Role of TcR signal strength in memory development

Alanis Villanueva | August Lab
Undergraduate: Biological Sciences
Vaccines can generate protective immunity

CDC, 2011
There are branches of immune cells

- **Innate vs adaptive**

- **Innate response**
  - Nonspecific response
  - Immediate (hours)
  - No immunological memory

- **Adaptive response**
  - Pathogen and antigen specific response
  - Delayed (days, weeks)
  - Immunological memory
The adaptive immune response is comprised of CD8$^+$ T cells
Antigen-induced development of CD8\(^+\) T cell memory

WT naïve CD8\(^+\) T cell → Teff Tbet → Tmem Eomes

Cell Number

Time

expansion → Death
Itk regulates TcR signal strength

Methodology

Adoptive transfer
naive CD8\(^+\) T cells

1

WT CD45.2 (OT-1/Rag-/-)  ltk -/- CD45.2 (OT-1/ltk-/-/Rag-/-)

2

Challenge
Listeria monocytogenes OVA

C57/B6 mice (CD45.1)  C57/B6 mice (CD45.1)

3

Collect
Effector and memory CD8\(^+\) T cells

Days

7  14  21  30
MPEC cell phenotype

Memory cell surface markers:
CD127 high
KLRG1 low

Adapted from Kaech and Cui, PMC (2012)
Reducing TcR signal strength increases memory precursor effector cell development.
Antigen-induced development of CD8$^+$ T cell memory
Itk tunes development antigen-induced development of CD8^+ T cell memory

- Itk^-/- naïve CD8^+ T cell
- Teff
  - Tbet
- Tmem
  - Eomes
Conclusions

• Reducing TcR signal strength leads to enhanced CD8⁺ memory T cell formation up until two weeks after infection.

• Itk is a potential target to increase memory precursor effector cells, thus Itk inhibitors may be developed that manipulate the CD8⁺ T cell response to enhance early development of memory without compromising memory recall responses.
Future directions

- What is the mechanism by which Itk enhances early development of CD8\(^+\) T cell memory cells?

- Can knocking out Itk in other adaptive immune cells also increase their propensity to develop into memory?

- Are immune cells in young mice similarly affected as compared to older mice?
Acknowledgments

**August Lab**

*Dr. Avery August*

Sabrina Solouki

Candice Limper

Amie Wood

Ling Zhang

**Funding**

Howard Hughes Medical Institute (HHMI)

NIH AI126814

Office of Academic Diversity Initiatives (OADI)

Cornell HHMI Accelerating Medical Progress through Scholarship (CHAMPS) Program