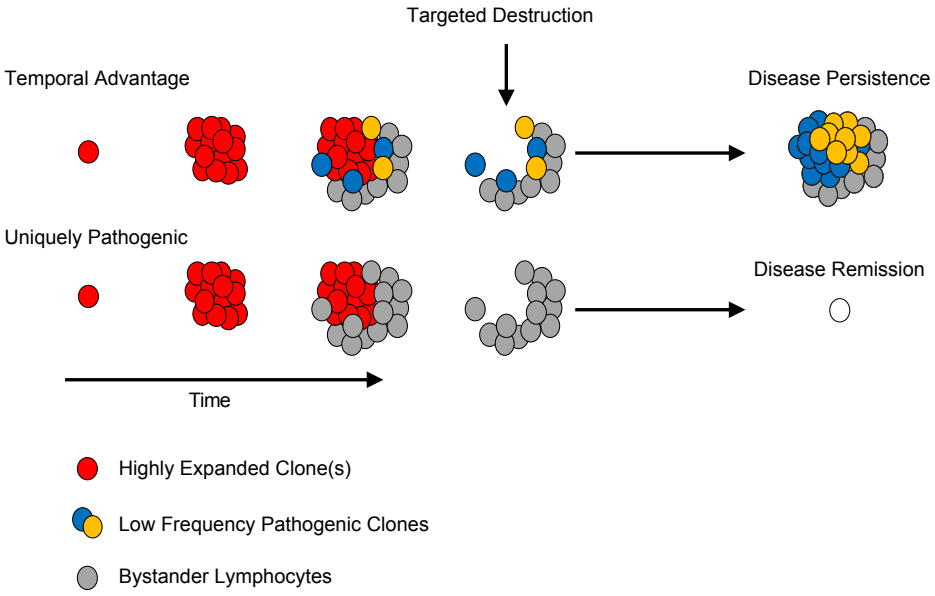
Supplemental Figure 12



Supplemental Figure 12: Proposed models for the emergence of highly expanded lymphocyte clones in granulomatous uveitis with hypothesized treatment response after targeted elimination of putative pathogenic clones. (Top Row) Early entry of antigen-specific clones (red) offers a competitive advantage to clonal expansion over late entrants (blue and yellow). This temporal advantage leads to the robust expansion of one or a select few clones with minimal expansion of late-arriving clones when the adaptive response is already underway. Targeted elimination of expanded clones is hypothesized not to affect long term disease activity as low frequency, late arriving clones would expand to perpetuate disease activity. (Bottom Row) Highly expanded clones are uniquely pathogenic (red) by initiating and perpetuating the inflammatory process. The remaining lymphocytes are largely bystander cells and are not antigen-specific (gray). Targeted destruction of highly expanded clones in this model would lead to elimination of the antigen-specific response and resolution of disease.