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BASIC IMMUNOLOGY

## CASE STUDY

# Common clonal origin of central and resident memory T cells following skin immunization

Gaide O, *et al.* (2015) *Nat Med* 21(6):647-53
**JANUARY 2015**

## WHY IMMUNOSEQ?

immunoSEQ repertoire analysis allows identification and tracking of unique TCRB clones

immunoSEQ metrics such as sample diversity and clonality allow evaluation of T-cell response after exposure to antigen

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**CASE STUDY:** Common clonal origin of central and resident memory T cells following skin immunization — Gaide O, *et al.* (2015) *Nat Med* 21(6):647-53

## BACKGROUND

- Resident memory T cells ($T_{RM}$) in peripheral tissues and central memory T cells ($T_{CM}$) in lymph nodes play different roles in immunity
- Both antigen-specific $T_{RM}$ and $T_{CM}$ are generated after Vaccinia skin infection
- Memory lineage commitment towards $T_{RM}$ and $T_{CM}$ in the skin is unclear

## AIM

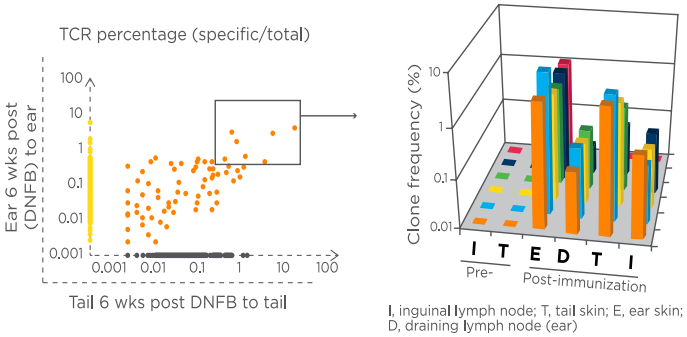
To determine how context of antigen exposure in skin can control memory T-cell lineage fate

## METHODS

1. Three different types of antigenic challenges were administered to the skin of mice *in vivo*
2. Genomic DNA (gDNA) was extracted from skin and lymph nodes at different time points, and high-throughput sequencing (HTS) of the mouse T-cell receptor beta (TCRB) locus was performed
3. For human studies, gDNA extraction and TCRB sequencing was performed on skin biopsies of individuals that were sensitized with diphenylcyclopropenone (DPCP)

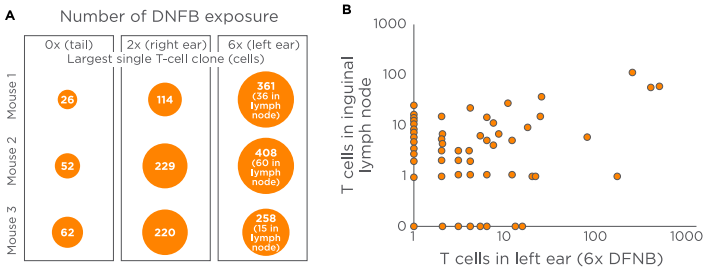
## RESULTS

Antigenic challenge in the skin generates T-cell receptor (TCR)-identical $T_{RM}$ and $T_{CM}$




I, inguinal lymph node; T, tail skin; E, ear skin; D, draining lymph node (ear)

Repetitive sensitization increases numbers of $T_{RM}$ in skin




- The six most abundant clones shared in tissues ($T_{RM}$), at treated (ear) and distant (tail) sites, were not present prior to immunization
- These clones were also present in the draining and distant lymph nodes ($T_{CM}$)

- Abundance of the single largest T-cell clone is highest in skin exposed six times to DNFB
- T cells were present in higher numbers in skin than in lymph nodes after six exposures

## CONCLUSIONS

Studies in human subjects and mouse models showed that antigen-reactive skin $T_{RM}$ and lymph node $T_{CM}$ cell clones were derived from a common naïve T-cell precursor after skin immunization

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