

## How to hit HIV where it hurts

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HIV continues to wreak havoc around the world, especially in developing countries. It is a highly mutable virus which can evade natural or vaccine induced immune responses by mutating at multiple sites linked by compensatory interactions. If one wishes to define the mutational vulnerabilities of HIV, these collective compensatory pathways need to be identified so as to not target the involved sites by a vaccine induced immune response. Moreover, the combinations of mutations that the virus cannot make and still maintain viability need to be determined, so as to target the pertinent sites by vaccination. Thus, knowledge of the fitness landscape of HIV could enable rational design of vaccines that can confront this scourge. We developed models to translate data on HIV protein sequences to knowledge of the prevalence landscape of the circulating HIV population. Theoretical analyses and biological reasoning led us to surmise that, unlike many other viruses, the relationship between the prevalence and fitness landscapes of HIV may be simple. I will show that this surmise is supported by positive correlations between predictions emerging from our inferred fitness landscape and in vitro experiments and clinical data obtained from patients. Based on these results, a therapeutic T cell-based vaccine was designed, which is now being advanced to pre-clinical studies in monkeys. I will also describe how scaling laws describe the HIV population and discuss an interesting analogy with Hopfield neural networks.