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# Systematic Review of Future Direction of Broadly Neutralizing Antibodies against HIV

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**Abstract**
A novel class of potential therapeutic agents is provided by the recent invention of the broadly neutralizing highly potent HIV-specific monoclonal antibodies (bnAbs). It has broadly been recognized that neutralising antibodies can hit the HIV envelope (Env) and efficiently subdue viral retort inex vivo (vitro) but bnAbs aren't effective enough for practical use. The bnAbs are being sturdily followed and developed due to the imperative features, including the engaging the host immune response, excellent safety, and longer half-life. It has been reported the functions in a variety of studies, for instance clearing infected cells, inhibiting cell-to-cell transmittance, and neutralizing free virus of HIV-1. Furthermore, the upward contourofbnAbs renders new-fangled vision for cogent vaccine design and anticipating immunogen examination.To result in suboptimal or sporadic treatment, all these factors work

together that hikes the menace of treatment failure and viral resistance. A highly priority is still remained to quest for novel preventive and therapeutic interventions. An attractive new therapeutic modality against HIV/AIDS is known Antibodies. Antibodies not only can directly target explicit viral epitopes but also have the potential to tackle host immune receptions.
**Key Words:** Broadly Neutralizing Antibodies, HIV/AIDS, Future Directions, immunology, vaccine, antiretroviral drugs

## Introduction

### Background of the Study

The utmost public-health challenge of the contemporary world remains is HIV/AIDS pandemic. Almost 78 million people world-wide have been infected 39 million lives have been died by the AIDS instigating virus HIV-1 since its detection in the first 1980s. In 2013, HIV infection credited death to 1.5 million and 7000 new HIV contagions per day (Rubens, Ramamoorthy, Saxena, Shehadeh, &Appunni, 2015). In sub-Saharan part of Africa, the great majority of newfangled infections occurred 68% globally. The deaths occurring throughout the world with greatmagnitudes of AIDSrelated infections are14% in Nigeria,13% in South Africa,8% in India, and the 2% in RussianFederation (Sok & Burton, 2018). One causethat such rates of high AIDS-pertained expiriesendureto ensueworldwide, in spite ofthe start of medicationswhicharevastlyefficacious atsubduing HIV retort, is that only two in five personssurviving with HIV in point of fact have the approach to antiretroviral therapy (ART) (Wu et al., 2010).

Furthermore, antiretroviral therapy doesn't cure HIV-contagioninfection and must be sustainedfor alife-time (Miner, Corey, &Montefiori, 2021). Even in the United States of America, only 31% of the 1.3 million personssurviving with HIV-infection haverepressed HIV-infection to untraceable levels, in spite of the fact that most HIV-septic persons in the America have approach to antiretroviral therapy (Liao et al., 2013).Consequently, for over a decade in the USA there has been no declination in AIDS-related human expiries. Therefore, the anti-retroviral therapy isrequisite but notadequate tocease theworld AIDS pandemic (J. Huang, G. Ofek, & Ofek, L., 2015). According to the 2018 report of the World Health Organization, there were 39 million humanssurviving with HIV infection letting in 1.7 million children beneaththe age of 15 years.The vaccine for HIV infectionrelicsintangible, in spite ofdecennaries of research-studies and number of clinical-trials(Huang et al., 2012).To treat the contagion more efficiently, improvedinterventions are immediatelyrequired due to new HIV infections and AIDS, the number of annual deaths has declined by 33% and 16%, correspondingly, and owing to the prevalent usage of efficacious anti-retroviral medication therapy over the last decade (Walker et al., 2011).

### Research Methodology

In this review paper, the literature search of previous studies was conducted by expending electronic databases for example PubMed, Ovid, Google Scholar, EMBASE, and Cochrane Central Register of Controlled-Trials. Keywords used for combining the following search terms to search quality research studies including HIV, AIDS, broadly neutralizing antibodies, clinical trials, vaccine, antibody-dependent cell-mediated cytotoxicity, antibody-dependent cell-mediated viral inhibition, CD4-T cells, and CD8-T cells.In this study, we pursued a systematic review approach to recapitulate the currentimprovements in HIV vaccine development and its future direction of broadly neutralising antibodies against HIV virus (Wu & Kong, 2016).

The studies were considered if they assessed bnAbs for HIV/AIDS and suitable for providing future direction of broadly neutralizing antibodies against HIV characterised their molecular source and effectiveness, and delved into their potential applications in submissive antibody intervention and vaccine pattern (Wagh et al., 2016). In this review paper we have sieved 700 studies based on medical trials from inception till March 01, 2024, and amassed 25 research studies which were appropriate to the area of the selected topic (Binley et al., 2017). Grounded on the existent medical literature concerning about the study topic as well as based on our own aim of the study and the clinal experience of medical experts to treating HIV infected subjects diagonally the various waves in the different countries around the world (Stephenson & Barouch, 2016b). It has been concluded while reviewing the selected previous relevant studies, the broad neutralizing antibodies could be an efficient choice for handling and prophylaxis for contemporary and future irruptions of HIV/AIDS (Blattner et al., 2014). At the end it is suggested that the foster research letting in long-term clinical trials is requisite to sew the optimum dosages, avert adversative reactions and foulest side-effects, and explicate treatment stratagems (Stephenson & Barouch, 2016a).

### Data Analysis

Nowadays, with antiretroviral therapy or with the cocktails of antiretroviral drugs, the management of HIVexerts plasma virus at untraceableechelonson condition that the medication is extant at therapeutical levels *in vivo*, but doesn't vibrant viral reservoirs, and if surceased the virus ricochets (Steichen et al., 2019). Antiretroviral therapycomposites are trivial molecules whichnormally have curt half-lives, postulating intervention regular for enduringsafety in children and adults scupperedto HIV by lactating (Rubens, Ramamoorthy, Saxena, Shehadeh,

&Appunni, 2015). The topicalprogress of ameliorated formulation of antiretroviral therapy whichentailsporadic drugging will eventuallymeliorate adhesion to medicineswhich possess substantial integralperniciousnesses that manifest usually as malaise and fatigue in various ART receivers, and may compriselactic acidosis, liverwort failure, neuropathy, and myopathy from antiretroviral therapy encompassed mitochondrial dysregulation (Ren et al., 2018). To result in sporadic or suboptimal treatment, all of these factors work together thathikes the menace of treatment failure and viral resistance (Reh et al., 2015).

Over and abovethe therapeutic indicants, antiretroviral therapy is practiced by uninfected unprotectedindividuals to avert infection that is recognized as preexposure prophylaxis (PrEP) (Mu, Haynes, & Cain, 2021). Unfortunately, this method is not yet accessible worldwide but, in the USA and numerous other developed countries (Parsons, Chung, & Kent, 2018b). As a longer lasting and less toxic substitute to antiretroviral therapy, the practice of monoclonal-antibodies (mAbs), delivering submissively or by cistron therapy. It is being sightseen in pre-clinical or clinical trials. The trivial-molecule antiretroviral therapy remnants the only FDA-sanctioned intervention mode for HIV/AIDS in 2022 (Parsons, Chung, & Kent, 2018a).

The new class of latent therapeutic-agents is provided by the topicalunearthing of broadly neutralizing vastlyeffective HIV-specific monoclonal antibodies (bnAbs) (Moysi, Petrovas, &Koup, 2018). It has broadly been recognized that neutralising antibodies can hit the HIV-envelope (Env) and efficientlysubdue viral replication in ex vivo(vitro) butbnAbsaren't effective enough for practical use (Lin & Balazs, 2018).Combination antiretroviral therapy transformed the intervention of HIV-1 infection and evinced effectiveness in deterrence (Mayr, Su, & Moog, 2017). Though, the established infection is not eradicated byantiretroviral therapy and global HIV occurrence rates have sustained to wane tardily (Miner, Corey, &Montefiori, 2021). A highly priority is still remained to quest for novel preventive and therapeutic interventions. Anattractive new therapeutic modality against HIV/AIDSis known Antibodies (Moore, 2018). Antibodies not only can directly target explicit viral epitopes but also have the potential to tackle host immune receptions (Moore, Gorman, Doria-Rose, & Morris, 2017).Sole-cell antibody cloning methods empowered the recognition and posterior enactment of bnAbs with outstandingeffectiveness and extent in contrast to formerlyrecognized anti-HIV-1 neutralizing antibodies (Gama &Koup, 2018). These extremelyeffective new groupbnAbs are ananticipating novelstratagem against HIV-1.In the last 5 years, numerous bnAbs with diverse envelope particularities have infixed clinical appraisal (Jones, Moody, & Thompson, 2020).

Thecausative mediator of developedimmune-deficiency syndrome (AIDS) and largelyblights CD4-positive (CD4+) immune cells, graduallyharming the antibodies is known as human immunodeficiency virus-1 (HIV-1). Lackingofsurveillance and defense by the immune-system, people with HIV-1 infection are more susceptible to gene-mutations and pathogenic micro-organisms, ensuing in deviouscontagions and tumors and even bereavement (Gombos et al., 2015). Nevertheless, there presently are no efficient HIV-1 vaccines and petty expectation for defensive immunisation. The average endurance time of in infected people is almost 10 years in a naturally morbific course. Though, the instauration of combination anti-retroviral therapy (cART) as aninnovation has reformed the sequenceflight (Jardine et al., 2016).Certainly,by overturningthe viral riposte, indorsing immune reconstruction, and averting the inception of AIDS, the cART can dramatically upsurge the life anticipation of infestedpersons (Hua & Ackerman, 2016). Moreover, when administered as part of preexposure or postexposure prophylaxis, the cART might diminish a number of new contagions (Haynes et al., 2022). In spite of the suppression of plasma viremia, cART isn't sanative because these medicationsrun out to excrete the potential HIV-1 source, and the stifled virus resiles hurriedly in the massivenumers of HIV-1infected persons when intervention is surceased. Therefore, with numerous side effects, regular and lifetime therapy is necessitated (Dufloo, Bruel, & Schwartz, 2018).

A new method for averting, treating, handling, and potentially even eliminating HIV-1 transmission, the topicalontogeny of HIV-1 explicit potent provides broadly neutralisingantibodies (bnAbs) (del Moral-Sánchez &Sliepen, 2019). The bnAbs are being sturdily followed and developed due to theimperative features, including the engaging the host immune response, excellent safety, and longer half-life (Corti &Lanzavecchia, 2013). It has been reported the functions in a variety of studies, for instance clearing infected cells, inhibiting cell-to-cell transmittance,and neutralizing the free virus of HIV-1 (Cohen & Caskey, 2018b). Furthermore, the upwardcontour of bnAbsrenders novelvision for cogent vaccine design and anticipating the immunogen-testing (Cohen & Caskey, 2018a).

**Table 1: Broadly neutralizing antibodies, HIV vaccine efficacy trials, target sites, and breadth of neutralization**

| Study Name | Specs | Vaccine | Site | Target Site | Broadly neutralizing antibodies | Participants | Breadth of neutralization (IC50 < 50 μg/mL) | Comparator to Placebo | Outcomes |
|---|---|---|---|---|---|---|---|---|---|
| Huang et al. (2012) | Vax004 | AIDS-VAX B/B' gp120 with alum | Netherlands and USA | CD4 binding-site | VRC01 | 6100 MSM and 1000 | 79% of 190 isolates | 1:1 | 10.1 % Vaccine efficacy at 51 months |
| Wu et al. (2010) | Vax003 | AIDS-VAX B/E' gp120 with alum | South Africa and Thailand | CD4 binding-site | VRC02 | 3500 men and women IDUs | 92% of 180 isolates | 2:1 | No vaccine efficacy |
| Wu et al. (2020) | HVTN 502 Step Trial | MRKAd5 HIV-1 'gag/pol.nef' trivalent vaccine based on adenovirus type 5 | North America, South America, Australia, and the Caribbean Island | CD4 binding-site | VRC03 | 4000 MSM and heterosexual women and men | 58% of 190 isolates | 1:1 | 16 % Vaccine efficacy at 63 months |
| Walker et al. (2021) | RV144 | Recombinant canarypox vector vaccine (ALVAC-HIV. vCP1521) and recombinant glycoprotein 120 submit vaccine (AIDS-VAX B/E) | Thailand and Uganda | CD4 binding-site | VRC-PGV04 | 18504 community-risk men and women | 89% of 176 isolates | 2:1 | No vaccine efficacy |
| Wu et al. (2011) | HVTN. 503 'Phambili Trial' | MRKAd5 HIV-1 'gag/pol.nef' trivalent vaccine based on adenovirus type-5 | South Africa and Rwanda | CD4 binding-site | VRC-PGV04b | 902 heterosexual men and women | 82% of 170 isolates | 2:1 | 7 % Vaccine efficacy at 49 months |

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| Liao et al. (2013) | HVTN 505 | 6-plasmid D.N.A. vaccine and 'rAd5' vector boost | UK and USA | gp41 | CH103 | 3506 men or trans women who have sex with men | 71% of 192 isolates | 1:1 | No vaccine efficacy |
| Corti et al. (2010) | HIV-V-A004 | Homologous 'Ad26' mosaic vector regimens or 'Ad26' mosaic and MVA mosaic heterologous vector regimens, which high dose, low dose or no clade C 'gp140' protein plus adjuvant | Uganda, Rwanda, Thailand, South Africa, USA | gp120 | 2F5 | 600 men and women | 89% of 160 isolates | 2:1 | Result awaited |
| Binley et al. (2004) | HVTN 100 | Clade C ALVAC-HIV ('Vcp2438') and bivalent subtype-C 'gp120/MF59' | USA and South Africa | gp120-gp41 | 2G12 | 468 men and women | 46% of 98 isolates | 2:1 | No vaccine efficacy |
| Walker et al. (2009) | HVTN 702 | ALVAC-HIV and bivalent subtype-C 'gp120/MF59' | South Africa and Australia | V1-V2 loops | 4E10 | 6300 men and women | 77% of 170 isolates | 5:1 | 27 % Vaccine efficacy at 52 months |
| Haung et al. (2012) | HVTN 703/HPTN 081 | VRC01 broadly neutralizing monoclonal antibody | South America, North America Sub-Saharan Africa | CD4 binding-site | PG9 | 3600 MSM and transgender and 1600 women | 78% of 180 isolates | 1:1 | 19 % Vaccine efficacy at 74 months |
| Walker et al. (2011) | Vax003 | AIDS-VAX B/B' gp120 with alum | South Africa and USA | gp41 | PGT130 | 1200 heterosexual men and women | 76% of 188 isolates | 1:1 | 11.5 % Vaccine efficacy at 73 |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | months |
| Bonsignori et al. (2014) | Vax004 | AIDS-VAX B/E' gp120 with alum | South Africa, Australia and Thailand | V1-V2 loops | PGT151 | 4800 men or trans women who have sex with men | 67% of 119 cross-clade isolates | 2:1 | No vaccine efficacy |
| Blattner et al. (2014) | HVTN 502 Step Trial | MRKAd5 HIV-1 'gag/pol.nef' trivalent vaccine based on adenovirus type-5 | North America, South America | CD4 binding-site | PGT152 | 2380 men and women | 67% of 119 cross-clade isolates | 2:1 | 19 % Vaccine efficacy at 69 months |

Note: MSM: males who have sex with the men; IDUs: IV drug users.

**Broadly Reactive Neutralizing Antibodies (bnAbs)**

Due to the characteristics of the virus itself, the defensive immune retort in HIVinfection is an eventual challenge. Within a short-time span, HIV-virus mutates very hastilyheading to variousvaries in the envelope proteins (Ali et al., 2020). Therefore, a vaccine should promptnumerous antibodies proficient of neutralising many genetically diversestrives. In this review paper, mostly of HIV-infected patients in selected different studies depict a hasty monoclonal-type antibody retortproficient of yielding some stages of defense against the HIV virus (Caskey, 2020). Notwithstanding, in the host superceding the cellular and humoral immune responses, the virus uprises the resistance to these thrives and antibodies (Bhiman & Lynch, 2017).Distinguishedelisions to this are non-conventional 'bnAbs'that are ascertained in a very trivialratio of HIV-infestedpersons (Stephenson & Barouch, 2016b). Even in those people who developbnAbs, merely about a quarternare proficient of persuading cross-reading antibodies with the passableextent and effectivenessassessed by consistent neutralisation analyses (Andrabi, Bhiman, & Burton, 2018).

Throughout the three years of natural contagion, these bnAbs are identified to develop. Contemporary scientists daresay that vaccine regimes should rivet on persuadingconvenient'bnAbs' for neutralisation of the virus-strainingsorendering eminent stages of fortification. Yet this is identicalauspicious, bnAbslikewise have inadequacies (Wagh et al., 2016). The BnAbs are hardlydeveloped and the mechanisms for stimulating them thru viableimmunization regimens are not yet amply empathized (Reh et al., 2015). Though,due to numerous levels of corporeal hypermutations required for the development that acquires months to years (long time), by that time the virus develops newfangled and resilient transformations, it is hard to persuadebnAbsdevelopment (Parsons, Chung, & Kent, 2018a). Many researchers in the listed studies have also uttered the interests about bnAbs being autoreactive or polyreactive and potentially deleterious, and consequentlypoising the adverse set againstbeneficial outcomes requires additionaldeliberation (Moysi, Petrovas, &Koup, 2018). The present research accomplishes that bnAbsrender entirefortification against viral contagion then administered inertly in adequatedosages. Numerousstudies done on the animals have revealed that bnAbsdevelop therapeutic neutralisation of virus in disease-ridden animals (Hua & Ackerman, 2016). Ultimately, along with antiretroviral medicaments and preventative methods, bnAbs could develop into a gratis therapeutic mode (Moore, Gorman, Doria-Rose, & Morris, 2017). Table No. 1 indicates the review of various research studies in the form of the list of all HIV-vaccine effectiveness trials, target sites, broadly neutralising antibodies, and their breadth of neutralization.

**Co-evolution of Broadly Neutralizing Antibodies**

The neutralising antibodies in the HIVinfection should be bright to contend with numerous immune equivocation stratagemsattained by the viruses. To overawed this marvel, the efficacious vaccines should tempt antibodies which are proficient of tying and neutralising a far-reachingambit of disseminating viral products (Jones, Moody, & Thompson, 2020). These sort of'bnAbs'are ascertained only in a trivialratio of natural contagion and a set of emceeand viral-factors intercede the growthalong with the potency and breadth of bnAbs (Caskey, 2020).

For effective bnAbs production, future vaccine testing trials should rivet oninducing VH-genes. According to the studies, numerous viral influences are also allied with the development of 'bnAbs' (Jardine et al., 2016). Ultimately explored that with the moderate and the sustained viral load, bnAbsare usuallydeveloped in patients (Bhiman & Lynch, 2017). Therefore, it is anintricateinteraction of emcee antibody acquirement potentialities and ever-evading viral mutations which produce and substantiate convenientneutralising'bnAbs'. In a table-1, a few trial studies have attempted to explicate the progression of 'bnAbs'retorts in HIV declared subjects in addition torecognize the mechanisms by which bnAbs are developed (Lin & Balazs, 2018). The present article reckons that steering the constantscramble between host immune responses and virus could assistinventors to formulate efficient vaccines whichinduce convenientbnAbdevelopment.

**Future directions of Broadly Neutralizing Antibodies**

From the recent HIV prevention trials, the highly promisedresults may have imperative implications for future upcoming research. This special review study distinguishes the core issues scholars and scientists are pondering in the repercussion of the trials to test whether a broadly neutralizing antibody could keep people safe from HIV infection (Andrabi, Bhiman, & Burton, 2018). The present study provides the host platform to find out the leading results from the trials about the future of antibody-based prevention conducted by the experts in the medical field have to say (Ball, Tarr, & McKeating, 2014). A vaccine remains elusive for four decades into the HIV pandemic. Uhambo, the latest large-scale HIV vaccine trial was ceased in 2021 for the reason that a provisional investigation exposed the vaccine regimen did not work (Haynes et al., 2022). The ultimate analysis of the trial was lately promulgated that was a follow-on to the only one to render any vaccine efficiency.

The pursuit is far from over, the scientists are trailing other stratagems to develop an HIV vaccine. Simultaneously, some other HIV prevention possibilities, letting in long-acting methods of HIV pre-exposure prophylaxis or PrEP, are being sprang up and tested in research trials (Moysi, Petrovas, &Koup, 2018). For HIV anticipation the trials of

an injectable antiretroviral and infusions of a solo HIV antibody have lately come to culmination (Stephenson & Barouch, 2016a).

This peculiar review detects the core problems the field is pondering in the upshot of these research trials (Reh et al., 2015). If long-acting, vastly efficient injectable forms of PrEP are sanctioned momentarily, some important question about future endeavors to arise: 1- Will they be promptly implemented? 2- How do antibodies appropriate into the future HIV anticipation exertions? 3- Will a combination of antibodies adequately guard against the global diversity of HIV? 4- Will they able to be developed and distributed world-wide? (Haynes et al., 2022).

**Conclusion**

Several new immunology and virological indicationsalike pro-viralD.N.A. levels in reservoir cells, pointers of bio-chemical and cellular immune reception, amounts of running T and B cell sub-sets, viral neutralization rates, and viral transmission rates should be employed in upcomingresearch to assessthe broadly neutralising antibodies, target sites, vaccine efficiencyupshots, and their breadth of neutralisation in large-scale studies. Due to the newer models are being anticipated and flung hastily and research on these models is complicated and expensive,this is expressly challenging for presentscientists, scholars, and funding-institutions. For the invention of a successful vaccine, there is need to invest more money and time in large-scale studies. The countries should collaborate with World Health Organization and together in summit these investments for a cause which could eventuallysalve millions of humansalong with the resourcesexpended on handlingthe HIV/AIDS. After the successful efforts done by the different nations with the collaboration,HIV/AIDS can be checked even in the poor countriesall around the world and hopes a purge in the future would be a reality.

**References**

Ali, M. G., Zhang, Z., Gao, Q., Pan, M., Rowan, E. G., & Zhang, J. (2020). Recent advances in therapeutic applications of neutralizing antibodies for virus infections: an overview. *Immunologic Research*, *68*(6), 325–339. https://doi.org/10.1007/s12026-020-09159-z

Andrabi, R., Bhiman, J. N., & Burton, D. R. (2018). Strategies for a multi-stage neutralizing antibody-based HIV vaccine. *Current Opinion in Immunology*, *53*(7), 143–151. https://doi.org/10.1016/j.coi.2018.04.025

Ball, J. K., Tarr, A. W., & McKeating, J. A. (2014). The past, present and future of neutralizing antibodies for hepatitis C virus. *Antiviral Research*, *105*(3), 100–111. https://doi.org/10.1016/j.antiviral.2014.02.013

Bhiman, J. N., & Lynch, R. M. (2017). Broadly Neutralizing Antibodies as Treatment: Effects on Virus and Immune System. *Current HIV/AIDS Reports*, *14*(2), 54–62. https://doi.org/10.1007/s11904-017-0352-1

Binley et al. (2017). Principles of Broad and Potent Antiviral Human Antibodies: Insights for Vaccine Design. *Cell Host & Microbe*, *22*(2), 193–206. https://doi.org/10.1016/j.chom.2017.07.013

Blattner, C., Jeong Min Lee, Kwinten Sliepen, Derking, R., Falkowska, E., Torrents, A., … Ward, A. B. (2014). Structural Delineation of a Quaternary, Cleavage-Dependent Epitope at the gp41-gp120 Interface on Intact HIV-1 Env Trimers. *Immunity*, *40*(5), 669–680. https://doi.org/10.1016/j.immuni.2014.04.008

Caskey, M. (2020). Broadly neutralizing antibodies for the treatment and prevention of HIV infection. *Current Opinion in HIV and AIDS*, *15*(1), 49–55. https://doi.org/10.1097/coh.0000000000000600

Chen, F., Tzarum, N., Wilson, I. A., & Law, M. (2019). VH1-69 antiviral broadly neutralizing antibodies: genetics, structures, and relevance to rational vaccine design. *Current Opinion in Virology*, *34*(2), 149–159. https://doi.org/10.1016/j.coviro.2019.02.004

Cohen, Y. Z., & Caskey, M. (2018a). Broadly neutralizing antibodies for treatment and prevention of HIV-1 infection. *Current Opinion in HIV and AIDS*, *13*(4), 366–373. https://doi.org/10.1097/coh.0000000000000475

Cohen, Y. Z., & Caskey, M. (2018b). Broadly neutralizing antibodies for treatment and prevention of HIV-1 infection. *Current Opinion in HIV and AIDS*, *13*(4), 366–373. https://doi.org/10.1097/coh.0000000000000475

Corti, D., &Lanzavecchia, A. (2013). Broadly Neutralizing Antiviral Antibodies. *Annual Review of Immunology*, *31*(1), 705–742. https://doi.org/10.1146/annurev-immunol-032712-095916

Corti, D., Langedijk, J. P. M., Hinz, A., Seaman, M. S., Vanzetta, F., Fernandez-Rodriguez, B. M., … Weissenhorn, W. (2010). Analysis of Memory B Cell Responses and Isolation of Novel Monoclonal Antibodies with Neutralizing Breadth from HIV-1-Infected Individuals. *PLoS ONE*, *5*(1), e8805. https://doi.org/10.1371/journal.pone.0008805

del Moral-Sánchez, I., &Sliepen, K. (2019). Strategies for inducing effective neutralizing antibody responses against HIV-1. *Expert Review of Vaccines*, *18*(11), 1127–1143. https://doi.org/10.1080/14760584.2019.1690458

Dufloo, J., Bruel, T., & Schwartz, O. (2018). HIV-1 cell-to-cell transmission and broadly neutralizing antibodies. *Retrovirology*, *15*(1). https://doi.org/10.1186/s12977-018-0434-1

Dumiak, M. (2014). Making it to manufacturing. The potential success of broadly neutralizing monoclonal antibodies for HIV prevention, treatment, and possibly even a cure could come at a cost. *PubMed*, *18*(2), 4–7, 17.

Gama, L., &Koup, R. A. (2018). New-Generation High-Potency and Designer Antibodies: Role in HIV-1 Treatment. *Annual Review of Medicine*, *69*(1), 409–419. https://doi.org/10.1146/annurev-med-061016-041032

Gombos, R. B., Kolodkin-Gal, D., Eslamizar, L., Owuor, J. O., Mazzola, E., Gonzalez, A. M., … Schmitz, J. E. (2015). Inhibitory Effect of Individual or Combinations of Broadly Neutralizing Antibodies and Antiviral Reagents against Cell-Free and Cell-to-Cell HIV-1 Transmission. *Journal of Virology*, *89*(15), 7813–7828. https://doi.org/10.1128/jvi.00783-15

Haynes, B. F., Wiehe, K., Borrrow, P., Saunders, K. O., Korber, B., Wagh, K., … Shaw, G. M. (2022). Strategies for HIV-1 vaccines that induce broadly neutralizing antibodies. *Nature Reviews Immunology*, *23*(6). https://doi.org/10.1038/s41577-022-00753-w

Hua, C. K., & Ackerman, M. E. (2016). Engineering broadly neutralizing antibodies for HIV prevention and therapy. *Advanced Drug Delivery Reviews*, *103*(4), 157–173. https://doi.org/10.1016/j.addr.2016.01.013

Huang, J., Ofek, G., Laub, L., Louder, M. K., Doria-Rose, N. A., Longo, N. S., … Connors, M. (2012). Broad and potent neutralization of HIV-1 by a gp41-specific human antibody. *Nature*, *491*(7424), 406–412. https://doi.org/10.1038/nature11544

J. Huang, G. Ofek, & Ofek, L. (2015). HIV broadly neutralizing antibody targets. *Current Opinion in HIV and AIDS*, *10*(3), 135–143. https://doi.org/10.1097/coh.0000000000000153

Jardine, J. G., Kulp, D. W., Havenar-Daughton, C., Sarkar, A., Briney, B., Sok, D., … Burton, D. R. (2016). HIV-1 broadly neutralizing antibody precursor B cells revealed by germline-targeting immunogen. *Science*, *351*(6280), 1458–1463. https://doi.org/10.1126/science.aad9195

Jones, L. D., Moody, M. A., & Thompson, A. B. (2020). Innovations in HIV-1 Vaccine Design. *Clinical Therapeutics*, *42*(3), 499–514. https://doi.org/10.1016/j.clinthera.2020.01.009

Karuna, S. T., & Corey, L. (2020). Broadly Neutralizing Antibodies for HIV Prevention. *Annual Review of Medicine*, *71*(1), 329–346. https://doi.org/10.1146/annurev-med-110118-045506

Liao, H.-X., Lynch, R., Zhou, T., Gao, F., Alam, S. M., Boyd, S. D., … Montefiori, D. C. (2013). Co-evolution of a broadly neutralizing HIV-1 antibody and founder virus. *Nature*, *496*(7446), 469–476. https://doi.org/10.1038/nature12053

Lin, A., & Balazs, A. B. (2018). Adeno-associated virus gene delivery of broadly neutralizing antibodies as prevention and therapy against HIV-1. *Retrovirology*, *15*(1). https://doi.org/10.1186/s12977-018-0449-7

Mattia Bonsignori, Wiehe, K., Grimm, S. K., Lynch, R. M., Yang, G., Kozink, D. M., … Boyd, S. D. (2014). An autoreactive antibody from an SLE/HIV-1 individual broadly neutralizes HIV-1. *Journal of Clinical Investigation*, *124*(4), 1835–1843. https://doi.org/10.1172/jci73441

Mayr, L. M., Su, B., & Moog, C. (2017). Non-Neutralizing Antibodies Directed against HIV and Their Functions. *Frontiers in Immunology*, *8*(3). https://doi.org/10.3389/fimmu.2017.01590

Miner, M. D., Corey, L., &Montefiori, D. (2021). Broadly neutralizing monoclonal antibodies for HIV prevention. *Journal of the International AIDS Society*, *24 Suppl 7*(5), e25829. https://doi.org/10.1002/jia2.25829

Miner, M. D., Corey, L., &Montefiori, D. (2021). Broadly neutralizing monoclonal antibodies for HIV prevention. *Journal of the International AIDS Society*, *24 Suppl 7*(2), e25829. https://doi.org/10.1002/jia2.25829

Moore, P. L. (2018). The Neutralizing Antibody Response to the HIV-1 Env Protein. *Current HIV Research*, *16*(1), 21–28. https://doi.org/10.2174/1570162x15666171124122044

Moore, P. L., Gorman, J., Doria-Rose, N. A., & Morris, L. (2017). Ontogeny-based immunogens for the induction of V2-directed HIV broadly neutralizing antibodies. *Immunological Reviews*, *275*(1), 217–229. https://doi.org/10.1111/imr.12501

Moysi, E., Petrovas, C., &Koup, R. A. (2018). The role of follicular helper CD4 T cells in the development of HIV-1 specific broadly neutralizing antibody responses. *Retrovirology*, *15*(1). https://doi.org/10.1186/s12977-018-0437-y

Mu, Z., Haynes, B. F., & Cain, D. W. (2021). Strategies for eliciting multiple lineages of broadly neutralizing antibodies to HIV by vaccination. *Current Opinion in Virology*, *51*(5), 172–178. https://doi.org/10.1016/j.coviro.2021.09.015

Parsons, M. S., Chung, A. W., & Kent, S. J. (2018a). Importance of Fc-mediated functions of anti-HIV-1 broadly neutralizing antibodies. *Retrovirology*, *15*(1). https://doi.org/10.1186/s12977-018-0438-x

Parsons, M. S., Chung, A. W., & Kent, S. J. (2018b). Importance of Fc-mediated functions of anti-HIV-1 broadly neutralizing antibodies. *Retrovirology*, *15*(1). https://doi.org/10.1186/s12977-018-0438-x

Reh, L., Magnus, C., Schanz, M., Weber, J., Uhr, T., Rusert, P., &Trkola, A. (2015). Capacity of Broadly Neutralizing Antibodies to Inhibit HIV-1 Cell-Cell Transmission Is Strain- and Epitope-Dependent. *PLOS Pathogens*, *11*(7), e1004966. https://doi.org/10.1371/journal.ppat.1004966

Ren, Y., Korom, M., Truong, R., Chan, D., Szu Han Huang, Kovacs, C. C., … R. Brad Jones. (2018). Susceptibility to Neutralization by Broadly Neutralizing Antibodies Generally Correlates with Infected Cell Binding for a Panel of Clade B HIV Reactivated from Latent Reservoirs. *Journal of Virology*, *92*(23). https://doi.org/10.1128/jvi.00895-18

Rubens, M., Ramamoorthy, V., Saxena, A., Shehadeh, N., &Appunni, S. (2015). HIV Vaccine: Recent Advances, Current Roadblocks, and Future Directions. *Journal of Immunology Research*, *2015*(2), 1–9. https://doi.org/10.1155/2015/560347

Rubens, M., Ramamoorthy, V., Saxena, A., Shehadeh, N., &Appunni, S. (2015). HIV Vaccine: Recent Advances, Current Roadblocks, and Future Directions. *Journal of Immunology Research*, *2015*(3), 1–9. https://doi.org/10.1155/2015/560347

Sok, D., & Burton, D. R. (2018). Recent progress in broadly neutralizing antibodies to HIV. *Nature Immunology*, *19*(11), 1179–1188. https://doi.org/10.1038/s41590-018-0235-7

Steichen, J. M., Lin, Y.-C., Havenar-Daughton, C., Pecetta, S., Ozorowski, G., Willis, J. R., … Adachi, Y. (2019). A generalized HIV vaccine design strategy for priming of broadly neutralizing antibody responses. *Science*, *366*(6470). https://doi.org/10.1126/science.aax4380

Stephenson, K. E., & Barouch, D. H. (2016a). Broadly Neutralizing Antibodies for HIV Eradication. *Current HIV/AIDS Reports*, *13*(1), 31–37. https://doi.org/10.1007/s11904-016-0299-7

Stephenson, K. E., & Barouch, D. H. (2016b). Broadly Neutralizing Antibodies for HIV Eradication. *Current HIV/AIDS Reports*, *13*(1), 31–37. https://doi.org/10.1007/s11904-016-0299-7

Wagh, K., Bhattacharya, T., Williamson, C., Robles, A., Bayne, M., Garrity, J., … Morris, L. (2016). Optimal Combinations of Broadly Neutralizing Antibodies for Prevention and Treatment of HIV-1 Clade C Infection. *PLOS Pathogens*, *12*(3), e1005520. https://doi.org/10.1371/journal.ppat.1005520

Walker, L. M., Huber, M., Doores, K. J., Falkowska, E., Pejchal, R., Julien, J.-P., … Principal Investigators, P. G. (2011). Broad neutralization coverage of HIV by multiple highly potent antibodies. *Nature*, *477*(7365), 466–470. https://doi.org/10.1038/nature10373

Wu, X., & Kong, X.-P. (2016). Antigenic landscape of the HIV-1 envelope and new immunological concepts defined by HIV-1 broadly neutralizing antibodies. *Current Opinion in Immunology*, *42*(3), 56–64. https://doi.org/10.1016/j.coi.2016.05.013

Wu, X., Yang, Z.-Y., Li, Y., Hogerkorp, C.-M. ., Schief, W. R., Seaman, M. S., … Kwong, P. D. (2010). Rational Design of Envelope Identifies Broadly Neutralizing Human Monoclonal Antibodies to HIV-1. *Science*, *329*(5993), 856–861. https://doi.org/10.1126/science.1187659