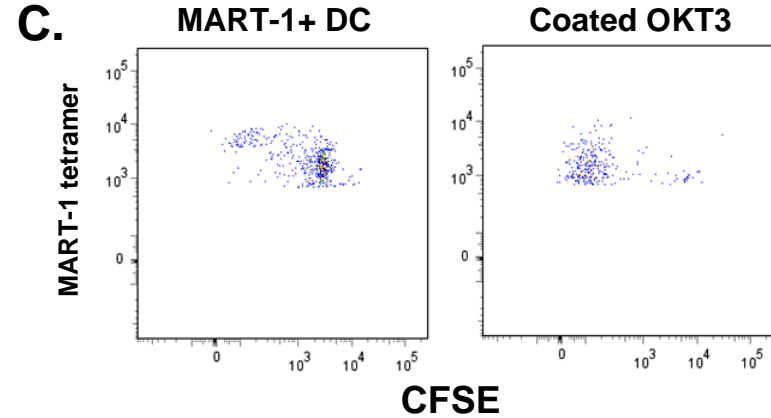
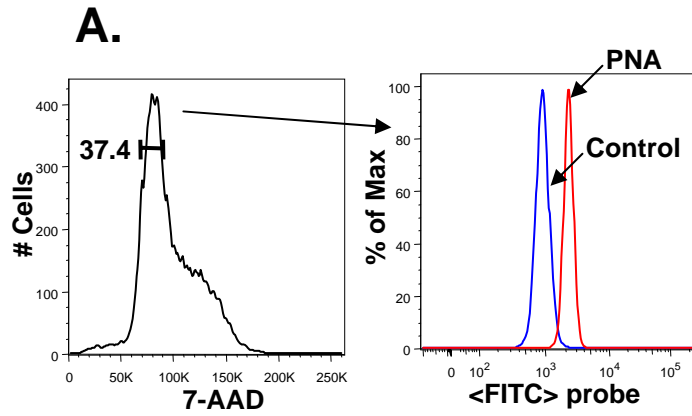
Pre-REP MART-1-specific TIL can expand better following Ag re-stimulation than post-REP TIL



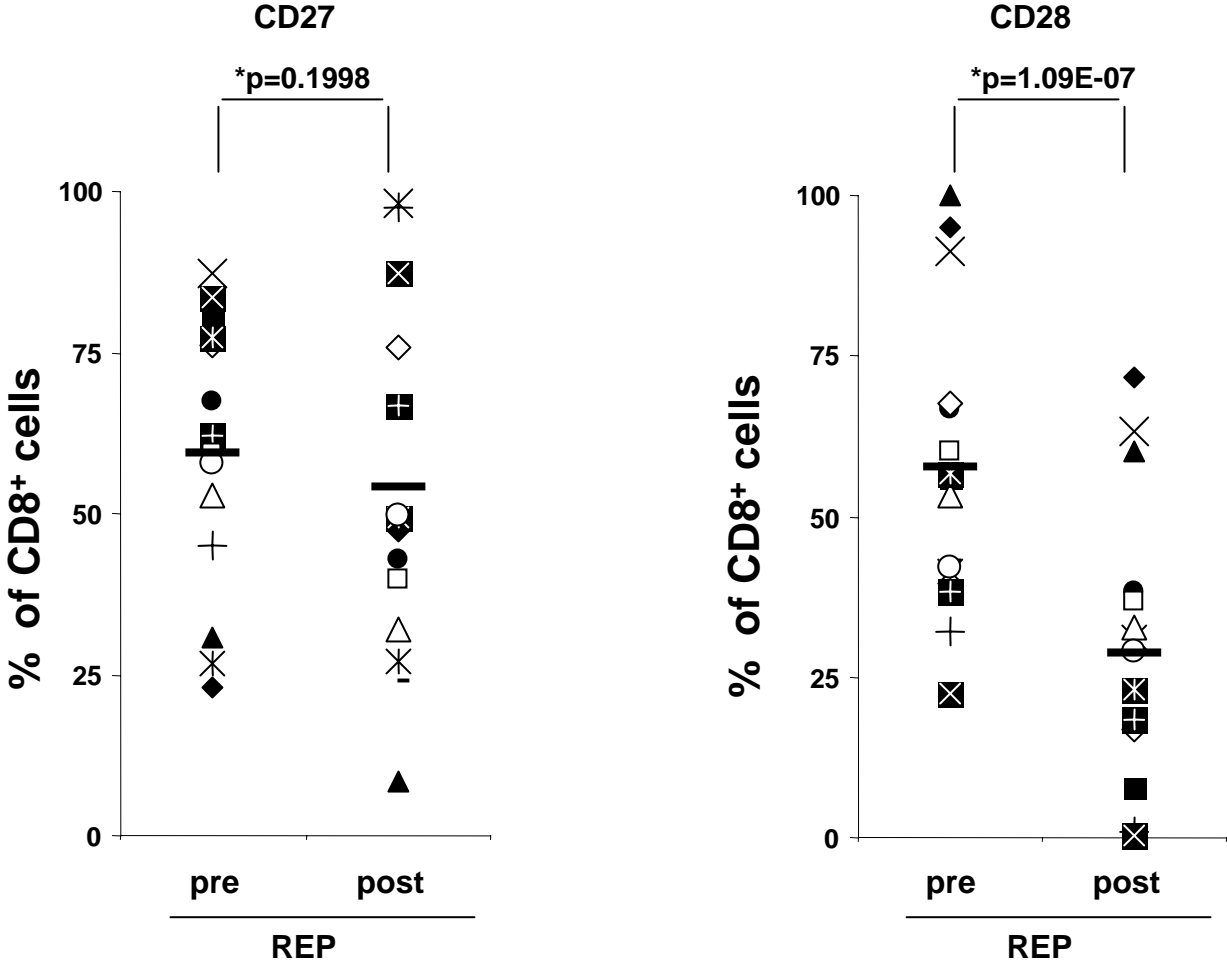
Reduced cell cycle entry and increased apoptosis in post-REP following Ag re-stimulation



Telomere length is shortened after REP, but TIL still retain capacity to divide

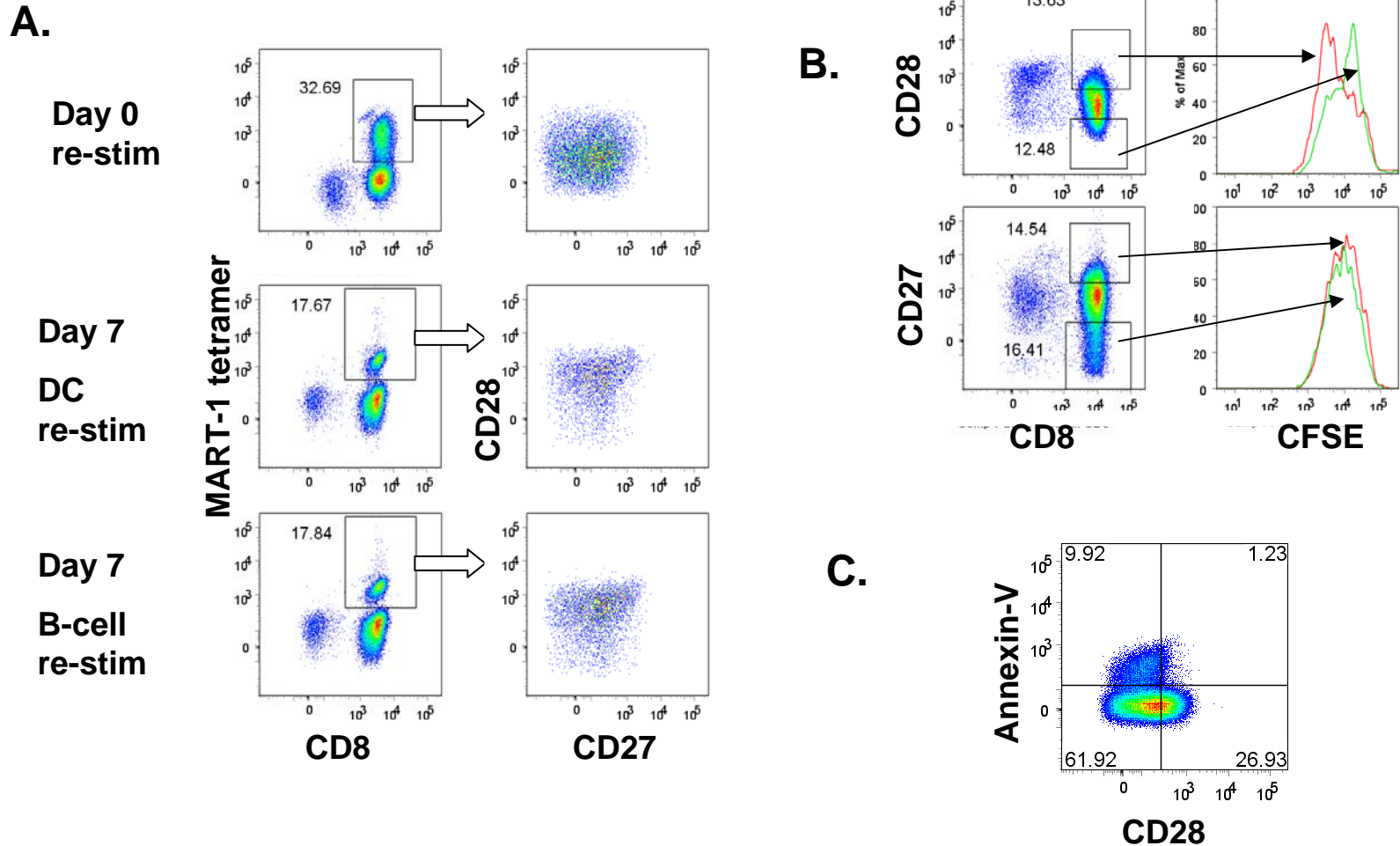


Post-REP MART-1-specific (and bulk) TIL lose CD28 expression, but not CD27

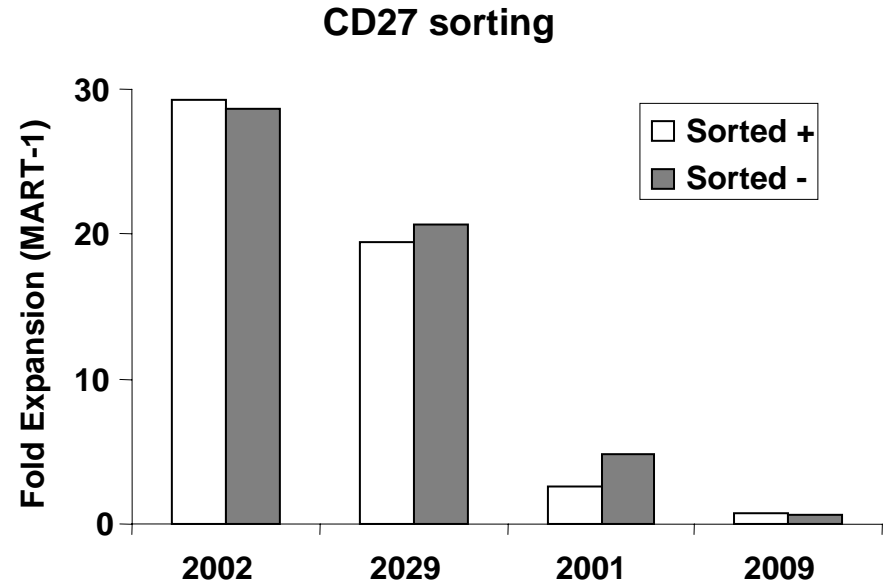
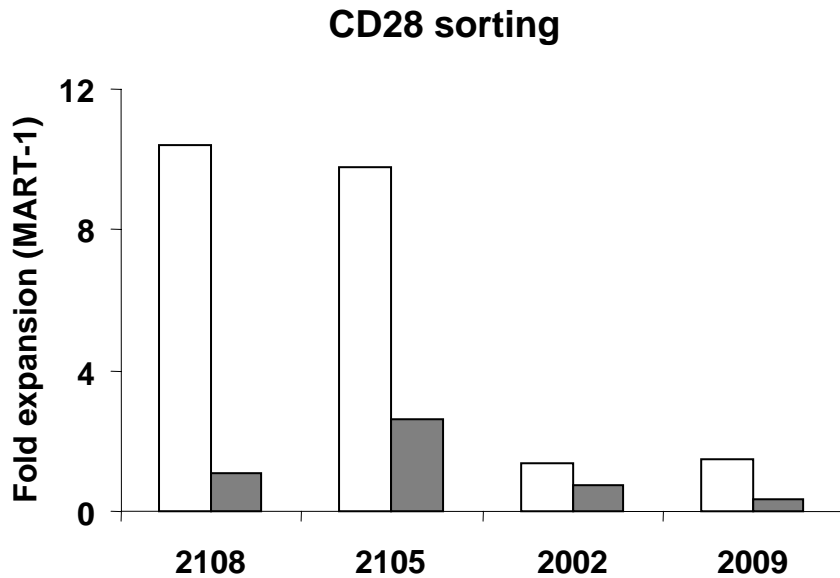


- No difference in TCR, PD1, or CTLA4 expression

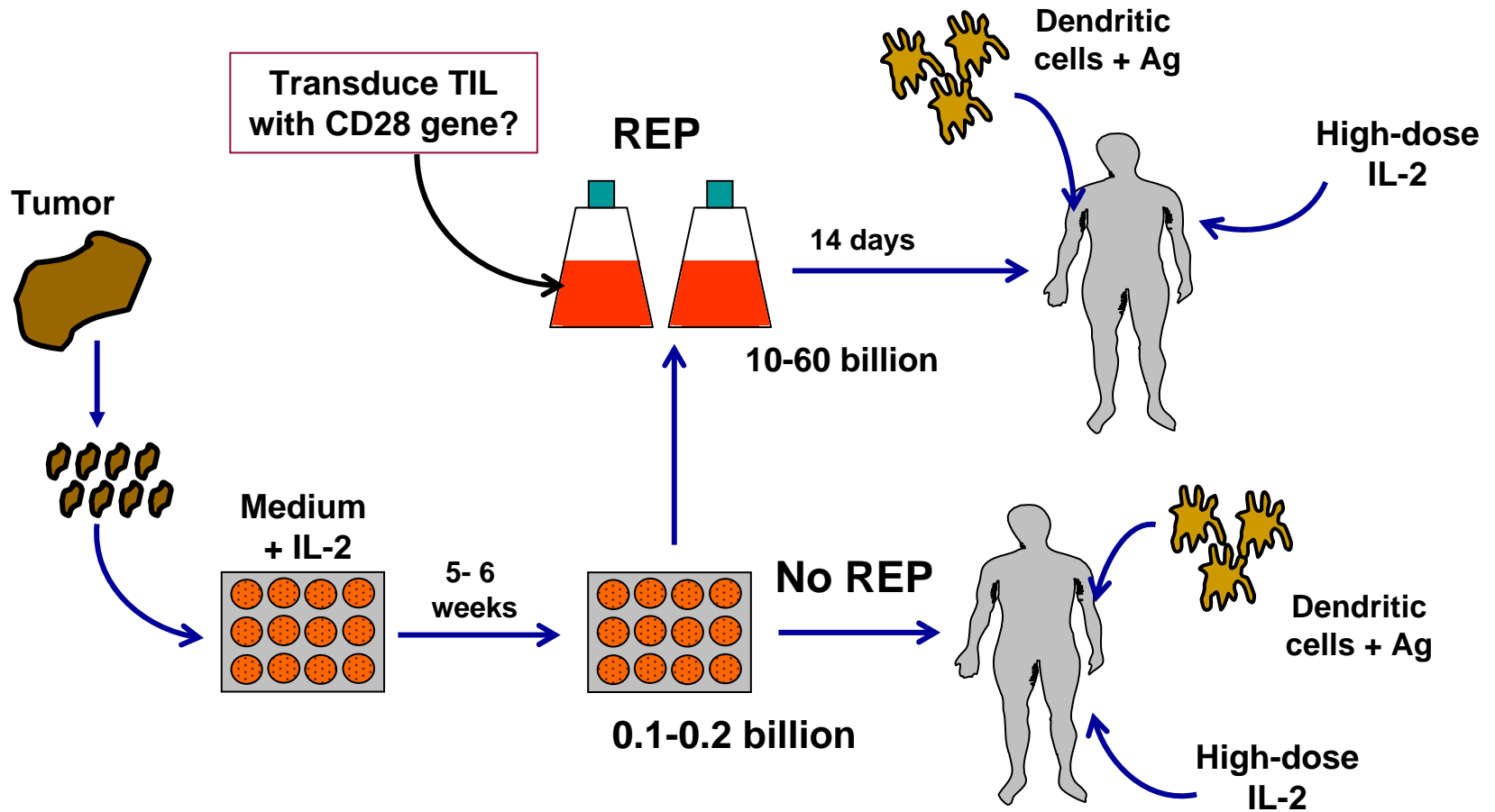
Few remaining CD28+ MART-1-specific post-REP TIL can persist and expand following Ag re-stimulation



CD28+ MART-1-specific post-REP TIL have expansion advantage while CD27+ do not



ACT: Possible new approaches



Acknowledgements

Laszlo G. Radvanyi
Patrick Hwu
Willem Overwijk
Kimberly Schluns
Krishna V. Komanduri
Miles Wilkinson

IMCL personnel
TIL lab personnel
CCIR FACS Facility
Laszlo and Patrick's lab