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Complex vaccination strategies prevent the emergence of vaccine resistance

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Background:
Vaccination is among the most effective tools to control infectious diseases. However, the evolution of vaccine resistance, exemplified by vaccine-resistance in SARS-CoV-2, Influenza or Hepatitis B, remains a concern. As an attempt at containing antigenic evolution, multi-epitope vaccines were proposed, but displayed varying success. Rapidly evolving pathogens call for alternative vaccination procedures.
Methods:
We model complex vaccination strategies against a pathogen with multiple epitopes, by diversification of available vaccine targets across the vaccinated population. Our analytical model incorporates within-host evolution in response to vaccination (in form of an evolutionary Wright Fisher model) as well as between-host pathogenic spread (in form of a stochastic transmission model). The model allows analyzing how the combined effects of different life history properties of a pathogen affect the evolution of novel resistant variants.
Results:
Vaccine resistance in highly infectious pathogens was prevented by the full-vaccine, one targeting all available epitopes, but only when the rate of pathogen evolution was low. Strikingly, a bet-hedging strategy of random administration of vaccines targeting different epitopes was the most effective in preventing vaccine resistance in pathogens with low rate of infection and high rate of evolution.
Conclusions:
Complex vaccination strategies utilizing a diversified vaccine portfolio may be preferable to the currently used single-vaccine approaches for long-term control of disease outbreaks. Depending on the rate of evolution and the transmissibility of a pathogen, an optimal vaccine portfolio may greatly reduce the risk of newly evolving variants. Given the biological feasibility and our knowledge about the life history of a pathogen, we recommend stronger consideration of diversification in vaccine design.
Key messages:
- Diversification of vaccine targets reduces the pathogens propensity to evolve vaccine resistance.
- Fast evolving pathogens are best contained by random administration of diverse multi-epitope vaccines.