Day 1, July 7 2022, Thursday

From sequence to specificity

New tools for the generation and analysis of T cell receptor sequences are released with increasing frequency. Despite significant advances in this area in the last decade, we still lack the ability to translate sequence into specificity without some prior knowledge of related TCR sequences and their target antigens. How close are we to solving this problem? What approach or approaches are likely to be successful? Will structural modeling be able to distinguish the fine specificity of closely related epitope or TCR sequences? Can a purely empirical approach, such as large-scale sequencing against an array of antigens, provide a workable solution? To what extent does cross-reactivity complicate any potential solution? Regardless of solving the precise specificity of a TCR sequence, what can we predict about TCR fate and function based on sequence alone, e.g. CD4 versus CD8 identity, unconventional subpopulations (IEL, MAIT, NKT, others), likely affinity, inclination towards exhaustion or effector fates?

9:30-10:30 Martin Meier-Schellersheim and Christopher Boughter (in person)
10:30-11:30 Andreas Mayer (in person)
11:30-12:30 Stefan Schattgen (in person)

12:30-14:00 Lunch and Discussion

2:00-3:00 Thomas Leitner (virtual, is this time zone OK, that is 6am in New Mexico)
3:00-4:00 Phil Bradley (virtual, is this time zone OK, that is 6am in Seattle)
4:00-5:00 Paul Thomas (in person) (I'm happy to move earlier if it will help Phil and Thomas)

Day 2, July 8 2022, Friday

From function to fate

T cell differentiation trajectories are the key determinant of their functional role in pathogen clearance, autoimmune pathology, tumor control, and long-term memory. A number of models for memory formation have been proposed, including linear models with specific intermediates, versus branching models driven by micro-environment, asymmetric cell division, or other factors. The success of tumor immunotherapy has driven focus towards terminal differentiation, the formation of dysfunctional T cell effector states, and the tools available to assess them and manipulate them. How many effector states are possible? How fixed are differentiation trajectories? What are the best methods for defining a T cell phenotype state (protein, gene expression, epigenetics)? What should be the ultimate reference? Are dysfunctional states truly dysfunctional or do they represent an alternate set of functional properties? How can trajectories be altered, and can they be reversed? Are there "precursor" states that are irreversible? What cells contribute to memory and do these precursors have distinct biological features or are they stochastically selected?

9:30-10:30 Veronika Zarnitsyna (in person)
10:30-11:30 Dietmar Zehn (in person)
11:30-12:30 Niroshina Anandasapathy (in person)

12:30-14:00 Lunch and Discussion

2:00-3:00 Rob de Boer (in person)
3:00-4:00 Evan Newell (virtual)
4:00-5:00 Weiguo Cui (virtual)

Day 3, July 9 2022, Saturday

From sampling to human heterogeneity of T cell responses

One of the most pressing challenges of immunology in the XXI century is to identify and quantify those parameters which regulate and determine the variability of human adaptive immune responses to pathogens, and in turn, disease severity and outcome. In our quest to understand human T cell immunology and immune responses, there is a need to examine T cell immune homeostasis. For instance, we still do not know if i) baseline (homeostatic) immune signatures reflect molecular or cellular mechanisms of immune responses, or do they merely reflect statistical correlations of yet-to-be-determined immunological factors? ii) predictive baseline signatures of disease outcome or severity similar or different across different populations? For example, do we know that public TCRs make up most of the diversity in homeostasis? iii) under the hypothesis that an individual's vulnerability to disease is encoded in its T cell immune homeostatic state, what are the timescales characterizing these baseline states, and how robust are these homeostatic states to perturbations, such as viral infections or vaccinations, and their concomitant immune responses? iv) to
Improve current quantitative approaches to human immunology and their potential for predicting disease severity and outcome, how can data-driven approaches (statistical) and hypothesis-based mechanistic (mathematical) modeling be best integrated? Finally, modern single-cell sequencing techniques allow the unique T cell receptor (TCR) signature of each of a sample of hundreds of T cells to be read. The mathematical challenge is to extrapolate from the properties of a human sample to those of the whole repertoire of an individual, made up of many millions of T cells. Where are we addressing this challenge?

9:30-10:30 Grant Lythe (in person)
10:30-11:30 Nicole La Gruta (in person)
11:30-12:30 Carmen Molina-París (in person)

12:30-14:00 Lunch and Discussion

2:00-3:00 John Tsang (virtual)
3:00-5:00 Paul Thomas, Veronika Zarnitsyna and Carmen Molina-París (summary of WG1) (in person)