Minutes of IARC meeting 101, July 21st, 2022

In attendance: Ayelet Peres, Andrew Collins, Martin Corcoran, Corey Watson, Mats Ohlin, James Heather

1. **Approval of minutes of meeting 100**
   Approved

2. **Novel gene nomenclature - effect on tool performance**
   Novel nomenclature affects performance of some tools as each allele is treated as a single gene.

3. **Human IGHV reference set**
   Awaits further discussion with WL

4. **Functional groups reference book - update**
   AP provided an update on the development of the Functional Groups Reference Book.

5. **Further assessment of inference IGHV4-59*01_G267A in P1_I39 (S00037)**
   IGHV4-59*01_G267A was inferred in subject S36 (VDJ-base: P1_I39_S1). The genotype carried one other allele of IGHV4-59. This sample carries few IGHV reads. The inference was consequently supported by a relative small number of sequences (60) and unmutated sequences (43), a relatively low overall frequency in the unmutated population (0.58%) and a small but diverse set of unique CDR3s (43) in the unmutated sequence set. Its allelic ratio was 31%. Haplotyping based on allelic diversity in IGHJ6 was possible with excellent separation from reads associated to IGHV4-59*01 (IGHV4-59*01_G267A: 0:100; IGHV4-59*01: 100:0). IARC affirms the sequence at level 1 up to and including base 319 in agreement with past practice. It is acknowledged that the allele most likely carries one additional base, typically A at base position 320. A trailing "." indicates IARC's opinion that the sequence is likely to contain one additional 3'-nucleotides for which there is insufficient evidence to make an affirmation. The allele is given the name IGHV4-59*i03.

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>IGHV4-59*i03 (IGHV4-59*01_G267A)
CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCC
CTCACCTGCACTGTCTCTGGTGGCTCCATCAGTAGTTACTACTGGAGCTGGATCCGG
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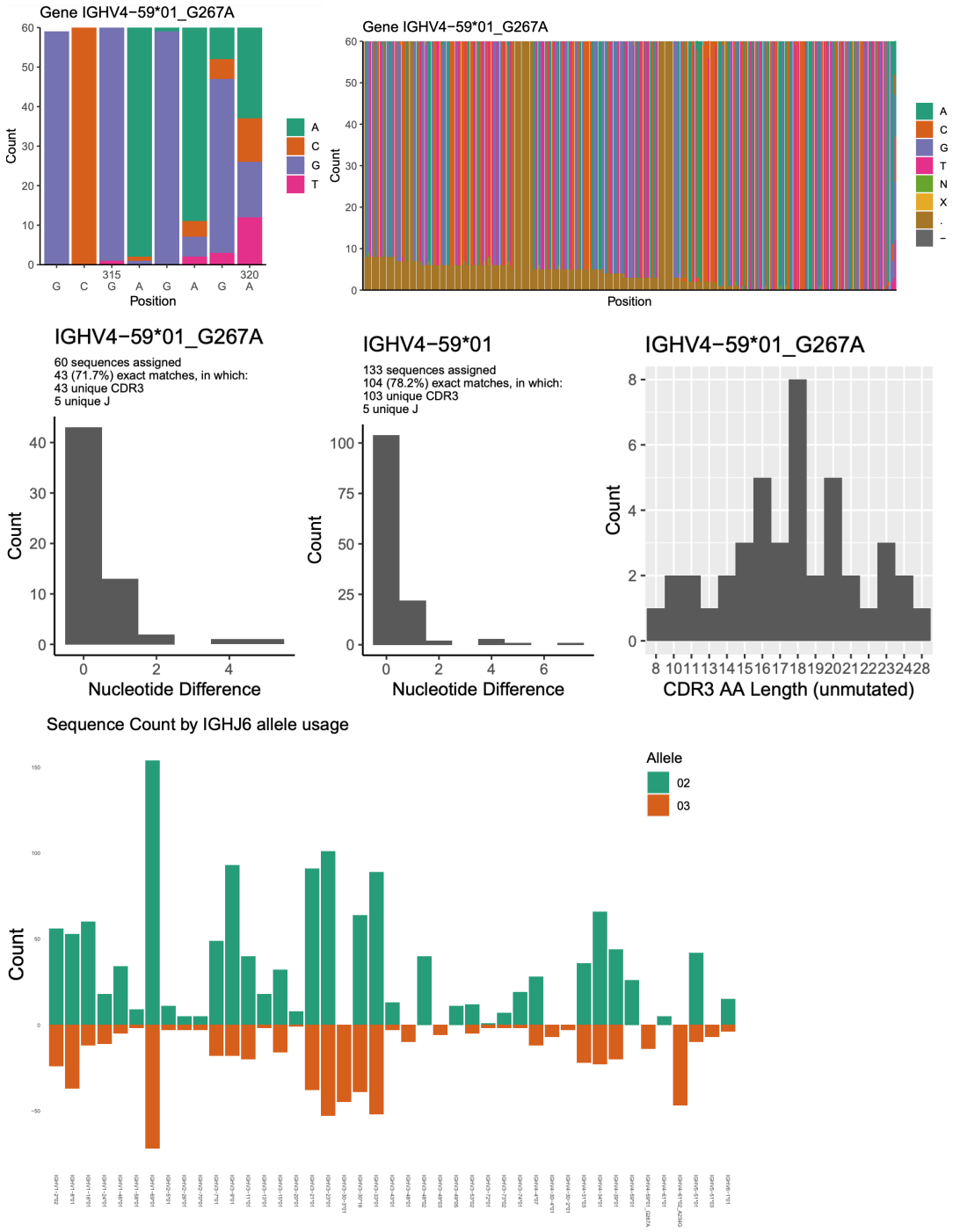
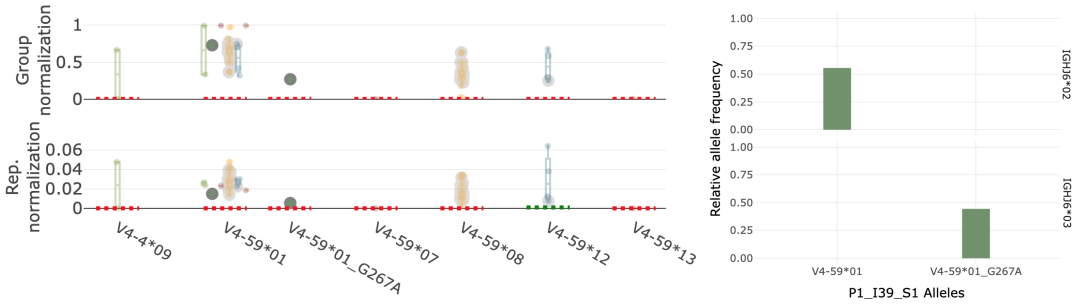
CAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTATATCTATTACAGTGGGAGCACC
AACTACAACCCCTCCCTCAAGAGTCGAGTCACCATATCAGTAGACACGTCCAAGAAC
CAGTTCTCCCTAAAGCTGAGCTCTGTGACCGCTGCGGACACGGCCGTGTATTACTGT
GCGAGAG.





6. **Public release/report of new affirmed alleles**
   AC agreed to proofread OGRDB entries. There is currently no obvious process in place to submit them to IUIS. They will be published on OGRDB.

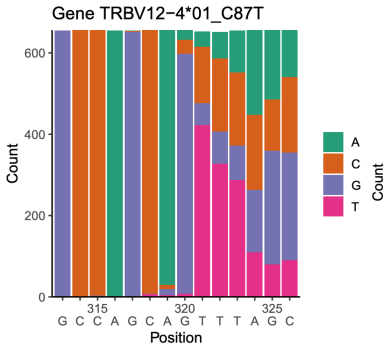
7. **Assessment of inference TRBV12-4*01_C87T in P4_I24_S1 (S00036)**
   TRBV12-4*01_C87T has been inferred in nine genotypes in the VDJbase P4 data set, including in VDJbase P4_I24_S1, a haplotypable data set (based on heterozygocity in TRBJ1-6). The genotype is also implied to carry TRBV12-4*01. No other gene apart from TRBV12-3 in the IMGT database is closely related to these alleles of TRBV12-4. The novel allele is the most expressed allele in the repertoire (72% allelic frequency; 1.47% of the total error-free population). It is represented by 499 error-free sequences and 467 unique CDR3s in the error-free set. Haplotyping based on allelic diversity in TRBJ1-6 demonstrates perfect separation from TRBV12-4*01. The validity of the inference was considered highly appropriate. The inference of the 3'-nucleotides, made problematic by the trimming that has occurred in many rearrangements, was extensively discussed. A final decision was postponed until a later meeting.

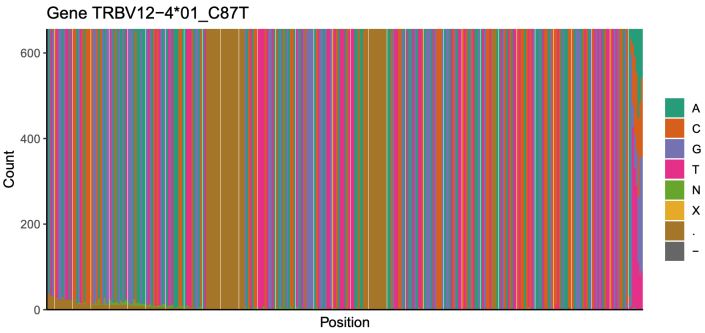
Result summary: TRBV12-4*01_C87T	No rearrangement found		
V-GENE and allele	Homsap TRBV12-4*01 F, or Homsap TRBV12-4*02 (F)	score = 1371	identity = 99.64% (275/276 nt)
FR-IMGT lengths, CDR-IMGT lengths	[5.6.X]		

1. Alignment for V-GENE and allele identification

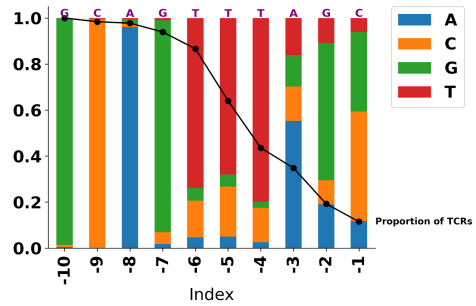
Closest V-REGIONs (evaluated from the V-REGION first nucleotide to the 2nd-CYS codon)

		Score	Identity
K02546	Homsap TRBV12-4*01 F	1371	99.64% (275/276 nt)
M14264	Homsap TRBV12-4*02 (F)	1371	99.64% (275/276 nt)
X07192	Homsap TRBV12-3*01 F	1326	97.83% (270/276 nt)
X07223	Homsap TRBV12-5*01 F	957	82.97% (229/276 nt)
X07224	Homsap TRBV12-1*01 P	867	79.35% (219/276 nt)

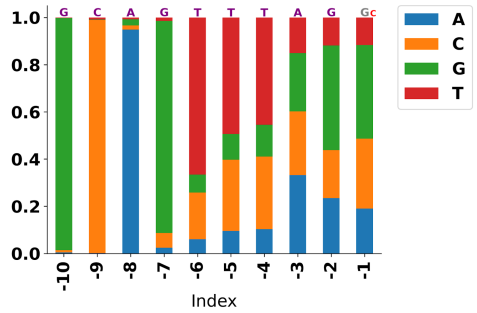


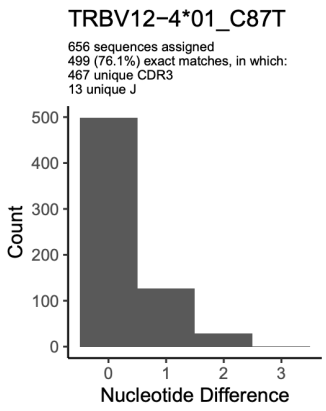


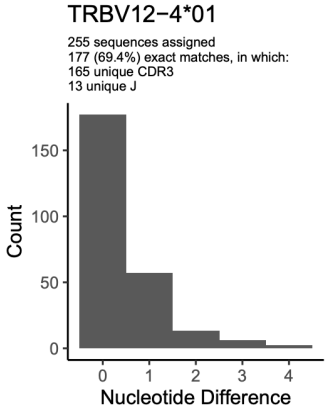
Consensus plot of 3’-end:

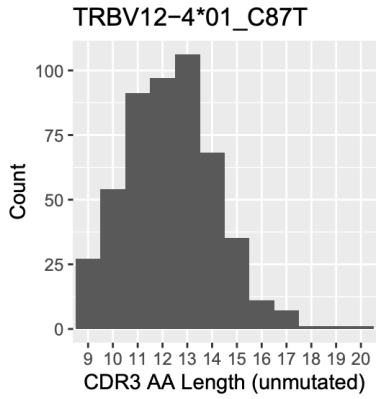


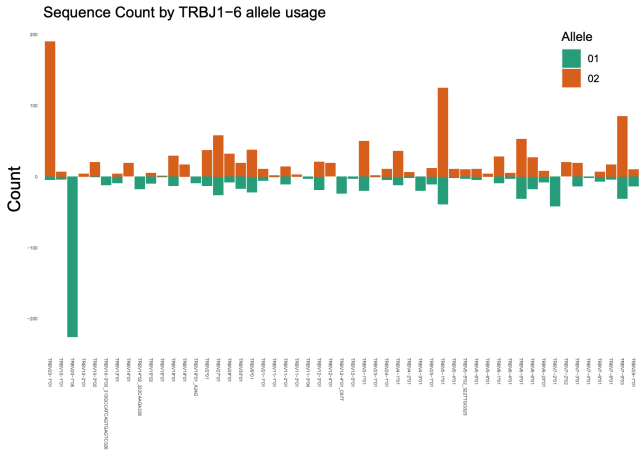
All data:











8. Next meeting

To be decided.