Vaccination Strategy Targets Fast-Changing Pathogens

A theory outlines an immunization protocol that fosters powerful antibodies while avoiding immune-cell death.

By **Rachel Berkowitz**

It is extremely challenging to design effective immunization schemes against fast-mutating viruses such as HIV and influenza. To help with this formidable task, Saeed Mahdisoltani and his colleagues at MIT propose a protocol for efficiently administering vaccinations in a way that targets both the original virus strain and mutants [**1**]. The approach is based on identifying the factors and mechanisms that steer how the body produces antibodies that are effective against a broad spectrum of pathogen strains.

Our adaptive immune system uses an accelerated evolutionary process to generate antibodies for previously unseen pathogens. This process is known as affinity maturation, and it works by changing the surface proteins expressed by so-called B lymphocyte cells (B cells). Vaccination strategies nudge affinity maturation forward by introducing appropriate antibody generators (antigens) in a controlled way. To optimize this design, Mahdisoltani and his colleagues developed a statistical physics-based model of the antibody–antigen dynamics. The model incorporates cell replication, death, and mutations while also accommodating spatial and temporal variations in vaccine-induced antibody effectiveness.

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Using this model, the researchers derived a formula that reveals qualitative features of an optimal vaccination protocol. In the initial stages of this protocol, the administered antigens are designed to allow the immature B-cell population to grow and diversify. Subsequent vaccines then contain antigens that gradually become more similar to the target viral protein sequence and focus on promoting B cells that have a better chance of generating broadly neutralizing antibodies. Past experiments in mice support the feasibility of this approach. The protocol, the researchers say, could result in a vaccination strategy that maximizes the evolutionary chance of producing valuable rare antibodies without risking B-cell extinction.

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REFERENCES

1. S. Mahdisoltani *et al.*, "Minimal framework for optimizing vaccination protocols targeting highly mutable pathogens," **Phys. Rev. E 110, 064137 (2024).**