OpenSource Immgen T proposal

TITLE

***Lab PI:***

***Institution:***

***Lab address:***

***PI email:***

***Investigator directly responsible:***

***Investigator phone contact:***

***Investigator email:***

***Total nb of populations:***

***General description of the cell populations proposed*** *(2-3 lines, pls be specific)****:***

*Example: CD3+ T cells in the toe infiltrate in ACB5.2 TCR transgenic mice, at 25 and 60 days of age.*

***Justification of the population(s) and experimental design: Why is multimodal single-cell RNAseq (RNA, TCR, Cite-seq) on the proposed cell populations of interest, and how does it complement the current game-plan?***

*(in relation to immgenT context, but also to your lab’s research)*

*Example: Autoimmune attack of the big toe is a poorly understood condition, and our lab has been working on understanding the determinants of T cells infiltration. The unusual physiology, relative to commonly studied sites of autoimmunity like the brain or pancreas, lead to unusual T cell populations in the toe infiltrate, which would be important for immgenT to capture (no toe datasets are currently proposed). It will be interesting to compare these T cells states to other autoimmune contexts (shared programs), and how epitope spreading in the lesion recruits additional*

*It is usually impossible to isolate enough cells from the native model, but ACB2.5. TCR transgenic mouse, whose TCR recognizes a toe-specific antigen, yields >30,000 cells/toe.*

*Two time points proposed: 25 days is the very onset of infiltration, where transgenic CD4+ T cells dominate; toeitis is fully blown at 60 days, when additional T cells have been recruited and epitopes/TCRs diversify.*

***Realistic? Profiling will require >20,000 cells/sample. Please indicate if that number is a problem, number of mice required, etc***

*Example: The XA14 model is readily available, and easily bred. From one mouse, at least 50,000 cells, mostly T cells, can be isolated from the toe. Isolation of toe-infiltrating cells is challenging, but XX, a postdoctoral fellow who would be involved in this study, could easily travel to Boston for this (and for the later analysis jamboree).*

***Dream list: For realism, we anticipate that investigators might contribute a 2-3 samples. If there were no financial constraints or other priorities, what would you add to the above?***

*Example: While autoimmune infiltrate is present in 100% of the mice, we know that microbiome alterations (skin painting with P. epidermis) and dietary variations (high-carb diet) influence the outcome, Profiling infiltrating T cells with these additional variations would be valuable to understanding the cellular and molecular mechanisms.*

***Why your group?***

*Pls indicate prior experience (publications?) with the proposed organ, cell types, or model*.

*Our lab has played a leading role in studying this unique autoimmune condition, as reflected in publications XXX, YYY and ZZZ, and we are fully versed in the challenging extraction of these cells, In addition, given our going work in the ACB2.5 model, we would be we placed to build on the CITEseq protein expression results obtained, with followup/validation studies by flow cytometry and/or Ab blockade experiments*