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INFECTIOUS DISEASE

CASE STUDY

Successive annual influenza vaccination induces a recurrent oligoclonotypic memory response in circulating T follicular helper cells

Herati RS, et al. *Science Immunology*. 2(8):eaag2152. 2017.
FEBRUARY 2017

WHY IMMUNOSEQ?

Allows tracking of sequences over multiple time points as well as between subsets to identify dynamics and relationship of various cell populations

The quantitative nature and clonality metric allows for evaluation of clonal expansion in response to vaccination at the repertoire and individual clone levels

Lack of a batch effect allows for prospective, near real-time results in longitudinal studies

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CASE STUDY: Successive annual influenza vaccination induces a recurrent oligoclonotypic memory response in circulating T follicular helper cells—*Herati RS, et al. Science Immunology. 2(8):eaag2152. 2017.*

BACKGROUND

T follicular helper cells (Tfh) located in the germinal center, play a key role in B-cell activity and responses to antigens and antibody production. A circulating set of $CD4^+$ T cells with similar phenotype and function as traditional Tfh, have been identified and termed circulating T follicular helper cells (cTfh). Assessment of cTfh in the blood could serve as a noninvasive way to monitor Tfh activity after vaccination. Previous studies have shown that changes in this subset, including increased expression of inducible costimulator (ICOS) are correlated with antibody production following influenza vaccine. However, the dynamics of the antigen specific cTfh cell response to vaccination has not yet been well characterized.

AIM

- Evaluate and compare repertoire and clonality of cTfh subsets before and after influenza vaccination using the immunoSEQ Assay.
- Investigate the influenza-specificity of these cells, using tetramers and cell stimulation assays.
- Track these responses over successive annual influenza vaccinations using the immunoSEQ Assay.

METHODS

Blood samples were drawn on day 0, 7 and 28 from 6 healthy adults who had not received a prior flu vaccination for six months. Study participants were tracked over a period of 2 or 3 years.

1. Sort activated and non-activated cTfh pre and post annual vaccinations → gDNA → Sequence using the **hsTCRB immunoSEQ Assay**
2. Compare clonality, repertoire and overlaps between time points and cell subsets.

RESULTS

- The increased frequency of activated ICOS+CD38+ cTfh cells were enriched for influenza-specific cells at 7 days post vaccination. This response was oligoclonal. (Figure 1)
- Longitudinal analysis, showed a high turnover in the activated cTfh pool at baseline (in the absence of vaccination). However, repeated flu vaccination led to re-emergence of influenza-specific memory clonotypes at day 7 after vaccination in year 2 and 3 in the activated cTfh. (Figure 1)
- The stable $ICOS^-CD38^-$ cTfh subset may represent a memory pool from which antigen-specific Tfh cells could be recalled following antigen exposure.

Figure 1.

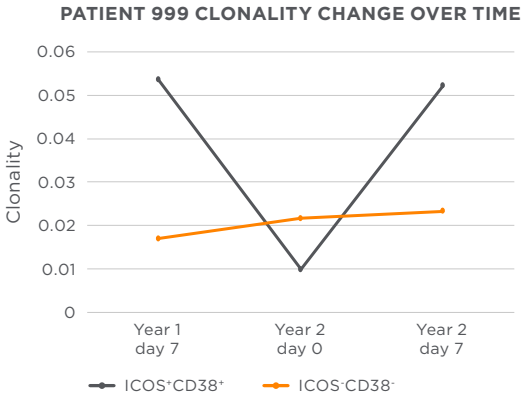

Figure 2.

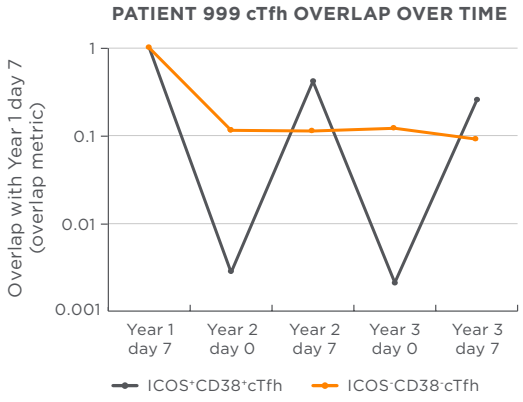

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Figure 1. Clonality changes in the subsets over time. The increased in clonality of the activated $ICOS^+CD38^+$ cTfh cells suggests an antigen-driven clonal expansion following vaccination, while the potential memory subset remains consistent, even following vaccination.

Figure 2. Overlap of $ICOS^+CD38^+$ (activated) cTfh and $ICOS^-CD38^-$ cTfh in patient 999. Successive vaccination induced similar repertoire responses each year in the $ICOS^+CD38^+$ subset, while the $ICOS^-CD38^-$ subset remained fairly stable, likely acting as a memory pool.

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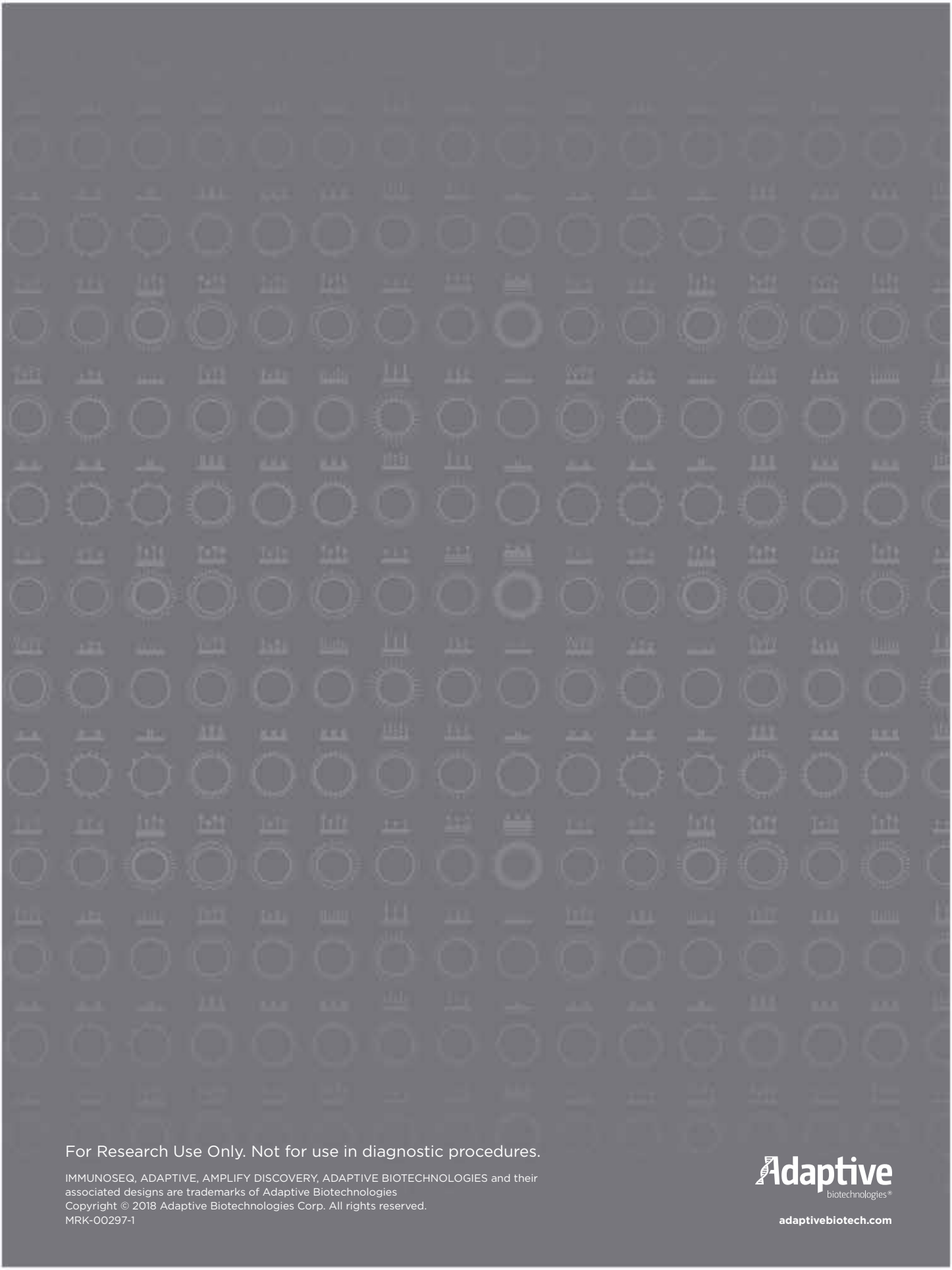
CONCLUSIONS

- Influenza-specific cells were identified in the $ICOS^+CD38^+$ cTfh subset of peripheral blood at day 7 after vaccination.
- Successive annual influenza vaccination resulted in the induction of recurrent clonal responses for each of the studied years.
- Activated $ICOS^+CD38^+$ cTfh cells converted to a memory pool and can be recalled with each successive vaccination.
- The combination of tetramer staining, in vitro stimulation and T cell repertoire studies used in this study demonstrated new ways to monitor antigen-specific Tfh cell responses in the peripheral blood to improve future vaccination strategies.



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