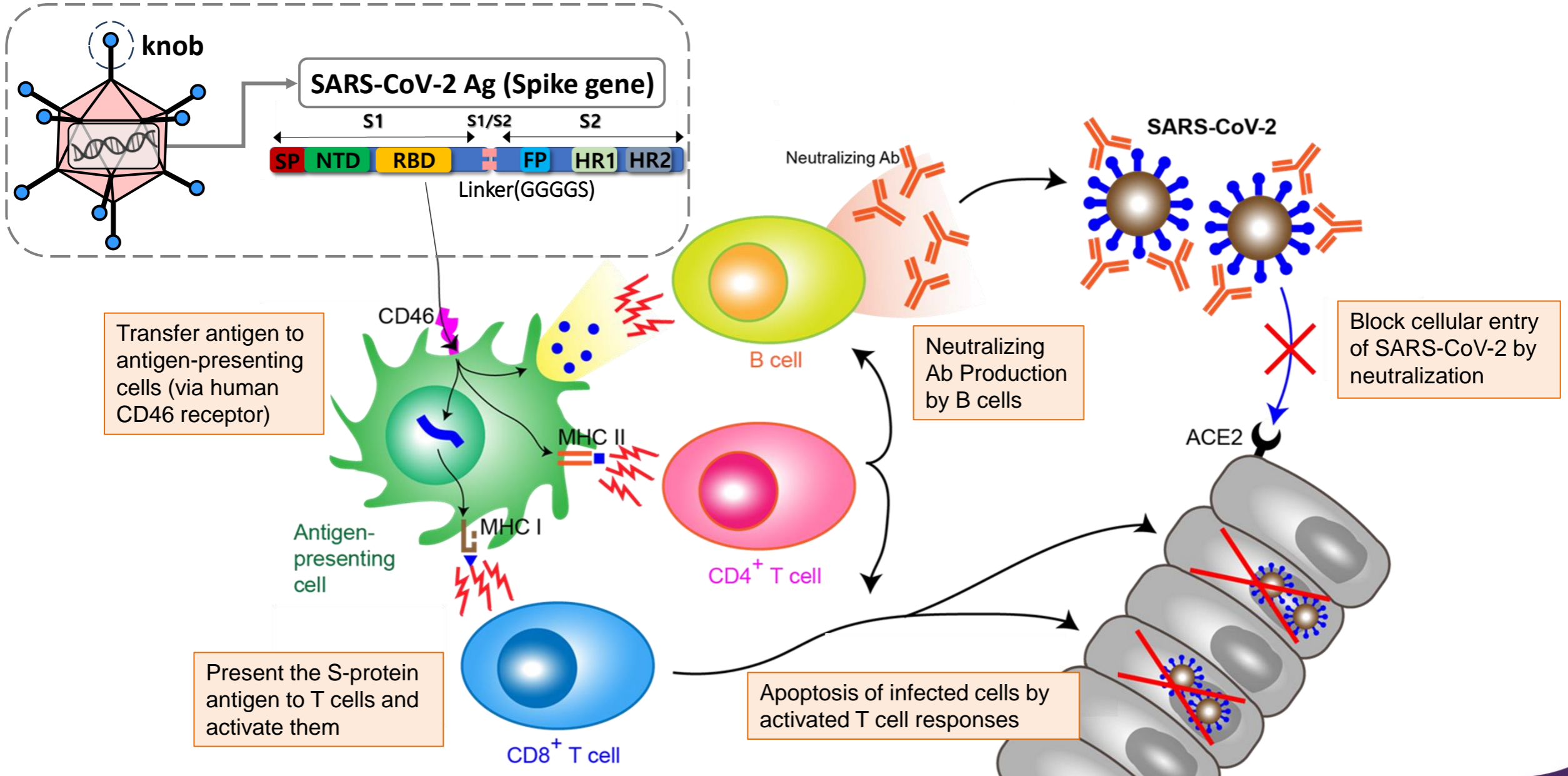


Polyvalent strategy to the development of broadly protective vaccines against COVID-19 subvariants

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Cellid Co., Ltd.

CELLID's COVID-19 vaccine platform

Adenovirus type 5/35 (Ad5/35) Cellid's proprietary vector backbone



CELLID's COVID-19 Vaccine: Current Clinical Trials

Pipeline	Antigen gene	Basic Research	Preclinical	Phase of Clinical trial			Remarks
				Phase 1	Phase 2	Phase 3	
AdCLD-CoV19	SARS-CoV-2 Spike						Primary vaccine (Discontinued due to limitations in recruiting clinical trial subjects)
AdCLD-CoV19-1 (Improved vaccine for mass manufacturing)	SARS-CoV-2 Spike						
AdCLD-CoV19-1 OMI (Omicron variant Vaccine)	SARS-CoV-2 B.1.1.529 Spike						Booster dose Vaccine (Completed clinical phase 2 administration 2023.02.09)

Developed **AdCLD-CoV19-1 OMI**, a vaccine against **Omicron BA.1 variant** using a replication-deficient recombinant adenovirus serotype 5/35 platform, **completed phase 2 clinical administration on February 9, 2023**, and scheduled to apply for phase 3 clinical trial around April.

Response to variants: Variant Vaccine Library

• Table 1. Variant-specific vaccine library

Variants	Vaccine construction & animal immunogenicity study
Wild type	Completed
Beta	Completed
Gamma	Completed
Delta	Completed
Lambda	Completed
Mu	Completed
BA.1	Completed
BA.2	Completed
BA.2.12.1	Completed
BA.4.1	Completed
BA.5	Completed
BA.2.75	Completed
BA.4.6	Ongoing
BA.2.75.2	Ongoing
BF.7	Ongoing
BQ.1	Ongoing
BQ.1.1	Completed
BN.1	Completed
XBB	Completed
XBB.1.5	Completed
XBB.1	Ongoing
BA.2.3.20	Ongoing
CH.1.1	Ongoing
XBF	Ongoing

• Table 2. Pseudovirus library for neutralization test

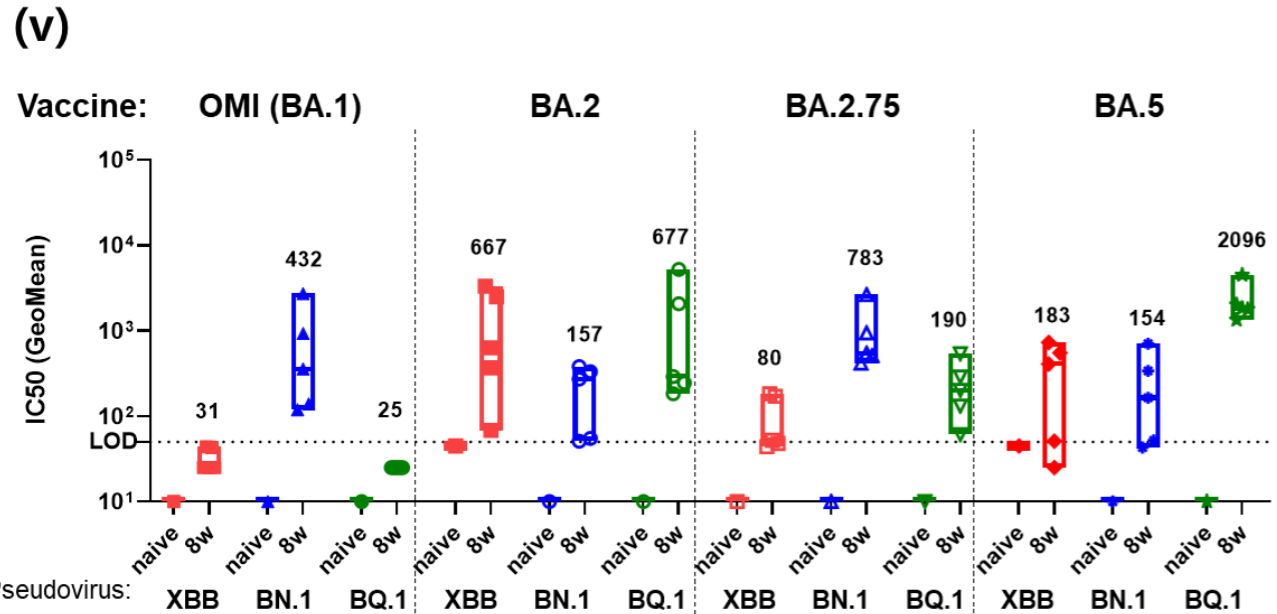
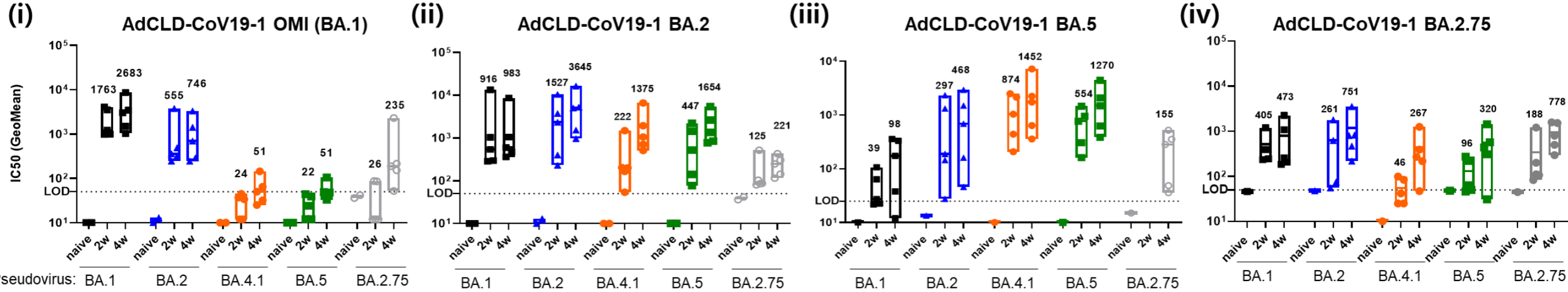
Variants Pseudovirus	Manufacturing	Evaluation
-	Wild type	Completed
Variants common	B.1.1.7/B.1.351/P.1/ B.1.617.2	Completed
	$\alpha/\beta/\gamma$ common	B.1.1.7/B.1.351/P.1
β/γ common	B.1.351/P.1	Completed
Beta (partial variant)	B.1.351 (Partial)	Completed
Delta (partial variant)	B.1.617.1 (Partial)	Completed
Delta (partial variant)	B.1.617.2 (Partial)	Completed
Alpha	B.1.1.7	Completed
Beta	B.1.351	Completed
Gamma	P.1	Completed
Delta	B.1.617.2	Completed
Delta plus (Delta subtype)	AY.1	Completed
	AY.4	Completed
	AY.4.2	Completed
	AY.43	Completed
	AY.69	Completed
Lambda	C.37	Completed
Mu	B.1.621	Completed
IHU	B.1.640.2	Completed
Omicron Stealth Omicron	BA.1	Completed
	BA.2	Completed
	BA.2.12.1	Completed
	BA.4.1	Completed
	BA.4/BA.5	Completed
	BA.2.75	Completed
	BA.4.6	Completed
	BA.2.75.2	Completed
	BF.7	Completed
	BQ.1	Completed
Omicron subvariant	BQ.1.1	Completed
	BN.1	Completed
	XBB	Completed
	XBB.1	Completed
	XBB.1.5	Completed
	BA.2.3.20	Completed
	CH.1.1	Completed
XBF	Ongoing	

- By using Ad5/35 platform, we have constructed different variant-specific vaccines for emerging threats (Table 1).
- Ad5/35 platform can be easily modified to respond variants by replacing antigen to that of VOCs.
- Additionally, we have various lentivirus-based pseudotyped virus to test the immunogenicity of our vaccine (Table 2). It enables us to facilitate the process of vaccine development.

Preclinical studies of Omicron subvariant vaccine 'AdCLD-CoV19-1 OMI'

- Immunogenicity of Omicron subvariant vaccines **after single administration**

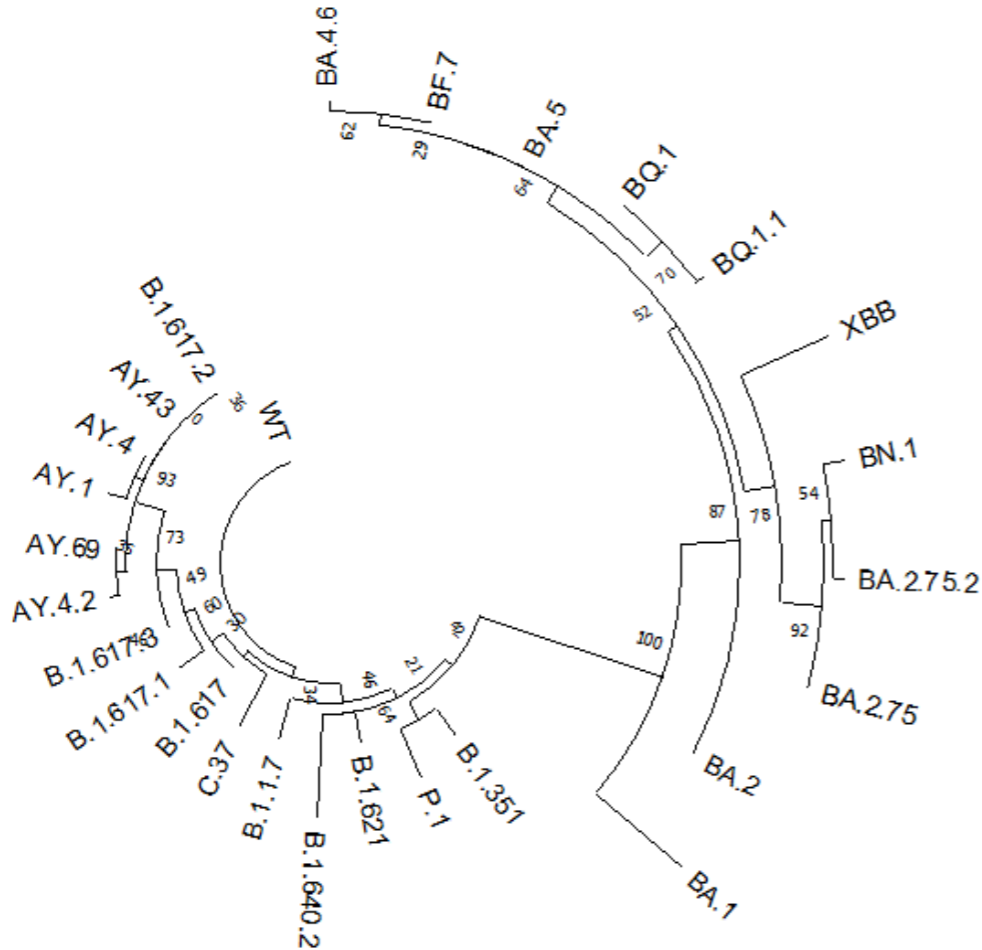
Neutralizing Ab responses (Pseudovirus NT)



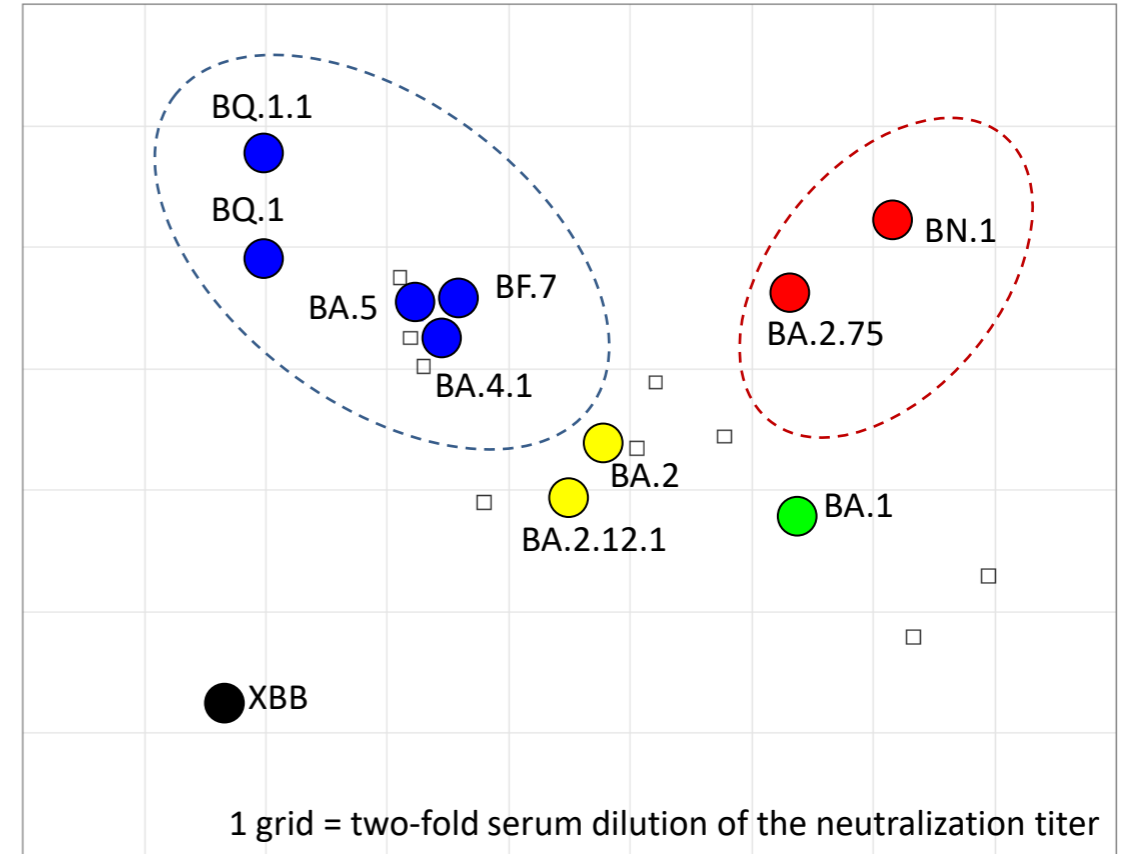
→ Each vaccine has a difference in Neutralizing Ab responses depending on variants.
 → It is difficult to respond to all variants with one vaccine.

Clustering based on the variant sequence and the immunogenicity of the vaccine

- COVID-19 variant spike sequence phylogenetic tree



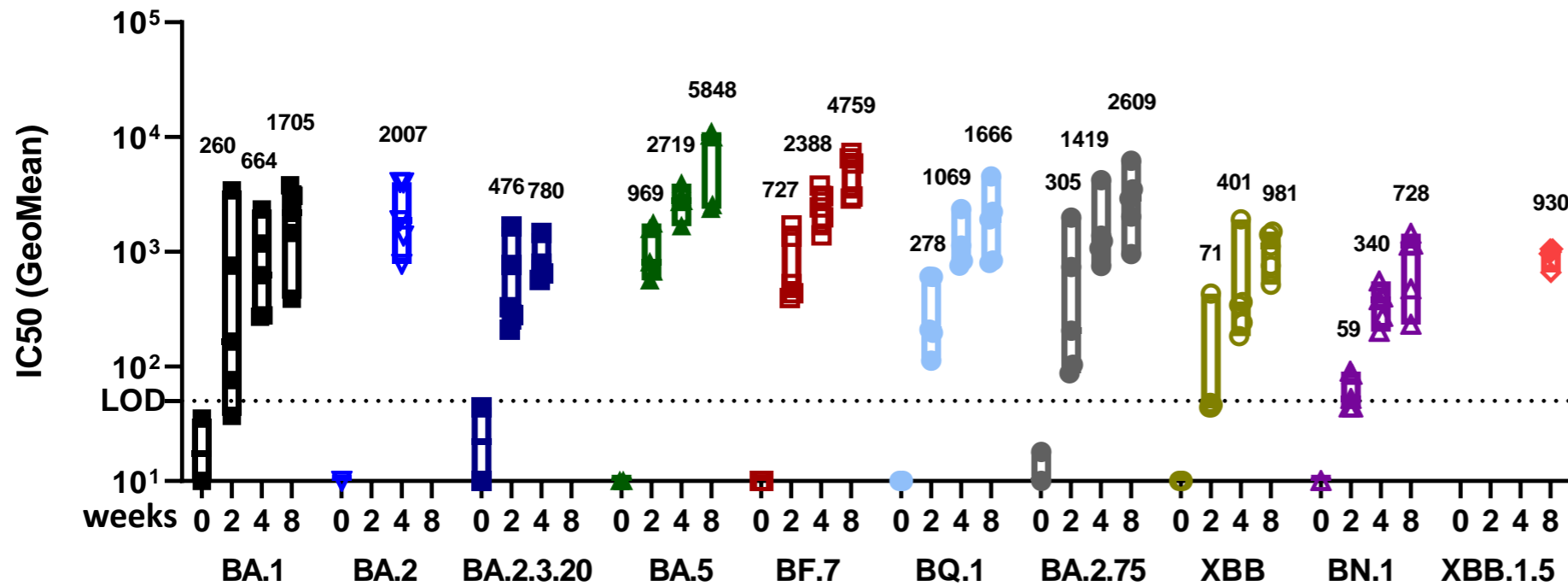
- COVID-19 variant spike antigenic cartography map (Single shot)



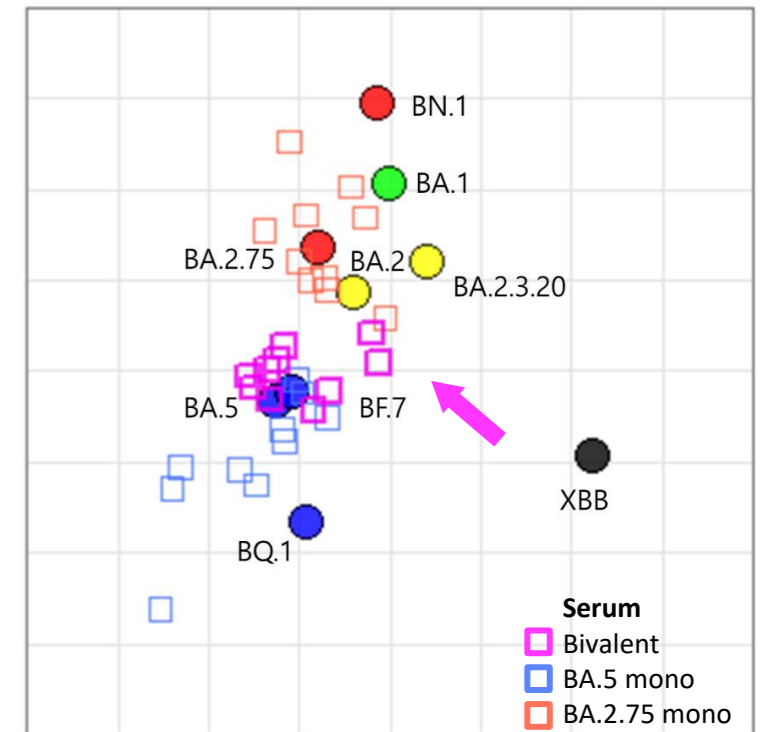
→ Through the variant sequence and antigenic cartography map-based clustering produced by cross-neutralization activity, we selected **BA.5 and BA.2.75 specific vaccines as the first candidate for the multivalent vaccine.**

Multivalent vaccine 1st candidate: BA.5/BA.2.75 bivalent vaccine

- Neutralizing Ab responses after **single** administration



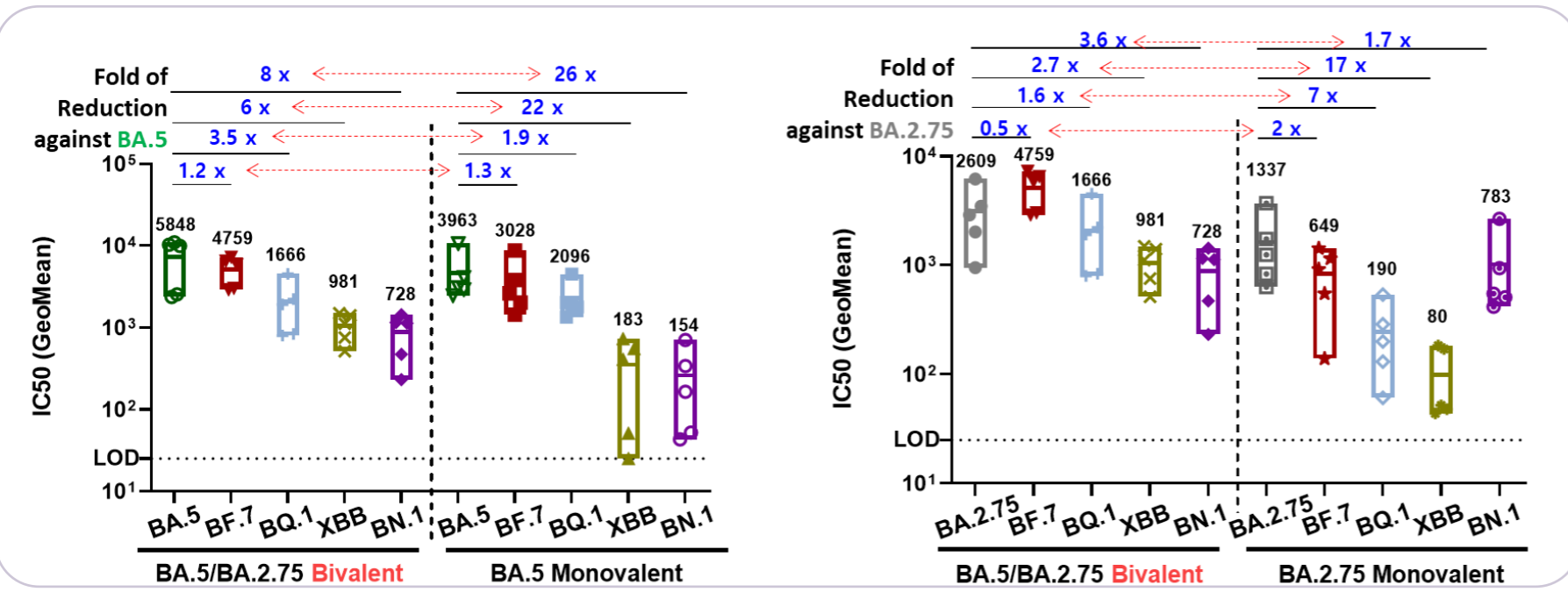
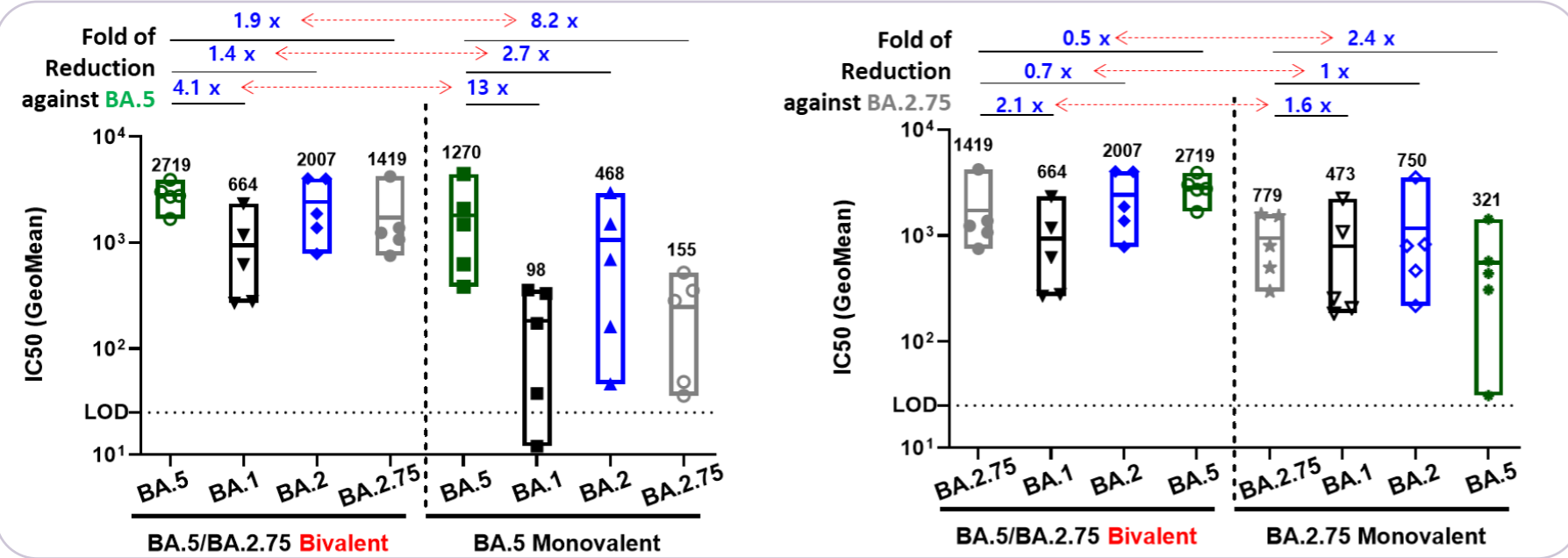
- Antigenic cartography map



1 grid = two-fold serum dilution of the neutralization titer

- By BA.5/BA.2.75 bivalent vaccine, the neutralizing antibody activity generally increased including the BN.1, BQ.1, and XBB1.5 that are currently prevalent in the world.
- A **wide range of neutralizing antibodies** was produced, and **antigenic distance was reduced**.

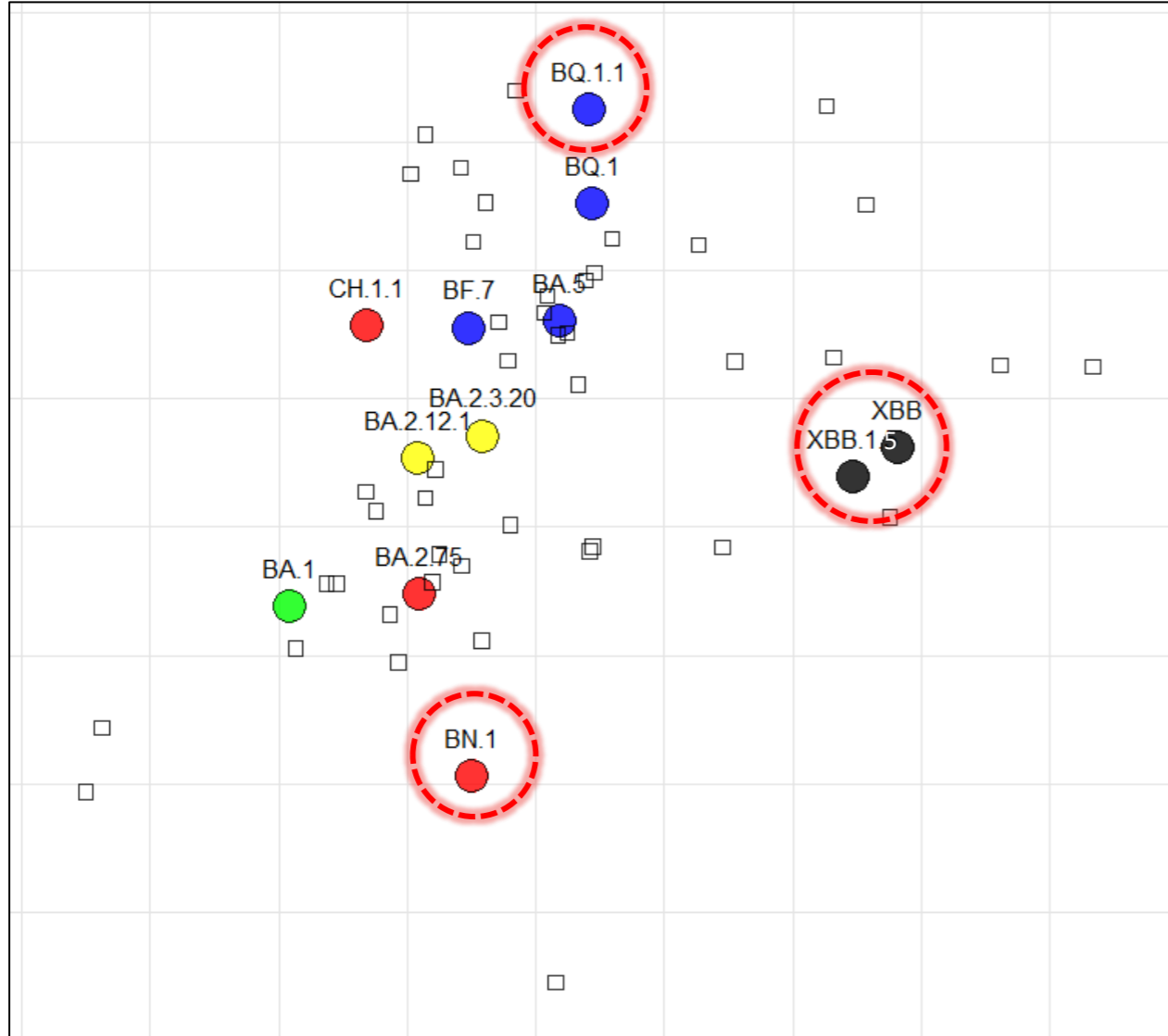
Multivalent vaccine 1st candidate: BA.5/BA.2.75 bivalent vaccine



→ By BA.5/BA.2.75 bivalent vaccine, the neutralizing antibody activity generally increased.

Clustering based on the immunogenicity of the vaccine

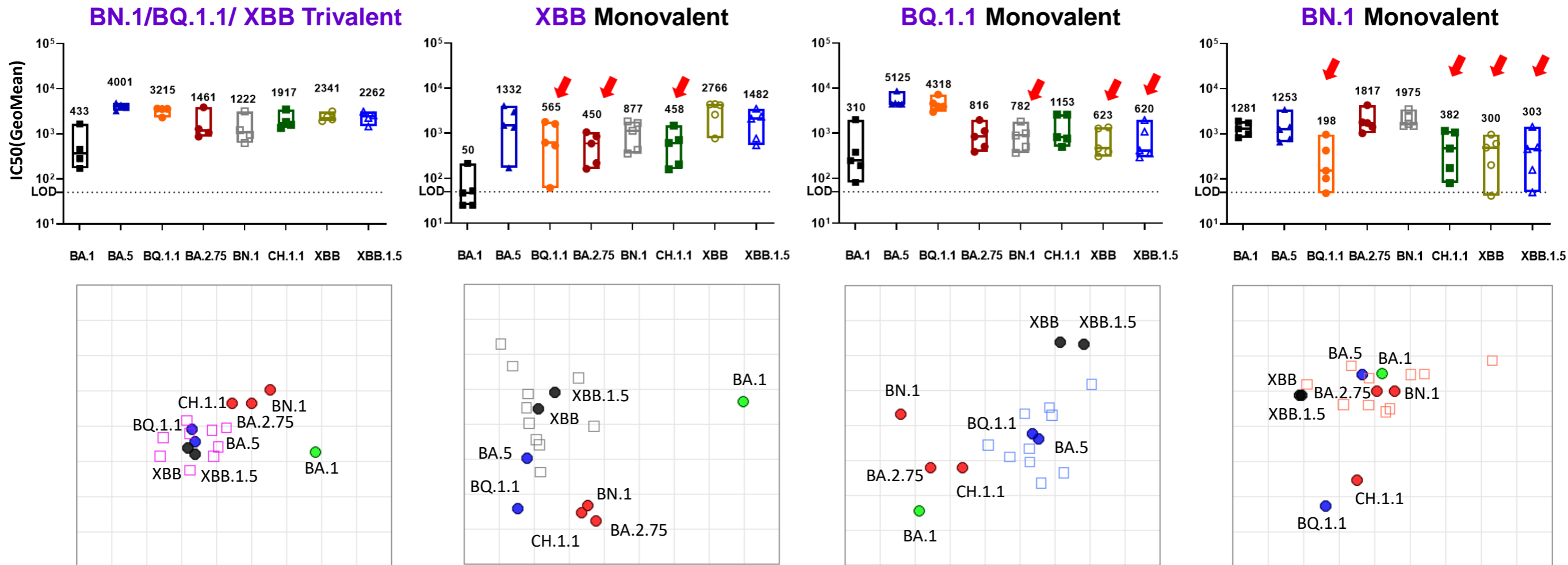
- COVID-19 variant spike antigenic cartography map (Single shot)



Trivalent vaccine using XBB, BN.1, and BQ1.1 specific vaccines was selected as the second candidate for multivalent vaccine through the variant sequence and antigenic cartography map-based clustering produced by the cross-neutralization activity.

Multivalent vaccine 2nd candidate: XBB/BN.1/BQ1.1 trivalent vaccine

- Immunogenicity of Omicron subvariant vaccines **after single administration**



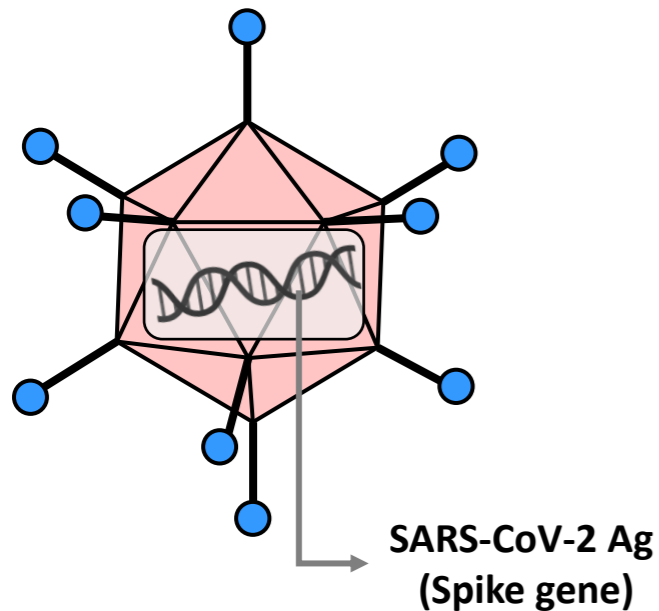
	Trivalent	XBB	BQ.1.1	BN.1
Variant-Variant	1.84	3.15	3.34	2.22
Serum-Variant	1.61	2.91	2.75	2.11

By XBB/BN.1/BQ1.1 trivalent vaccine, a **wide range of neutralizing antibodies** was produced, and **antigenic distance was reduced**.

CELLID's COVID-19 vaccine platform : Competitiveness

AdCLD-CoV19-1

AdCLD-CoV19-1 OMI



01

Long-term efficacy

- Induction of neutralizing Ab and T cell immune response

02

Competitive cost

- Available at a lower cost compared to other vaccines such as mRNA vaccine
- Suitable for middle to low-income countries

03

Convenient storage and distribution

- Stored and distributed at 4 °C
- Cold-chain system not required

04

Fast development and manufacturing process

- Rapid response to COVID-19 variants or emerging threats