IMMREP22: Dynamics of Immune Repertoires: Exploration and Translation
Meeting agenda for Working Group 2 (July 7–10)
Evolutionary Footprints in Immunoglobulin V Genes

Thursday July 7th, Day 1

Morning session (9:00-12:00)
(Morning coffee 10:30-11:00)

Introduction to the Working Group:

- Icebreaker
- Overview talk (Victor Greiff)
- Exercise to map disciplines
  - Who are we? Who is connecting remotely?
  - What expertise do we bring to the table? What disciplines do we represent?)

Topic of the day: the evolution "within" us.

- Overview presentation. (Corey Watson)
  - What needs to be true for natural selection on IG genes to be plausible? How does genetic variation in IG genes influence the evolution of antibodies in the repertoire during the response?

Brief talks on Key Questions

1. Can/does evolution act on germline IG genes to reduce self-reactivity in the antibody repertoire? (Uri Hershberg)
2. TBD (Felix Breden)
3. Can allelic variation at different IG amino acid positions help us better understand which residues are critical to antigen binding, and other functions? Are these positions targets for natural selection? (Mats Ohlin)
4. On the definition of specificity, polyreactivity, cross-reactivity (Victor Greiff)
5. Is clonal expansion correlated to epitope specificity? (Alex Yermanos)

Lunch 12:00-1:00 (MPI Cafeteria)

- Informal discussions at lunch will help drive the afternoon group discussion

Afternoon Session (1:30-4:30)
Coffee break: (2:30 – 3:00)

Discussion (and additional short presentations) arising from morning talks (Discussion leader: Matt Pennell).

- What to "discuss"? Other suggested topics related to the Theme of the Day.
- 10-year plan: what are the subquestions, datasets, methods
- Brainstorm all ideas centering around the key questions
- Build a mind map/model around those questions

- How could these hypotheses be addressed, and are there any preliminary investigations that could be carried out now?

Free time / analysis (4:30 – 6:00)

Friday July 8th, Day 2:

Morning session (9:00-12:00)
(Morning coffee 10:30-11:00)

Topic of the day: The evolution "within" populations?

- Overview presentation. (TBD)
  - How important is germline variation between individuals of a species? What drives this variation between individuals?

Brief talks on Key Questions

1. Host-pathogen interactions and consequences for genetic diversity (Ailene MacPherson: remote presentation)
2. What do human IGHV Haplotype Blocks and Crazy Mice tell us about the process of IGH evolution? (Andrew Collins)
3. Human IG repertoire variation (Ayelet Peres)
4. Variation in non-coding regions influence the composition of the "baseline" repertoire (Oscar Rodriguez)

Lunch 12:00-1:00 (MPI Cafeteria)

- Informal discussions at lunch will help drive the afternoon group discussion

Afternoon Session (1:30-4:30)
Coffee break: (2:30 – 3:00)

Discussion (and additional short presentations) arising from morning talks, as per Day 1
(Discussion leader: Matt Pennell).

Free time / analysis (4:30 – 6:00)

Saturday July 9th, Day 3

Morning session (9:00-12:00)

Topic of the day: How have repertoires evolved to meet the varying immunological needs of different species?
Overview Presentation: Andrew Collins

Brief talks on Key Questions

1. Have IG genes helped drive the process of vertebrate speciation? (Andrew Collins)
2. IG/TCR diversity in marsupials and reptiles (Robert Miller)
3. IG diversity: Rhesus vs Human (Martin Corcoran)

4. Comparative analysis of antibody repertoires and immunoglobulin loci reveals convergent evolution of the adaptive immune systems in mammals (Yana Safonova)

Lunch 12:00-1:30 (Local cafes)

- Informal discussions at lunch will help drive the afternoon group discussion

Afternoon Session (1:30-4:30)

Discussion (and additional short presentations) arising from morning talks, as per Day 1

(Discussion leader: Matt Pennell).

Free time / analysis (4:30 – 6:00)

Sunday July 10th, Day 4

Ad hoc agenda to be determined by participants, based on Days 1–3

Other Possible Discussion Topics

Below are some other topics for discussion that have been suggested by various participants in the Working Group. If you have ideas you would like to add, please email them through to the organisers via a.collins@unsw.edu.au.

1. Are Neanderthal and Denisovan IGHV to be found in Melanesia? If so, does this imply these genes brought biological advantages during the human migration through South East Asia and beyond? If so, can the targets of these IGHV and therefore the advantages be determined??
2. What is the meaning of the conservation of the human IGHV7-27 sequence across species as remote from the human as the mouse? The sequence is not (apparently) found in all mammalian species. Why? More generally, what is the meaning of D gene conservation and divergence between species? What other genes are conserved? Any IGHV? Why?
3. Isotype mysteries - what are the consequences of isotype variation between species? Is it possible to have a general model of isotype function across mammalian species? What are the consequences of allelic variation in isotype genes and why is there so much allelic variation within the human population?
4. Could it be possible to look at phylogenies of pathogens; can we say when a given pathogen or class of pathogens invaded a clade (humans? primates? mammals?); can we see some evolutionary footprint of that invasion in the immune genes?

5. It is intriguing to compare the evolutionary history of the IG genes through evolutionary time versus the evolution/development of repertoires through developmental time. Are the same genes/SNPs selected? probably not. Certain

mutations are always seen in IGHV3-23 as one develops a response to flu. Why isn't that mutation coded into the germline genes?

6. Why are some genes stable, while others are enormously divergent? Human IGHV6-1 versus IGHV1-69. What are the consequences of diversification through copy number versus allelic diversity in IG. 1/2 of the genes appear in CNV. Do they have more allelic variants per gene than single copy genes? Are there positional effects that contribute to outcomes?
7. Does chromosomal position affect duplication probability versus allelic diversity
8. How can we assess the likely accuracy of an IGH assembly and annotation, and thereby determine whether or not it is time to give names to the identified genes?
9. Comparison between species, with a specific focus on how regions of diversification are conserved
10. Do different CDR regions have different roles?
11. Are the shape spaces of B cell and T cell repertoires related? Can we see it in the repertoires?