

IARC Meeting 8: March 19th 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 reviewed, revised and accepted.
2. The recent meetings of the Germline Gene Working Group, and a meeting between the AIRR-C executive and Andrew Collins were discussed. AC reported that the minutes of the IARC should be posted soon to the IARC website.
3. The definitions of aspects of the IgDiscover output were discussed. MC agreed to update the IARC_submission_sheet under development by the subgroup chaired by William Lees, to make clear definitions available to interested parties.
4. It was agreed that, as per the decision relating to the IGHV1-2*01_allelic variant affirmed at the previous IARC meeting, sequences will only be affirmed, at present, up to and including nucleotide 319. Where nucleotide 320 is submitted, such nucleotides will be reported, but not affirmed. It was noted that the default setting for TIgGER results in inferences up to and including nucleotide 312. AC will write to Steven Kleinstein to suggest that advice should be offered, or changes should be made to the default parameters of TIgGER, so that users understand that the utility is capable of inferring longer sequences. IARC will, as defined at the 3rd AIRR community meeting, only assess inferences that include nucleotides at least up to and including nucleotide 318.
5. The committee notes the formation of a subgroup of the Germline Gene Working Group, which will consider the nature of chimeric sequences arising from cross-over events during PCR amplification, and which will be developing strategies to reduce the frequency of such events, and to assist IARC in the detection and measurement of such events. The view was expressed that wet lab work may be required by this group, and IARC will advise the subgroup of what we would like to see them do, when this becomes a bit clearer to the committee. IARC believes it should discuss chimerism with researchers who submit data, and MC and MO will liaise to draft a suitable email.
6. IARC will complete the evaluation of data from subjects B12 and B16, as supplied to the Germline Gene Working Group by Davide Bagnara.
7. From dataset B16, the committee evaluated a variant of IGHV4-4 (IGHV4-4*01_S5769 as identified by IgDiscover). CS advised that this is an extension of IGHV4-4*03. The committee considered their policy towards inferences that extend sequences that have previously been reported as truncated sequences. AC will write to Marie-Paule Lefranc to ask what the policy of IMGT will be towards advice of this kind, sent from IARC to IMGT. A preliminary assessment of this inference found no reason to immediately exclude the sequence. It is expressed at high frequency (0.6% of exact matches) but haplotype analysis was not supportive due to the assignment of another common allele of IGHV4-4 to this haplotype. TIgGER and partis also inferred this allele. CDR3-based cross-over analysis was not highly supportive but values were not worse than those of other alleles of this particular sample. In light of the need to liaise with IMGT regarding the extension of previously reported truncated (incomplete) sequences, this sequence was designated as a Level 0 sequence, that should be re-evaluated at a later date. It was noted that this sequence can be considered a member of the IGHV4-4/4-59/4-61 gene cluster, and as such affirmation of the validity of this inference will be approached with particular caution.
8. From dataset B12, the committee evaluated a variant of IGHV2-70 (IGHV2-70*01_S4660 as identified by IgDiscover). A preliminary assessment of this inference found no obvious reason to

exclude the sequence, but as the frequency of reads was very low (<0.05%) and as the sequence was inferred by IgDiscover but not by Partis or TIGGER, this sequence was designated as a Level 0 sequence, that should be re-evaluated at a later date.

9. From dataset B12, the committee evaluated a variant of IGHV1-69 (IGHV1-69*14_S3451 as identified by IgDiscover). A preliminary assessment of this inference found no reason to exclude the sequence. It was inferred by IgDiscover and TIGER but not by Partis. The sequences unique CDR3 with exact matches to the inferred sequence were present as 2.35% of all sequences with exact matches to the inferred sequence. The sequence could not be explained as an artefact of cross-over events, but the inference was not supported by IGHJ6-based haplotype analysis although such analysis is complicated by a likely major duplication in this haplotype. The committee finally designated this as a Level 0 sequence, because of the complex duplication events that are apparent for IGHV1-69 sequences in the B12 haplotype analysis, and will finalise its deliberations at its next meeting.
10. The next meeting will be held on Wednesday March 28th at 22:00 AEST.

The meeting finished at 23:15 AEST.