November 29, 2021

DYADIC®

C1 Technology Platform

Supporting the fight against SARS-CoV-2 Variants of Concern with a **rapid response** to current pandemic and future biological threats utilizing the **gene expression technology of tomorrow to combat the threats of today**

Safe Harbor Regarding Forward-looking Statements

Certain statements contained in this presentation are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, including those regarding Dyadic's expectations, intentions, strategies and beliefs pertaining to future events or future financial performance. Actual events or results may differ materially from those in the forward-looking statements as a result of various important factors, including those described in Dyadic's most recent filings with the SEC. Undue reliance should not be placed on the forward-looking statements in this presentation, which are based on information available to us on the date hereof. Dyadic assumes no obligation to update publicly any such forward-looking statements, whether as a result of new information, future events or otherwise. For a more complete description of the risks that could cause our actual results to differ from our current expectations, please see the section entitled "Risk Factors" in Dyadic's annual reports on Form 10-K and quarterly reports on Form 10-Q filed with the SEC, as such factors may be updated from time to time in Dyadic's periodic filings with the SEC, which are accessible on the SEC's website and at www.dyadic.com

Our Mission, Transforming Biomanufacturing

"Improving how we feed[1], fuel[1], and heal the world by utilizing modern biotechnology to revolutionize science, medicine, agriculture[1]."

"Providing a cost-effective solution that increases outputs and to meet the growing demand for protein production."

"Ultimately fulfilling the unmet need of affordable biologic drugs, vaccines and biologic products and processes."

-Mark Emalfarb, CEO Dyadic

[1] *Dyadic has achieved certain ports of the above "Mission" through its twenty plus years of experience in industrial biotech. Currently, we are primarily focused on animal and human health applications while opportunistically exploring if and how we may enter/re-enter certain industrial biotechnology applications.*

"C1-cells" are an exceptional strain of genetically engineered fungus

Broad application of C1 has expanded through 20 years of commercial engineering

1992

C1 wildtype strain produces commercially valuable catalytic enzymes

C1 mutation leads to commercial launch of C1 enzymes for industrial textile manufacturing

C1 molecular toolkit optimized for development in other industries including human therapeutics

Genome sequenced and cell line refined for high purity in industrial manufacturing

2005

Enzyme library developed

Generally Recognized as Safe (GRAS) designation by FDA

C1 launched in biofuels industry

Launch of human development for vaccines and biosimilars

ZAPI project initiated

2016

Acceleration of Proof-of-Concept collaborations with pharma industry

Funded R& D, pre-clinical trials with top global pharma and leading animal health companies

Covid-19 vaccine Collaborations

- **Rubic Consortium: Africa**
- **Medytox: S. Korea / SE Asia**
- **Syngene, Epygen[1]: India**
- **Sorrento[2]: Americas, Europe, Others**

Today

C1 Platform

1st in human trials

1. *Epygen – Awaiting investment funding to initiate pre-clinical and phase 1 & phase 2 clinical trials in India (BIRAC approved Co-funding)*
2. *Sorrento - the parties are continuing to negotiate the License Agreement, the terms of which may be materially different than the terms set forth in the binding term sheet announced on August 11, 2021; we can give no guidance if or when the License Agreement will be executed, but in the interim, technology transfer to Sorrento for DYAI-100 and the C1 platform has been initiated.*

C1-Cell Technology: Proven, Rapid, Efficient Antigen Manufacturing

Robust, versatile and scalable platform for production of Covid-19 variant of concern and others

- ***Status of C1-based DYAI-100 COVID-19 vaccine development***
  - Stable C1-cell expressed RBD-CTag antigen Stable C1-cell expressed was developed by Dyadic in < three months.
  - A C1 cell line (single gene copy) expresses RBD at a level of .75 g/L in 4 days under GMP with high purity.
  - Since the gene is inserted into a single site and it is being expressed by promiscuous strong promoter there is no need for induction.
  - The single-copy integrated gene is very stable - No need for transient stage.
  - Pre-clinical studies in mice confirmed that the DYAI-100 vaccine candidate induced high level of neutralizing antibodies and generated protection in two (2) Human ACE2 mice challenge studies.
  - Phase I clinical study is planning to start first half of 2022.
  - Current production development is aiming to increase the titer to 2-3 g/L at production scale as already achieved in several lab scale fermentations.
- ***Toxicology study demonstrated complete safety by using C1-RBD antigen & Alhydrogel***
  - The Toxicology study involved 2 groups of n=20 rabbits each (n=10 males and n=10 females per Test Group). One group was subjected to ×4 injections of the Test Item and the second group served as Control Administrations will take place at an interval of 1 week between each injection during the study.
  - Toxicology study will support two or three doses of the DYAI-100 vaccine candidate
  - "In view of the reported findings and under the conditions of this study, it can be concluded that the Test Item C1-RBD Vaccine (Batch: 21Q-DY-02) Vaccine was not associated with major systemic adverse effects and the Test Item is considered safe".
- ***Rapid generation of stable C1-cell lines for different variants***
  - We can rapidly insert RBD variant's genes into the same cell line (same genotype).
  - In addition to the Wuhan RBD, the following variants: Alpha (UK), Beta (SA) Gamma (BR) and Delta (Ind) RBD's have been successfully expressed in C1 cell line (e.g., RBD-delta-CTag: 1.36 g/L in 5 days fermentation before fermentation optimization)
  - ***Rapid generation of stable C1-cell lines to produce Omicron (SA) being initiated***
    - ***Anticipate stable C1-cell producing Omicron antigen in two months after gene synthesis***

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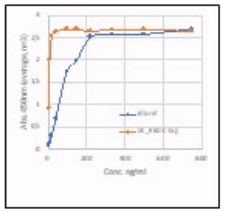
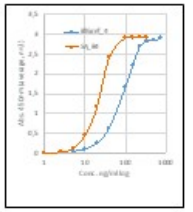
ACE2 - ELISA Assay

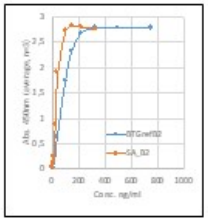
Alpha



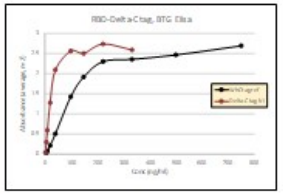
Beta



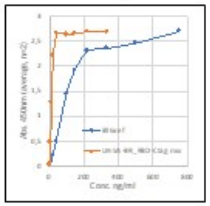
Gamma



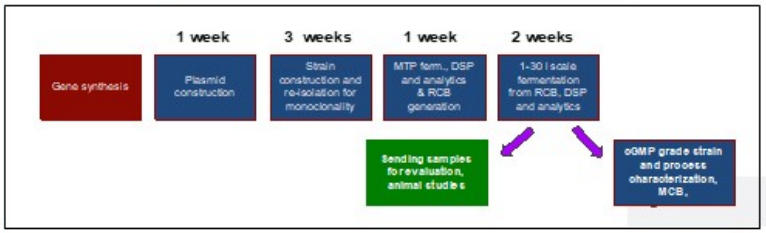
Delta



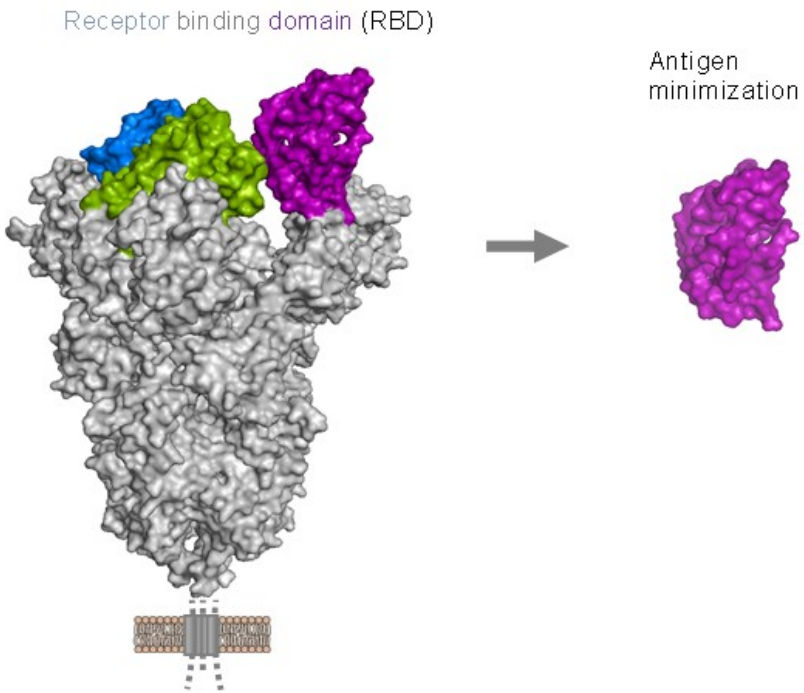
Alpha, Beta ,Gamma Co-expressed



Rapid Development Timeline



SARS-CoV-2 RBD Variants have key advantages as a vaccine antigen



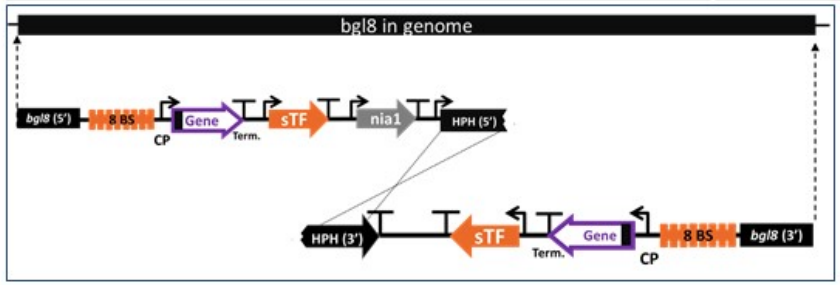
Minimization advantage of spike protein antigen to the RBD:

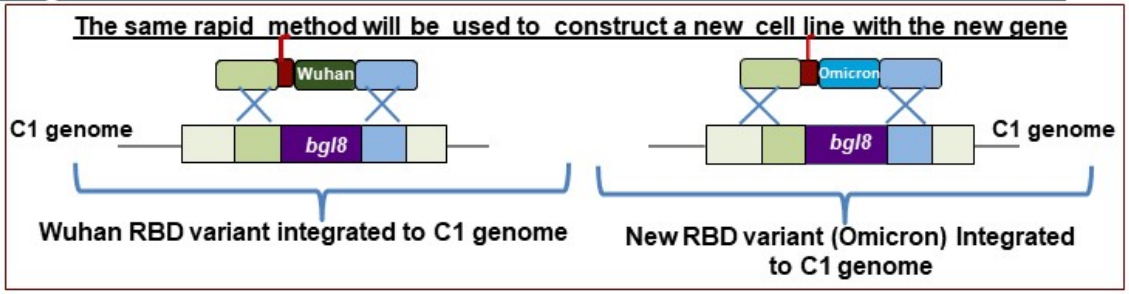
- Exposure of key neutralizing epitopes on the RBD to the immune system that are hidden in the closed spike conformation
- Efficient induction of neutralizing antibodies by focusing the immune response to primary neutralizing epitopes
- RBD is much easier to produce (18x smaller than the spike trimer, much higher yields) compared to full size S
- Immune response to RBD is sufficient to protect from disease
- Recombinant protein vaccine: use as 'booster' vaccine, no interference by 'vector immunity'
- Stand-alone vaccine and potential universal boost strategy
- Reduced probability of Antibody Dependent Enhancement (ADE) / Enhanced Respiratory Disease (ERD)

C1 Protein Production Platform

Site Directed Transformation Method yields Rapid generation of Stable RBD Variant Cell Lines

Site specific integration for stable cell line





- Set of strong promoters native and synthetic
- No need for induction or transient stage
- Stable single-copy integration

- Wuhan RBD variant is located in the *bgl8* gene locus
- New RBD variants replacing the Wuhan variant at exactly the same *bgl8* locus.
- C1 Site Directed Transformation leads to quick generation of stable C1 cell lines

Rapid Development Timelines

- High Productivity – large quantities
- Microbial single use or stainless-steel bioreactors
- Purity
- Stability
- Robust Manufacturing Process
- Flexible Commercial Scales
- Low Cost

	1 week	3 weeks	1 week	2 weeks
Gene synthesis	Plasmid construction	Strain construction and re-isolation for monoclonality	MTP ferm., DSP and analytics & RCB generation	1-30 l scale fermentation from RCB, DSP and analytics

Sending samples for evaluation, animal studies

cGMP grade strain and process characterization, MCB,

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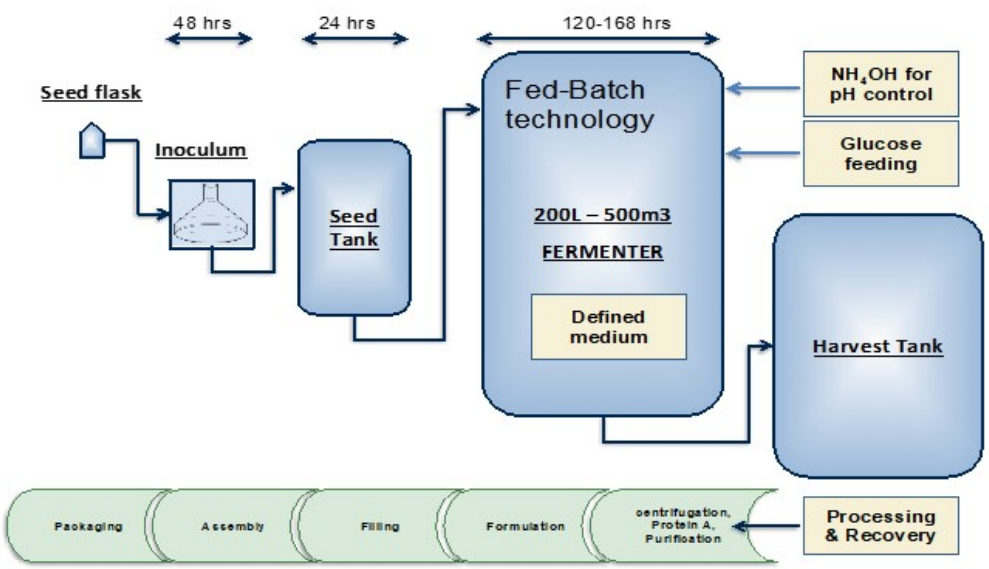
C1 Fermentation Technology – Microbial

Fed-Batch Process Well Defined easy Technology Transfer at flexible scaling

Fed-batch Process



- Fully defined low-cost medium
- Fed-batch technology with glucose feeding
- Wide range of conditions pH: 5-8, Temp: 20 - 45°C
- Low viscosity culture
- ~ 4 to 7-day process
- 1L to 500,000L fermentation scale, stainless steel or single use stirred tank fermenters
- At the end 30-40% biomass, 60-70 % supernatant* Protein production requires no inducer
- Protein is secreted to the media

MTP to large scale mAbs productivity

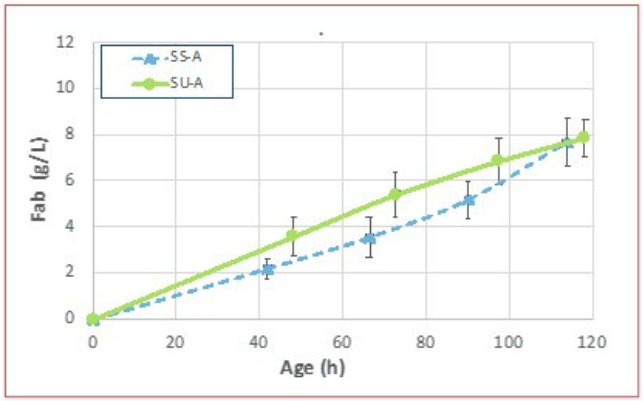
24 wells MTP – 1mg/4ml
1L fermentor – 1.7/g/l/d
30L fermentor – 2.4 g/l/d

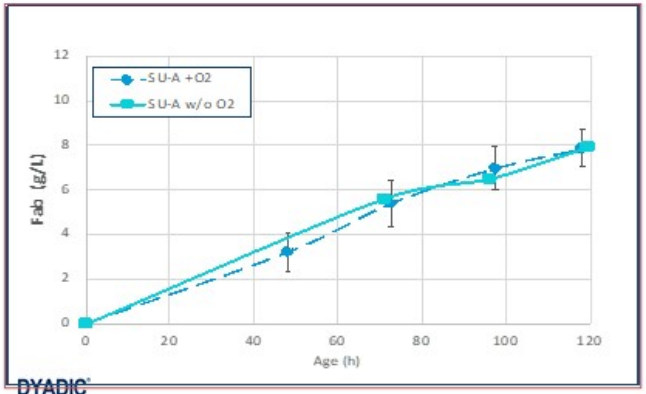
*titers refer to the supernatant

Comparison of Fab production in SSB or SUB under different conditions

Certolizumab production with C1 in Single use Bioreactor (SUB)

Conditions A



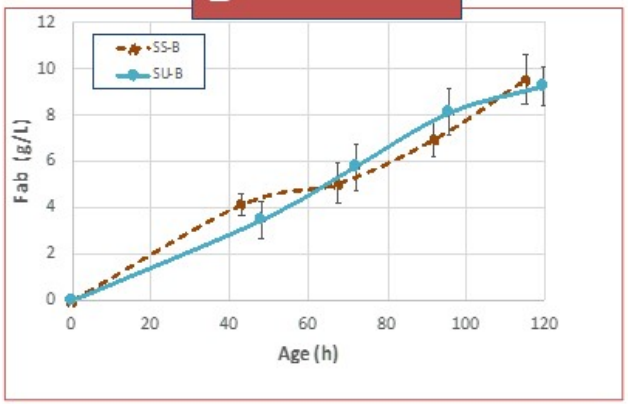


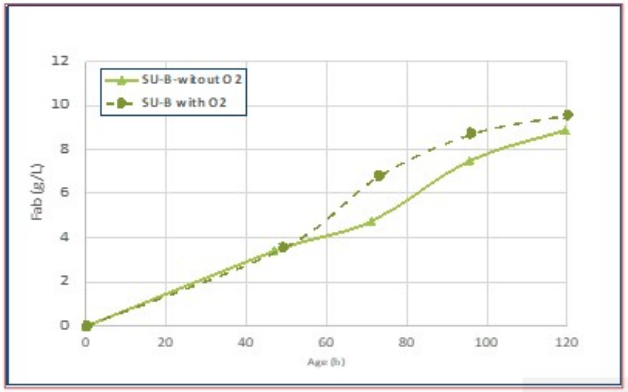
GE's Xcellerex™ XDR-50 MO

Fab production kinetics in either SSB or SUB under two different operating conditions

- Six batches were tested in 2 different conditions with or without O_2 supplementation.
- Conditions B have been shown to be more productive than A in both SSB and USB.
- Supplementation of O_2 slightly improve Certolizumab productivity

Conditions B





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SARS-CoV-2 Spike RBD Is A Key Target For Potent Neutralizing mAbs

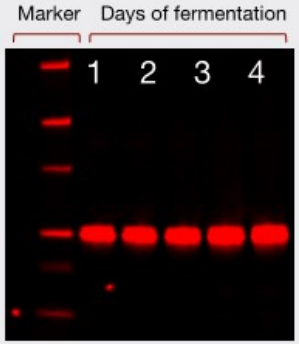
Advancing Towards Phase I clinical study 1H 2022[1]

- **In ~ 2 months, we developed a C1 cell line expressing the Receptor Binding Domain (23kDa) of SARS-CoV-2 spike protein**
- **C1 stable cell line was developed that expressed the RBD originally at a level of ~ 1 g/L – no need for transient stage [2]**
  - **Fermentation optimization 2-3 g/l in 5 days in 22L fermenter [3]**
- **C1 fermentation is based on Fed-batch technology with glucose feeding and cGMP synthetic media**
- **The RBD antigen was secreted to the media – no need for induction**
- **Transgenic mice challenge test demonstrated full protection**

Receptor binding domain:

- Single folded polypeptide chain
- All potent neutralizing Ab target the RBD
- Ag minimization -> focused immune response

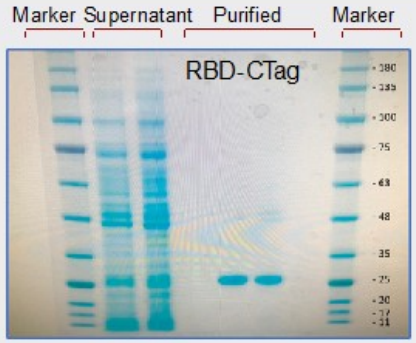
C1 cell line in Ambr250 fermenter system



C1 RBD strain was run in Ambr250 for 5 days

WB analysis off fermentation broth

C1 cell line in 1L fermenter system



C1 RBD strain was run in 5L scale fermentation

The RBD was purified twice with CaptureSelect™ C-tag 10ml column.

98% purity

70% recovery

1. See Slide # 2 Safe Harbor Forward Looking Statements
2. & 3. Reported yields are based on research & development results reported by third parties

Potential Commercial Scale Production of C1-RBD With/Without MPSP

❖ **C1-RBD fermentation capacities for different dose requirements based on 5 days fermentation at various scales [1]**

C1 productivity (2.0 g/L)	Doses (30µg and 30µg)			Doses (15µg+15µg)		
	10M	100M	1000M	10M	100M	1000M
Total volume (g)	600	6 000	60 000	300	3 000	30 000
Productivity (g/L)	2.0	2.0	2.0	2.0	2.0	2.0
RBD purification Recovery (%)	60	60	60	60	60	60
Total fermentation volume (%)	80	80	80	80	80	80
Calculated fermentation volume C1 (L)	625	6 250	62 500	313	3 125	31 250

❖ ***C1-expressed SARS-CoV-2 RBD has the potential to be an effective low-cost vaccine candidate that can be rapidly manufactured at flexible commercial scales***

1. *This slide demonstrates the potential for C1 expressed RBD doses if scale up from laboratory scale (~ 2 g/l of Wuhan variant) if further optimization in upstream fermentation and downstream processing is successfully achieved in cGMP manufacturing .*

Phase I with C1-cell SARS-CoV-2 RBD Recombinant Vaccine in 2021

Prove Safety and Efficacy of DYAI-100 Vaccine Candidate in Humans

✓ Coordination of clinical trials for anti-viral vaccines — CRO

✓ cGMP manufacturing of Toxicology & Clinical Trial Material — BTG, A FERRING COMPANY

✓ Toxicology Study — ENVIGO

✓ Support with regulatory & CMC consultation towards accelerated licensure — parexel

DYADIC — Developed the C1 –SARS-CoV-2 RBD protein based rVaccine (DYAI-100 Vaccine Candidate) ✓

Universiteit Utrecht — Development of Monovalent RBD characterization / evaluation ✓

Erasmus MC — Collaboration on preclinical evaluation of the vaccine candidates in small animal ✓

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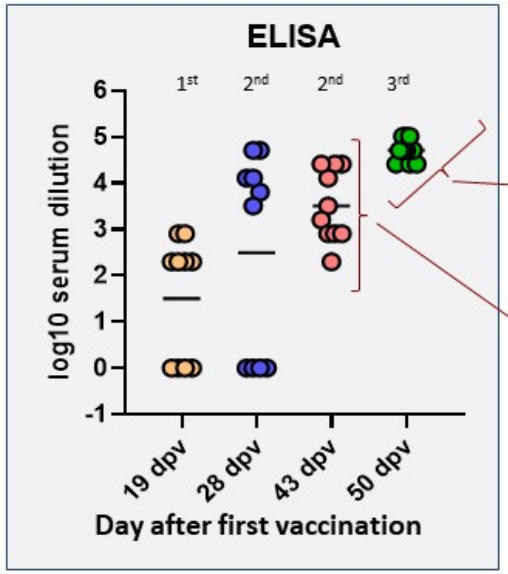
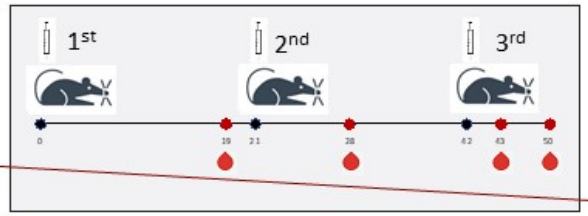
✓ = Completed

Pre-Clinical Study (1)

Mice study demonstrated that the C1-RBD-CTag induced neutralizing antibodies at high level





Plaque reduction neutralization test (PRNT)

SARS-CoV-2 and Vero E6 cells

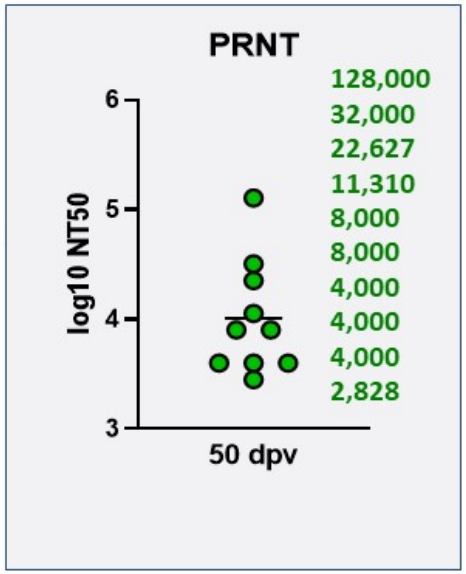
NT_{50} **Dilution** that neutralizes 50% of the virions

Conducted on pooled sera According to Titer (GEOMEAN OF THE titers):

Range 1:1,600 -3200 (Low) - **1,280**

Range 2: 6,400 -12,800 (Mid) - **5,120**

Range 3: 25,600 - 51,200 (High) - **20,400**



Direct RBD ELISA

Serum samples obtained at 19, 28, 43 and 50 dpv were tested in a direct ELISA assay. For each mouse (n = 10) serum dilutions scoring positive in the ELISA are plotted, bars represent geometric means for each sampling time-point.

PRNT

Serum samples obtained at 50 dpv were tested in a PRNT against SARS-CoV2 on Vero E6 cells. NT50 values are plotted for each mouse (n=10) and the geometric mean value is indicated.

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DYAI-100 Vaccine Candidate

Pre-Clinical Study (2)

Challenge Mice study demonstrated that the C1-S-RBD induced full protection

A. Vaccination of K18-hACE2 transgenic mice:

B. 2 groups of transgenic mice were vaccinated with 20 µg of RBD-C formulated with Alhydrogel.

Group I of 8 mice were vaccinated: Prime = Day 1 and Boost at Day – 21. There were 3. Placebo Control Mice. At day 42- Challenge with 2000 PFU of SARS-CoV-2.

1. Bleedings – At Day 20 and Day – 35.
2. Antibodies against RBD were determined by ELISA
3. After 2 days All Control Mice were dead. 7 out of 8 Mice survived with almost no weight loss.

Injection No.	Prime	Boost I		Challenge
Mouse #	Titer dilution 1st	Titer dilution 2nd	PRNT rVSV-SARS-CoV-S	2,000 PFU SARS-CoV-2
1	800	102,400	11,314	Live
2	0	25,600	2,828	Live
3	3,200	3,200	453	Live
4	3,200	512,00	8,000	Live
5	0	102,400	32,000	Live
6	0	6,400	905	Live
7	800	51,200	32,000	Live
8	0	400	40	*Dead
Placebo 1	0	0	0	Dead
Placebo 2	0	0	0	Dead
Placebo 3	0	0	0	Dead
GEOMEAN	40	16,600	2,845	

Group II of 8 mice were vaccinated: Prime = Day 1 and Boost at Day – 21. And Boost at Day-42 There were 2. Placebo Control Mice. At day 57- 4 mice were Challenged with 2000 PFU of SARS-CoV-2.

i. Bleedings – At Day 20 and Day – 41 and 56
ii. After 2 days All Control Mice were dead. 4 out of 4 Mice survived with no weight loss.

Injection No.	Prime	Boost I	Boost II		Challenge
Mouse #	Titer dilution 1st	Titer dilution 2nd	Titer dilution 3rd	PRNT rVSV-SARS-CoV-S	2,000 pfu SARS-Cov-2
1	0	12,800	102,400	32,000	Live
2	0	12,800	204,800	64,000	Live
3	0	3,200	204,800	22,627	Live
4	0	51,200	204,800	128,000	Live
5	800	102,400	204,800	512,000	No Challenge
6	0	6,400	204,800	32,000	No Challenge
7	0	6,400	25,600	22,627	No Challenge
8	0	6,400	409,600	512,000	No Challenge
Placebo 1	0	0	0	0	Dead
Placebo 2	0	0	0	0	Dead
GEOMEAN	0	12,800	169257	53817	----

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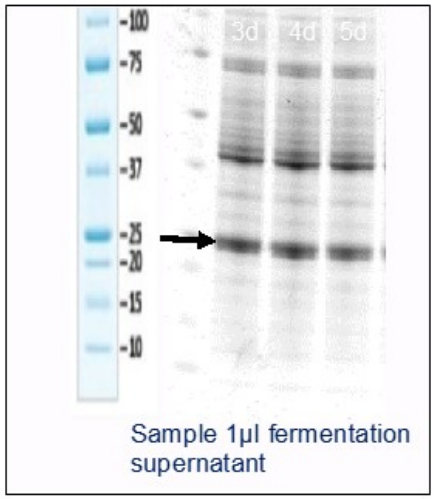
*This mouse succumbed during the anesthesia preceding the intra nasal instillation of SARS-CoV-2.

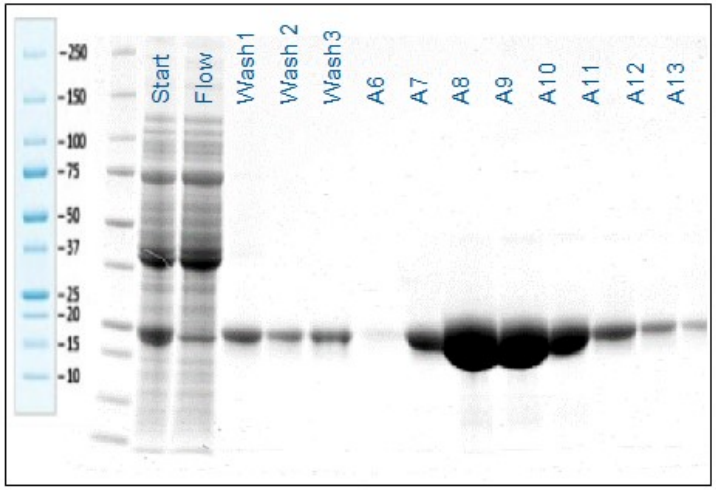
Production of ALPHA-RBD-C-tag variant

Expression in 1L Fermenter

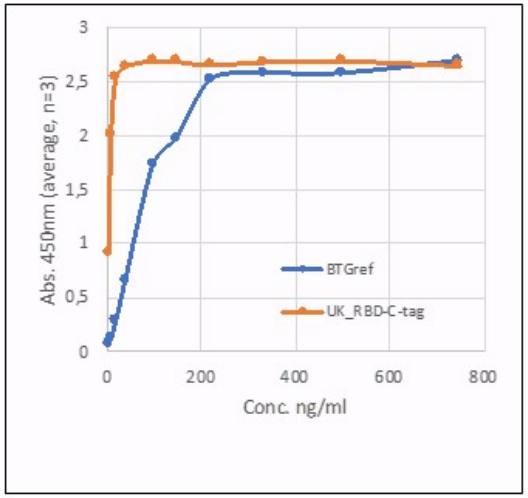
Fermentation and Small-scale purification



Larger scale purification



ACE2 ELISA Assay



Time point	C-tag g/l	Repligen v1 g/l
95h	0,96	1,38
118h	1,19	1,75

- Titer of supernatant 1,75 g/l Purification yield 0,45 g/l
- Recovery 25%
- No fermentation optimization was applied to the UK strain
  - Not optimal purification process

- UK-RBD-C-tag has over 11x activity compared to Wuhan reference in this assay

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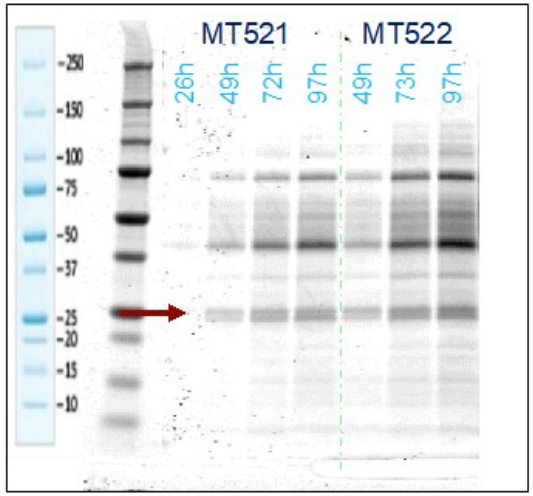
Production of Covid-19 BETA-RBD-C-tag variant

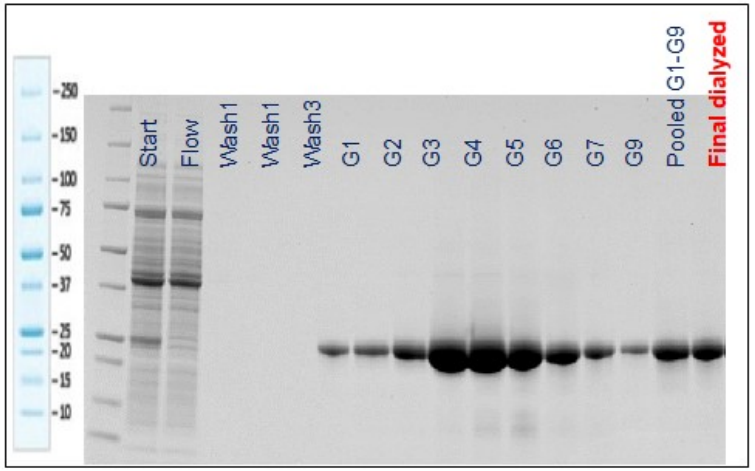
Expression in 1L Fermenter

Fermentation and Small-scale purification



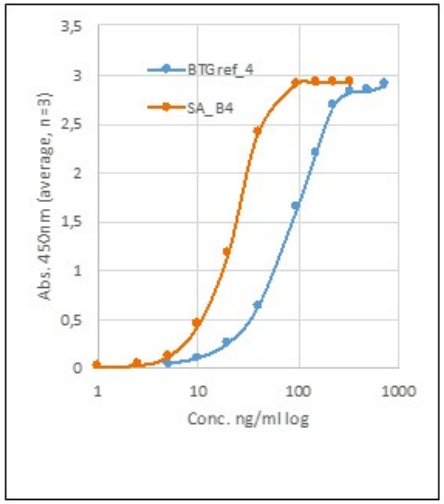
Culture	Time point	Repligen v2 g/l
MT521	72h	0,46
MT521	97h	0,48
MT522	73h	0,51
MT522	97h	0,48

Larger scale purification



- Titer of supernatant 0,48 g/l
- Purification yield 0,48 g/l
- Recovery ~100% purification protocol optimized
- Fermentation process optimization was initiated with the SA cell line

ACE2 ELISA Assay

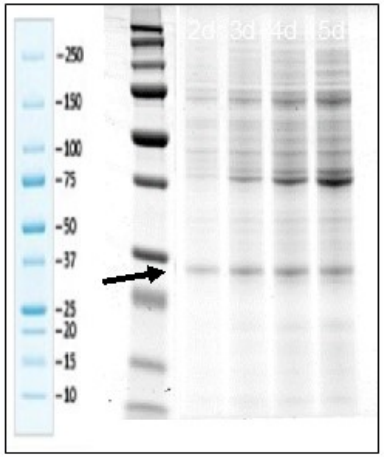


- SA-RBD-C-tag has 3,7-2,7x activity compared to Wuhan reference in these assays

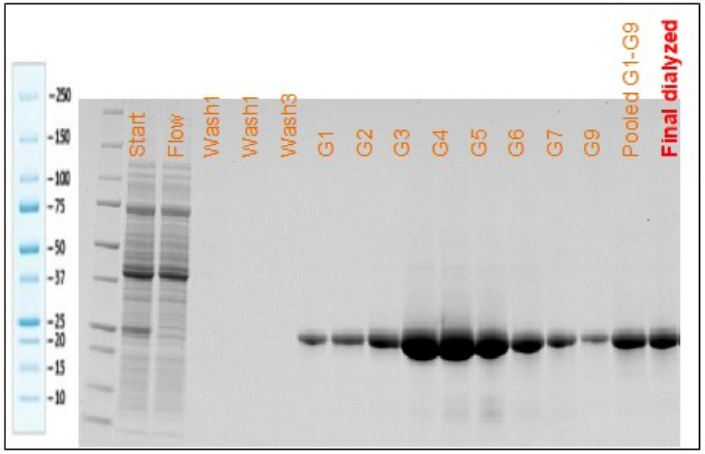
Production of Covid-19 Gamma-RBD-C-tag variant

Expression in 1L Fermenter

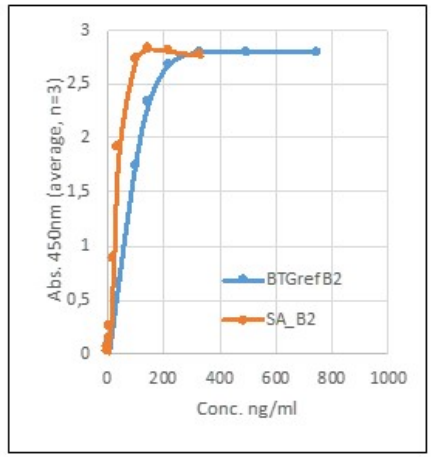
Fermentation and Small-scale purification



larger scale purification



ACE2 ELISA Assay



Time point	C-tag g/l	Repligen g/l
95h	0,54	ND*
118h	0,51	ND*

- Titer of supernatant 0,51 g/l
- Purification yield 0,46 g/l
- Recovery 90%
- No fermentation optimization was applied to the BR strain

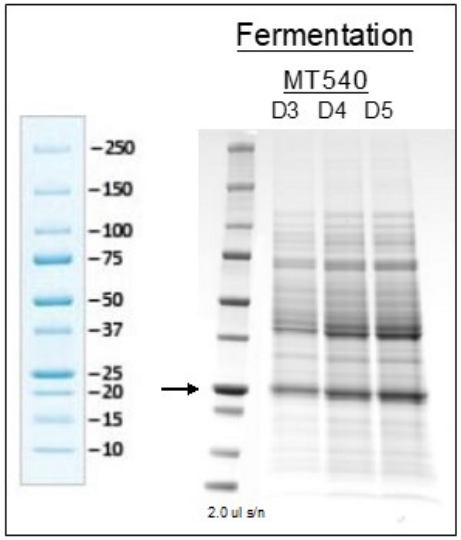
- BR-RBD-C-tag has 7,5x activity compared to Wuhan reference in this assay

DYADIC

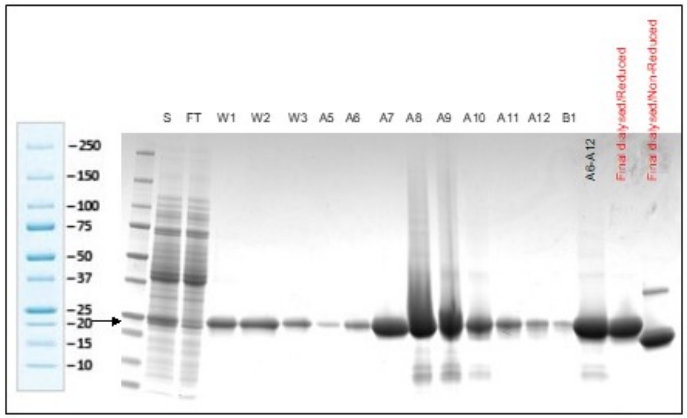
Production of Covid-19 Delta-RBD-C-tag variant

Expression in 1L Fermenter

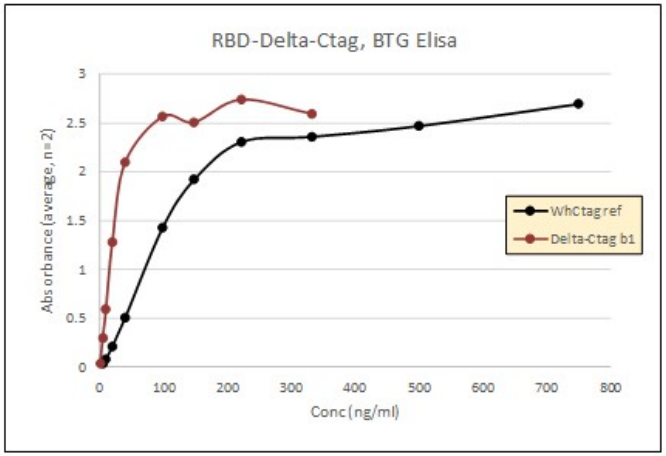
Fermentation and Small-scale purification



Larger scale purification



ACE2 ELISA Assay



Time point	Repligen v1 g/l	C-tag resin g/l
D 5	1.31	1.36

- Titer of supernatant 1.31 g/l
- Purification yield 0.41 g/l
- Recovery 31%
- No fermentation optimization was applied to the Delta-Ctag strain

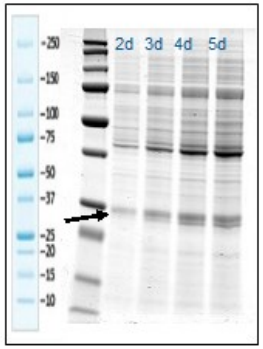
- RBD-Delta-Ctag has 4.3x activity compared to Wuhan reference in this assay

DYADIC

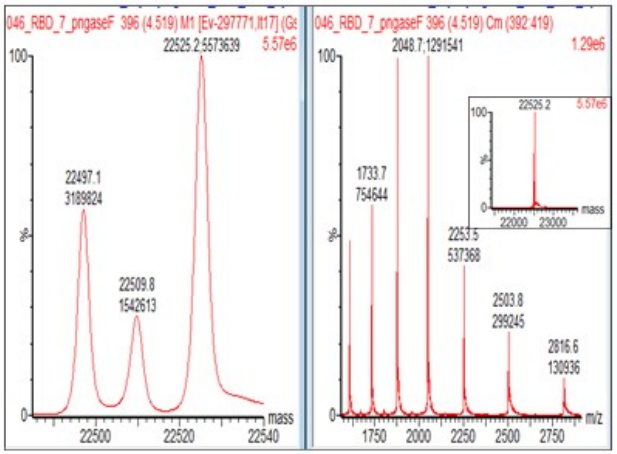
Production of Alpha, Beta, Gamma - SARS-CoV-2 C-Tag Variant RBD's

Co-Expression of 3x Covid-19 RBD's variants in One C1 Strain

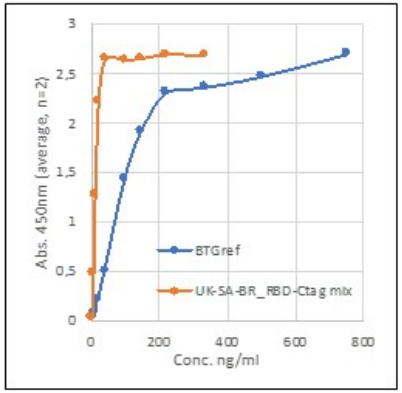
5 days Fermentation



Intact LC-MS



ACE2 ELISA Assay



C-tag and Repligen purification:

- In 121 hr. – 1.34 g/L-1.42 g/L (5 day fermentation.)

Intact LC-MS analysis:

- 1.1.2007 (BR) = 0.46 g/L - 30.95%
- B.1.351 (SA) = 0.23 g/L - 14.97%
- 1.1.28.1 (UK) = 0.81 g/L - 54.08%

UK-SA-BR-RBD-C-tag mix has nearly 9x activity compared to Wuhan reference in this assay

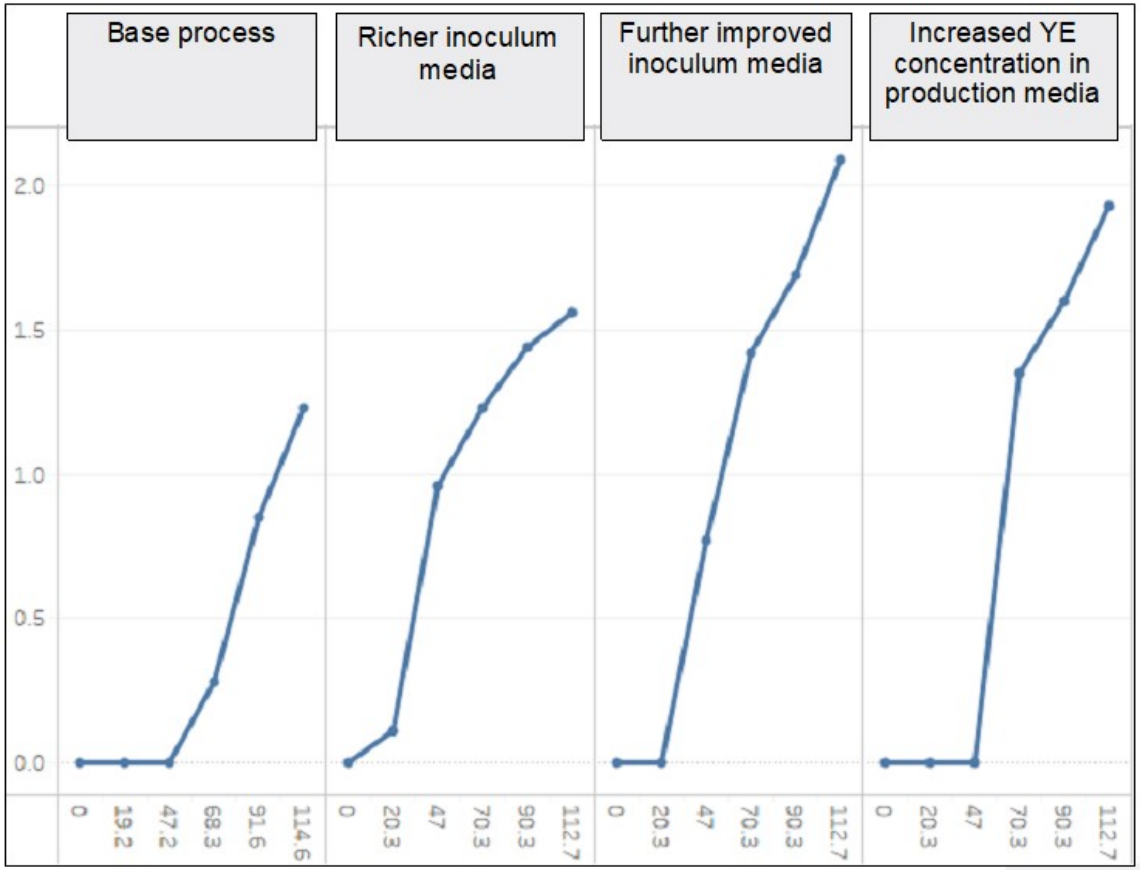
DYADIC's can construct C1 cell line that co-expresses 4 different RBD-variant genes!

- **Three RBD variants were integrated into 2 genomic sites**
- **The expression of each variant was evaluated by LC-MS**
- **The ratio of the expression levels can be modified by adjusting the expression constructs**
- **The reproducibility of the expression was confirmed by 2 fermentation batches**

Optimization of C1-SARS-Cov-2 RBD Fermentation is in Process

Further Fermentation Optimization based on Media, Inoculum and Feeding Regimen

- **Fermentation was done with the single gene copy Wuhan cell line.**
  - Fermentations were run at the 22L scale for 4.6-4.8 days
  - Further fermentation improvement is ongoing



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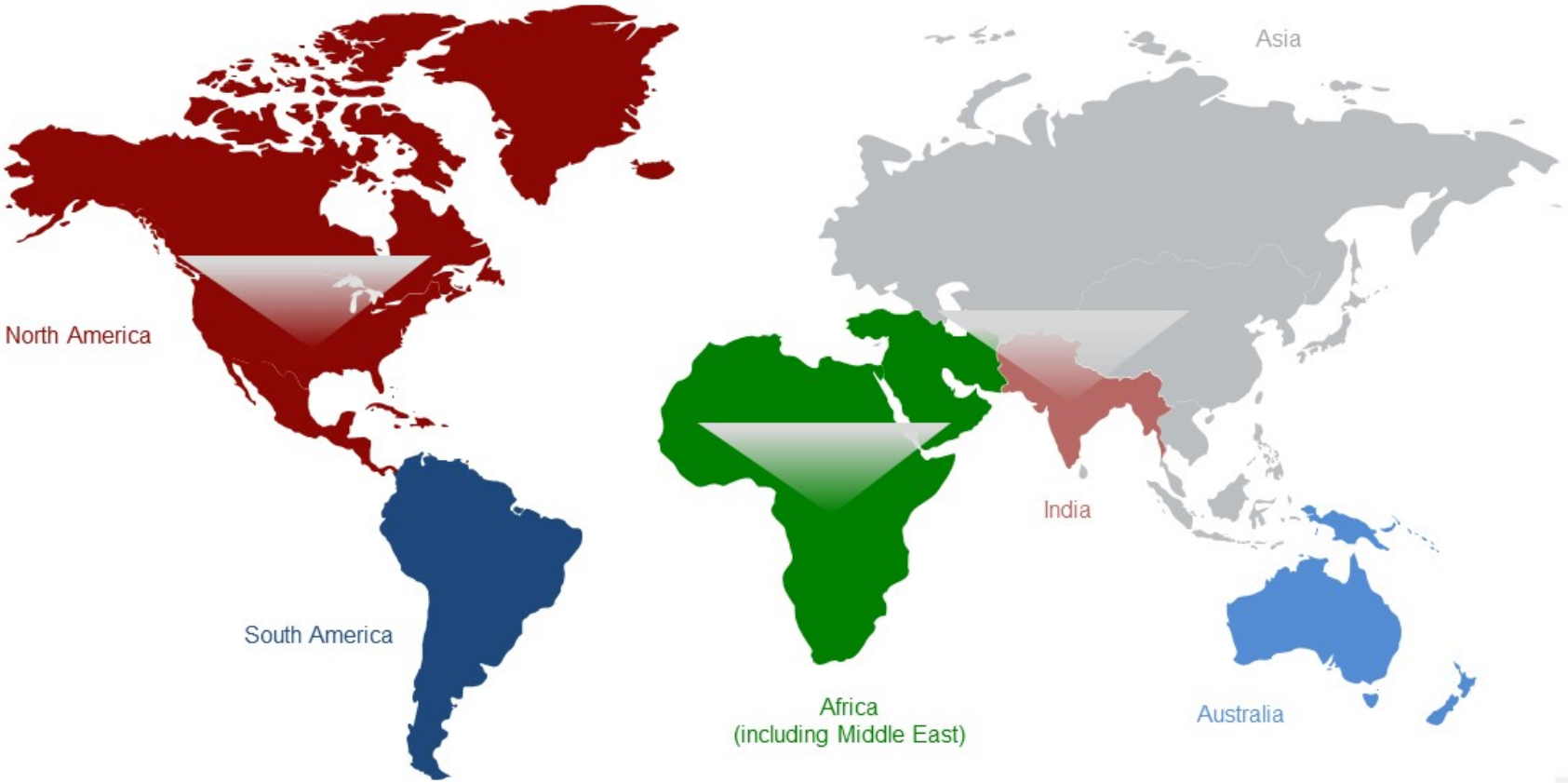
GLOBAL HEALTH ACCESS, AFFORDABILITY & EQUITY

C1 Technology has the Power to Transform Global Health



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