

IARC Meeting 47: December 9th 2019: minutes

The meeting commenced at 10:30 UTC. AC, MC, CS, MO, WL and CW were in attendance. CS was unable to attend the whole meeting.

1. The minutes of meetings 45 and 46 were considered. The minutes of Meeting 45 (with changes to the naming of Level 0 sequences) were accepted. The minutes of Meeting 46 were discussed at length to amend the text relating to the end of the sequence IGHV4-4*102, and to include the judgement of the committee regarding the likely identity of nucleotide 319. The minutes were then accepted.
2. The committee continued to discuss the nature of light chain sequences and the challenges of assessing light chain inferences. The higher levels of mutation in light chain sequences from unsorted cells was noted. The presence of numerous mutational hotspots in the light chain V-region CDR3 was also noted. There has been little analysis of light chain sequences, but AC pointed to a 2008 study from his group that reported 33% of sequences had lost 3 nucleotides by exonuclease removals, and more than 20% of the sequences had higher levels of removals (DOI: 10.1007/s00251-008-0325-z). These features of the light chain will make it very difficult to affirm the final few nucleotides in a sequence, and such truncated sequences will likely be overlooked by some alignment software. A solution to this problem will need to be found as soon as possible, if the reporting of light chain polymorphisms is to have value for the AIRR community.
3. The committee considered an excel spreadsheet produced by WL, showing inferences in VDJbase, and the committee also considered a document showing AC's comments on these sequences. Using these comments, WL has produced a list of 36 sequences that are most likely to represent valid inferences. These sequences came from 5 studies:
 - P1: 21 sequences
 - P4: 5 sequences
 - P7: 2 sequences
 - P8: 2 sequences
 - P9: 6 sequences
4. MC reported on discussions with IMGT staff at the Genoa meeting of the AIRR Community, in which they expressed interest in documenting IG sequences that had been flagged as potentially problematic. The view was expressed that it would be easier and more appropriate to document sequences for which functionality had been validated through repertoire studies. VDJbase should provide a means of easily generating a listing of validated sequences, and this could be made available to IMGT and others via the VDJbase site.
5. MO highlighted the need to complete entries of affirmed sequences into OGRDB. MO and AC will make and check the entry of these data. MO also indicated the need to complete

submission of affirmed sequences to IMGT. AC agreed to make the submissions prior to the December 18th virtual meeting with IMGT.

6. The next meeting (Meeting 48) will be held on January 27th at 10:30 UTC, subject to email confirmation from CS.

The meeting ended at 12:00 UTC.