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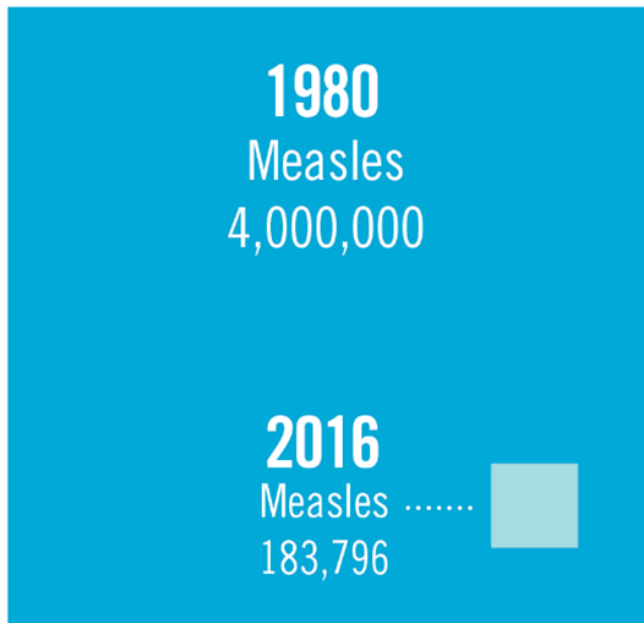


Progress toward an HIV vaccine

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Vaccines

Vaccines **teach** our **immune systems** to memorize **harmful agents** and **respond to them quickly** if seen again.



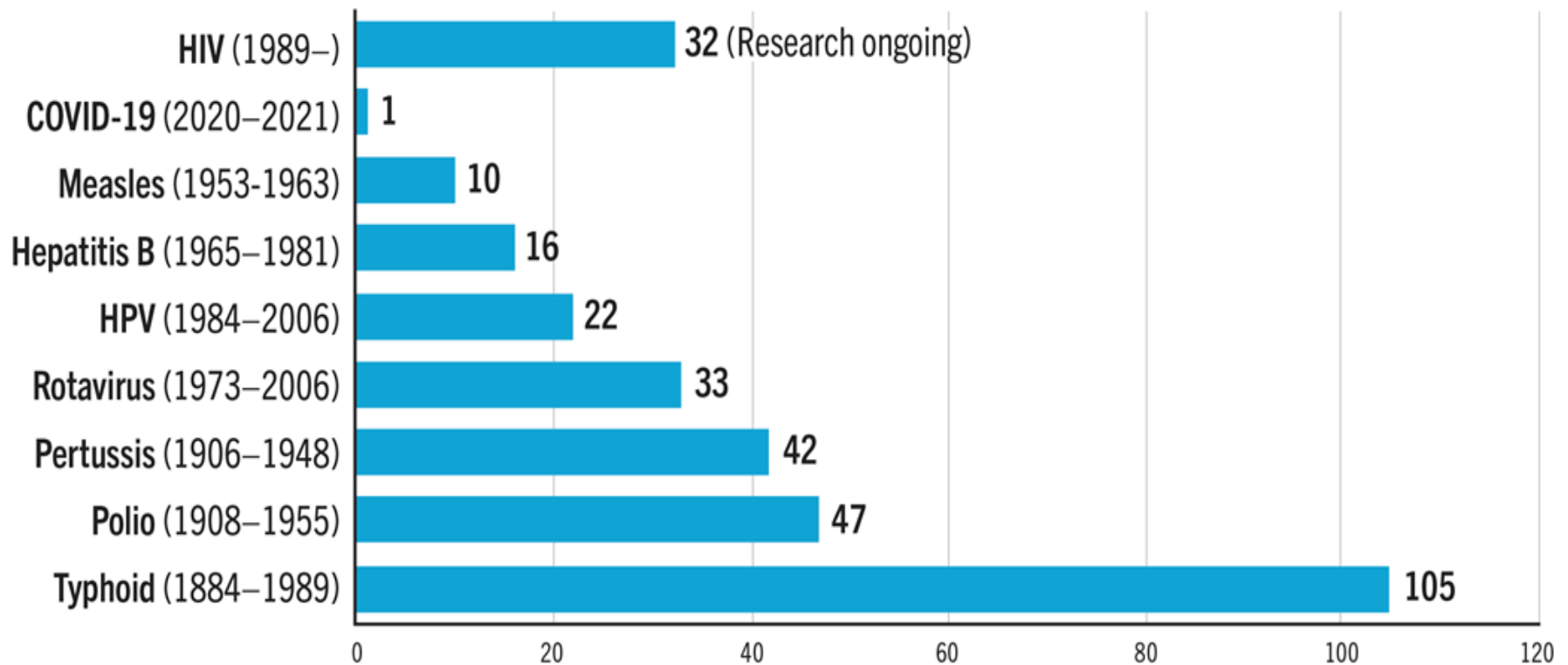
EPIDEMICS SUCCESSFULLY COMBATED WITH VACCINES (CASES 1980 – 2016)



Vaccine Development History

Time to Develop a Vaccine: Duration between discovery of microbiologic cause of selected infectious diseases and development of a vaccine

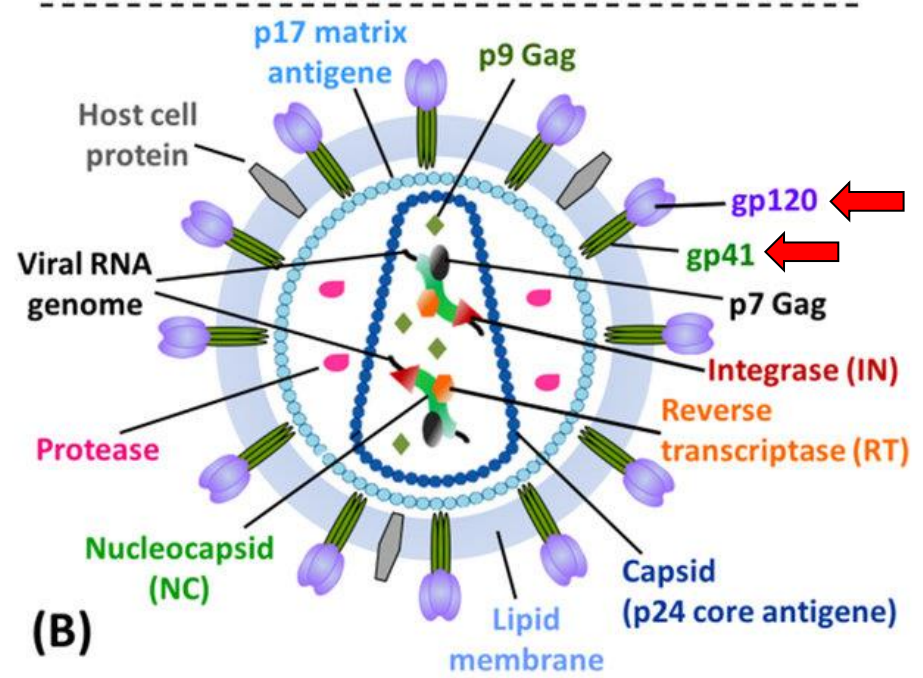
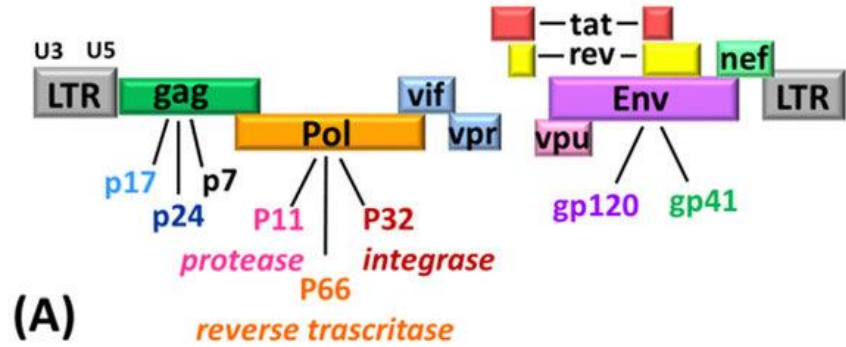
Time to develop a vaccine (in years)



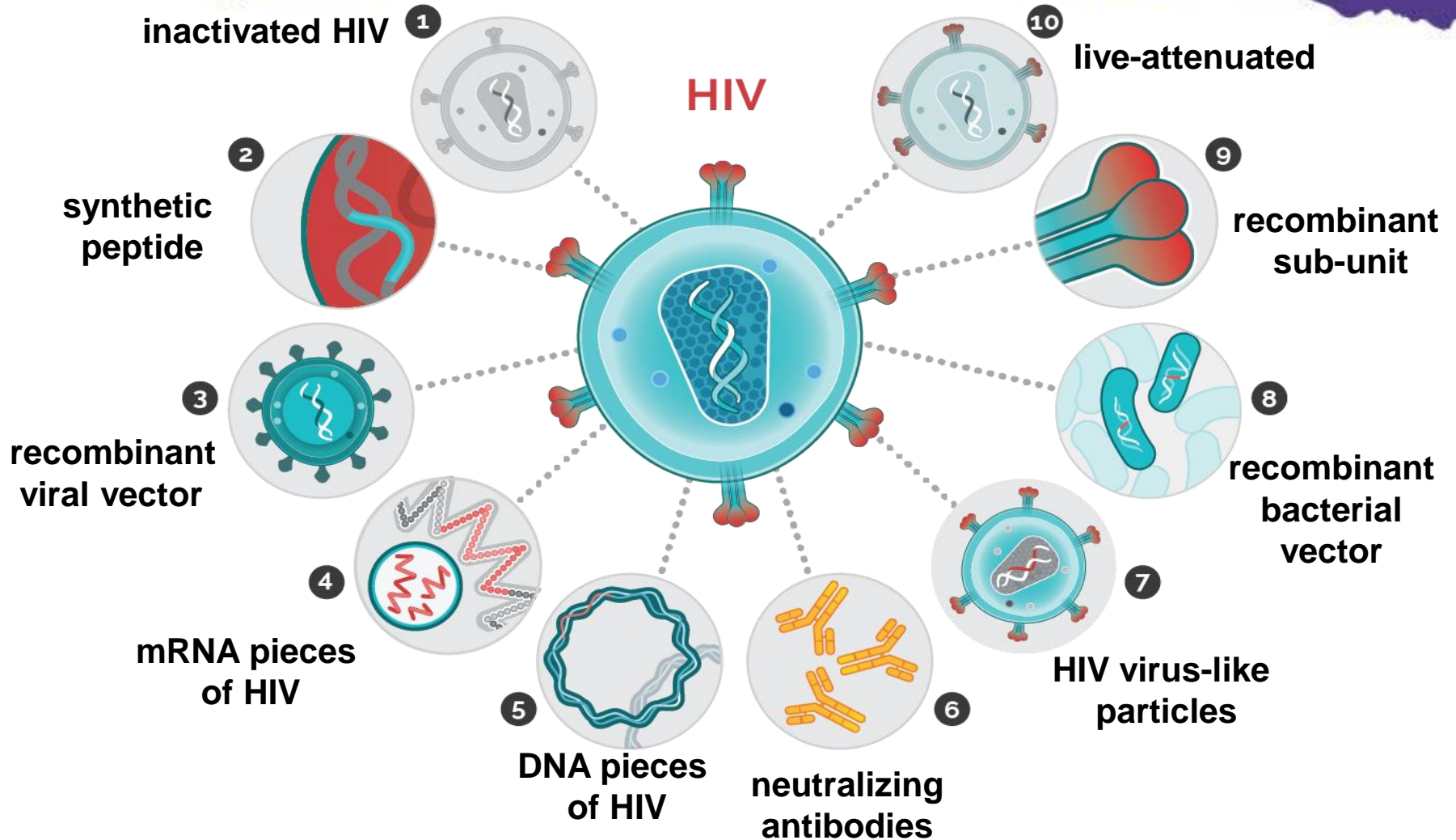
HIV vaccine

- HIV/AIDS is a leading cause of mortality and morbidity worldwide.
- Safe, effective HIV vaccines remain a necessity for the durable control of the epidemic.
- An HIV vaccine may induce an immune response against HIV (**active vaccination**) or consist of preformed antibodies against HIV (**passive vaccination**).
- An HIV vaccine is a potential vaccine that could be **either a preventive vaccine or a therapeutic vaccine**.

HIV genome (A) and structure (B)



Types of Vaccines

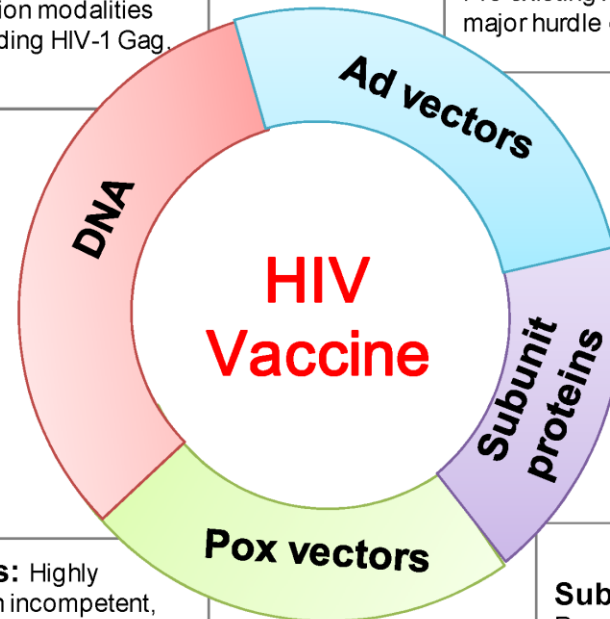


HIV vaccines in clinical trials

Vaccine Modality	No. of Trials
DNA/Pox Virus	8
DNA/Ad Virus	5
DNA/Pox/Protein	3
Viral vector - Pox	3
Viral vector - Ad	11
Protein	8
Protein/Pox	3

DNA Vaccines: Non-replicating plasmid DNA encoding HIV proteins. Employed as a prime in heterologous prime-boost vaccination modalities e.g., pGA2/JS2 encoding HIV-1 Gag, Pol, Env

Adenovirus (Ad) vectors: Broad tropism, highly immunogenic. Pre-existing Ad-specific immunity major hurdle e.g., Ad5, Ad26, Ad34



Pox-virus vectors: Highly attenuated, replication incompetent, extensive safety record; efficient expression vectors with large capacity for added DNA e.g., MVA, NYVAC, ALVAC

Subunit proteins: Recombinant HIV proteins e.g., gp120, trimeric gp140, gp41, Gag



HIV vaccine development challenges



No roadmap of protection

Nobody has ever eliminated HIV with their own immune system



Viral Variability

HIV makes many copies of itself and mutates, making it unrecognizable to the immune system and leading to different subtypes of the virus throughout the world



Immune-targeting

HIV kills the very immune cells the body uses to defend against disease

Eliciting HIV Immune Responses



T cell-mediated response: Stimulate branch of immune system (mainly T cells) that recognizes and destroys cells infected with HIV so it cannot multiply and spread



Neutralizing antibody response: Induce antibodies that block HIV in the blood, preventing HIV from infecting the body's cells



Non-neutralizing antibody response: Induce antibodies that recognize HIV and recruit other immune cells to help destroy the virus

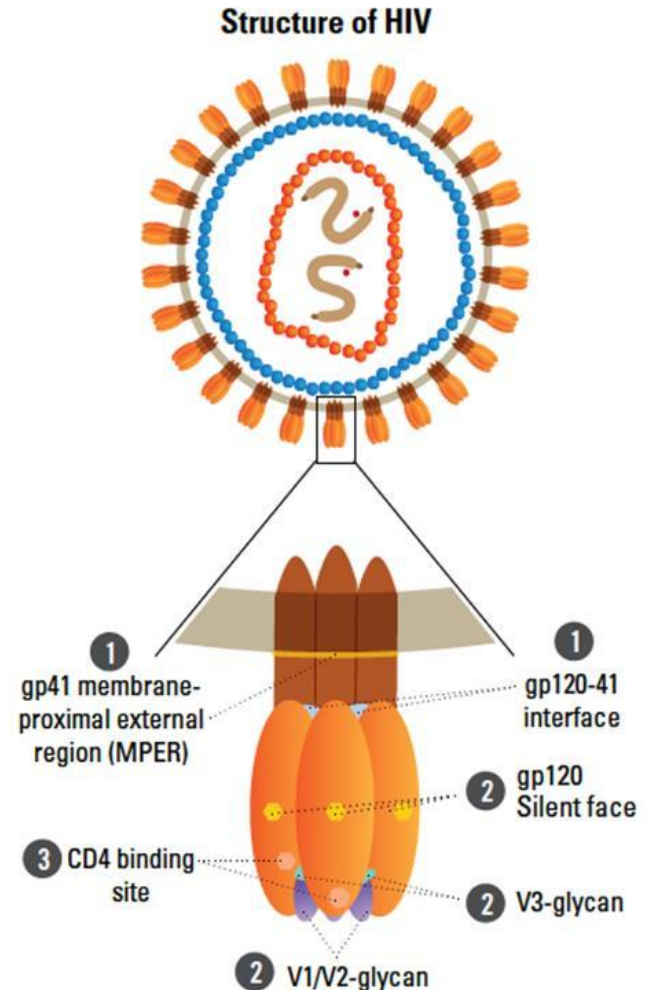


Combination responses: Stimulate multiple parts of the adaptive immune system to recognize and defend the body against HIV

- With the exception of RV144, the so-called Thai Trial, which found a 31% lower infection rate among those who received the vaccine, **strategies that elicit non-neutralising responses have not been effective.**

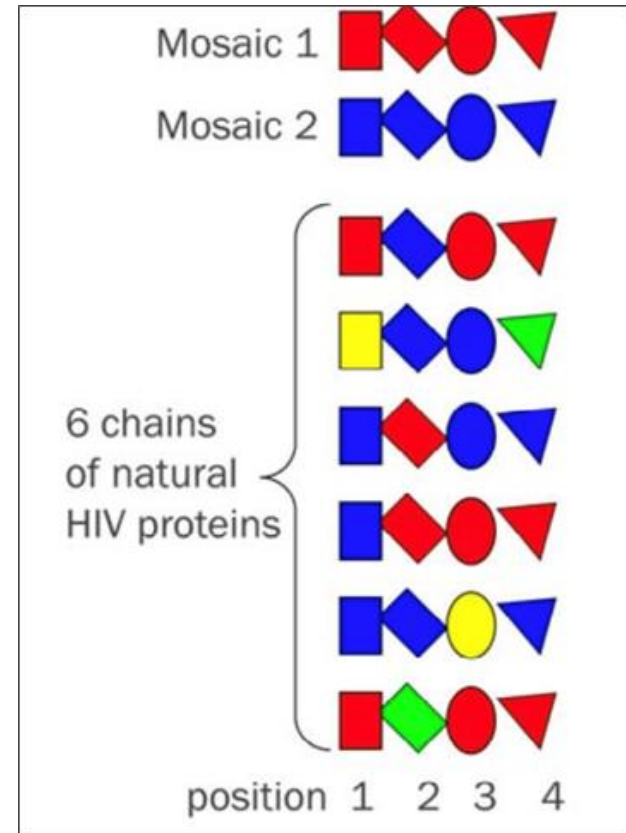
Broadly neutralizing antibodies (bNAbs)

- Specialized antibodies that bind to and neutralize multiple strains of HIV
- Numerous bNAbs discovered since 2009
- Five main targets of bNAbs on the virus envelope



Mosaic Vaccines

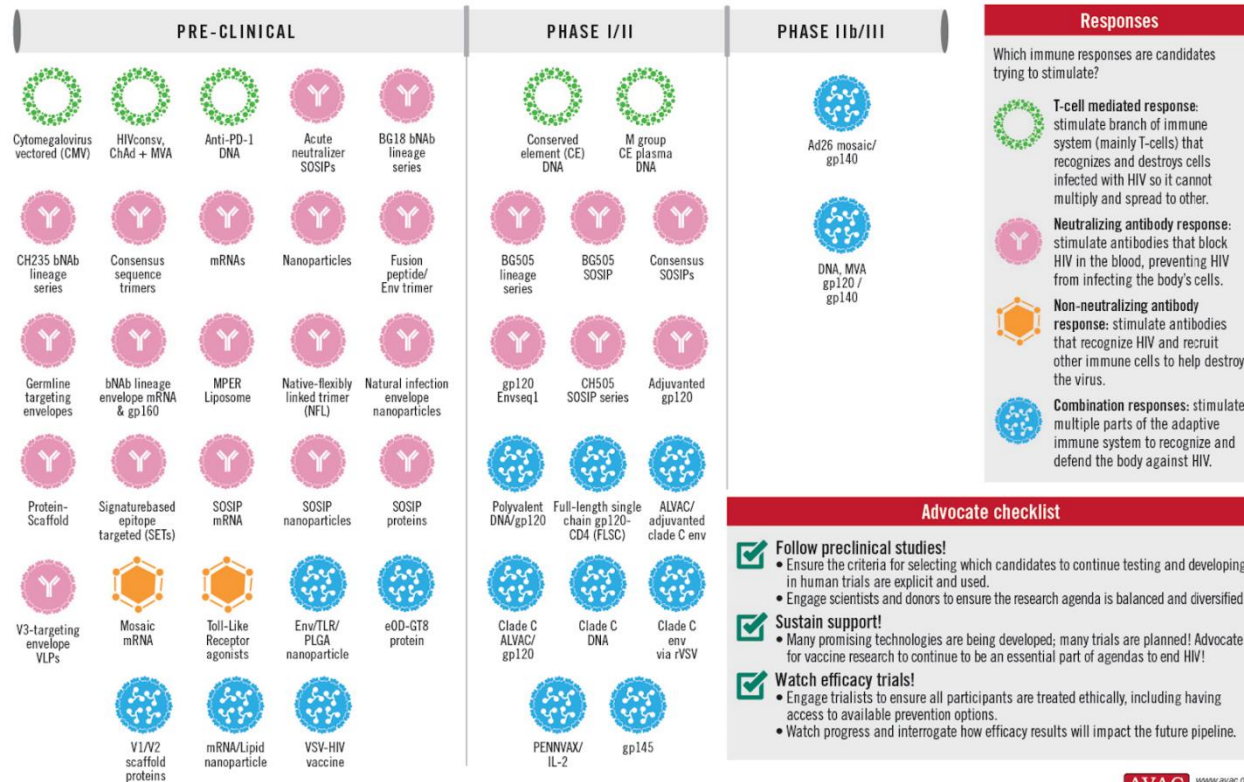
- A so-called “mosaic” vaccine is designed to create immune responses to multiple HIV clades
- Several mosaics used together in a vaccine could provide broader coverage
- Mosaic immunogens can be inserted into viral vectors, e.g. Adenoviruses



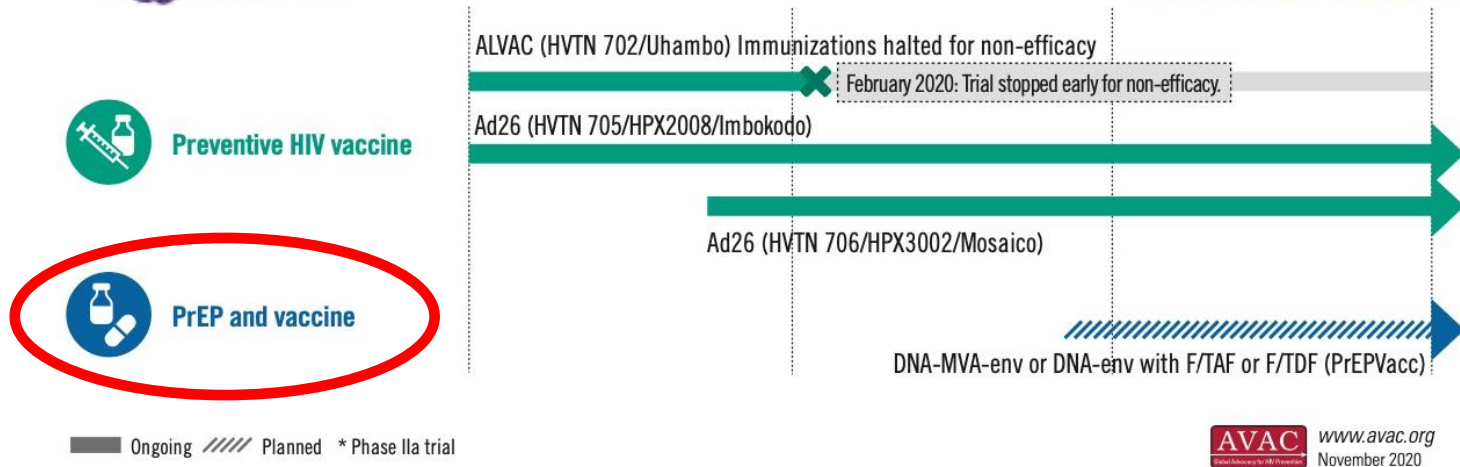
Sustaining HIV Vaccine Research

HIV VACCINE RESEARCH PIPELINE (FEBRUARY 2020)

Scientists are exploring many types of vaccines to try to elicit immune responses that would protect from HIV. These vaccines can be organized, imperfectly, under three buckets: vaccines designed to elicit broadly neutralizing antibodies, non-neutralizing antibodies or T-cell responses. Some vaccines are trying to elicit a combination of these responses. We don't yet know which of these immune responses will protect against HIV. To learn more about immune responses and the vaccine regimens below, check out: www.avac.org/hvad



HIV Vaccine Trials



- The past few years have been difficult for HIV vaccine research, with several high profile trials being stopped early and with negative results.
- Now the focus seems to be on broadly neutralising antibodies (bnAbs), either by giving infusions of bnAbs or by eliciting the immune system to generate its own bnAbs.

Key Resources

- AVAC: www.avac.org/vaccines
- Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery (CHAVI-ID)
 - At Duke: www.chavi-id-duke.org
 - At Scripps: www.cavi-id.org
- Collaboration for AIDS Vaccine Discovery: www.cavd.org
- European AIDS Vaccine Initiative (EAVI 2020): www.eavi2020.eu
- European HIV Vaccine Alliance (EHVA): www.ehv-a.eu
- Global HIV Vaccine Enterprise: <https://www.iasociety.org/Global-HIV-Vaccine-Enterprise>
- HIV Px R&D Database (PxRD): <http://www.avac.org/pxrd>
- HIV Vaccines & Microbicides Resource Tracking Working Group: www.hivresourcetracking.org
- HIV Vaccine Trials Network (HVTN): www.hvtn.org
- International AIDS Vaccine Initiative (IAVI): www.iavi.org
- NIAID: www.niaid.nih.gov/topics/hivaids/research/vaccines/Pages/default.aspx

با سپاس از توجه شما

