

Research Article

Opinion; Heterologous Prime-Boost as COVID-19 Vaccine Strategies: Towards a Nationwide Implementation

Ibrahim MS Shnawa*

Department of Anesthesia, Hilla University College and Department of Biotechnology College of Biotechnology, University of Qasim, Babylon, Iraq

*Corresponding author: Dr. Ibrahim MS Shnawa, Department of Anesthesia, Hilla University College and Department of Biotechnology College of Biotechnology, University of Qasim, Babylon, Iraq; Tel: 09647800188929

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Abstract

The specific immune priming can be either through immunization or hyper-immunization approach. Priming of mammalian animals models initiate primary immune response events leading to effector cells formation. Boost activates immune cell to be memory immune cells that are involved in the secondary immune response events. Immunization protocols based either on prime, homologous prime-boost and/or heterologous prime-boost strategies. This theme is operable both in mammalian laboratory animals and human beings. Murine, lapin and primates immune system functions are similar but not identical to that of human beings. So far concerning vaccine development and manufacture. On transition from mammalian laboratory animal to man, there may be variations in responses and/or in vaccine adverse effects. Homologous prime-boost is being the classical and traditional strategy in the national and international vaccination schedules of vaccine preventable infectious diseases for human welfare. Heterologous prime boost strategies are being less sounded in vaccine care givers and in health professional communities. Day by day current trials all over the world were conducted to uncover the validity of use of heterologous prime-boost in mass vaccination of COVID-19. Workers reached one of three conclusions as; i) it reactivate immunogenicity, reactogenicity and/or efficacy ii-Are of comparable efficacy and iii) Preference advise to apply it for mass vaccination of COVID-19. International authority recommendation in this concern is still not in hand. Though, there were few published human volunteer trails for heterologous COVID-19 vaccine strategies.

Keywords: Animal, Boost, COVID-19, Homologous, Heterologous, Prime, Vaccine

Introduction

From the down of COVID-19 till date, the pandemic is circulating, vaccine developed and emergency licensing obtained for few vaccines and vaccine adverse effects were being currently reported in vaccine all over the world. COVID-19 pan mass vaccinations pose to a number of interesting and fascinating topics among which the theme of heterologous prime-boost validity in combating the burden of the sars-cov-2 infections especially those concerning the newly rising variants [1-3]. The objective of the present opinion was to shed a light on the current experimental Coid-19 vaccine designs and vaccine strategies for the application of heterologous prime-boost theme across the globe.

Prime-Boost Theme

In any immunization protocol or schedule, the first applied vaccine shot is known as prime shot, while the following vaccine shots term as booster or boosting shots. The time period between the prime and boost shots depends onto; nature of the vaccine, nature of the receiving immune system, vaccine dose, rout of the proper administration and cautions of the manufacturer. Booster shot induce; memory B cell, memory T cell and both of the memory cells to produce mediator as that for B the antibodies and that of T the cytokines [4,5].

Mammals and Vaccine Development

Small mammalian laboratory animals are eligible for the vaccine laboratory development phase of a newly invented or known vaccines to determine; safety, identity, immunogenicity and efficacy. Efficacy in this case measured from live vaccine challenge model through calculation of morbidity and mortality rate among vaccinated and non-vaccinated test animals. Large primate animals can serve for the preclinical development of a vaccine but mostly used for clinical development of human fetal pathogen as a doublebar similar to man [6,7].

Vaccine Prime-Boost in Mammals

Vaccine prime-boost theme is operable both in mammals and man. When a boost shot is of an identical vaccine nature to the prime shot. The schedule is known as homologous prime boost. While when the boosting vaccine shot is for the same pathogen but using different vaccine design and/or different strategies the protocol is termed heterologous prime-boost [5-8].

Mammals-Human Immune Simlulatin

Mammalian immune system is rather similar but not identical to the human immune system. There were found percentages of genetic relatedness between the human genome and genomics and

the genome and genomics for mice, rabbit and chimpanzee [9,10]. Rabbit and chimpanzee are genetically more related to human being than mice in the major aspects of the human immune system. Shnawa [10] report about nine immune models of the lapin immune system that simulate for the human immune system among which the vaccine development models [5,6,10]. Though, on transmission from mammalian immune system models to human immune system, there found differences in the nature of in the immune response, efficacy and in the post vaccination vaccine adverse effects. What so ever the nature of these mammalian immune system differences than that of man they stand as an eligible indispensable developmental tool for human vaccine development due to high genetic and immune simulation percentages.

Prime-Boost Theme and Human Vaccine Preventable Diseases

Almost all of the human licensed vaccination schedules in the national and international vaccine list for vaccine preventable

Table 1: Vaccines recommended for children aged 0-6 years as homologous prime boost.

Bacterial Vaccines	Viral vaccines
Diphtheria toxoid, tetanus toxoid, acellular pertussis	Hepatitis A
Haemophilus influenza type b[Hib]	Hepatitis B
Meningococcal	Influenza
Pneumococcal	Measles, Mumps, rubella, polio inactivate, Rotavirus, Varicella

Source: Adapted from [11].

Table 2: The timeline of heterologous Prime Boost in small mammals and primate.

Date	Vaccine Strategy	Vaccine immunity	Reference
1991	Priming with live recombinant virus, boost with subunit recombinant protein	More effective than either vaccines. It is considered as key principle of heterologous prime boost	16
1991	Prime with recombinant vaccine virus boosted by multiple time with mixture of HIV protein or synthetic peptide	Increase in HIV specific antibodies	17
1992	First trail for Heterologous prime boost in nonhuman primates	Increase In HIV specific antibody, promising and promote HIV vaccine development	18
1999	DNA-viral vector based in nonhuman primates	Good protection. Good inducer to T cell mediated immunity	19
2005-2006	DNA prime-recombinant protein boost with primary HIV Env antigen in nonhuman primates	Increase in HIV specific antibodies	20,21,22
2006	DNA prime-protein boost in nonhuman primates	Proved effective vaccine strategy, provide active sterilizing immune protection	23
2008 2021	DNA prime-protein boost Heterologous prime-boost COVID-19 vaccine strategy in nonhuman primate	High frequency responders, HIV specific Antibodies, functional T cell immune responses Increase in antibody titres Balanced Th1/TH2 cells More CD8+ T cells response	24-26

Table 3: The timeline of heterologous prime boost vaccination strategy in human being.

Date	Vaccine strategy	Vaccine immunity	References
1988	Recombinant vaccine virus HIV coding gene an boosted by recombinant envelope protein	First human done by the author himself by inoculating this vaccine strategy gave reasonable individual immunity	27
2005	Vector prime-Protein boost HIV vaccine strategy	Induce high antibody and high CD* T cells	28
2008	DNA prime-Protein boost HIV vaccine strategy	More significant immunity	21
2016-2019	Ebola heterologous prime-boost vaccine strategy	1a,1b clinical trial in healthy human beings	29,30,31,32
2021	Astrazinicka prime-Pfizer boost COVID-19 heterologous prime boost in human volunteers	Significant rise in antibody titre and T cell reactivity	33
2022	Hetero and homologous COVID-19 vaccine strategies for modrena J&J,Pfizer using 458 participant	Increase of 6to 73 fold in hetero and 4 to 20 folds rise in neutralizing antibodies and durable T cell mediated immunity	34

communicable infectious disease are of homologous-prime boost type and it is common notion among vaccine care giver and health professionals. Heterologous prime-boost theme is not sounded among vaccine care givers and health professionals. On limited scale it has been tried in HIV, Deng, Ebola [and now it is being experimentally in practice for COVID-19 vaccination in more than one country all over the world (Table 1) [11-15].

Heterologous Prime-Boost Time Line

DNA prime-protein boost and/or protein boost DNA boost, vector-protein, protein-vector as well as the mRNA-vector, vector-mRNA vaccine strategies were noticed all-over the timeline of heterologous prime boost vaccine designs both in mammals [16-26] and man [27-34] as depicted in Tables 2 and 3.

Heterologous Prime Boost Strategies and COVID-19 Vaccination

Lessons derived from mass vaccination of COVID-19, showed that the nature of the emergency licensed vaccines and vaccine strategies are of homologous prime-boost nature. Currently, there were reports in more than area across the globe showed that they were tempting heterologous prime boost strategies at an experimental levels. They reached to one of the following conclusions; i) heterologous yield more reactogenicity, more immunogenicity and efficacy than the homologous, ii) homologous and heterologous were of comparable vaccine efficacy and iii) Cautious recommendation for mass vaccination. Strategies tempted for heterologous prime boosts were; i) starting prime boost mono-epitopic followed by multi-epitopic ii)

Table 4: Heterologous, homologous prime –boost versus single vaccine dose in human beings.

Priming Nature	Vaccine design and strategy	Response nature	References
Prime	Astrazinicka	Efficacy up to 76% in day 22 to the day 90 post to single vaccine shot	34
Homologous Prime-boost	Pfizer-Pfizer, Astrazinicks-Astrazinka	Appreciable neutralizing ab rising and CD8+ T cells	35
Heterologous prime-boost	Mix Watch of the above makes	Higher Ab titre 73 fold High CD8+ T cells	35

Table 5: The immune features of heterologous prime boost vaccine strategies in mammal and man.

Recipient Immune System	Immune features	References
Mammals; Mice And nonhuman primates	i) Make use of existing vaccine candidates ii) Produce high long term antibody titres especially the neutralizing antibody iii) Robust germinal center responses iv) Long term T cell responses Balanced TH1/TH2 responses v) High memory CD8+ cells vi) Immunogenic and effective vii) Improve TH1 biased T cell responses viii) Safe, fast and economic	36 37
Human	i) Safe, effective. high systemic reactogenicity ii) Lend profile flexibility for future vaccines	38
Human	iii) Increase in the levels of neutralizing antibodies iv) Provide better protection v) Combine the best characteristic of each vaccine to enhance the immune system vi) Advisable to be used in shortage, emergency, low and middle income countries vii) Heterologous give 6-73 fold rise in neutralizing ab as compared to 4-20 folds in homologous	35,39

multi-epitopic followed by mono-epitopic vaccines using variable time periods, Table 4, between the prime and the booster shots. Till date no evident international health authority recommend frankly heterologous prime-boost theme in mass vaccination of human against COVID-19 [12,13,34,35].

Immune Features of Hetrologous Prime Boost both in Mammal and Man

The immune feature of vaccinated small mammals and non-human primate [36,37] as well as that for human beings [35,38,39] are depicted in Table 5. The similarity appeared to be evident in both of the cases.

Conclusions

Prime and homologous prime-boost vaccine strategies were classically and traditionally known among vaccine care giver and health profession involved in the vaccine community. Heterologous prime-boost, seems to be not known among vaccine workers before 1988. From 1988 onwards to 2022 the scientific community became gradually familiar with the heterologous prime-boost both in; mammals and man. Few current phase I/II human trail using mix and match vaccine strategies for COVID-19, with cautious recommendation for use in low and middle income countries. Though till now international vaccine authority recommendation for mass vaccine implementation concerning heterologous prime boost COVID-19 vaccine strategies is not in hand. Hopes in the coming couple of months or a year, the international vaccine authority be in a position able to license any of experimental and/or the field trail proved heterologous prime boost COVID-19 vaccine strategies.

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