IARC Meeting 7: March 9th 2018: minutes

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

1. The minutes of the previous meeting were accepted.

2. The committee again discussed the issue of cross-over artifacts (chimeric sequences). It was agreed that we need a better understanding of the causes of higher levels of cross-over artifacts, and IARC needs access to tools that can assist in the estimate of errors arising from cross-over events. It is the hope of the committee that the Germline Gene Working Group can give this issue its attention, and report back to the IARC.

3. The committee considered the inferences from both B12 and B16, and chose to initially evaluate a single inference from each dataset.
4. From dataset B12, the committee chose to evaluate a variant of IGHV1-2*01 (IGHV1-2*01:T163C).

   >IGHV1-2*02_T163C
   CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGA
   AGGTCTCCTGCAAGGCTTCTGGATACACCTTCACCGGCTACTATATGCACTGGGTGC
   GACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGACGGATCAACCCTAACAGTGG
   TGGCACAAACTATGCACAGAAGTTTCAGGGCAGGGTCACCATGACCAGGGACACGT
   CCATCAGCACAGCCTACATGGAGCTGAGCAGGCTGAGATCTGACGACACGGCCGT
   GTATTACTGTGCGAGAGA

   The sequence was inferred by Martin Corcoran using IgDiscover, and by Duncan Ralph using both Partis and TIgGER. The number of unique CDR3 used by sequences with exact matches to the inferred germline allele represents 1.9% of all unique CDR3 associated to exact IGHV matches in the genotype, according to IgDiscover. There were at least 739 unique rearrangements, utilizing 19 D genes and 7 J genes, and hundreds of exact matches. The allele was the more frequently utilized allele, with an expression ratio of 70:30 with the *01 allele. The inference was supported by haplotype analysis using IGHJ6*02/*03. The sequence is present in the IgPdb as IGHV1-2*p06. The full length sequence was first reported to IgPdb in 2015 by Scheepers and colleagues (see J Immunol 194:4371-8) from genomic sequencing, and it was separately reported to IgPdb in 2016 by Kirik and colleagues (see Mol Immunol 87:12-22), as an inference from VDJ rearrangements.

   The sequence was accepted by IARC up to nucleotide 319
   >IGHV1-2*02_T163C
   CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGA
   AGGTCTCCTGCAAGGCTTCTGGATACACCTTCACCGGCTACTATATGCACTGGGTGC
   GACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGACGGATCAACCCTAACAGTGG
   TGGCACAAACTATGCACAGAAGTTTCAGGGCAGGGTCACCATGACCAGGGACACGT
   CCATCAGCACAGCCTACATGGAGCTGAGCAGGCTGAGATCTGACGACACGGCCGT
   GTATTACTGTGCGAGAG

5. From dataset B16, the committee chose to evaluate a variant of IGHV1-3*01 (IGHV1-3*01:G172A).

   >IGHV1-3*01_G172A
   CAGGTCCAGCTTGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGA
   AGGTTTCCTGCAAGGCTTCTGGATACACCTTCACTAGCTATGCTATGCATTGGGTGC
   GCCAGGCCCCCGGACAAAGGCTTGAGTGGATGGGATGGATCAACACTGGCAATGG
   TAACACAAAATATTCACAGAAGTTCCAGGGCAGAGTCACCATTACCAGGGACACATC
   CGCGAGCACAGCCTACATGGAGCTGAGCAGCCTGAGATCTGAAGACACGGCTGTGT
   ATTACTGTGCGAGAG

The sequence was inferred by Martin Corcoran using IgDiscover, and by Duncan Ralph using both Partis and TIgGER. The number of unique CDR3 used by sequences with exact matches to the inferred germline allele represents 1.3% of all unique CDR3 associated to exact IGHV matches in the genotype, according to IgDiscover. There were at least 775 unique rearrangements, utilizing 22 D genes and 7 J genes. The allele was the more frequently utilized allele, with an expression ratio of 56:44 with the *01 allele. The inference was supported by haplotype analysis using IGHJ6*02/*03.

The meeting finished at 23:00 AEST.