

1 **Neutralization of SARS-CoV-2 VOC 501Y.V2 by human antisera elicited by both**
2 **inactivated BBIBP-CorV and recombinant dimeric RBD ZF2001 vaccines**

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24 **Abstract**

25 Recently, the emerged and rapidly spreading SARS-CoV-2 variant of concern (VOC)
26 501Y.V2 with 10 amino acids in spike protein were found to escape host immunity induced
27 by infection or vaccination. Global concerns have been raised for its potential to affect
28 vaccine efficacy. Here, we evaluated the neutralization activities of two vaccines developed in
29 China against 501Y.V2. One is licensed inactivated vaccine BBIBP-CorV and the other one is
30 recombinant dimeric receptor-binding domain (RBD) vaccine ZF2001. Encouragingly, both
31 vaccines largely preserved neutralizing titres, with slightly reduction, against 501Y.V2
32 authentic virus compare to their titres against both original SARS-CoV-2 and the currently
33 circulating D614G virus. These data indicated that 501Y.V2 variant will not escape the
34 immunity induced by vaccines targeting whole virus or RBD.

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46 **Maintext**

47 The rollout of vaccines is the hope to control the coronavirus disease 2019 (COVID-19)
48 pandemic and reboot economy and society(1). However, the recent emergence of severe acute
49 respiratory syndrome coronavirus-2 (SARS-CoV-2) variants raised global concerns because
50 of their enhanced transmission and potential viral escape of host immunity elicited by natural
51 infection or vaccination. Variants containing D614G mutation in spike (S) protein was first
52 reported from the middle of 2020, which significantly increased the transmission rate and
53 became dominant in circulating strains ever since(2). Evolved from D614G mutants, recent
54 circulating isolates from Republic of South Africa (501Y.V2 variant) introduced further
55 mutations that escape neutralization by COVID-19 convalescent plasma and sera from human
56 receiving licensed mRNA vaccines expressing SARS-CoV-2 S protein(3-5). It also
57 dramatically decreased the protective efficacy for trimeric S protein-based vaccine in phase 3
58 clinical trial in South Africa(6).

59 501Y.V2 variant emerged in more and more countries, and was first isolated in China on
60 January 6, 2021 from an airline pilot of South African nationality(7). This variant, GDPCC
61 strain, contains 10 amino acid mutations sites in S protein corresponded to the features of the
62 variant of concern (VOC) South African 501Y.V2, with 5 (D80A, ΔL242, ΔA243, ΔL244 and
63 R246I) located at N-terminal domain (NTD), 3 (K417N, E484K and N501Y) in

64 receptor-binding domain (RBD) , and the other two in CTD2 domain and S1/S2-S2' region
65 (Fig.1).

66 The effectiveness of current vaccines against this VOC is of high importance to guide the
67 ongoing vaccination program worldwide. To answer this question, we evaluated two
68 representative COVID-19 vaccines developed in China for their neutralizing activities against
69 501Y.V2 variant. One is BBIBP-CorV, a licensed COVID-19 inactivated vaccine(8, 9). The
70 other one is ZF2001, a protein subunit vaccine targeting S protein RBD currently in phase 3
71 clinical trials(10, 11). Both vaccines showed good immunogenic in their clinical trials(9, 11).
72 For instance, ZF2001 induced neutralizing GMTs two times greater than that from
73 convalescent samples(11). We chose 12 serum samples for each vaccine from clinical trial
74 participants covering a range of different neutralizing titers (Table 1). The neutralizing
75 activities of these serum samples against live SARS-CoV-2 strains GDPCC (501Y.V2) were
76 measured by microcytopathogenic effect assay. SARS-CoV-2 strains HB02 (WT) (12, 13) and
77 BJ01 (D614G) (14) were tested as the control. Impressively, all 12 serum samples from either
78 ZF2001 or BBIBP-CorV recipients largely preserved neutralization of 501Y.V2 variant, with
79 slightly reduced geometric mean titres (GMTs) compared with their titres against WT or
80 D614G strain (Fig. 2 and Table 1). For ZF2001, the GMTs declined for 1.6-fold from 106.1
81 (95% CI, 75.0-150.1) to 66.6 (95% CI, 51.0-86.9) (Fig.2A). While for BBIBP-CorV, the
82 decline is also 1.6-fold, GMTs from 110.9(95% CI, 76.7-160.2) to 70.9(95% CI, 50.8-98.8)
83 (Fig.2B). These reductions are significantly less than those reported previously for
84 convalescent plasma (more than 10-folds)(4) or antisera from mRNA vaccine recipients (more

85 than 6-folds) (3, 5).

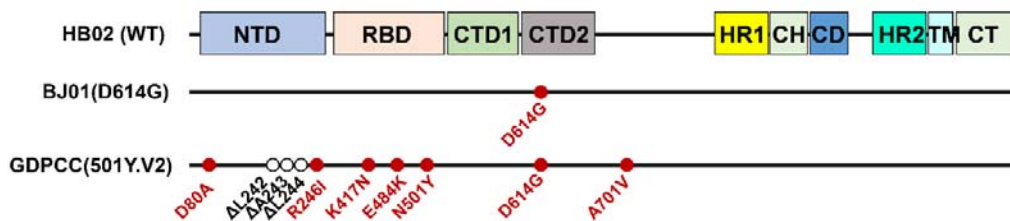
86 These results suggest that the 501Y.V2 variant does not escape the immunity induced by
87 vaccines targeting S protein RBD (ZF2001) or whole virus (BBIBP-CorV). The potential
88 1.6-fold reduction of neutralizing GMTs should be taken into account for its impact for the
89 clinical efficacy of these vaccines. For both vaccines, antisera neutralize both variant 501Y.V2
90 and D614G, the one currently circulating globally, without statistical significances. For
91 ZF2001, a slight significance ($P=0.04$) between variant 501Y.V2 and the HB02 may due to
92 the sample selection and size. For the neutralization-reduction discrepancy between our
93 protein-based vaccine and mRNA vaccine needs further investigation in the future.

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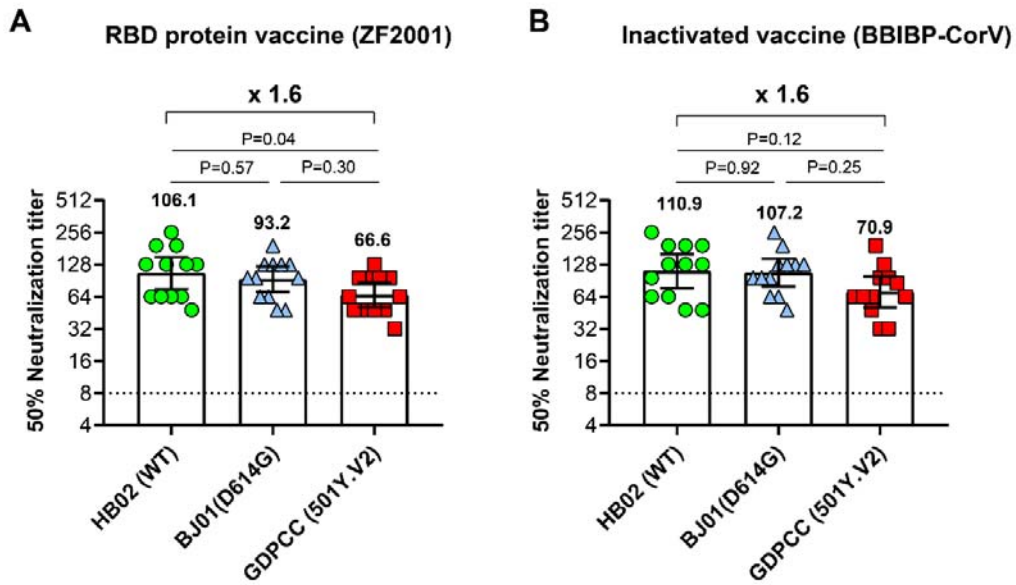


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103 **Fig.1. Schematic demonstration of the spike protein of SARS-CoV-2 HB02 (WT), BJ01**

104 **(D614G) and GDPCC (501Y.V2).** The mutation sites were denoted and marked as cycles,

105 with the point mutation colored in red and the deletion colored in white.



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107 **Fig.2. Neutralization titres of 24 antisera from vaccine BBIBP-CorV or ZF2001**

108 **recipients against authentic SARS-CoV-2 and its variants, D614G and 501Y.V2. (A-B)**

109 N=12 representative antisera each from ZF2001 (A) and BBIBP-CorV (B) vaccine recipients

110 were tested for their neutralizing activity to authentic SARS-CoV-2 HB02 (WT), BJ01

111 (D614G) and GDPCC (501Y.V2) via microcytopathogenic effect assay. Shown are the

112 geometric mean with 95% CI. P values were analyzed with One-way ANOVA test.

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121 **Table 1: Information for serum samples tested in this study**

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RBD protein vaccine (ZF2001)				
	50% Neutralization titer			
Serum ID	Clinical trials	HB02 (WT)	BJ01 (D614G)	GDPCC (501Y.V2)
012-6-(5)	128	128	96	64
014-6-(5)	256	256	128	128
024-6-(5)	64	64	48	48
082-6-(5)	96	64	64	32
088-6-(5)	96	48	96	48
102-6-(5)	256	128	128	96
135-6-(5)	384	192	192	96
153-6-(5)	128	128	96	64
154-6-(5)	64	64	64	48
233-6-(5)	256	128	128	96
290-6-(5)	128	64	48	48
308-6-(5)	256	192	128	96
Inactivated vaccine (BBIBP-CorV)				
	50% Neutralization titer			
Serum ID	Clinical trials	HB02 (WT)	BJ01 (D614G)	GDPCC (501Y.V2)
B867-2	192	128	128	96
B850-2	256	192	192	128
B848-2	64	48	64	32
B875-2	96	96	64	48
B841-2	256	192	128	64
B843-2	256	192	128	64
B844-2	192	128	128	96
B856-2	96	64	96	86
B851-2	192	128	96	64
B890-2	64	48	48	32
B845-2	384	256	256	192
B869-2	96	64	96	64

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Supplementary Materials for

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Neutralization of SARS-CoV-2 VOC 501Y.V2 by human antisera

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elicited by both inactivated BBIBP-CorV and recombinant dimeric

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RBD ZF2001 vaccines

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This PDF file includes:

184 **Materials and Methods**

185 **Supplemental references**

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190 **Material and methods**

191 **Viruses and titration**

192 The SARS-CoV-2 virus 19nCoV-CDC-Tan-HB02 (short as HB02), 19nCoV-CDC-Tan-BJ01
193 (short as BJ01) and 19nCoV-CDC-Tan-GDPCC (short as GDPCC) were used in our
194 experiments(1-4). Virus titer was determined by a micro-cytopathogenic efficiency (CPE)
195 assay on Vero cells as described previously(5).

196 **Neutralization assay**

197 The serum were inactivated in a 56°C water bath for 30 min, then successively diluted 1:4 to
198 the required concentration by a 2-fold series. An equal volume of challenge virus solution
199 containing 100 CCID₅₀ virus was added. After neutralization in a 37°C incubator for 2 h, a
200 1.0~2.5×10⁵/ml cell suspension was added to the wells and cultured in a CO₂ incubator at 37°C
201 for 4 days. Titers expressed as the reciprocal of the highest dilution protecting 50% cell from
202 virus challenge. A neutralization antibody potency < 1:4 is negative, while that ≥1:4 is
203 positive.

204 **Serum samples from clinical trial participants**

205 For the 12 Serum samples from BBIBP-CorV vaccination(6, 7), vaccine recipients received
206 BBIBP-CorV containing 4 µg total protein on days 0 and 21, blood samples were taken from
207 participants for serology tests 28 days after second vaccination, covering a range of different
208 neutralizing titers, the ClinicalTrials.gov Identifier is NCT04510207.

209 For the 12 Serum samples from ZF2001 vaccination (8), vaccine recipients received ZF2001
210 containing 25 µg vaccine dose on days 0, 30, 60. Blood samples were taken from participants

211 for serology tests 14 days after third vaccination, covering a range of different neutralizing
212 titers, the ClinicalTrials.gov Identifier is NCT04466085.

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