Attrition of Immune Memory

A Summer at Emory University

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Math Biology Seminar

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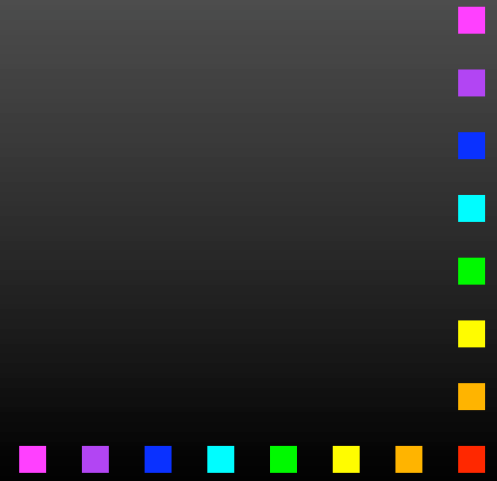
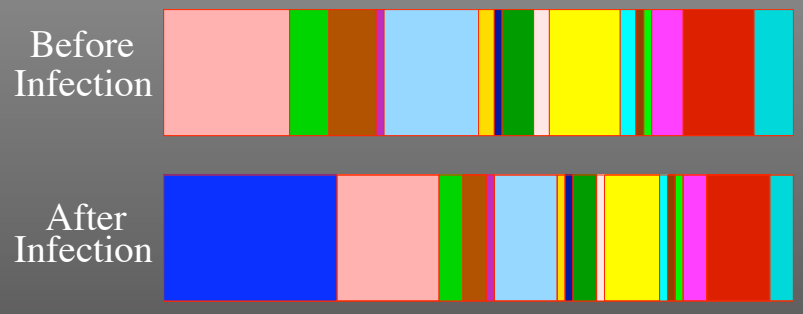


Immune Memory Repertoire and Passive Attrition

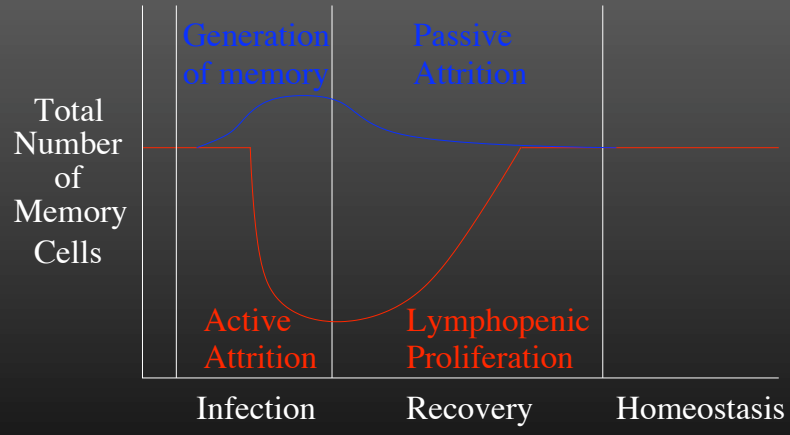


Following an infection:

- The total number of memory T cells returns to pre-infection levels. (homeostatic regulation)
- Some existing memory to other diseases must be lost to accommodate new memory cells.
- Reducing an overfilled memory compartment to homeostatic levels is likely controlled by resource competition for survival and death signals.
- The reduction process, which occurs after infection, is called *Passive Attrition*.

Active Attrition

- Some viral infections induce killing of up to 75% of existing memory, resulting in lymphopenia.
- This process, which occurs early in infection, is called *Active Attrition*.
- Later, remaining memory cells and some naive cells proliferate/differentiate to refill the memory compartment. (lymphopenic proliferation)



Research Questions

Does active attrition significantly and lastingly reduce memory lineage size/diversity? Is its impact greater than that of passive attrition on the memory repertoire in the long run?

Hypothesis in the literature: Selin et al. (2006)

"There may still be accommodation issues in competing for protective niches later in infection, but its relative importance seems less than the active attrition in these models of infection."

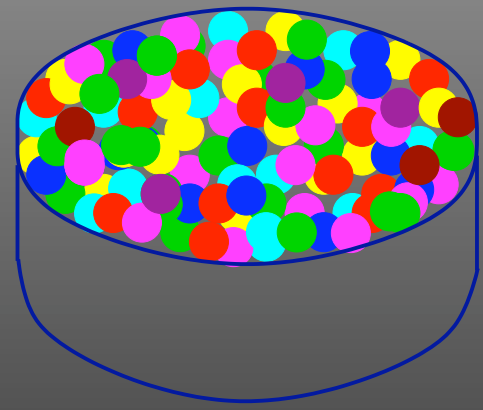
My hypothesis:

Since lineage sizes are usually large and since lymphopenic proliferation restores total compartment size, active attrition will have only minor effects on lineage size and diversity. The effects of passive attrition will be more lasting.

Simulation Approach

Active attrition:

- Sample from a multivariate hypergeometric distribution
- Initial memory distribution from Baron et al. (2003)
- Produces a new, smaller m.h.d.

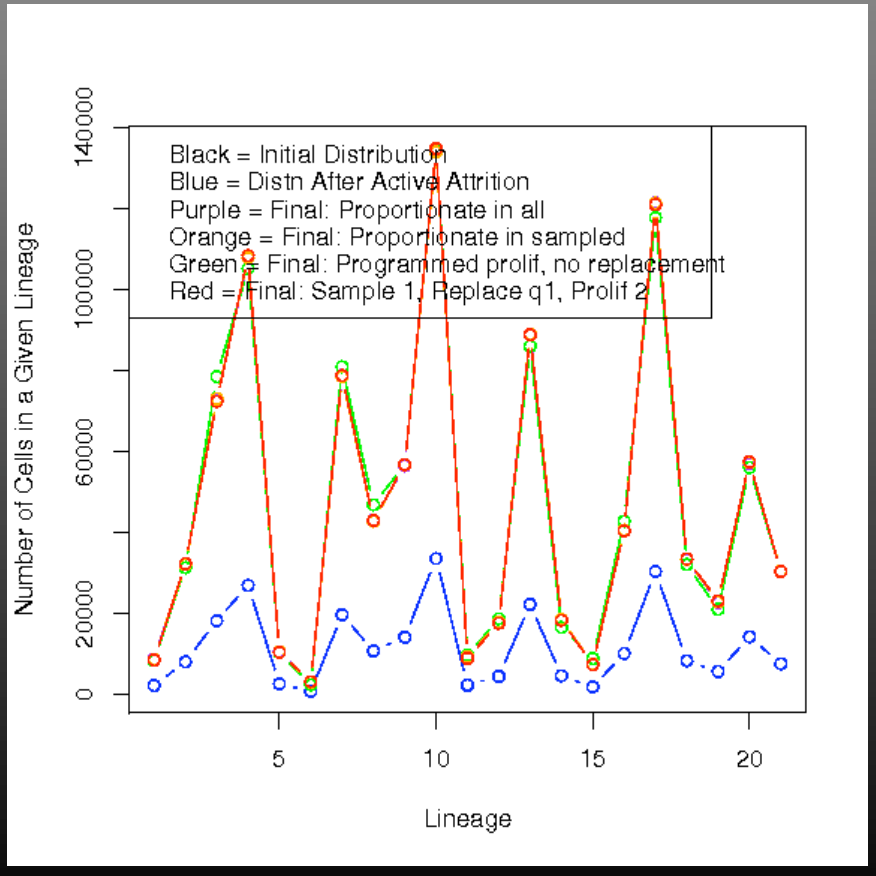


Lymphopenic proliferation:

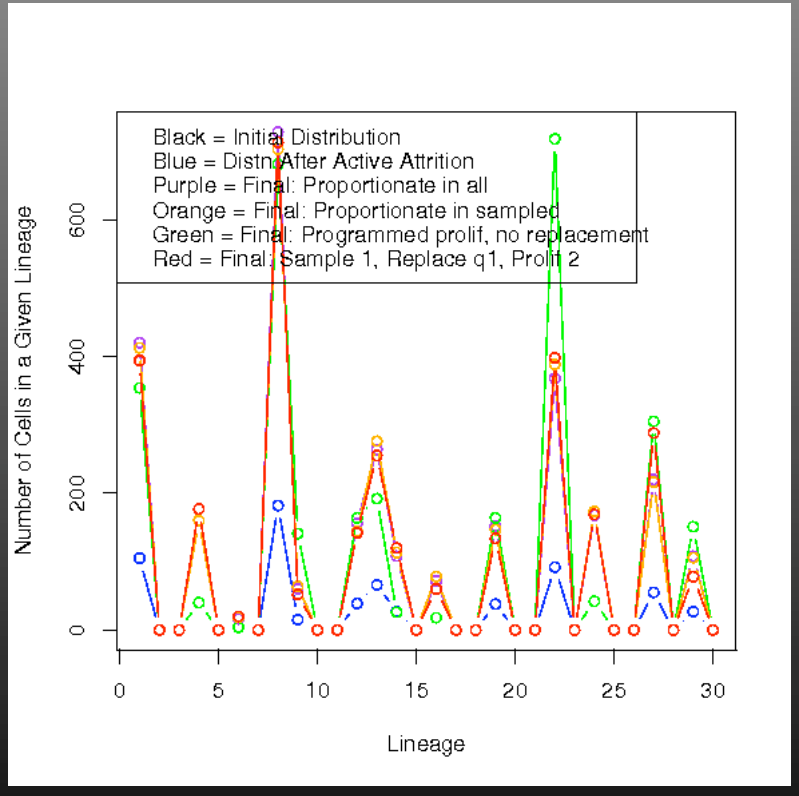
Use one of these proliferation regimes until memory compartment is refilled:

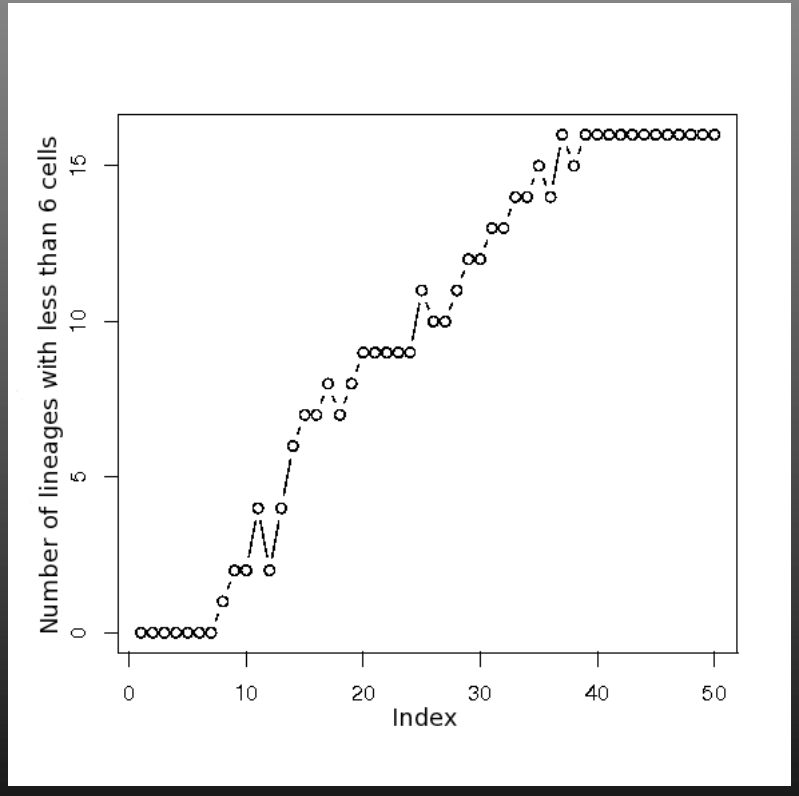
- Proportionate increase
- Random division
- Programmed division

Simulation Results: Initial Distribution from Data



Simulation Results: Uniform Initial Distribution





Observations and Conclusions

- Lymphopenic proliferation counters active attrition and, if lineage sizes are large, roughly returns lineages to their previous sizes and diversity.
- Random division best restores a lymphopenic memory compartment to its initial distribution.
- Even with an average of 100 cells per lineage, loss of lineages due to active attrition is relatively rare.
- Passive attrition permanently reduces lineage sizes and therefore likely contributes more to long-term lineage decay. This remains to be corroborated.

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