

# The TCR repertoire of circulating $\gamma\delta$ T lymphocytes in psoriasis vulgaris varies with age and disease severity

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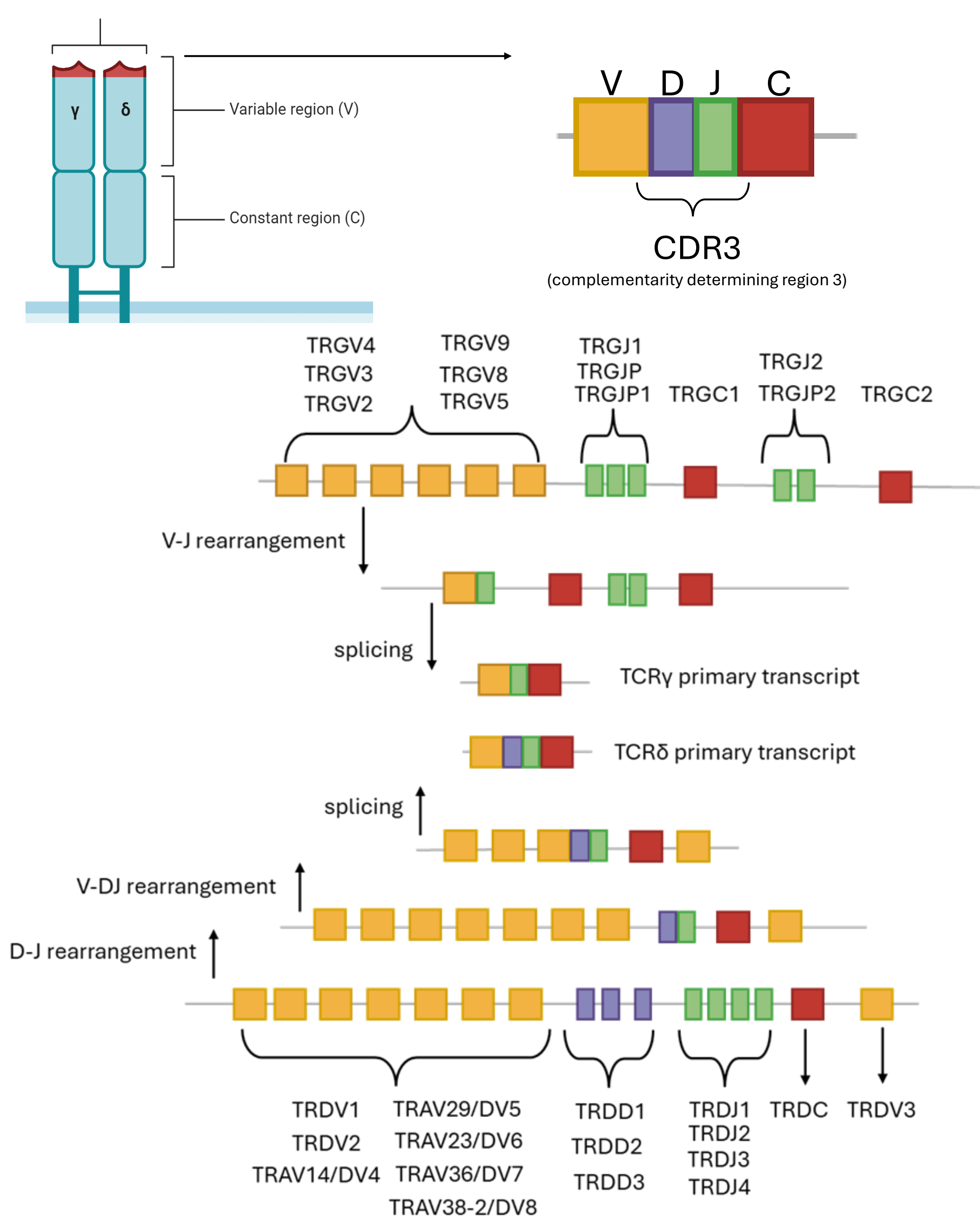
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## INTRODUCTION

- **Psoriasis vulgaris** – a recurring **autoinflammatory skin disease** that often **manifests systemically**
- underlying immune aberrations **predominantly driven by T cells**
- emerging evidence indicates that  **$\gamma\delta$  T cells may contribute to PV pathogenesis**
- **healthy peripheral  $\gamma\delta$  T cell repertoires are largely composed of V $\gamma$ 9V $\delta$ 2 cells**; however,  **$\gamma\delta$  TCR repertoires can undergo significant changes in disease**
- the **diversity and composition of the  $\gamma\delta$  TCR repertoire in PV remain largely unknown**

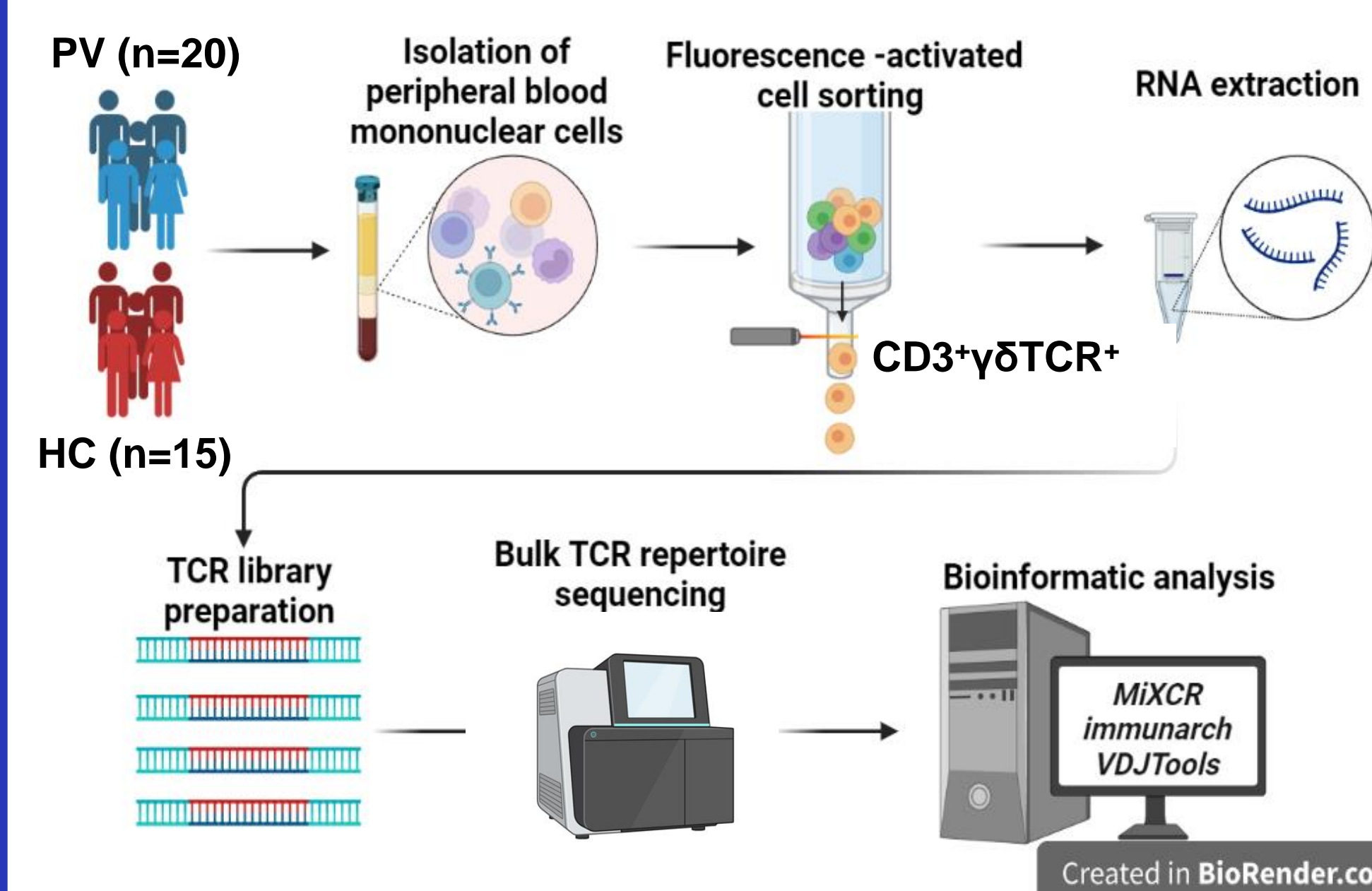


## $\gamma\delta$ TCR structure and V(D)J recombination



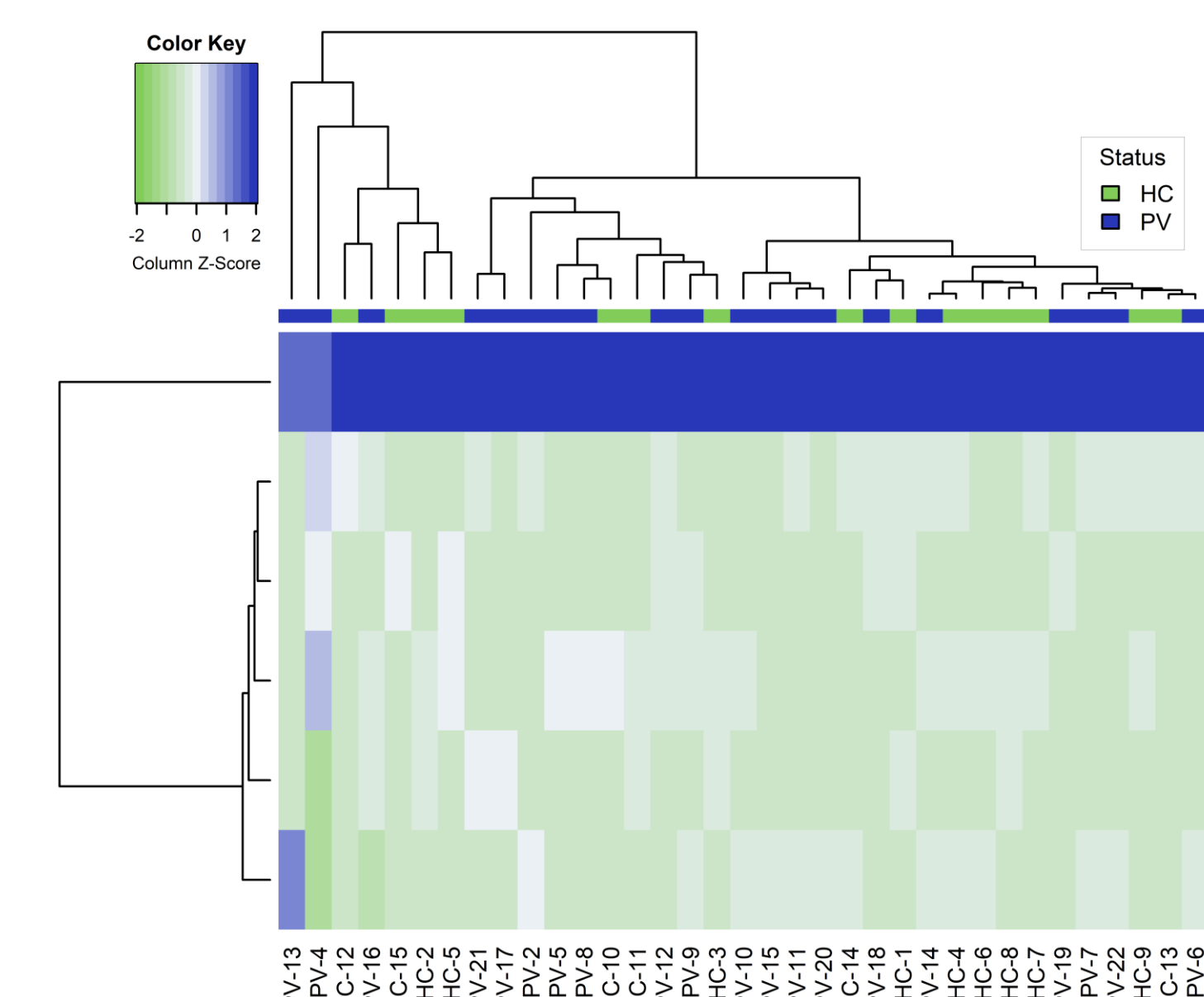
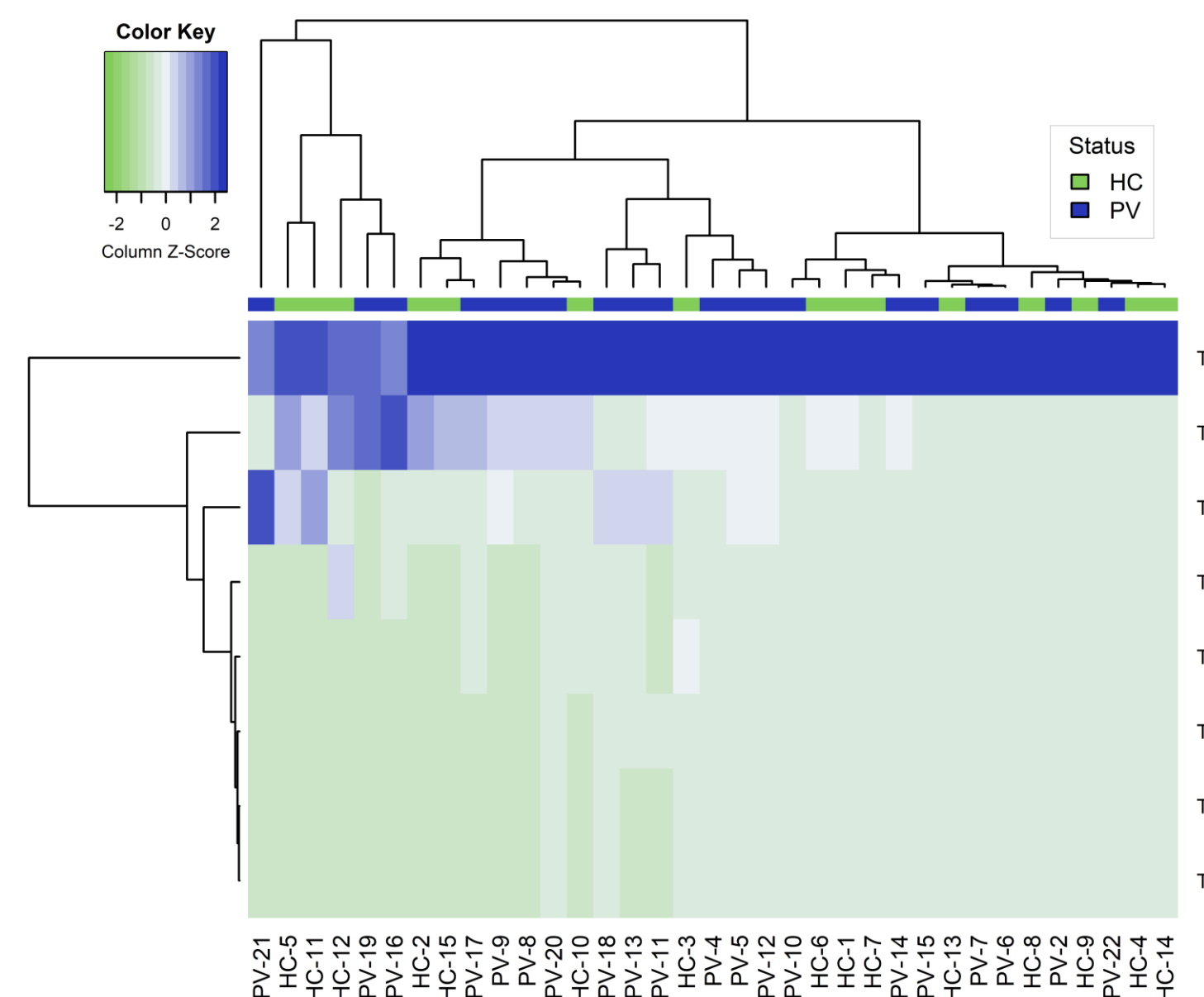
## METHODS

- **bulk TCRSeq analysis** (Archer Immuniverse™ HS TCR, NextSeq Illumina, MiXCR, VDJTools and immunarch pipeline) from **flow-sorted, peripheral  $\gamma\delta$  T cells**

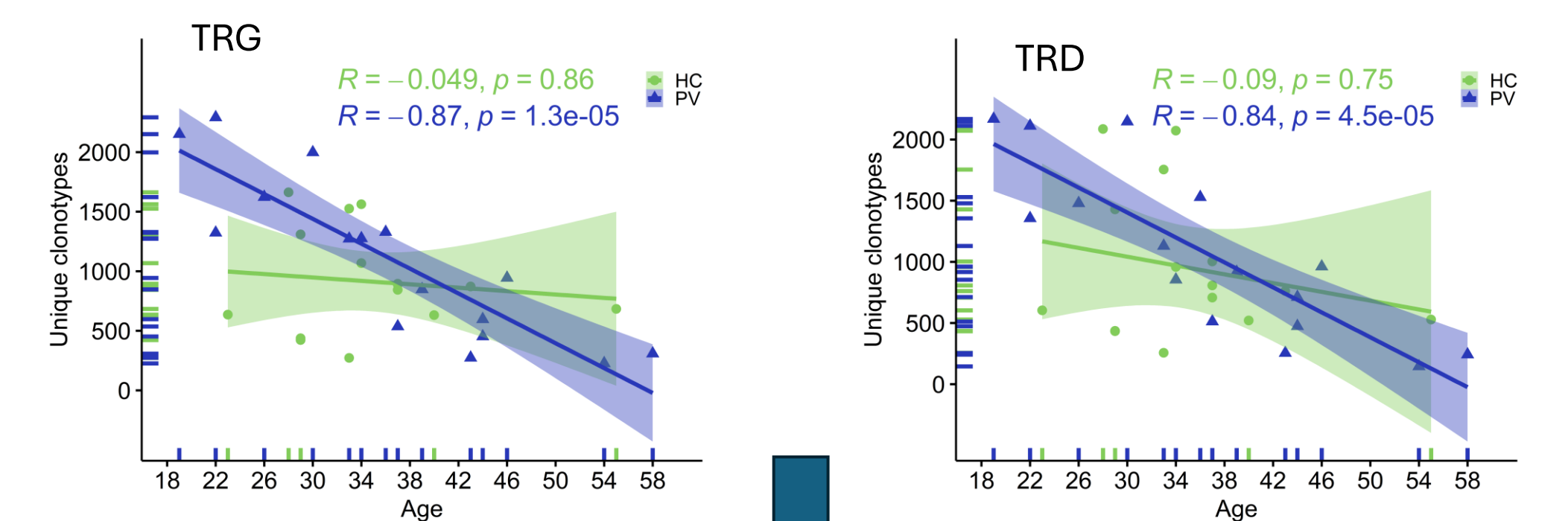


## RESULTS

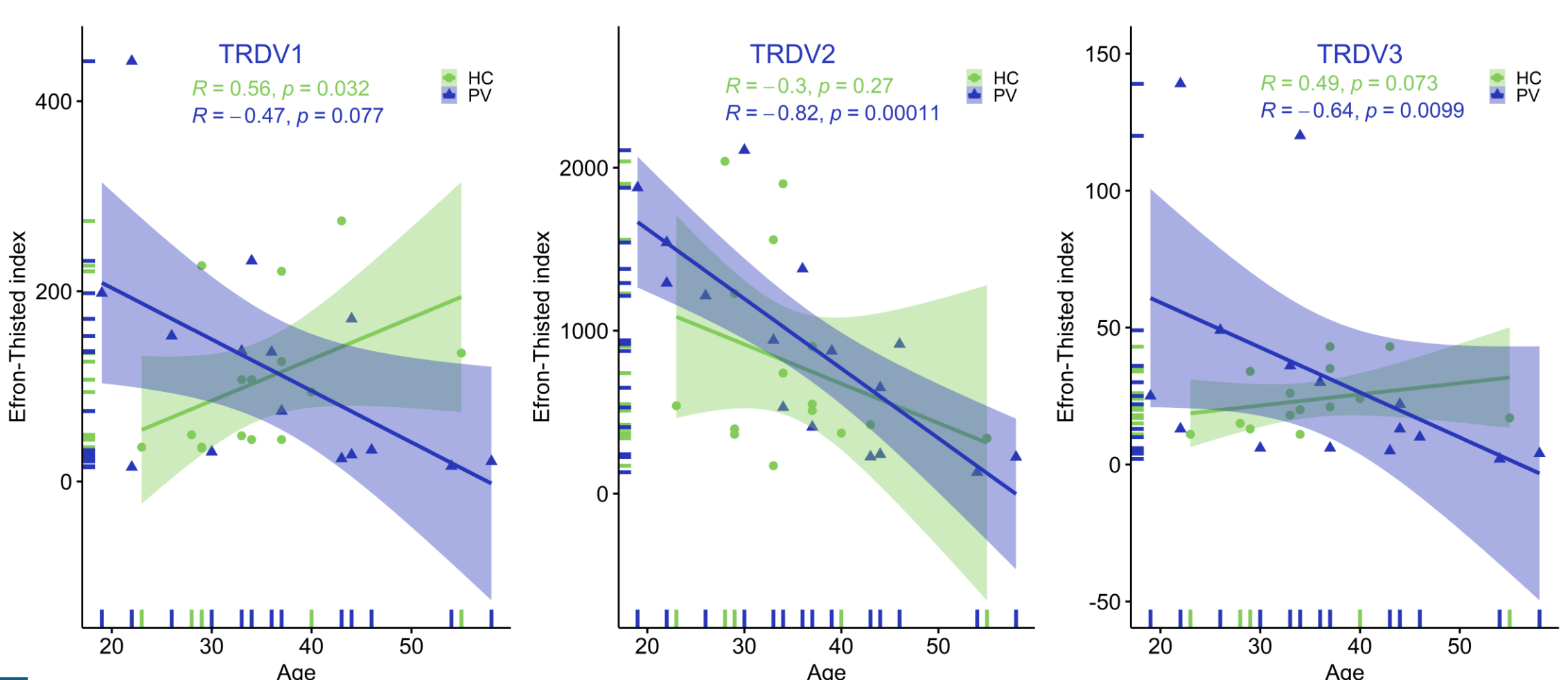
- **TRDV2-TRDJ1 and TRGV9-TRGJP clonotypes dominated the repertoire in most samples, with no significant differences between cases and controls**



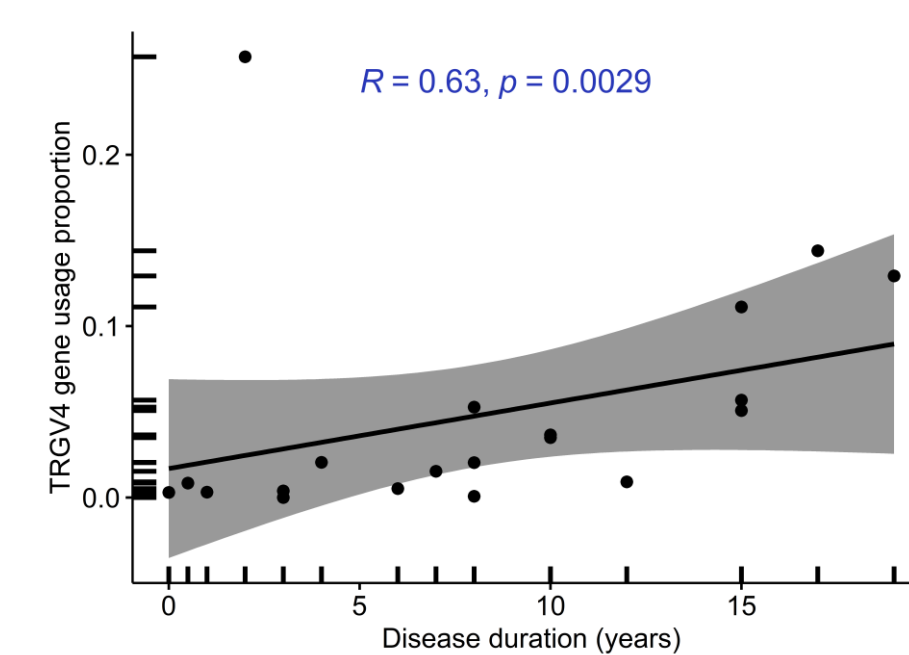
- **THE DIVERSITY OF THE TRG AND TRD REPERTOIRE DECREASES SIGNIFICANTLY WITH AGE IN PV, BUT REMAINS STABLE IN AGE-MATCHED HEALTHY CONTROLS**



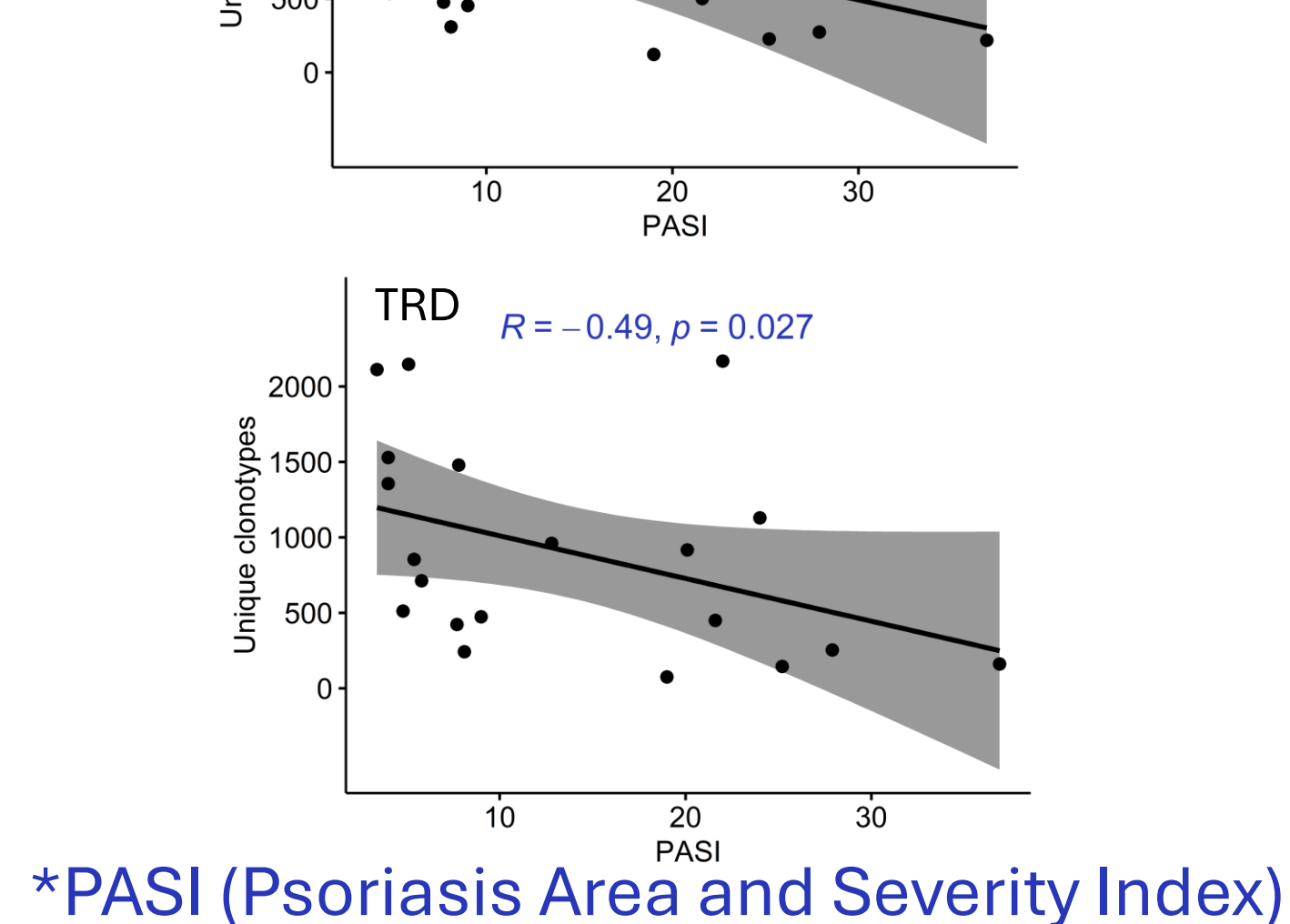
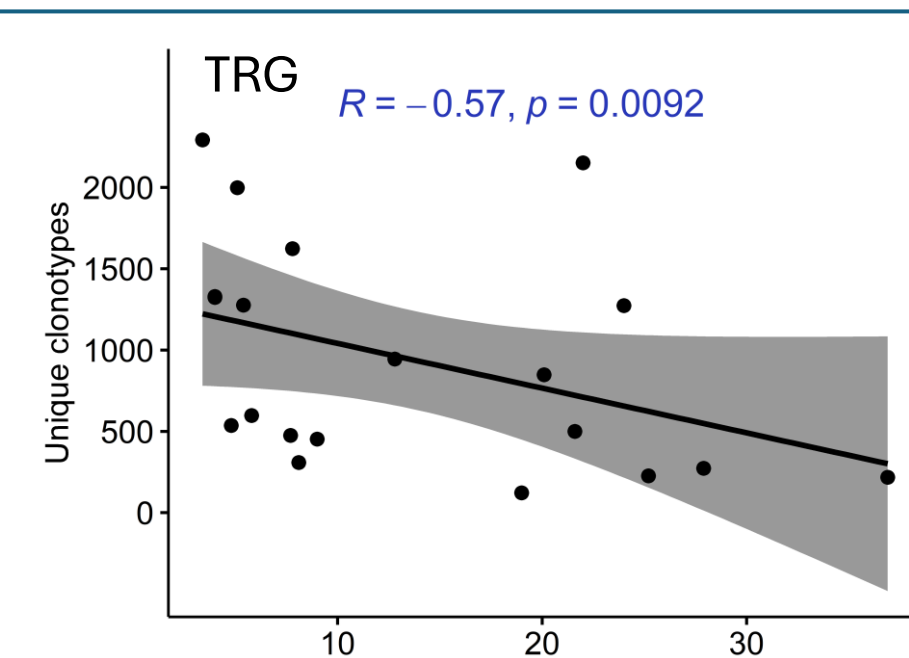
- **SIGNIFICANT AGE-RELATED LOSS OF RARE TCR $\delta$  CLONOTYPES IN PV, IN CONTRAST TO INCREASED TRDV1 AND TRDV3 DIVERSITY IN HEALTHY CONTROLS**



- **LONGER DISEASE DURATION IS ASSOCIATED WITH A HIGHER PREVALENCE OF TRGV4 CLONOTYPES**

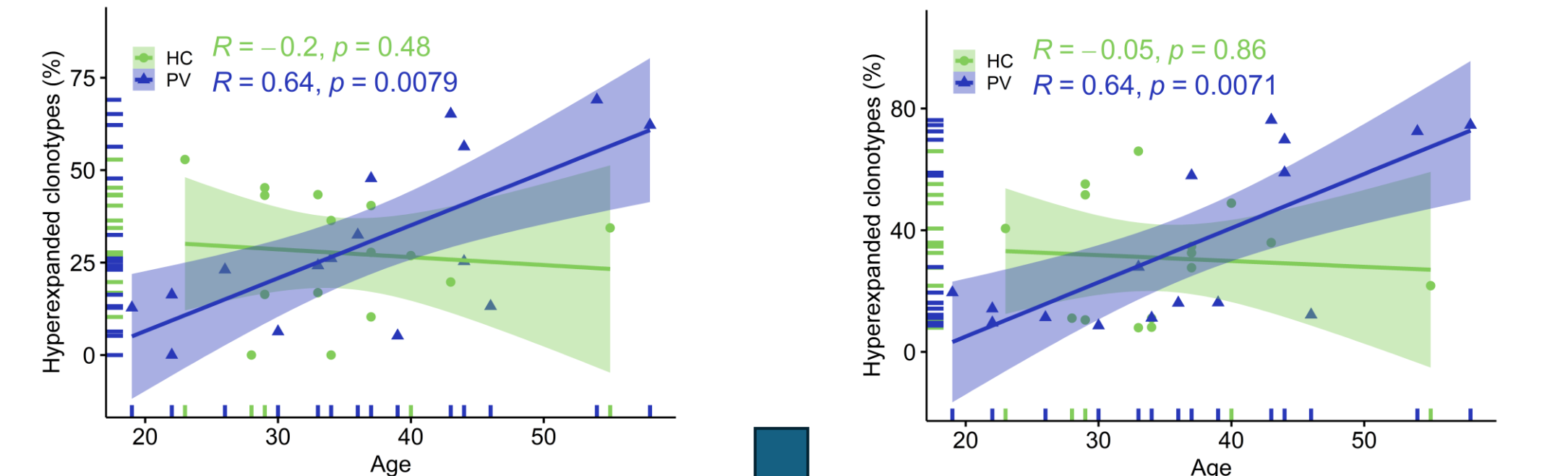


- **DISEASE SEVERITY\* NEGATIVELY CORRELATES WITH TRG AND TRD CLONOTYPE DIVERSITY**

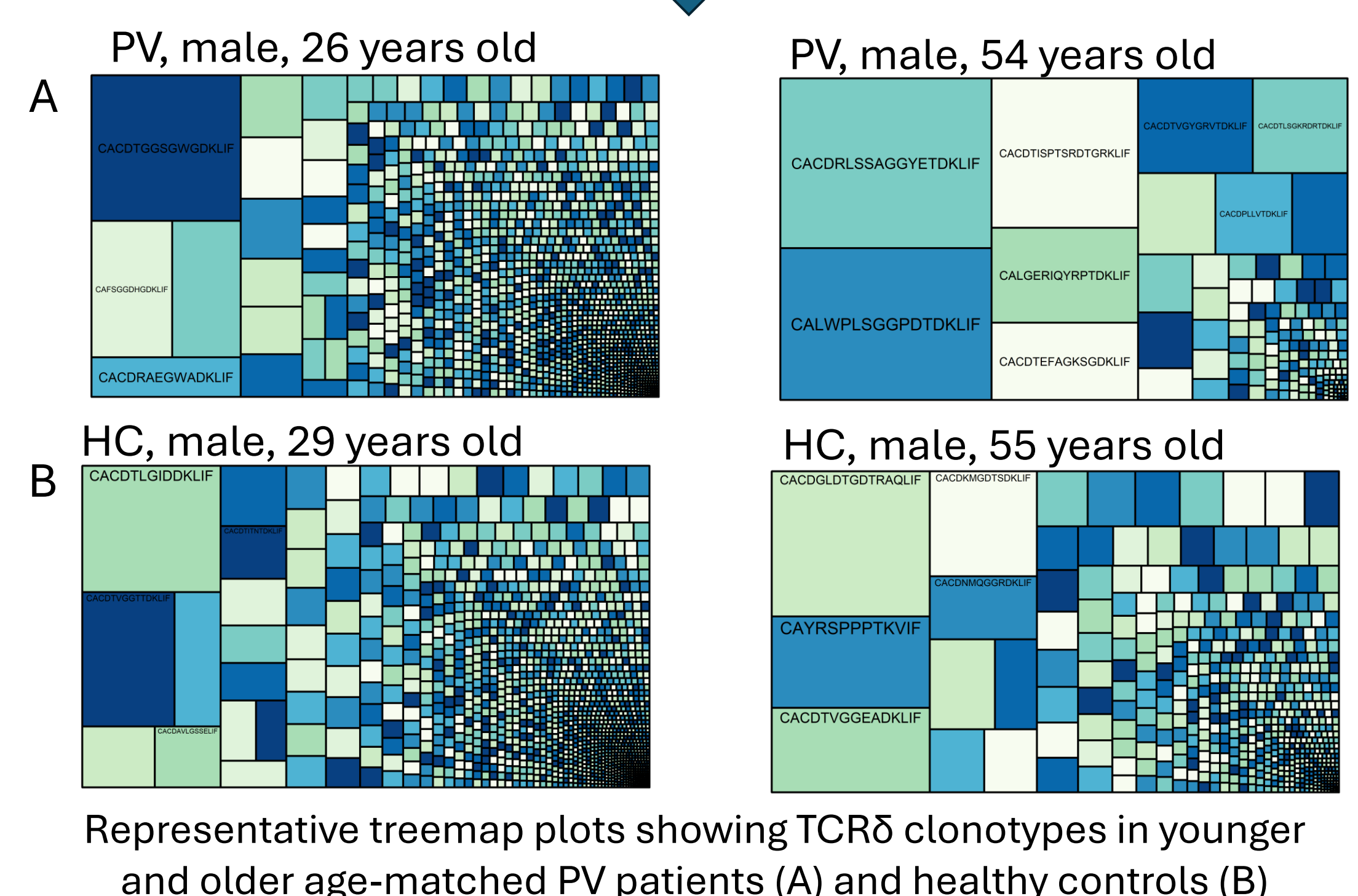


\*PASI (Psoriasis Area and Severity Index)

- **IN PV PATIENTS, AGING IS LINKED TO A SIGNIFICANT INCREASE IN THE FREQUENCY OF HYPEREXPANDED\* CLONOTYPES**



\*clonotypes that occupy >5% of repertoire



## CONCLUSION

- **age and disease severity exert a complex, multilayered influence on  $\gamma\delta$  TCR repertoire diversity and CDR3 characteristics in psoriasis vulgaris**
- **this intricate interplay emphasizes the need for further investigation of the underlying mechanisms driving TCR repertoire dynamics in PV**