

IARC Meeting 10: April 4th 2018: minutes

The meeting commenced at 22:00 AEST. AC, MC, MO and CS were in attendance.

1. The minutes of Meeting 8 were accepted, and the minutes of Meeting 9 will be edited along the lines suggested by MO. The minutes of Meeting 9 will be reconsidered at the next meeting.
2. An email from Steven Kleinstein regarding the operation of TIgGER was discussed. It was agreed that AC would write again to SK, seeking further clarification.
3. The committee discussed whether or not sequences in IgPdb stand as evidence in favor of the existence of an inferred allele. IgPdb includes some sequences derived by genomic sequencing, which can be considered separately from inferred alleles in the database. MO commented that genomic sequences should not be considered the 'gold standard'. It was agreed that it would be useful for the GLWG to address the question of how standards can be set and applied to genomic sequencing. CS drew attention to issues in the past as to whether or not MiSeq was reliable enough for MiSeq-derived sequences to be incorporated into the IMGT database. It was suggested that it would be valuable for the GLWG to also consider the suitability of PacBio sequencing.

4. The committee considered

>IGHV4-61*01_S9594 (C93T; C136G; A138C) from B12

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CAGGTGCAGCTGCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACC
TGCAGTGTCTCTGGTGGCTCCGTCAGTAGTGGTAGTTACTACTGGAGCTGGATCCGGCAGCCCC
CCGGGAAGGGACTGGAGTGGATTGGGTATATCTATTACAGTGGGAGCACCAACTACAACCCCTC
CCTCAAGAGTCGAGTCACCATATCAGTAGACACGTCCAAGAACCAGTTCTCCCTGAAGCTGAGC
TCTGTGACCGCTGCGGACACGGCCGTGTATTACTGTGCGAGAG
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The sequence is present at high frequency (1.22%) in the IgDiscover analysis, and was inferred by IgDiscover, TIger and partis. Haplotype analysis shows the inferred sequence to be carried on a chromosome along with another IGHV4-61 allele. The issue of similarities of IGHV4-4, IGHV4-59 and IGHV4-61 was discussed, and it was agreed that the sequence should be moved to Level 0.

5. The committee considered

>IGHV1-69*01_S5096(G163A) from B16

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CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCTCGGTGAAGGTCTCC
TGCAAGGCTTCTGGAGGCACCTTCAGCAGCTATGCTATCAGCTGGGTGCGACAGGCCCTGGA
CAAGGGCTTGAGTGGATGGGAAGGATCATCCCTATCTTTGGTACAGCAAACACTACGCACAGAAGT
TCCAGGGCAGAGTCACGATTACCGCGGACGAATCCACGAGCACAGCCTACATGGAGCTGAGCA
GCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAGAG
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Note that IGHV1-69*01 and IGHV1-69D*01 are identical sequences, and that this sequence is also just one nucleotide different from IGHV1-69*14 (C6G).

This sequence is present at very high frequency (6.75%) in the IgDiscover analysis, and was inferred by IgDiscover, TIger and partis. Haplotype analysis is inconclusive because two alleles appear to be present on one chromosome and three alleles on the other.

CDR3-based crossover analysis was not strongly supportive, but did not highlight particular issues with this sequence. The sequence was moved to Level 0.

6. The next meeting (Meeting 11) will be on Friday April 13th at 21:00 AET.

The meeting ended at 22:00 AET.