Next Generation of Antibody Therapeutics for Treating Infectious Diseases

Sheila Keating PhD MSPH
VP Immunology
May 21, 2026

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Disclosures

- Employee of Grifols

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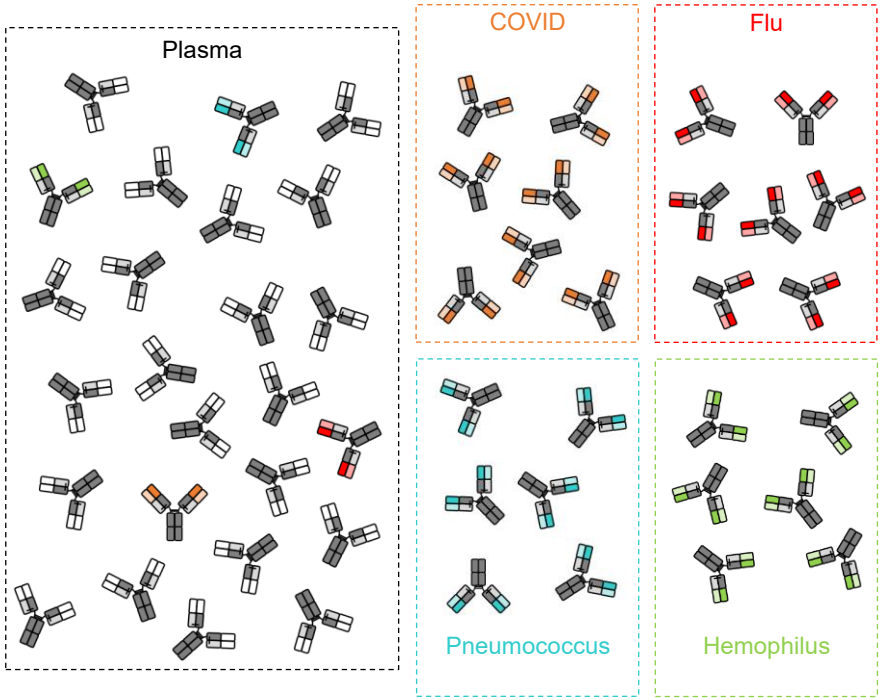
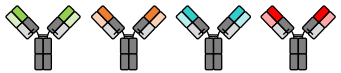
Natural polyclonal responses to infectious diseases



- B cells make antibodies against pathogens, such as:
  - Virus
  - Toxins
  - Bacteria
- Antibodies against these pathogens are in our plasma but are at a low frequency
- GigaGen captures anti-pathogen sequences from B cells to make **highly potent, recombinant antibody therapeutics** that are enriched to target important pathogens


= Ab against unknown pathogens


= mAb against known pathogens

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A platform to generate polyclonal antibody therapies

Immunized or convalescent human donor

Grifols, CSL, Takeda

Convalescent plasma

Isolate IgG

Plasma hyperimmune

- Hyperimmune antibody titer can be around 10-30x higher than IVIG
- Post-COVID IVIG and Hyper-COVID have higher titers
- Requires hundreds of donors per lot

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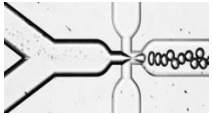
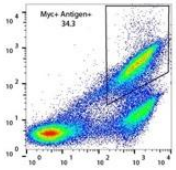
Droplet microfluidics



Yeast display



CHO library

Recombinant hyperimmune

- Antigen-specific antibody sequence enrichment
- Antibody titer typically >1,000x higher than plasma hyperimmune
- Only requires a few donors

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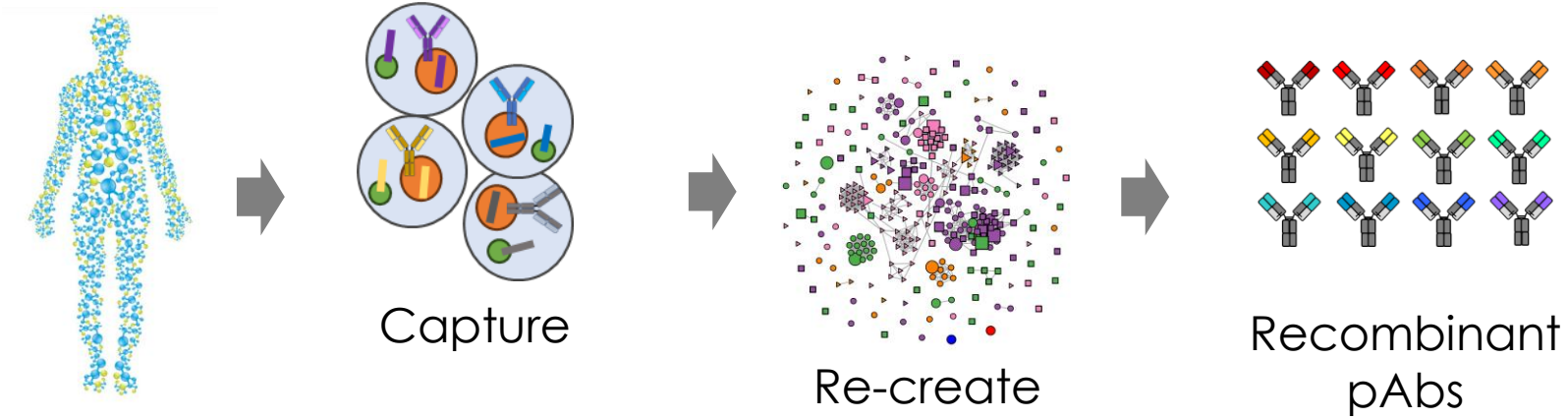
What is a recombinant polyclonal antibody (pAb)?

- Captures and recreates naturally occurring antibodies
- Contains natively paired heavy and light chains
- Maintains high diversity (>1000 antibodies)
- Created by Isolating individual B cells and produced in CHO cells



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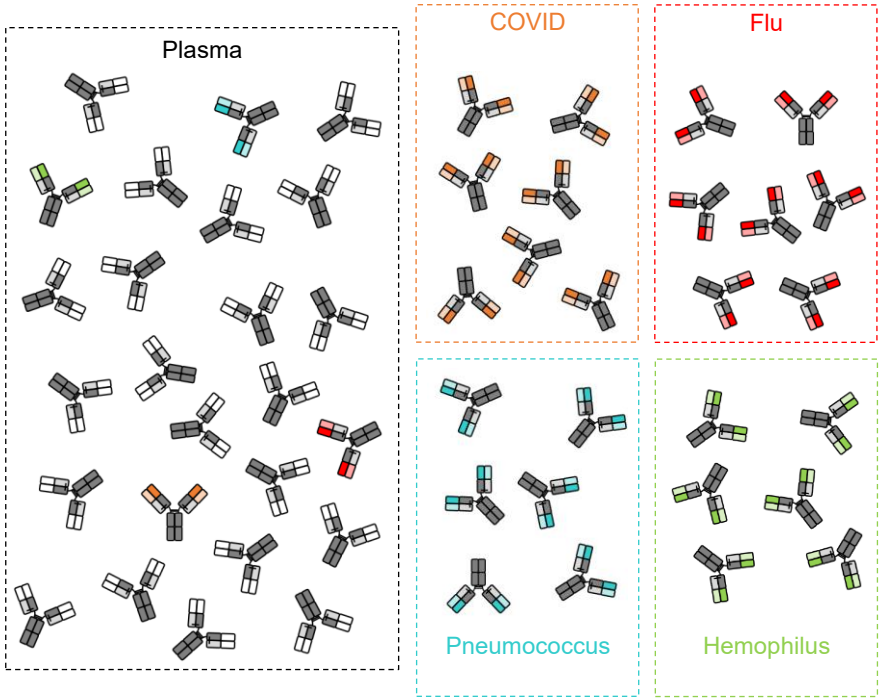
Natural polyclonal responses to infectious diseases



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= Ab against unknown pathogens

= mAb against known pathogens

SARS-COV-2
Recombinant Polyclonal Antibody Therapeutic
GIGA-2050

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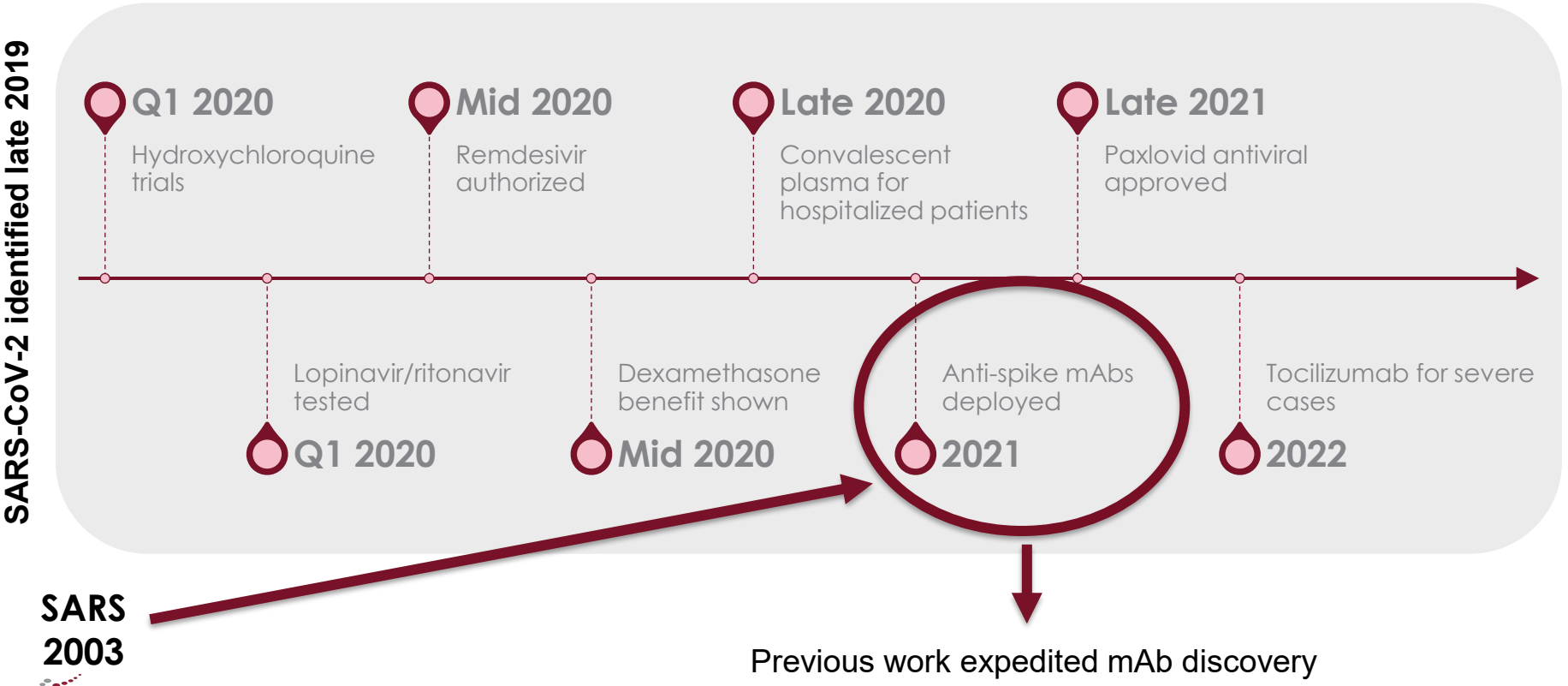
COVID-19 drug development timeline



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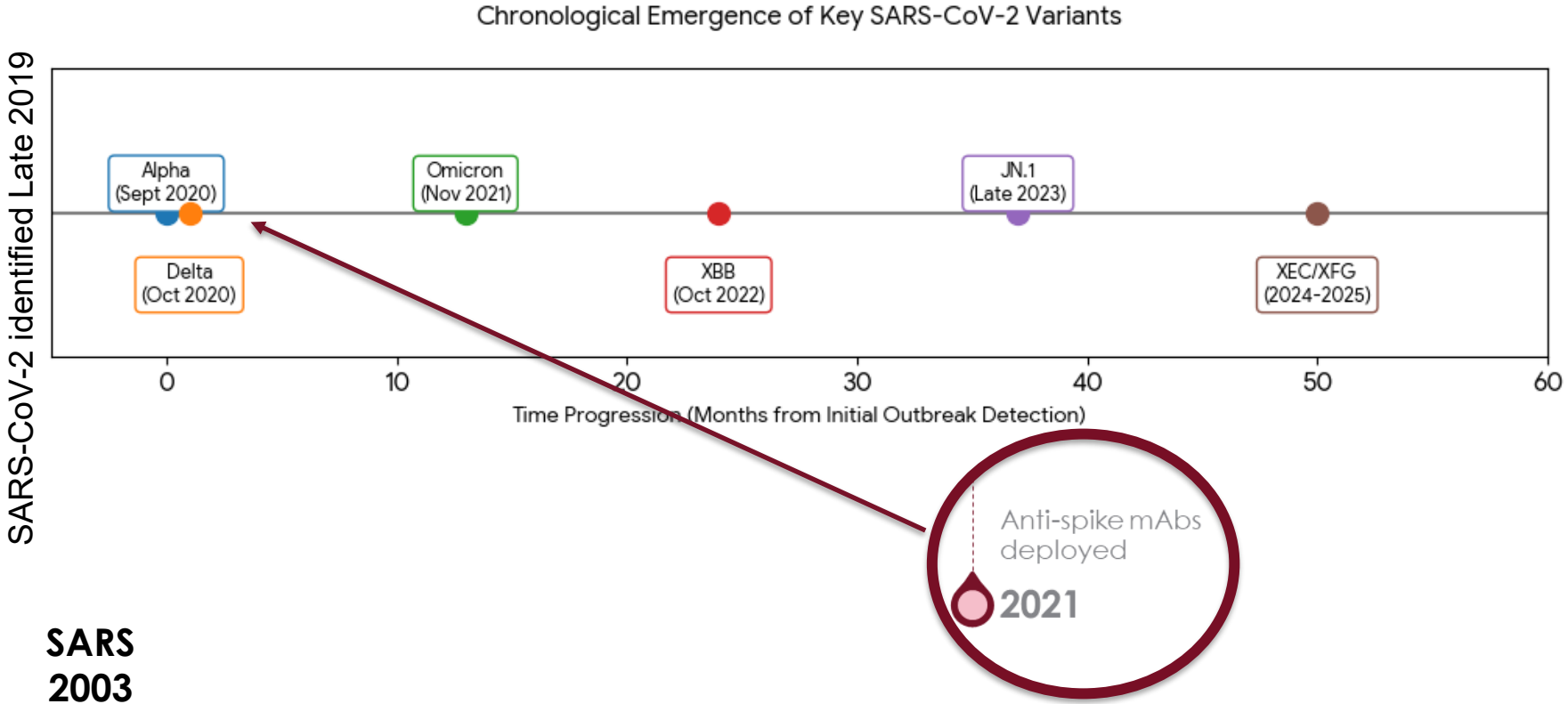
COVID-19 variant timeline



SARS 2003

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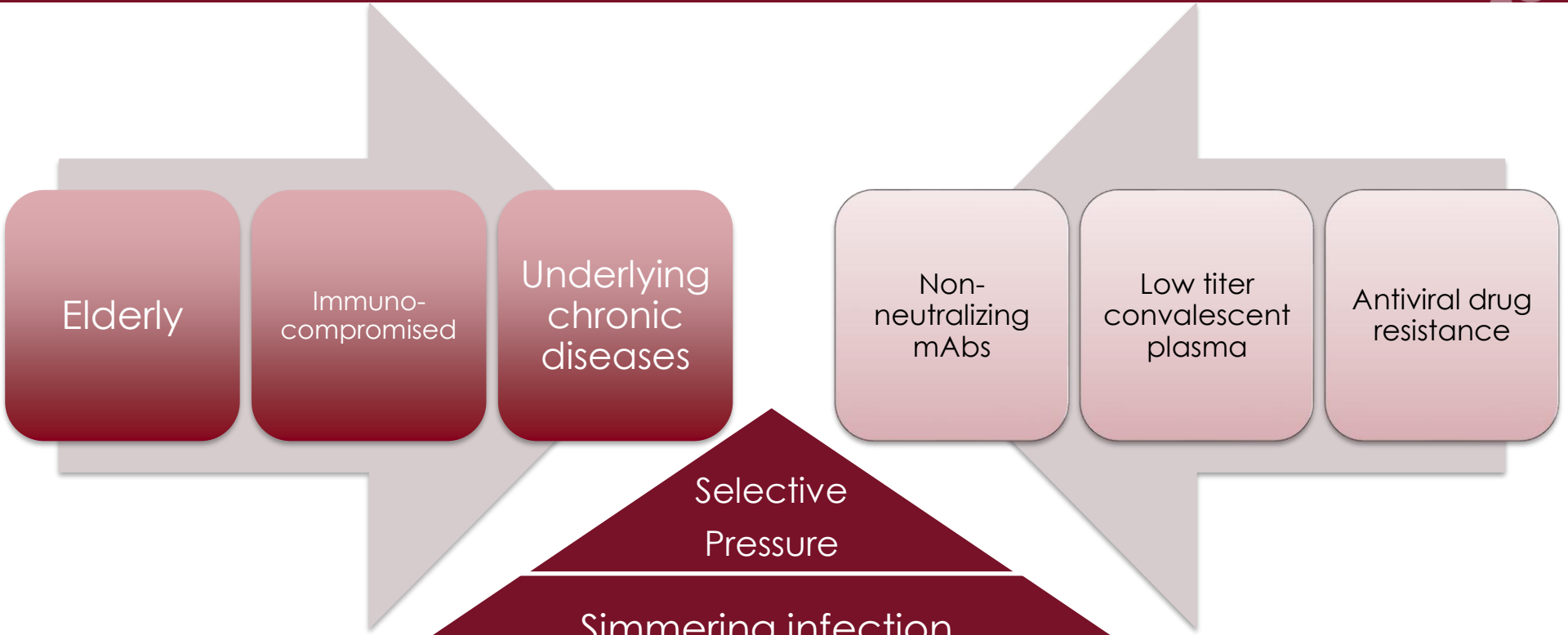
Drivers of SARS-CoV-2 variants



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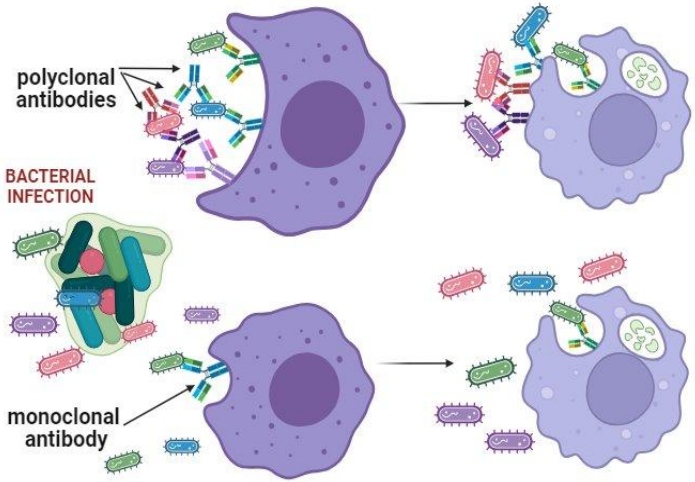
Yoon et al. Lancet 2025
Bansal et al. Transfus Clin Bio 2021

Polyclonal antibodies provide protective coverage



Monoclonal Antibody	Polyclonal Antibodies
Binds to only one pathogen	Contains natural diverse immune responses to pathogens
Limited to a single binding site	Targets multiple antigens, serotypes/variants, and toxins
Lower avidity and engagement cellular responses	Better at inducing high avidity cell mediated responses
May not neutralize viral mutants	Provides coverage for viral mutants and bacterial serotypes
Each Master Cell Bank produces a single mAb	Thousands of unique antibodies produced from in a single drug
GMP manufacturing costs applied to each mAb; Mixing mAbs magnifies cost	GigaGen Platform can produce polyclonal antibodies from a single MCB in a single GMP run

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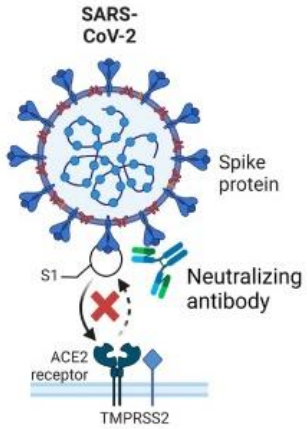
Neutralizing and non-neutralizing polyclonal antibodies are essential for viral clearance



Izadi et al, Trends in Immunology 2024

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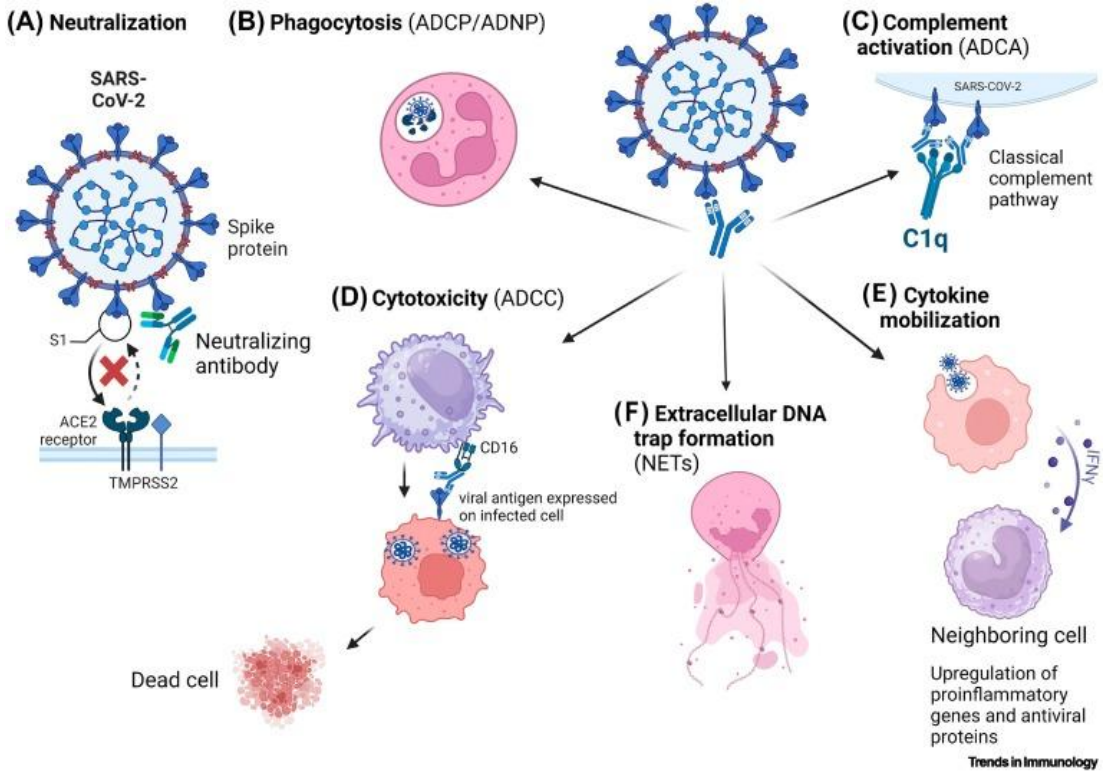

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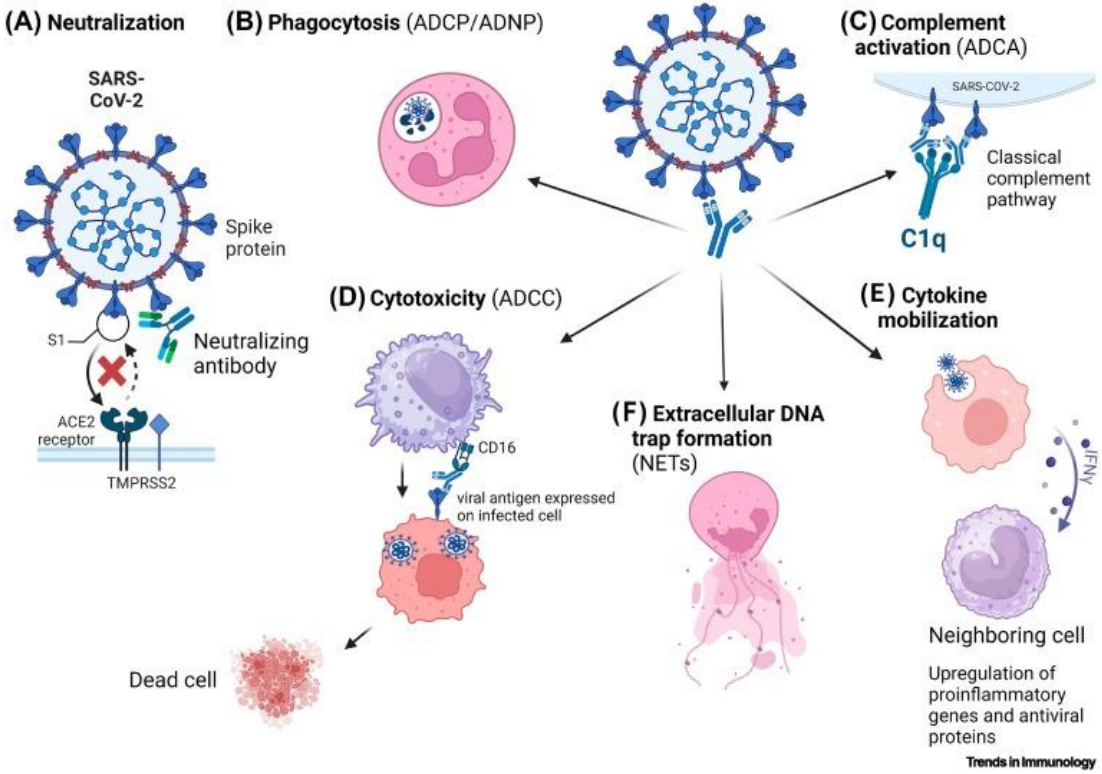

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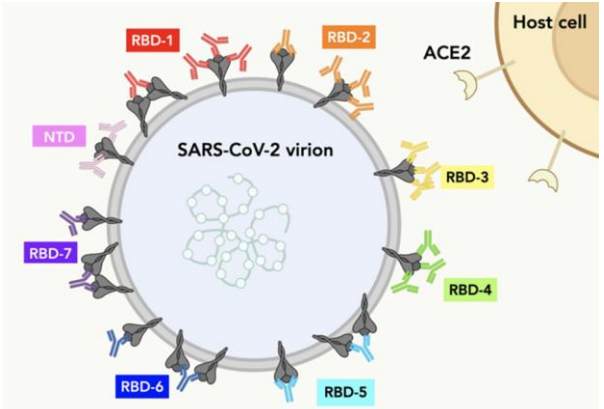
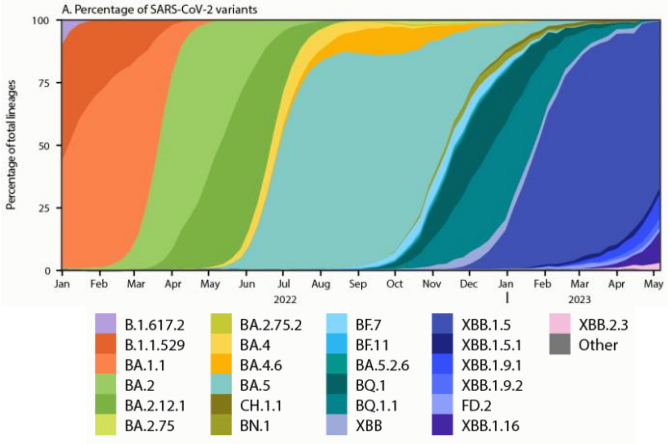


Brian Doctorow, NIH 2021



MMWR, vol 72

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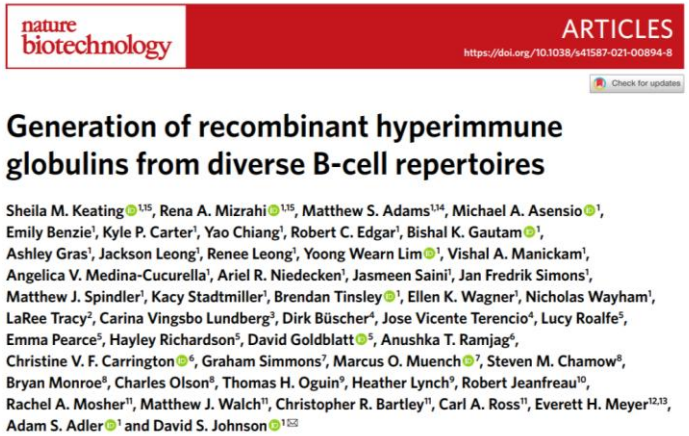
GigaGen's recombinant polyclonal therapies



nature biotechnology

ARTICLES

https://doi.org/10.1038/s41587-021-00894-8

Check for updates

Generation of recombinant hyperimmune globulins from diverse B-cell repertoires

Sheila M. Keating[1,15], Rena A. Mizrahi[1,15], Matthew S. Adams[1,14], Michael A. Asensio[1], Emily Benzie[1], Kyle P. Carter[1], Yao Chiang[1], Robert C. Edgar[1], Bishal K. Gautam[1], Ashley Gras[1], Jackson Leong[1], Renee Leong[1], Yoong Wearn Lim[1], Vishal A. Manickam[1], Angelica V. Medina-Cucurella[1], Ariel R. Niedecken[1], Jasmeen Saini[1], Jan Fredrik Simons[1], Matthew J. Spindler[1], Kacy Stadtmiller[1], Brendan Tinsley[1], Ellen K. Wagner[1], Nicholas Wayham[1], LaRee Tracy[2], Carina Vingsbo Lundberg[3], Dirk Büscher[4], Jose Vicente Terencio[4], Lucy Roalfe[5], Emma Pearce[5], Hayley Richardson[5], David Goldblatt[5], Anushka T. Ramjag[6], Christine V. F. Carrington[6], Graham Simmons[7], Marcus O. Muench[7], Steven M. Chamow[8], Bryan Monroe[8], Charles Olson[8], Thomas H. Oguin[9], Heather Lynch[9], Robert Jeanfreau[10], Rachel A. Mosher[11], Matthew J. Walch[11], Christopher R. Bartley[11], Carl A. Ross[11], Everett H. Meyer[12,13], Adam S. Adler[1] and David S. Johnson[1]✉

MABS
2022, VOL. 14, NO. 1, e2069075 (11 pages)
https://doi.org/10.1080/19420862.2022.2069075

Taylor & Francis
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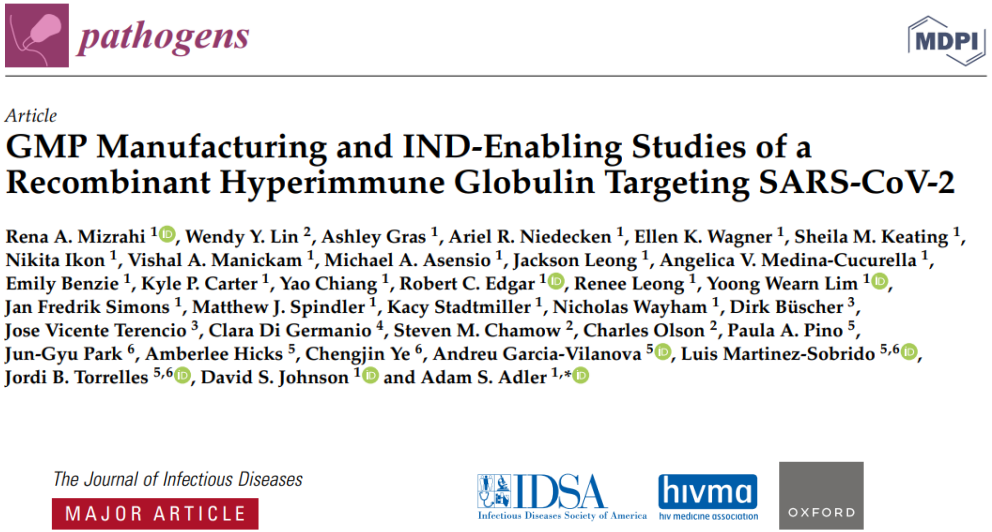
REPORT

OPEN ACCESS Check for updates

Predicting antibody binders and generating synthetic antibodies using deep learning

Yoong Wearn Lim, Adam S. Adler, and David S. Johnson

GigaGen Inc. (A Grifols Company), South San Francisco, CA, USA



pathogens

MDPI

Article

GMP Manufacturing and IND-Enabling Studies of a Recombinant Hyperimmune Globulin Targeting SARS-CoV-2

Rena A. Mizrahi [1], Wendy Y. Lin [2], Ashley Gras [1], Ariel R. Niedecken [1], Ellen K. Wagner [1], Sheila M. Keating [1], Nikita Ikon [1], Vishal A. Manickam [1], Michael A. Asensio [1], Jackson Leong [1], Angelica V. Medina-Cucurella [1], Emily Benzie [1], Kyle P. Carter [1], Yao Chiang [1], Robert C. Edgar [1], Renee Leong [1], Yoong Wearn Lim [1], Jan Fredrik Simons [1], Matthew J. Spindler [1], Kacy Stadtmiller [1], Nicholas Wayham [1], Dirk Büscher [3], Jose Vicente Terencio [3], Clara Di Germanio [4], Steven M. Chamow [2], Charles Olson [2], Paula A. Pino [5], Jun-Gyu Park [6], Amberlee Hicks [5], Chengjin Ye [6], Andreu Garcia-Vilanova [5], Luis Martinez-Sobrido [5,6], Jordi B. Torrelles [5,6], David S. Johnson [1] and Adam S. Adler [1,*]

The Journal of Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

A Potent Recombinant Polyclonal Antibody Therapeutic for Protection Against New Severe Acute Respiratory Syndrome Coronavirus 2 Variants of Concern

Nicholas P. Wayham,[a] Ariel R. Niedecken,[a] Jan Fredrik Simons, Yao Y. Chiang, Angélica V. Medina-Cucurella, Rena A. Mizrahi, Ellen K. Wagner, Ashley Gras, Ilana Segal, Peyton Witte, Alexis Enstrom, Aristea Bountouvas, Sabrina M. Nelson, Tess Weinberger, David Tan, Michael A. Asensio, Alagu Subramanian, Yoong Wearn Lim, Adam S. Adler, and Sheila M. Keating

GigaGen, Inc. (A Grifols Company), San Carlos, California, USA

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GigaGen Platform Technology

Donor / Immunization

Human donor (convalescent, vaccinated)

Ig humanized mouse, rat, or chicken

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Pandemic Response for SARS-CoV-2 – **GIGA-2050**

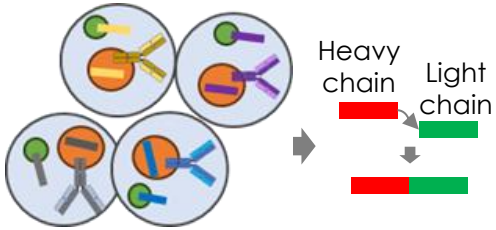
Donor / Immunization

16 Human donor (convalescent)

High titer donors

1-2 weeks

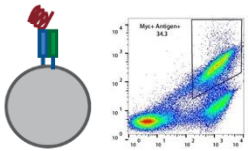
Capture complex antibody repertoires



Capture B cells in droplets, linked heavy and light chain, expressed single chain variable fragment (scFv) sequences on yeast and pooled to create 16 libraries

3 days

Create highly diverse libraries, enrich for binders, & express full-length pAb



Sorted receptor binding domain (RBD)-specific scFv sequences - each library contained hundreds of unique RBD-specific sequences

2-4 weeks

Cloned sequences into full-length vectors and transfected into a single site integration CHO cell line – *en masse* – 1 antibody produced per cell

1 week

Stable cell line generation; pool RCBs to make MCB

2-4 weeks

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Process takes 2 - 4 months

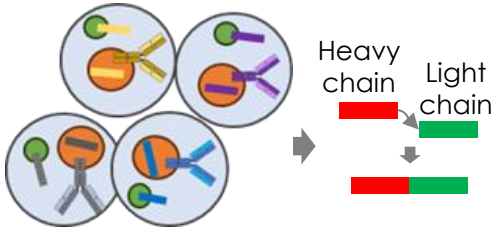
Pandemic Response for SARS-CoV-2 – **GIGA-2050**

Donor / Immunization

16 Human donor (convalescent)

High titer donors

Capture complex antibody repertoires



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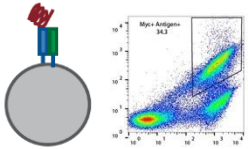

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Cloned sequences into full-length vectors and transfected into a single site integration CHO cell line – *en*
– 1 antib
produced p

Stable cell line generation; pool RCBs to make MCB

Final recombinant COVID polyclonal antibody drug (GIGA-2050) produced from MCB contained 12,000 unique antibodies

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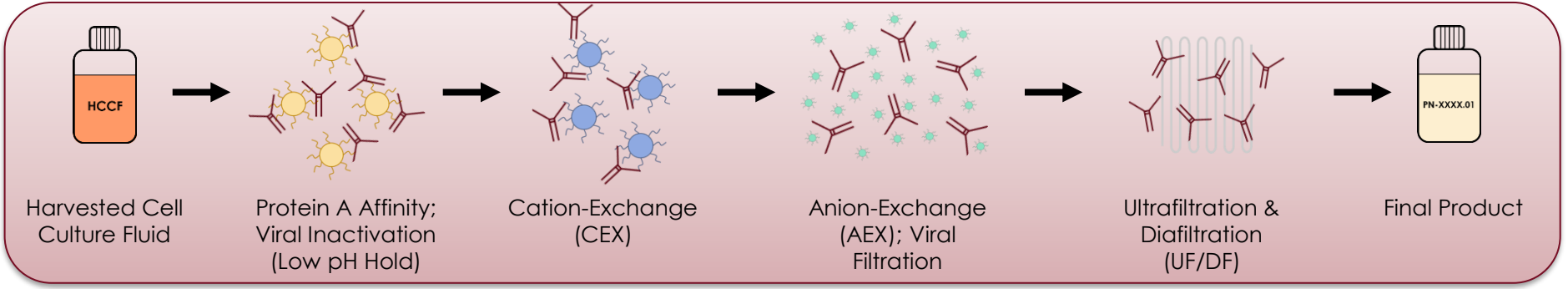
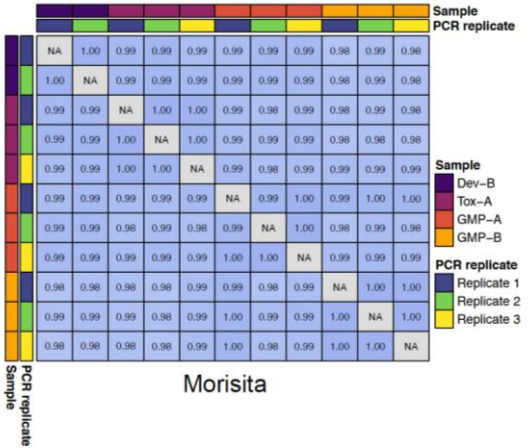
Overview of the Polyclonal Hyperimmune purification process – same as monoclonal



- Manufacture 12,000 antibodies from 1 vial of CHO cell produced GIGA-2050
- Consistent CHO cell antibody sequence diversity with each manufacturing run

Lot-to-Lot: Reproducible in Ab quality and function & Reproducible in sequencing

		Acceptance Criteria	Dev-A	Dev-B	Dev-C	Dev-D	Dev-E	Tox-A	GMP-A	GMP-B
Purity	Native Size Distribution by SEC-HPLC	Monomer: ≥ 90% Main Peak	98.30%	97.90%	98.70%	99.40%	96.70%	99.60%	98%	98%
		HMWS: Report	1.30%	1.60%	1.30%	0.50%	3.20%	0.40%	1.40%	1.60%
		LMWS: Report	0.40%	0.50%	0%	0.10%	0.10%	0%	0.70%	0.00%
	Denatured Size Distribution by CE-SDS (Non-Reduced)	>85% Intact	92.50%	93.90%	91.00%	87.30%	93.50%	85.20%	94%	95%
	Denatured Size Distribution by CE-SDS (Reduced)	>85% Heavy Chain + Light Chain	100%	99.80%	100%	99.80%	100%	100%	98%	98%
	Residual CHO DNA	<1 ppm	ND	ND	<1.1 ppm	ND	ND	<0.9 ppm	<0.7 ppm	<0.6 ppm
	Residual CHO HCP ELISA	<50 ppm	5.6 ppm	6.3 ppm	11.5 ppm	3.8 ppm	11.4 ppm	3.0 ppm	8.0 ppm	< 1.9 ppm
Potency	Anti-SARS CoV-2 Binding ELISA	Relative Potency: 100 ± 40%	N/A[1]	99%	92%	94%	88%	112%	100%[2]	74%[2]
	Pseudotype neutralization assay	Relative Potency: 100 ± 40%	N/A[1]	87%	112%	101%	125%	123%	97%[2]	74%[2]



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Timeline of GIGA-2050 development: <10 months from first blood sample to IND filing

March 9, first COVID-19 case in New Orleans

April 1, 2020, First blood sample received at GigaGen

May 5, All RBD-specific antibody libraries captured and cloned

June 11, RCB transferred to CDMO for production optimization

June 23, Research production and polyclonal characterization

September 9, Lot release assay development completed and transferred to CROs

December 9, GMP-lot completed

December 15, GLP tox study completed

January 15, 2021, Filed IND

February 15, IND approved

August 3, Phase I first patient dosed

- The timing from the first blood sample to a final drug was incredibly fast
- The timing of the clinical trial initiation was poor given the course of the pandemic (before the Omicron wave; mAb cocktails available through EUA)

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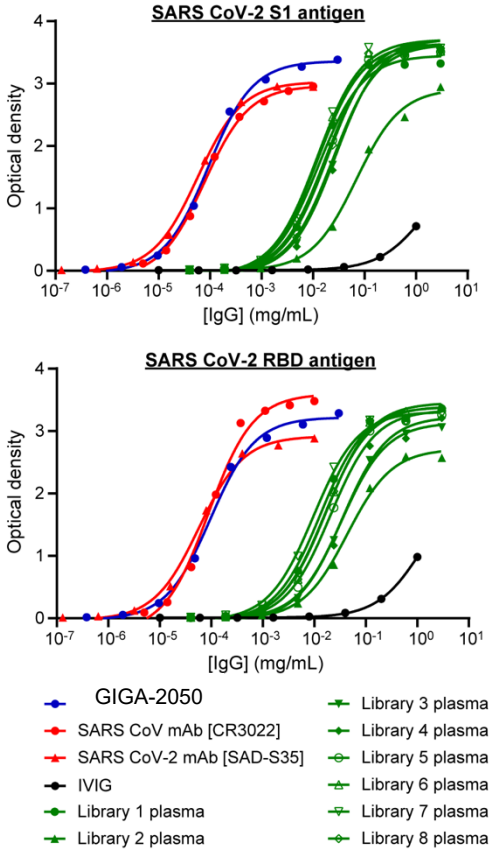
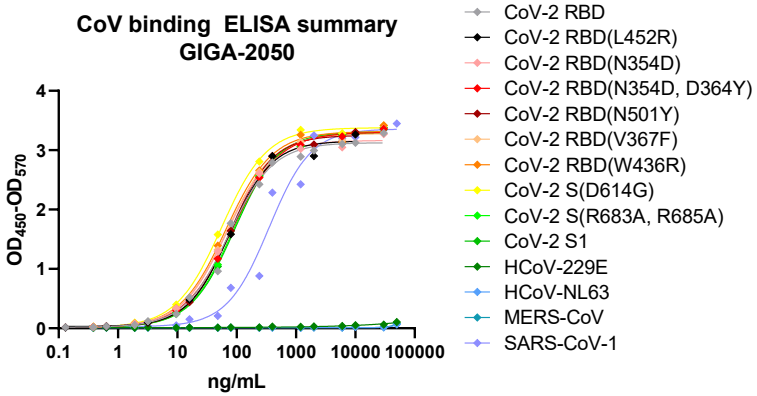
SARS-COV-2 pAb Libraries: ELISA binding



- GIGA-2050 EC50 values up to 750x higher than convalescent plasma from the same donors weeks after infection
- EC50 values remain consistent across all variants tested



Keating et al., Nature Biotechnology, 2021

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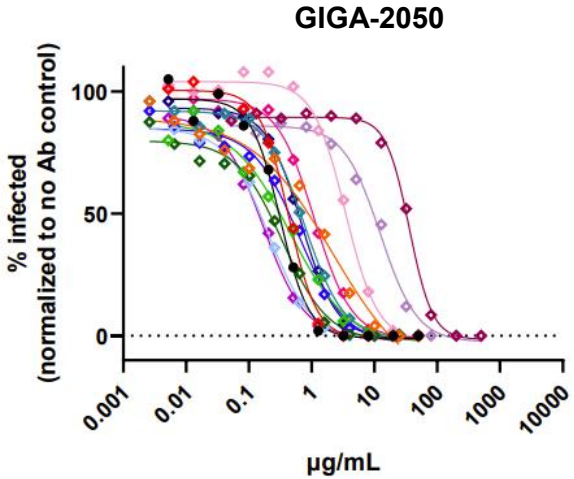
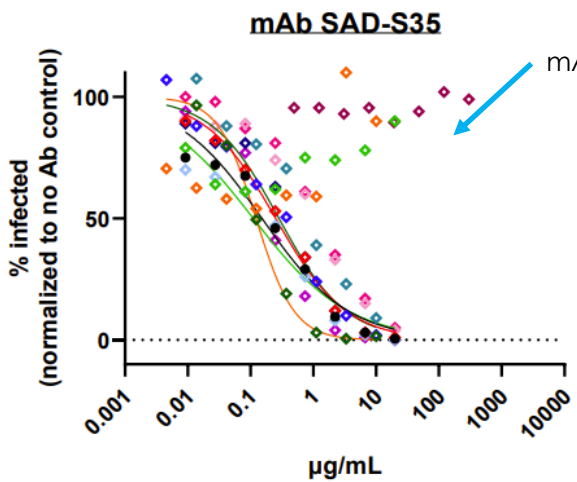
Polyclonal antibodies neutralize future viral variants

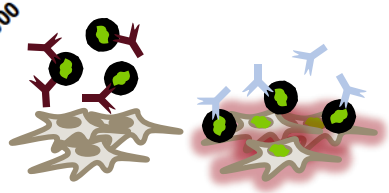
- Better than mAbs for infectious disease; target multiple epitopes to prevent viruses or bacteria from mutating around your drug.

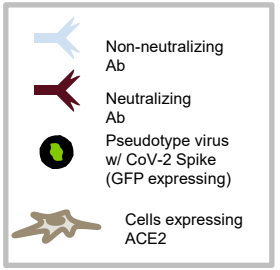




mAb unable to neutralize multiple variants

- ancestral
- alpha
- beta
- gamma
- delta
- epsilon
- eta
- iota
- kappa
- lambda
- mu
- omicron BA.1
- omicron BA.2
- zeta





Wayham et al., *JID*, 2023

GIGA-2050: recombinant anti-SARS-CoV-2 immunoglobulin
SAD-S35: reagent mAb binding to SARS-CoV-2 receptor binding domain

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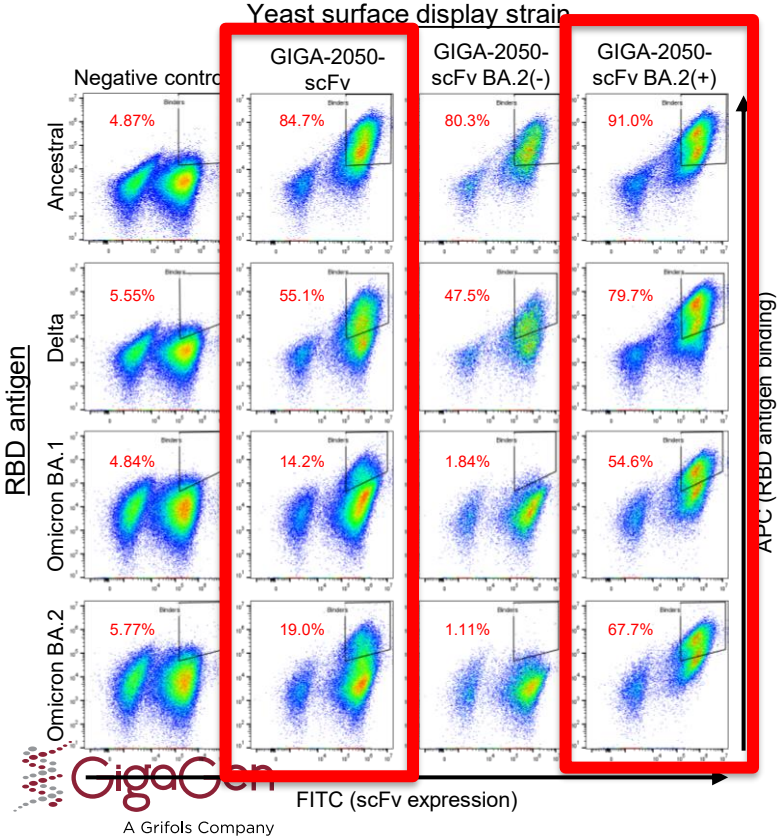
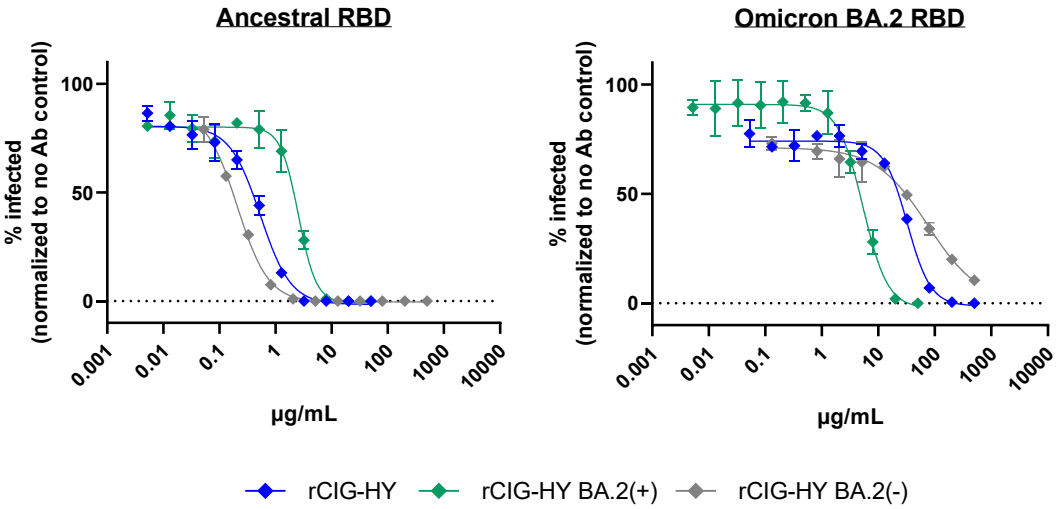
Polyclonal antibodies can be tuned to bind new variants

- Potential to update antibody libraries based on new variants





Pandemic Lessons Learned

- Diagnostics come first: antibody and antigen
- Consortium establishment takes time
- Benchmarking against neutralizing mAbs may miss the value of pAbs
- Contribution of non-neutralizing antibodies is difficult to measure in *in vivo* models
  - Clearance of virus
  - Initiating secondary immune response
- Find ways to prepare for the future:
  - Surveillance
  - Banking
- Identify resources to support

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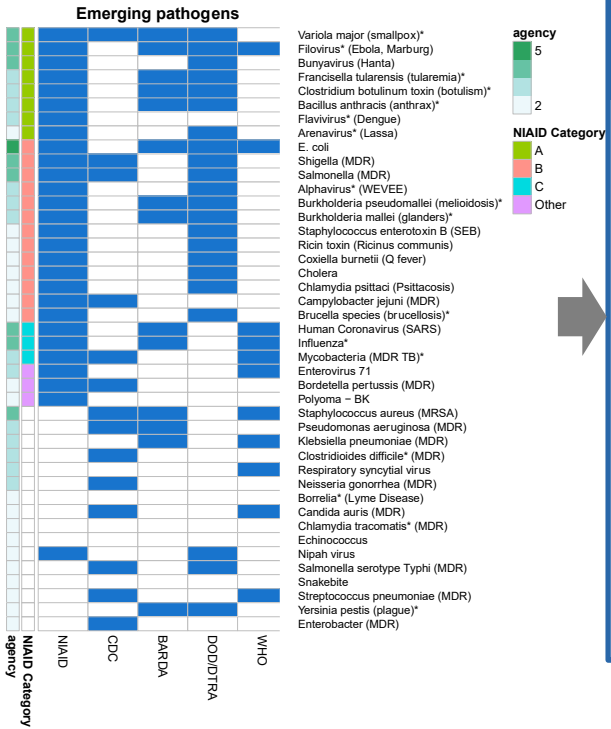
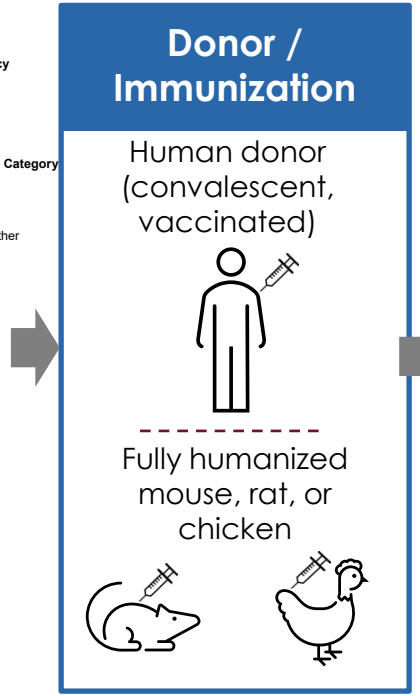
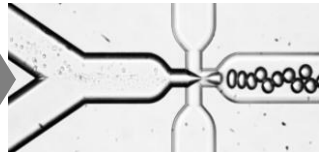
Health Emergency Preparedness and Response (HERA): major threat categories

1. **respiratory or contact-based viruses** with pandemic potential: highly transmissible viruses with a history or likelihood of causing large-scale outbreaks
2. **vector-borne or animal-reservoir viruses** with epidemic potential: viruses whose spread is accelerated by climate change and other environmental factors, which are qualified as a specific threat category due to their growing relevance for the Europe (the fastest warming continent according to the European Environment Agency);
3. **armed conflict-related threats** and chemical, biological, radiological and nuclear (CBRN) threats;
4. **antimicrobial resistance (AMR):** a rising global concern that threatens the efficacy of existing treatments and increases the burden of infectious diseases.

Rapid Response: Cell banks for emerging pathogens







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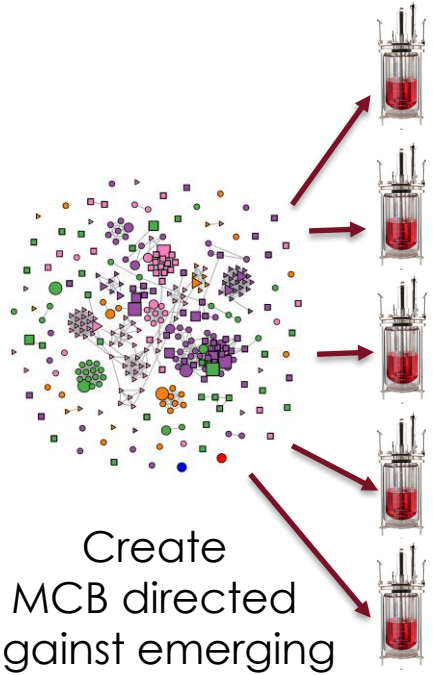

Create MCB directed against emerging pathogens to deploy for manufacturing

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Awarded DoD and BARDA contracts

September 15, 2022

GigaGen Awarded Contract by U.S. Department of Defense to Discover Synthetic Human Antibody Treatments for High-Priority Toxins and Pathogens

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South San Francisco, Calif., Sept. 15, 2022 (GLOBE NEWSWIRE) -- GigaGen Inc., a biotechnology company advancing transformative antibody drugs for immune deficiencies, infectious diseases and checkpoint resistant cancers, and a subsidiary of Grifols, announced today it has entered into a co
Program Executive Office for Chemical, Biological, Radiological
of its first-in-class recombinant human polyclonal antibody dis
DOD.

October 3, 2024

GigaGen Awarded U.S. BARDA Contract to Develop Recombinant Polyclonal Antibody Therapies for Botulinum Neurotoxins and an Additional Biothreat

Download PDF

- **The contract will provide an initial commitment of $19.6 million and up to $135.2 million over a six-year period, supporting drug manufacturing and phase 1 trials for the two programs**
- **GigaGen's recombinant polyclonals are part of Grifols' robust innovation strategy and commitment to delivering the next generation of antibody drugs for patients and healthcare professionals**

Pandemic Lessons Learned

- Diagnostics come first: antibody and antigen
- Consortium establishment takes time
- Benchmarking against neutralizing mAbs may miss the value of pAbs
- Contribution of non-neutralizing antibodies is difficult to measure in *in vivo* models
  - Clearance of virus
  - Initiating secondary immune response
- Find ways to prepare for the future:
  - Surveillance
  - Banking
- Identify resources to support

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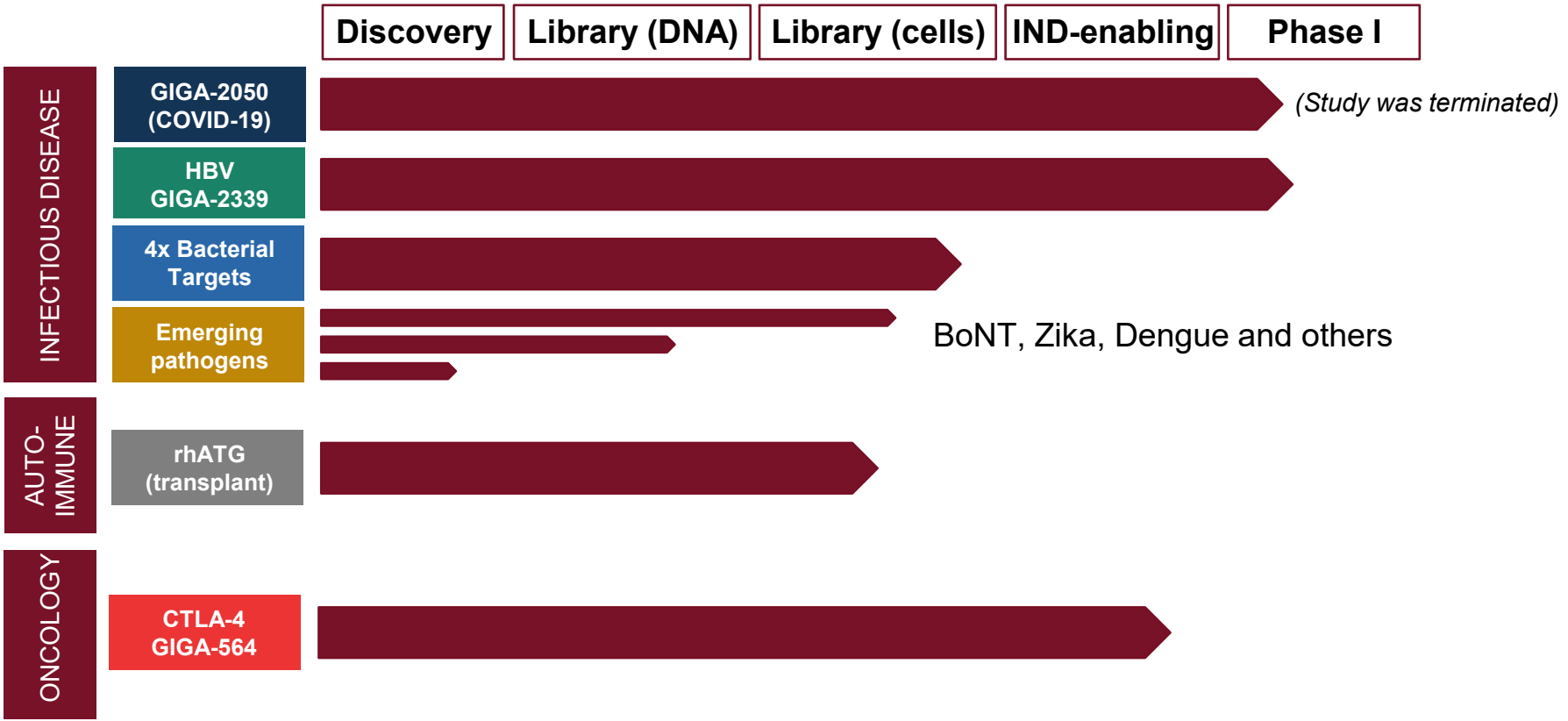
GigaGen's therapeutic pipeline overview



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Thank You

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