

Minutes of IARC meeting 118, March 20th, 2023

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

1. Approval of minutes of meeting 117

Approved

2. Next meeting

April 3rd, 2023 at 10.00 UTC

3. Proofreading of novel OGRDB entries

Done. Affirmed sequences have been published on OGRDB.

4. Discussion on the AIRR-C Executive Sub-committee - Special Meeting with WG/SC Co-leads on March 16, 2023

Update and discussion.

5. Discussion on the AIRR-C governance document

Discussion. Text amended.

6. Germline reference set manuscript

Discussion. AC will provide data to AP/WL/CW to generate updated figures. Discussions with potential additional contributors will be initiated (AC).

7. TRBV5-6*i01

This sequence now has genomic validation that provides the 3'-most base that is missing in the inferred sequence.

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>MZ339401.1 Homo sapiens T-cell receptor TRB locus  
TRBV5-6*01_S3655 gene, partial cds  
GGCAGGACAGGTAGAGAGTCCAGTGTCTGGAGCACTAGACCTAAGGAAGGCTGCAT  
GGGGAGGACAAAGGACAGTGACATCACAGGATACCCCTCCCATCAGGAAAATCAAGG  
CCCAGAACTCACTCGGCTCTTCCCCAGGAGAACCAAGCCCTGAATCAGATGCAGTGC  
TTCTGTCCCTCTGTGCCATGGGCCCGGGCTCCTCTGCTGGGCACTGCTTTGTCTC  
CTGGGAGCAGGTGAGTCCTGGGCACAGGACAGCAGCCCCATTCTCAGCTTTCCCACC
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CCTGTGTCCTCCACTTTACCTTGGGGAGGACCTCCAGGCTGTCCCTGTGCTCATCCT
CCATCTGCTTTTCCCACAGGCTTAGTGGACGCTGGAGTCACCCAAAGTCCCACACAC
CTGATCAAACGAGAGGACAGCAAGTGAAGTCTGAGATGCTCTCCTAAGTCTGGGCAT
GAACTGTGTCTGGTACCAACAGGCCCTGGGTGAGGGCCCAAGTTTATCTTTTCAG
TATTATGAGGAGGAAGAGAGACAGAGAGGCAACTTCCCTGATCGATTCTCAGGTCAC
CAGTTCCCTAACTATAGCTCTGAGCTGAATGTGAACGCCTTGTGGCTGGGGACTCG
GCCCTCTATCTCTGTGCCAGCAGCTTGGCACAGCCATCAGAGTCACTGACGTTCTG
TATATAAACTTCCTGCCTTAGCTTTGCCTTGAGAGCTGCAGGCCCCACCCAGATTTC
ACTCCTTCAAGGAAGC

IARC decides to update the sequence of TRBV5-6*01 with the 3'-terminal (G) base based on the information of this genomic record.

8. Consideration of inferences with limited inference-supporting reads that however also have genomic support.

On meeting 97 it was decided not to affirm or consider inferences like TRBV6-9*01_A303G in P4_I31_S1 and TRBV12-2*01 T187C in P4_I16_S1 that had very few supporting sequences. There are, however, genomic sequences in support of two of these inferences.

Genomic support exist for TRBV6-9*01_A303G:

>MZ339402.1 Homo sapiens isolate KI T-cell receptor TRB locus TRBV6-9*01_S0733 gene, partial cds

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GGAGACTGAGGTCTCAGAATGACTCCCTTGAGAGTCTGTTCCTTCCCTTTCATCAA  
TGCACAGACCCAGAAGACCCCTATGTCCTGCAGCCCCTGCCATGAGCATCGGGC  
TCCTGTGCTGTGTGGCCTTTTCTCTCCTGTGGGCAGGTGGGTCTGGGCAGAGC  
CCCTTGCCTGGATGTCAAGGCCCATCCCCTTCCACTGGGGCTGCAGCATCAGC  
TTTGTTCTTCTCTGCAGGTCCAGTGAATGCTGGTGTCACTCAGACCCCAAAT  
CCACATCCTGAAGACAGGACAGAGCATGAACTGCAGTGTGCCAGGATATGAA  
CCATGGATACTTGTCTGGTATCGACAAGACCCAGGCATGGGGCTGAGGCGCAT  
TCATTACTCAGTTGCTGCTGGTATCACTGACAAAGGAGAAGTCCCCGATGGCTA  
CAATGTATCCAGATCAAACACAGAGGATTTCCCGCTCAGGCTGGAGTCAGCTGC  
TCCCTCCAGACATCTGTGTACTTCTGTGCCAGCAGTTATTCCACAGCGCTGCA  
AGCCTGTCTCCTCTCTGCACATAAAGGCA  
heptamer 23-mer nonamer
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Genomic support exist for TRBV12-2*01 T187C:

>AC233282 (part of a sequence of a BAC clone)

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CCTGATTCATCTCCCAAAAATGTAGTCTGCCTGATTCATCTCCCAAAAATGTAG  
CCTCCGCTTAAAGGAGCTTCAAGTTGGGGGTGGTGGGCCATTCAGTGTGTCA
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CTAACAGATGCATCTTGTGGGGTAAAATGTCCCAAAGTATCTTTTCTTGCTTA
TGTTCATAAGGGCGCTGGTCTGGAATGTGCCACATCTGTTCTCACTCTGCCATG
GACTCCTGGACCTCTGTGTGTCCCTTTGTATCCTGGTAGCGAGTGAGTCCTCA
TGTATTTATCATCCTCATGCTGGGCCTCTGTATAGATGACTTCCTGTATTTTCC
TTATTCTGTTTCCTAATTTTGCCTTCTTTTATAGCATGCACAGATGCTGGCATT
ATCCAGTCACCCAAGCATGAGGTGACAGAAATGGGACAAACAGTGACTCTGAGA
TGTGAGCCAATTTTGGCCACAATTTCTTTTCTGGTACAGAGATACCTTCGTG
CAGGGACTGGAATTGCTGAGTTACTTCCGGAGCCGATCTATTATAGATAATGCA
GGTATGCCACAGAGCGATTCTCAGCTGAGAGGCCTGATGGATCATTCTCTACT
CTGAAGATCCAGCCTGCAGAGCAGGGGACTCGGCCGTGTATGTCTGTGCAAGT
CGCTTAGCCACAGCGCTGCAGAAATCTCCCTCCCTGTGCAGAAACTCTGGTGC
TTCTCTTTTCTCACAGCTCCCAGCAGTCCTGAGCAAAGTCTTTCCC
heptamer 23-mer nonamer

It was decided that these sequences will be assessed by IARC given the additional support from genomic sequencing data. Further assessment of criteria must be set from a policy standpoint.

9. Assessment of inference TRBV7-7*01_C315T in P4_I9_S1 (S00036)

TRBV7-7*01_C315T has been inferred in seventeen genotypes in the VDJbase P4 data set, including in VDJbase P4_I9_S1, a haplotypable data set (based on heterozygosity in TRBJ1-6). The genotype is also implied to carry TRBV7-7*01. No other gene apart from IGHV7-6 (alleles of which also carry C315) in the IMGT database is highly similar to these alleles of TRBV7-7. The novel allele is the most expressed allele in the repertoire (58% allelic frequency; 0.16% of the total error-free population). It is represented by 37 error-free sequences and 33 unique CDR3s in the error-free set. Haplotyping based on allelic diversity in TRBJ1-6 demonstrates association of TRBV7-7*01_C315T with only one of the haplotypes (only few recorded cases; TRBV7-7*01 was not associated with any allele of TRBJ1-6).

The allele has also been identified as TRBV7-7*01_S0326 and Sanger validated (GenBank MZ339373) (Corcoran et al. (2023) Immunity 56, 635-652.E6 (DOI: 10.1016/j.immuni.2023.01.026)).

>MZ339373
TTGAGAGAGGAAGTGATGTCACTGTGGAACTGCCCTGTGGAGACAAGGACATC
CCTCATCCTCCGCTCCTGCTCACAGTGACACTGATCTGGTAAAGCCCCATCCT
GGTCTGACACTGTC**ATGGGTACCAGTCTCCTATGCTGGGTGGTCTGGGTTTCC**
TAGGGACAGGTGAGTCCTCAAACACAAAGTAGTTTCATATTTTTTCTGTATGT
AGGTGTGTGTGTATGCATGTGTGTCTGTGTGTGTGTGTGTGTGTGTGTGTGT
GTGTGAGATGACTACAAATGTTTTCTTATTCTGTTGCCAGATTCTGTTTCCAC
AG**ATCACACAGGTGCTGGAGTCTCCAGTCTCCAGGTACAAAGTCACAAAGAG**

GGGACAGGATGTAACCTCAGGTGTGATCCAATTTTCGAGTCATGCAACCCTTTA
TTGGTATCAACAGGCCCTGGGGCAGGGCCAGAGTTTCTGACTTACTTCAATTA
TGAAGCTCAACCAGACAAATCAGGGCTGCCAGTGATCGGTTCTCTGCAGAGAG
GCCTGAGGGATCCATCTCCTACTGACGATTCAGCGCACAGAGCAGCGGGACTC
AGCCATGTATCGCTGTGCTAGCAGCTTAGCCACAGCATGGCACAGTCGCCTCCT
TCCTGTTACAAAACCTCATCCTTCT
heptamer 23-mer nonamer

It has also been identified in a BAC clone with accession number AC229888.
This inference will be further discussed at the next meeting.