

IARC Meeting 58: July 20th 2020: minutes

The meeting commenced at 10:00 UTC. AC, MO, CS and WL were in attendance. MC, Corey Watson and Gur Yaari joined the meeting at 10:30UTC.

1. The minutes of Meeting 57 were approved by the meeting attendees. MO was thanked again for his careful checking of the minutes.
2. The meeting considered the inference of the variant IGLV6-57 sequence in Genotype A007 VL, Submission S00028. The submitted sequence is as follows:
>IGLV6-57*01_S1429
aattttatgctgactcagccgactctgtgtcggagtctccggggaagacggtaaccatctcctgcacccgcagcagtgccagca
ttgccagcaactatgtgcagtggtaccagcagcgcggggcagtgccccaccactgtgatctatgaggataaccaagaccc
tctggggtccctgatcgggtctctggctccatcgacagctcctccaactctgcctccctcaccatctctggactgaagactgaggac
gaggctgactactactgtcagtcattatgatagcagcaatca
The sequence was seen in 1.49% of all unmutated rearrangements, with 14,472 sequences including 1776 perfect alignments to the inferred allele. There was abundant variation in the CDR3 regions of the aligned sequences. The IGLV6-57*01 allele was also present in the genotype, at a somewhat lower frequency. Haplotype data is unavailable. Plots of the final 3' nucleotides were considered, but the variability seen made it impossible to be certain of the final two nucleotides of the germline sequence. The sequence, up to and including nucleotide 333, was affirmed as the Level 1 sequence, IGLV6-57*i01. Uncertainty regarding nucleotides 334-335 will be indicated in IARC and OGRDB publications by two dots at the end of the affirmed sequence. The accepted sequence is as follows:
>IGLV6-57*i01
aattttatgctgactcagccgactctgtgtcggagtctccggggaagacggtaaccatctcctgcacccgcagcagtgccagca
ttgccagcaactatgtgcagtggtaccagcagcgcggggcagtgccccaccactgtgatctatgaggataaccaagaccc
tctggggtccctgatcgggtctctggctccatcgacagctcctccaactctgcctccctcaccatctctggactgaagactgaggac
gaggctgactactactgtcagtcattatgatagcagcaat..
3. The meeting re-considered the inference of the variant IGLV7-46 sequence in Genotype A007 VL, Submission S00028. This sequence had been rejected at the previous IARC meeting because of insufficient data - a low percentage of apparently unmutated sequences, and a low total number of sequences aligned to the variant. The sequence has been independently reported in Genbank, and a genomic sequence has been submitted to Genbank. The IARC members all agreed that the sequence is likely to be a real variant. Discussion again resulted in agreement that it is the task of the IARC to evaluate the data that is before it, though it was also agreed that other separate evidence can be noted. As a consequence it was agreed that the sequence should be affirmed as a Level 0 sequence.
4. Discussion continued regarding the use of VDJbase for the identification of further inferences that could be considered by the IARC. It pointed out that many variants were associated with the study of Gidoni et al (2019), of which AC and GY were co-authors. This would facilitate consideration of sequences, within the current guidelines of IARC. It was also noted that for the completion of the IARC process, Select Sets will have to be compiled,

and each inference will need to be submitted to Genbank. GY indicated that his group would be able to assist with this, for studies that they have been associated with. It was agreed that the process of review can proceed in parallel with the preparation of the Select Sets, given that data is available to the committee via VDJbase. It is hoped that for each variant, an 'exemplar' dataset can be identified. This will serve as a focus of review by the IARC, and can be used to direct interested parties to accessible evidence of the validity of these inferences.

5. The possibility was discussed that VDJbase data relating to IMGT sequences could also be considered by the IARC, either as an official IARC project, as a Germline Gene Working Group project, or as an independent project involving IARC members and others. 'Exemplar' datasets for previously reported genes could also be identified and flagged in VDJbase. All those present agreed that this would be useful, and that they would like to participate.
7. AC advised members that he would ask appropriate members of the IARC to review OGRDB entries for recently affirmed sequences, before their submission to IMGT. This will be done via email.
8. The next meeting (Meeting 59) will be held on Monday August 10th at 10:00 UTC.

The meeting ended at 11:17 UTC.