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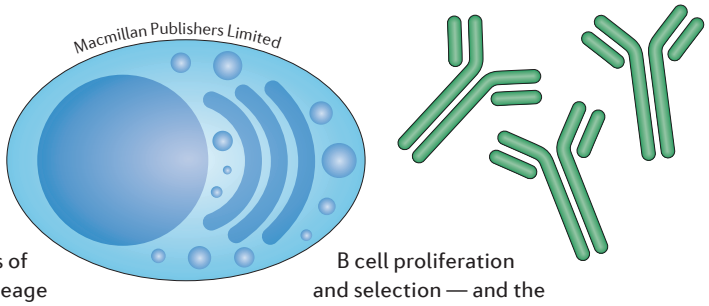
Journal club

RAGING EVOLUTION OF A B CELL RESPONSE TO A VIRAL INFECTION



This 2013 paper from the group of Barton Haynes is a rather extraordinary demonstration of the power of evolution of an antibody response by affinity maturation, and the concurrent power of HIV to escape the furious efforts of that affinity maturation.

Haynes and colleagues catalogue, in fine detail, the evolution of a broadly neutralizing antibody response in a single HIV-1-infected individual starting from 4 weeks post-infection, and concluding at more than 3 years post-infection when broadly neutralizing antibody activity developed. The authors accomplished this by single-cell sequencing of many antigen-specific memory B cells from the blood of the patient, complemented by bulk sequencing for related lineage members, followed by expressing key members of the clonal lineage as individual recombinant antibodies. In conjunction with those efforts, they also completed single-genome sequencing of HIV-1. All of that effort is encapsulated in Figure 5b of the orginal research paper. Due to the nature of the epitope, it was possible to obtain a crystal structure of the broadly neutralizing antibody bound to the envelope glycoprotein GP120 of HIV-1 and thereby, to beautifully model the evolution of the B cell receptor and HIV-1 mutations over time.

> “it is a study that makes it easy to imagine a virus wiping out the human species”

I regularly show Figure 5b in my research seminars, as a demonstration of the exceptional capacity of the immune system to evolve in real time — representing countless rounds of germinal centre B cell proliferation and selection — and the slippery nature of viruses, HIV in particular. Frankly, it is a study that makes it easy to imagine a virus wiping out the human species. Separately, I also find this paper to be an outstanding example of human immunology; the amount of knowledge learned from the in-depth study of a single individual was groundbreaking.

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ORIGINAL RESEARCH PAPER Liao, H.-X. *et al.* Co-evolution of a broadly neutralizing HIV-1 antibody and founder virus. *Nature* **496**, 469–476 (2013)