

Barcoding in TCR and IG repertoires profiling and comparative post-analysis of TCR repertoires

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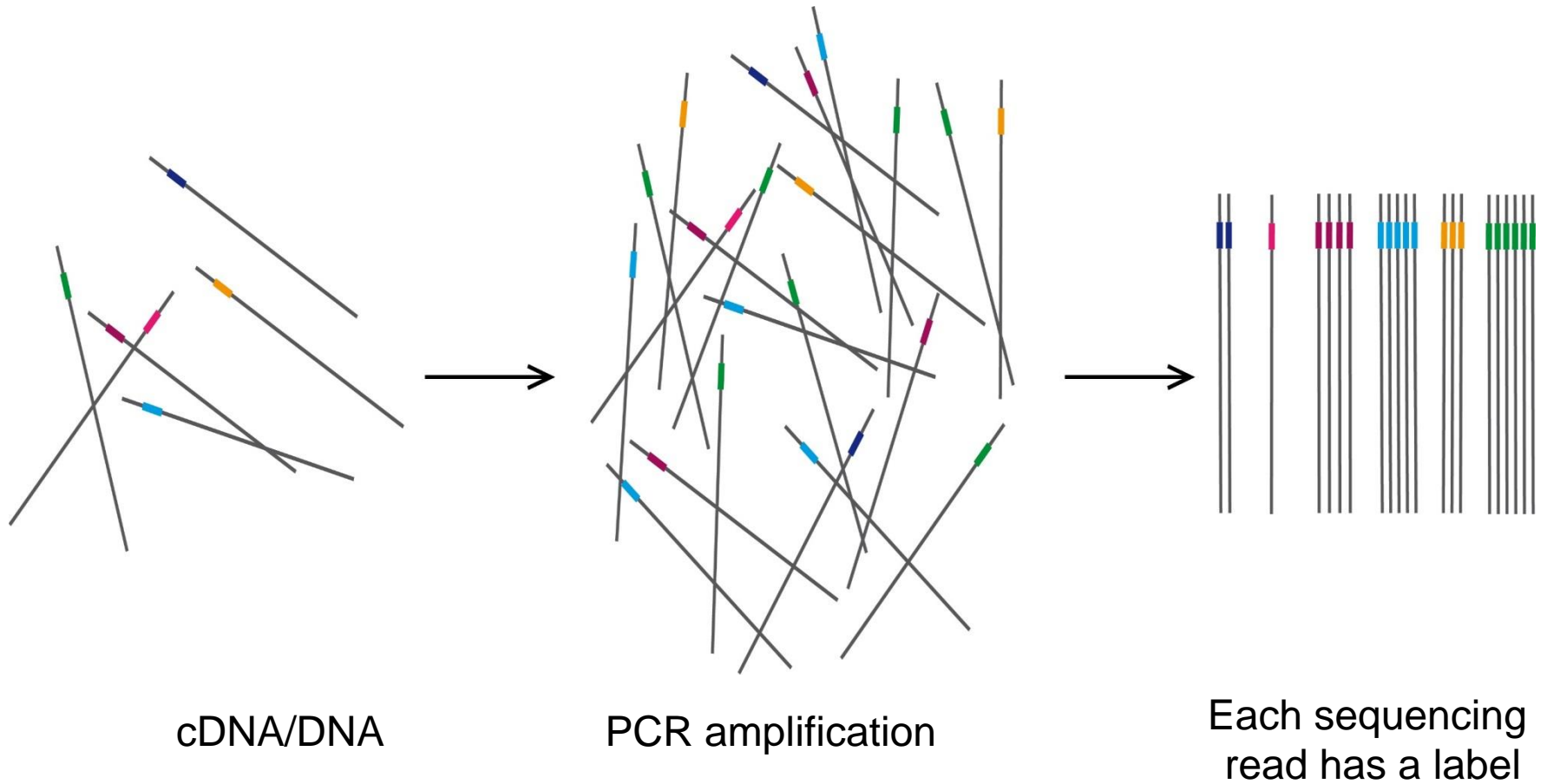


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- BCR and TCR repertoires are complicated
 - It is interesting to look at them
 - We can not do it reliably
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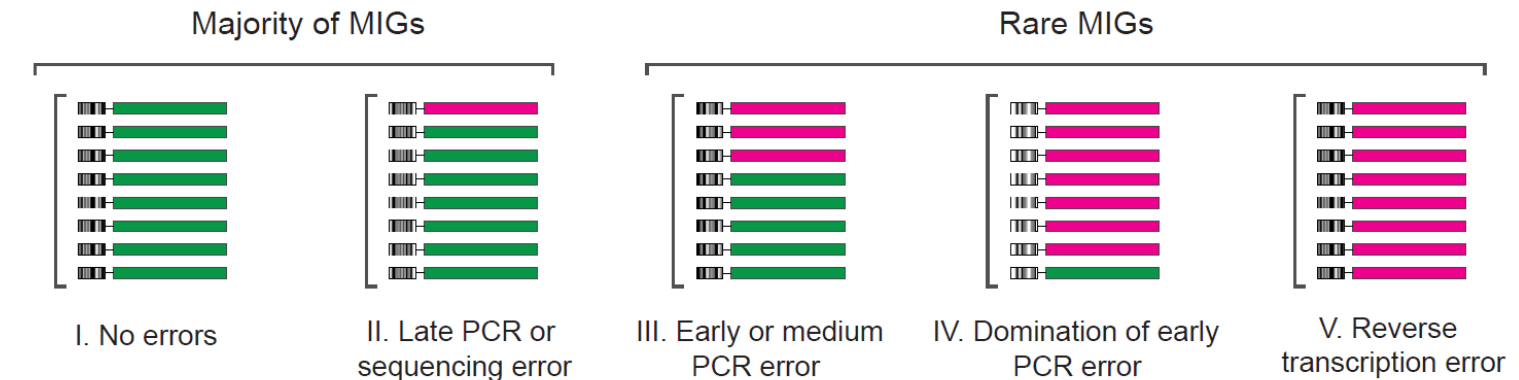


Power of molecular barcoding in HTS of immune repertoires

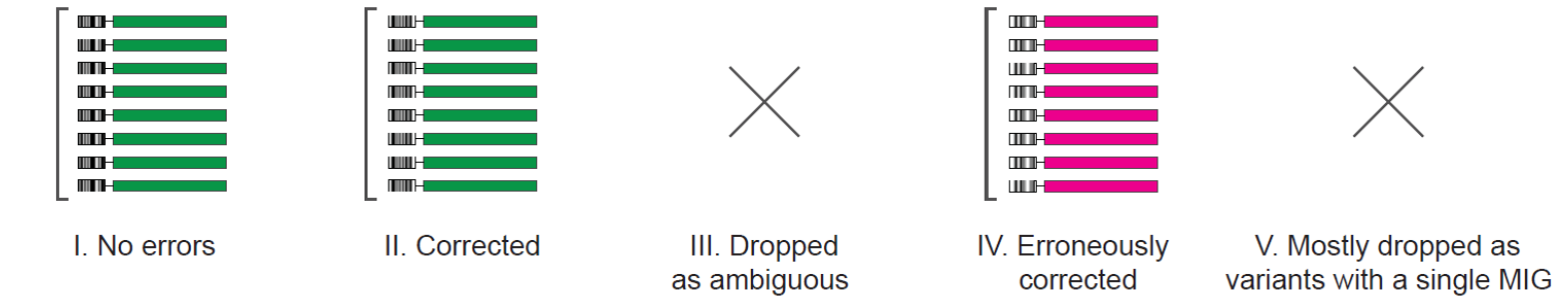
Molecular barcoding: normalization



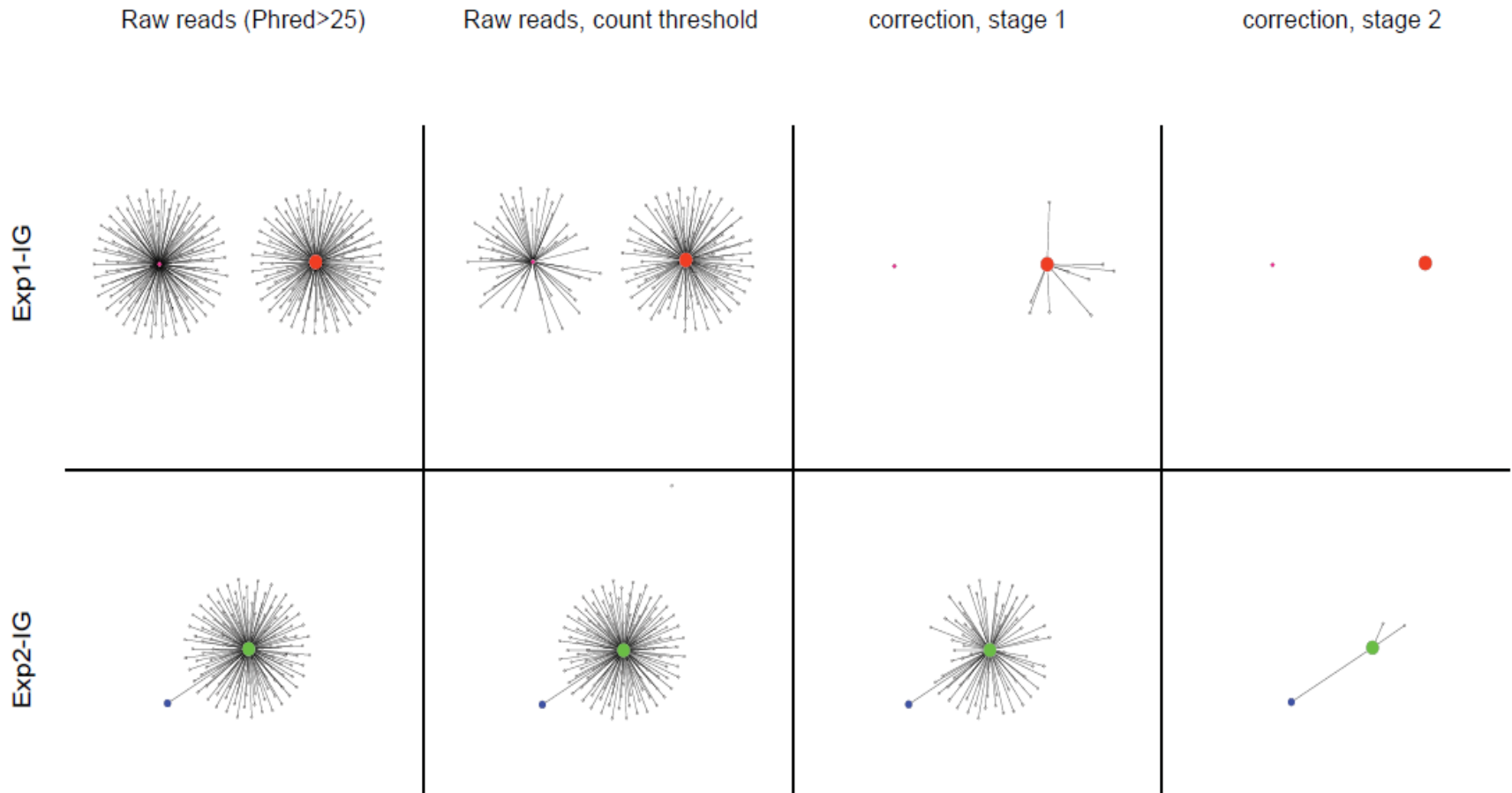
Error correction



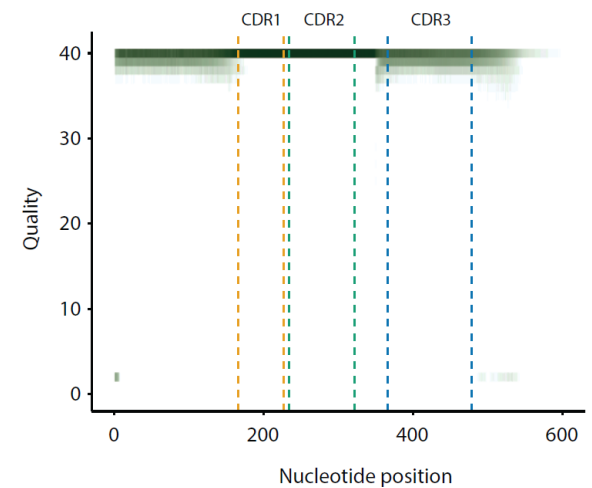
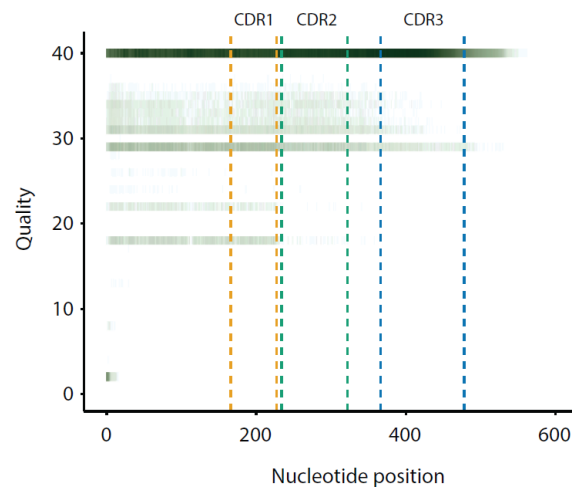
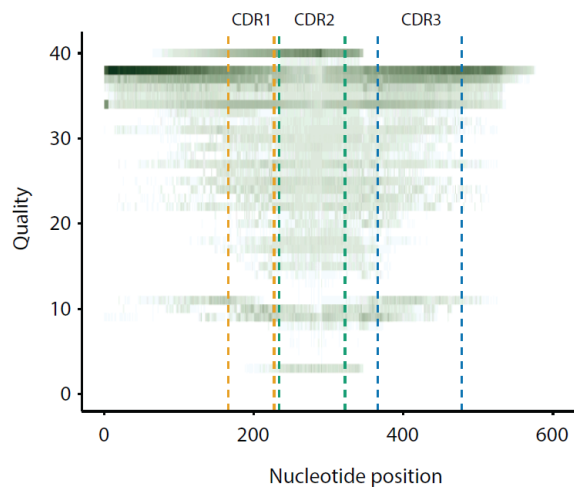
1st stage MIG-correction. Identification of the dominant sequence variant within each MIG and correction of minor sequence variants.



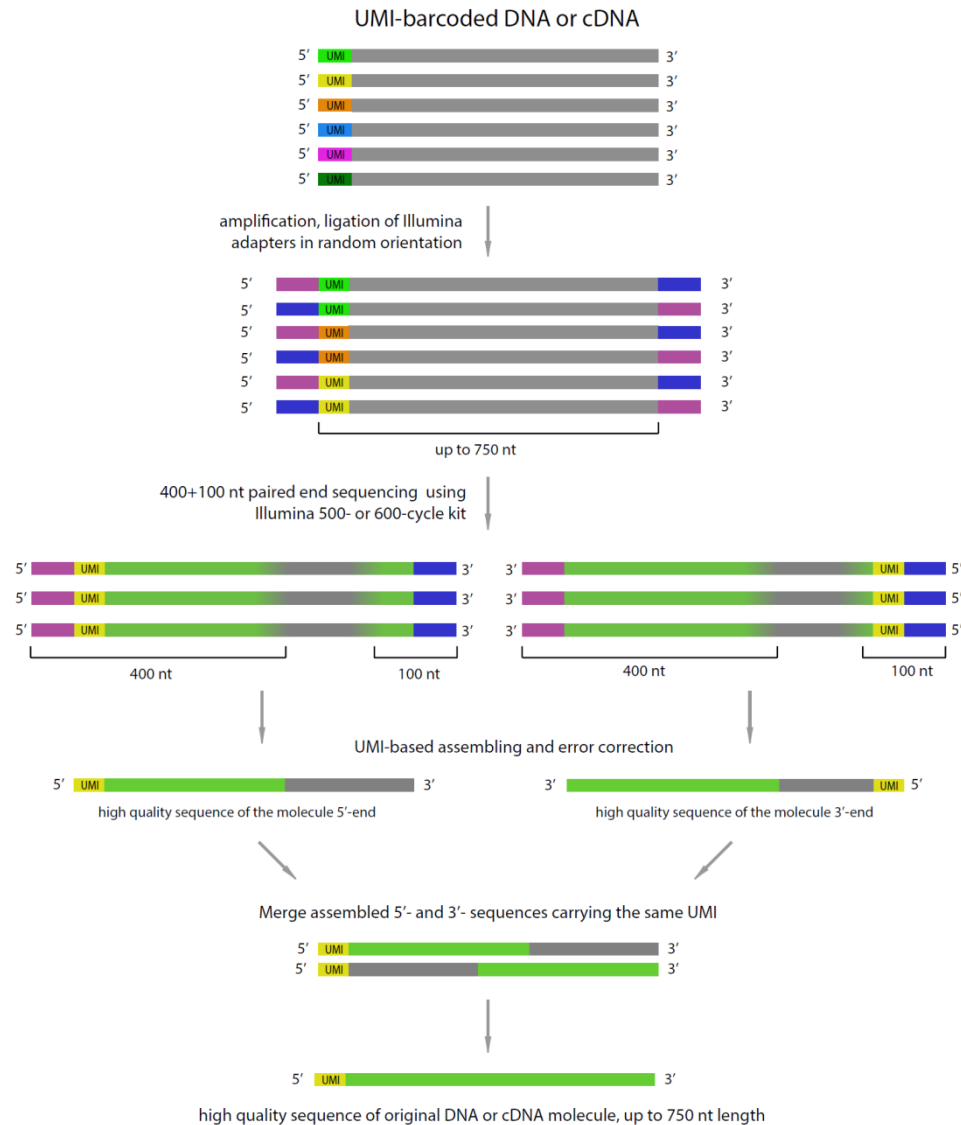
Deep antibody sequencing, control clonotypes



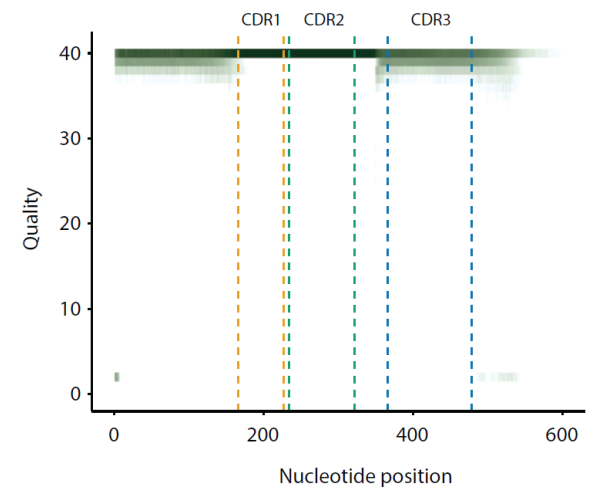
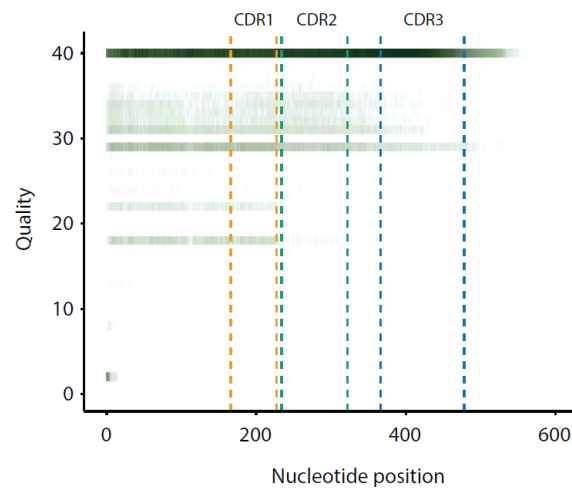
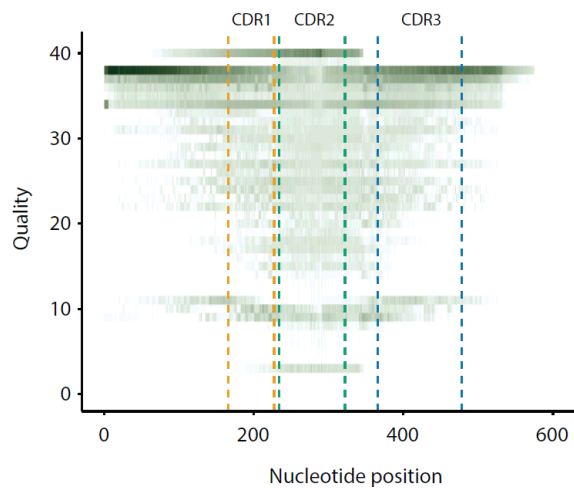
Molecular barcoding: dramatic improvement of long range sequencing quality



750 nt length (!) nearly error-free (!) sequencing on Illumina - asymmetric logic:



Molecular barcoding: dramatic improvement of long range sequencing quality





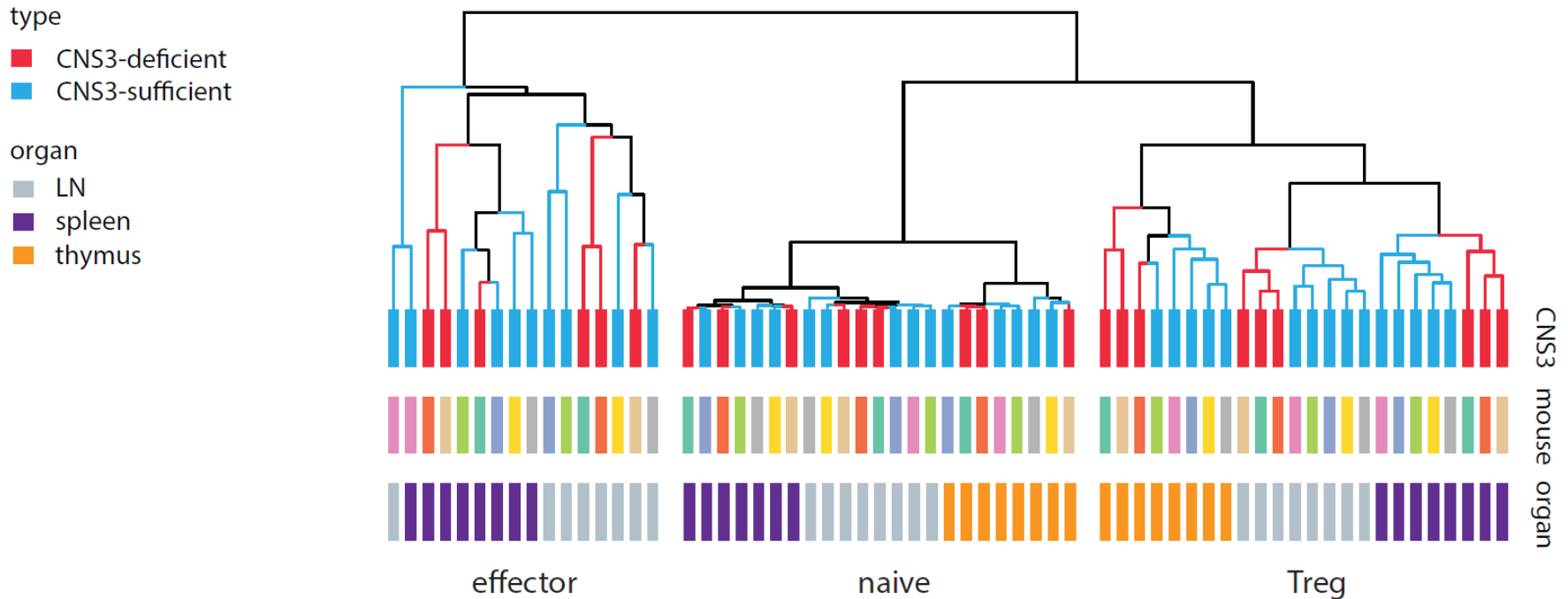
With molecular barcodes

- Know the numbers
 - Can normalize
 - Eliminate errors
 - Improve/rescue sequencing quality
 - Make it longer
-



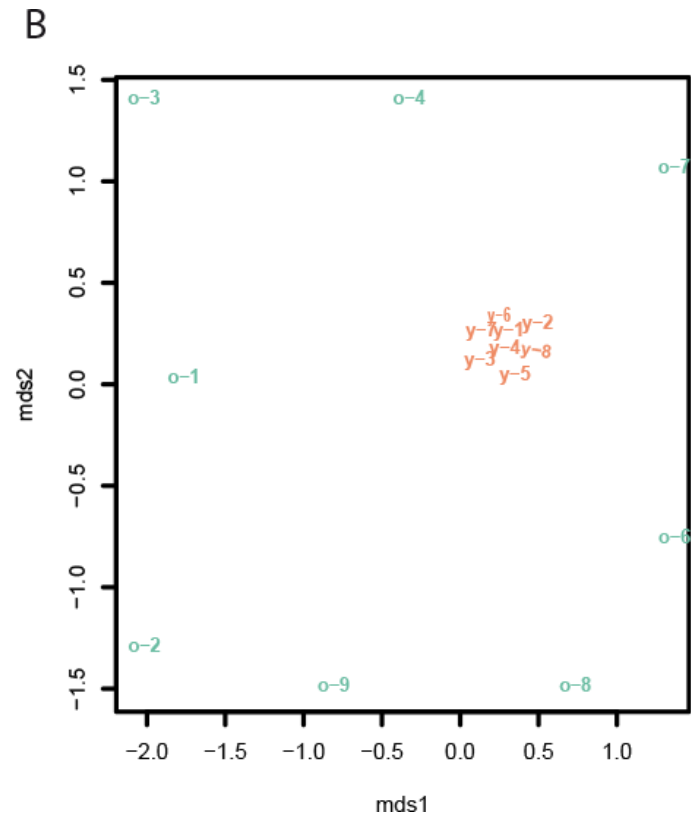
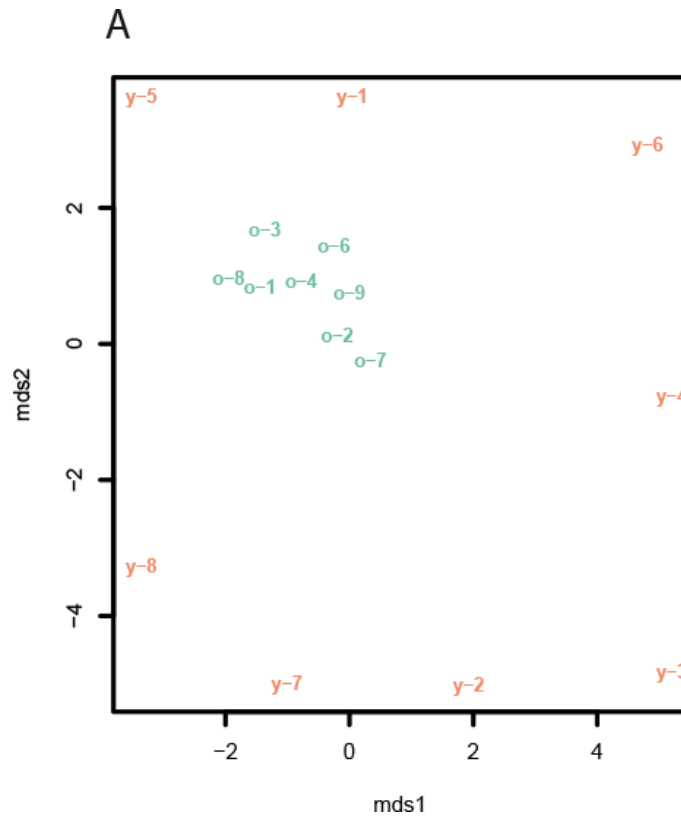
Comparative post-analysis of TCR repertoires

TCR repertoire distinguishes subsets and organs



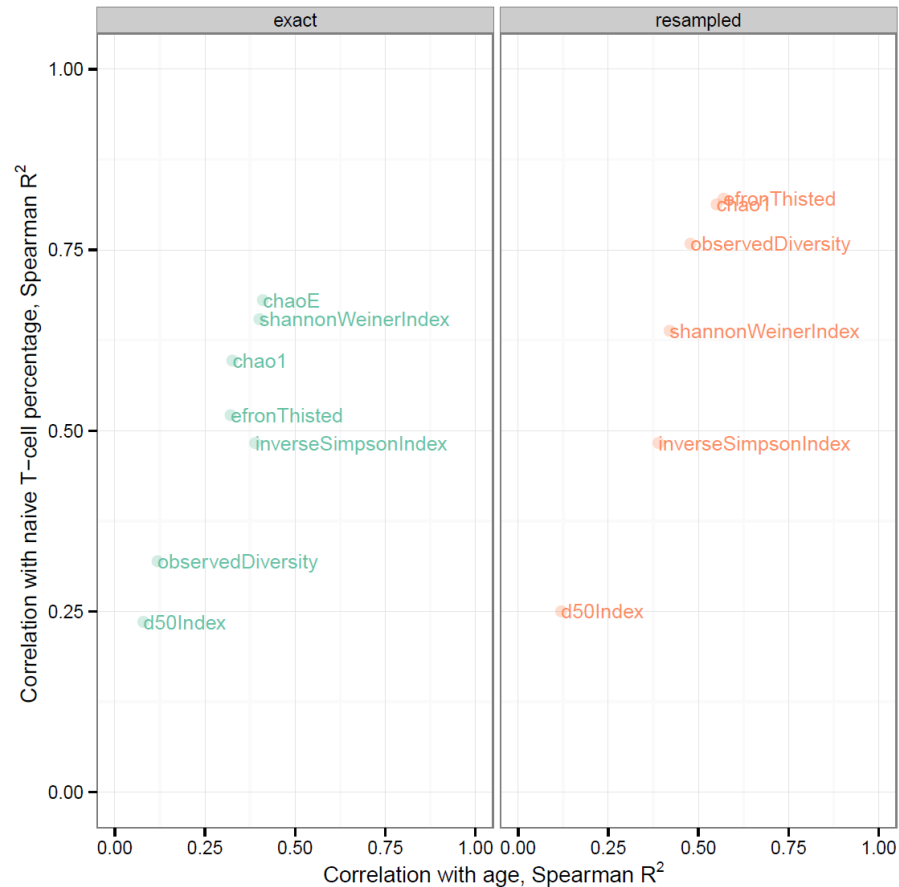
Mice TCRalpha amino acid CDR3 rep; mice mutant, factor important for Tregs

MDS



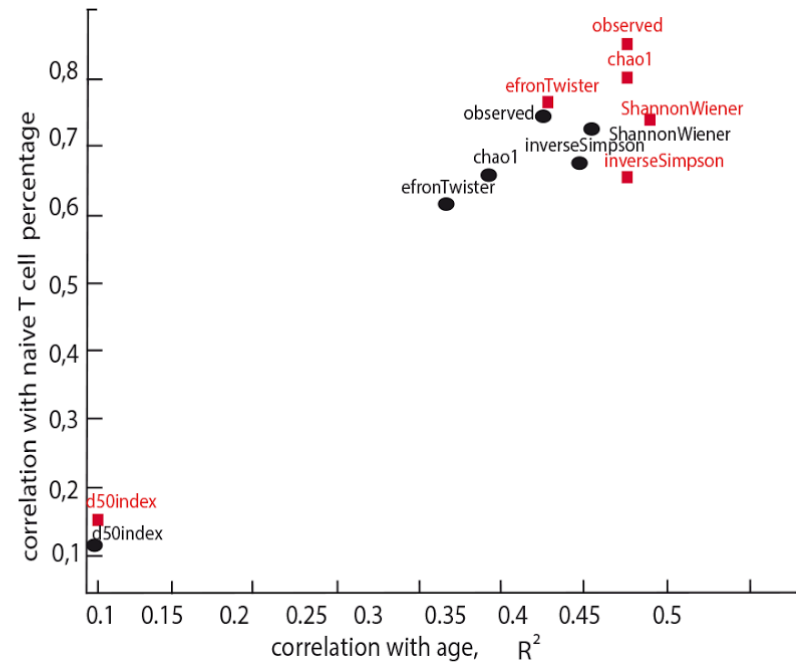
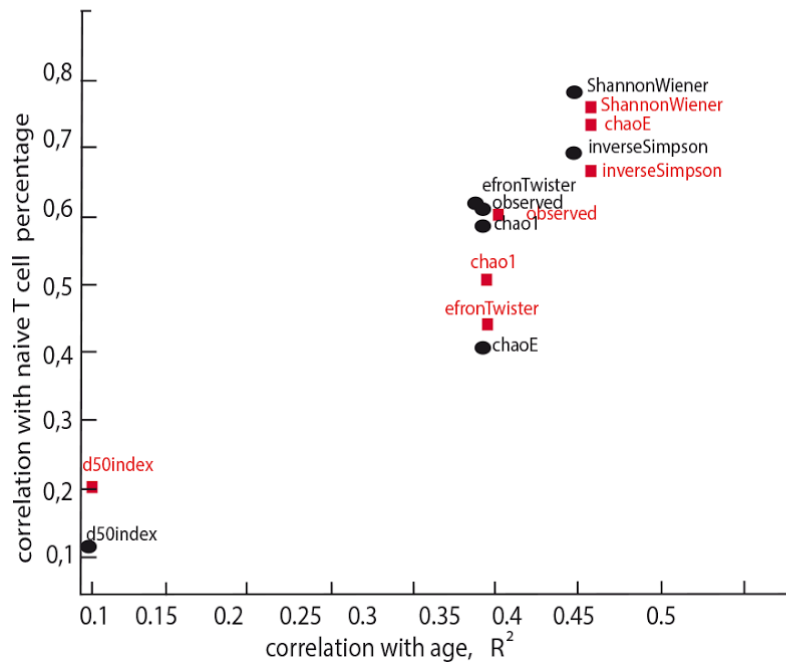
Old and young mice, TCRbeta repertoire, different metrics

Diversity metrics



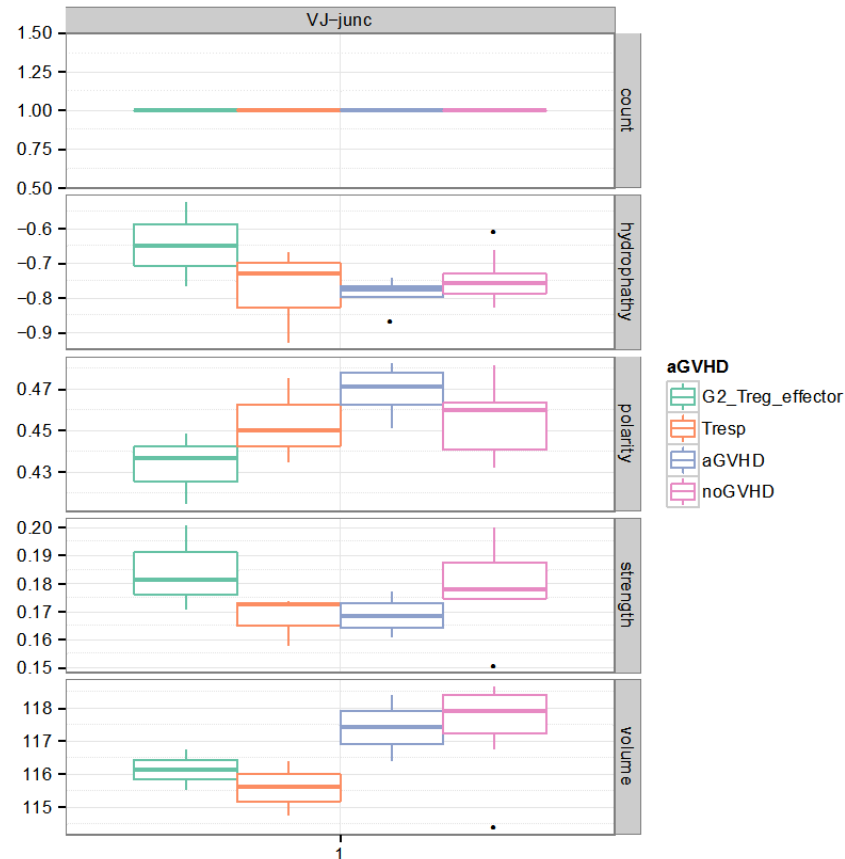
~100 humans, aging, naïve%, total blood TCRbeta diversity

Diversity metrics



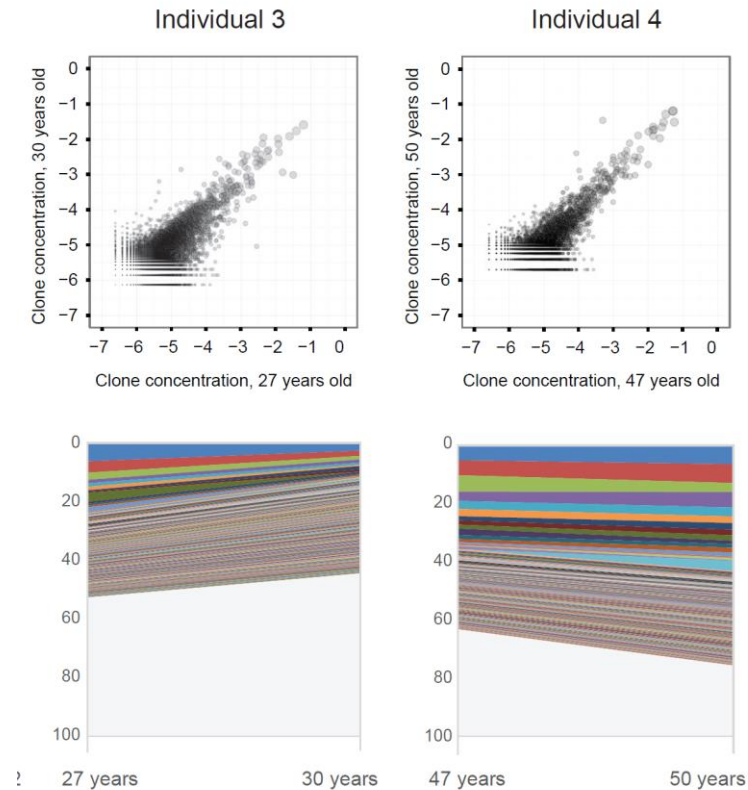
~5+5 mice, 2 ages, naïve%, total blood TCR diversity

Biophysical characteristics



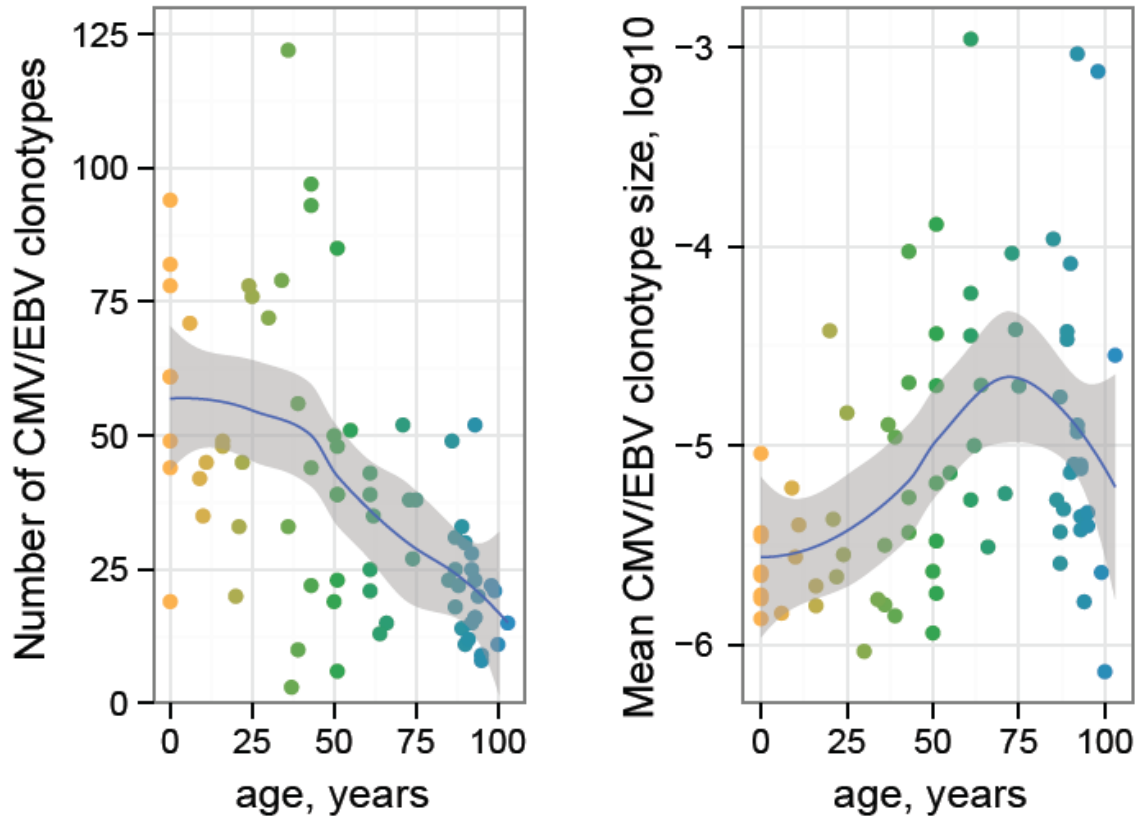
Tregs/non-Tregs; aGVHD/non-GVHD

Clonal tracking



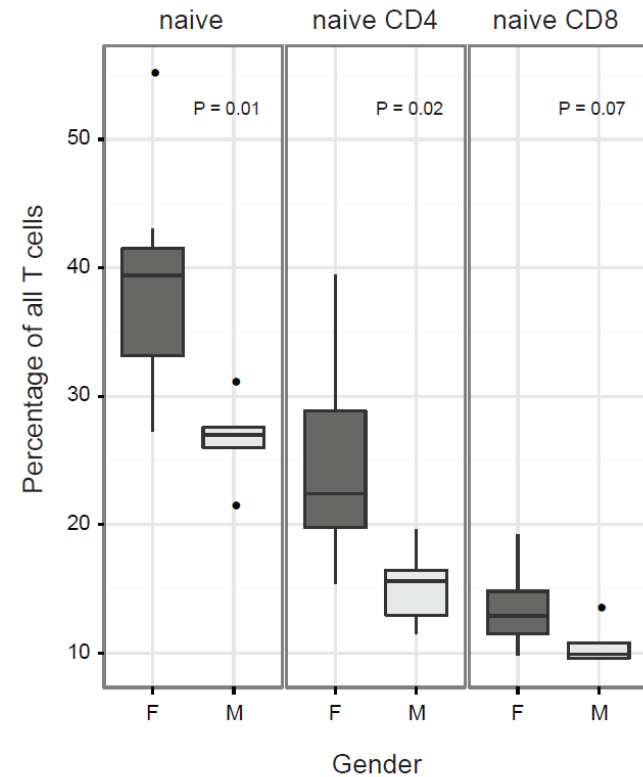
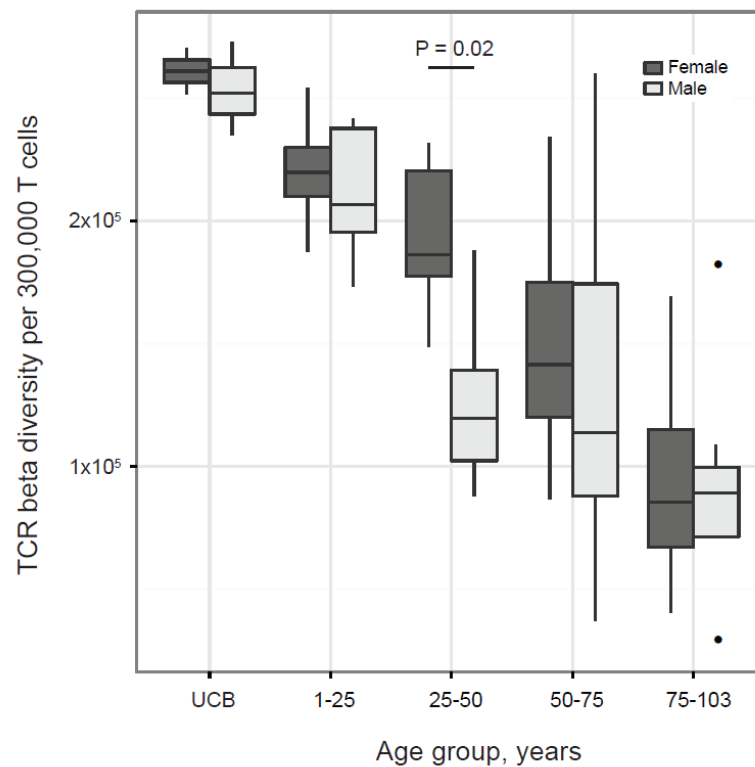
Stability in human blood, 3 years, total TCR beta

Scanning versus known TCRs



EBV/CMV clonotypes in human blood, 100 donors

Aging – gender differences



Bulk TCRbeta diversity, naïve %, human blood, 100 donors



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Some key Collaborations



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