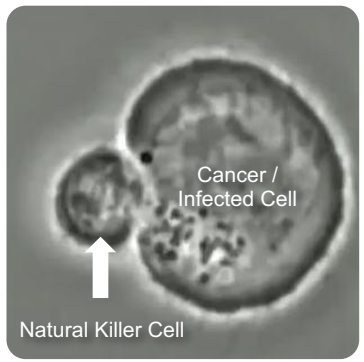
Core Mission:

Orchestrating Cross Talk Between the Natural Killer Cell and the T Cell to Drive Immune Memory

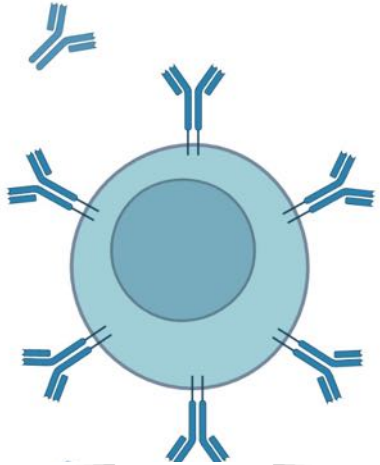
Forward Looking Statement

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Statements in this press release that are not statements of historical fact are considered forward-looking statements, which are usually identified by the use of words such as “anticipates,” “believes,” “continues”, “could”, “estimates,” “expects,” “intends,” “may,” “plans,” “potential”, “predicts”, “projects,” “seeks,” “should,” “will,” and variations of such words or similar expressions. These forward-looking statements are neither forecasts, promises nor guarantees, and are based on the current beliefs of ImmunityBio’s management as well as assumptions made by and information currently available to ImmunityBio. Such statements reflect the current views of ImmunityBio with respect to future events and are subject to known and unknown risks, including business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about ImmunityBio, including, without limitation, (i) potential adverse effects or changes to relationships with employees, suppliers or other parties resulting from the completion of the merger , (ii) the outcome of any legal proceedings that may be instituted against the parties and others related to the merger, (iii) unexpected costs, charges or expenses resulting from the merger, (iv) uncertainty of the expected financial performance of the combined company following completion of the merger, including the possibility that the expected synergies and value creation from the merger will not be realized or will not be realized within the expected time period, (v) the ability of ImmunityBio to continue its planned preclinical and clinical development of its development programs, and the timing and success of any such continued preclinical and clinical development and planned regulatory submissions, (vi) inability to retain and hire key personnel, and (vii) the unknown future impact of the COVID-19 pandemic delay on certain clinical trial milestones and/or ImmunityBio’s operations or operating expenses. More details about these and other risks that may impact ImmunityBio’s business are described under the heading “Risk Factors” in the Company’s Form 8-K filed with the U.S. Securities and Exchange Commission (“SEC”) on March 10, 2021 and in subsequent filings made by ImmunityBio with the SEC, which are available on the SEC’s website at www.sec.gov. ImmunityBio cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date hereof. ImmunityBio does not undertake any duty to update any forward-looking statement or other information in this press release, except to the extent required by law.

Orchestrating Cross Talk of the Immune System

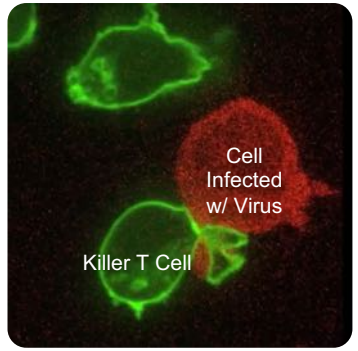


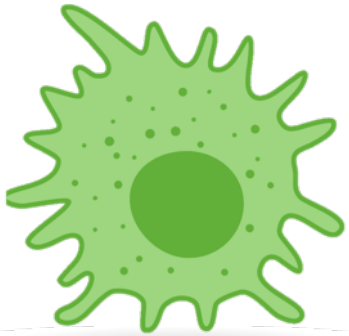
Natural Killer Cell



Memory B Cell

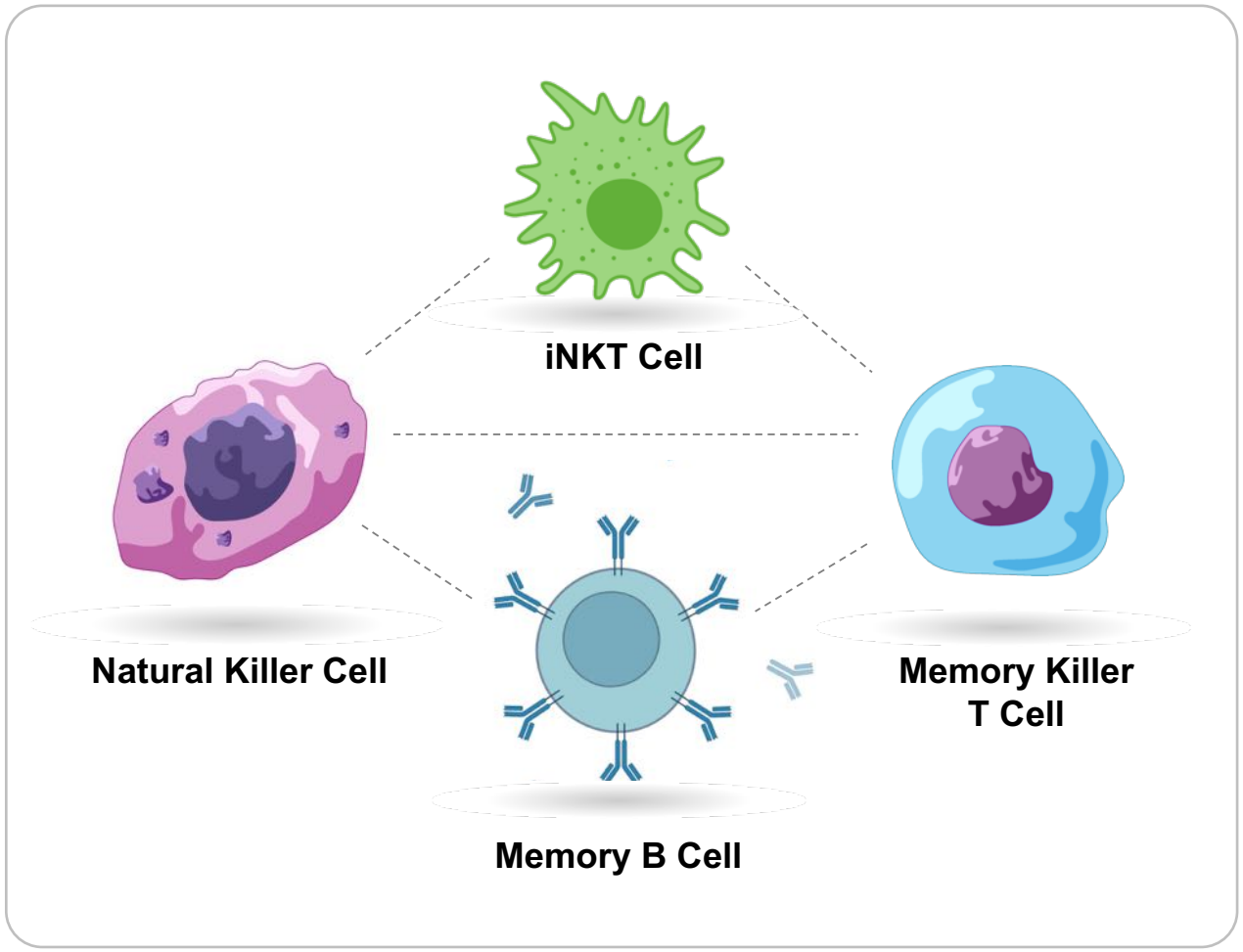
Memory Killer T Cell





iNKT Cell

First-in-Class Immunotherapy Platforms



Natural Killer Cells

- NK-92 Off-the-Shelf
- Autologous m-ceNK
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Memory B & T Cells

- Adenovirus
- Yeast
- Toll Receptor Activators
- saRNA

NK + T Cells

- IL-15 Fusion Proteins

NANT Vaccine Platform: Clinical Development

Cancer

Cancer – 2009-2013

A Preliminary and Comparative Evaluation of a Novel Ad5 [E1-, Eb2-] Recombinant Based Vaccine Used to Induce Cell Mediated Immune Resp

Elizabeth S. Gabitz
Andrea Amalfitano
* Etubics Corporation,

Cancer CEA - 2010

Cancer Immunol Immunother (2010) 59:1131–1135
DOI 10.1007/s00262-010-0847-8

SHORT COMMUNICATION

Anti-tumor immunotherapy despite immunity to adenovirus using a novel adenoviral vector Ad5 [E1-, E2b-]-CEA

Multiple Antigens - 2019

The Oncologist

Clinical Trial Results

A Phase I Trial Using a Multitargeted Recombinant Adenovirus 5 (CEA/MUC1/Brachyury)-Based Immunotherapy Vaccine Regimen in Patients with Advanced Cancer

Neoepitope - 2019

Research Article

Cancer Immunology Research

Efficient Tumor Clearance and Diversified Immunity through Neoepitope Vaccines and Combinatorial Immunotherapy

Karin L. Lee[1], Stephen C. Benz[2], Kristin C. Hicks[1], Andrew Nguyen[2], Sofia R. Gameiro[1], Claudia Palena[1], John Z. Sanborn[2], Zhen Su[3], Peter Ordentlich[4], Lars Rohlin[5], John H. Lee[6],

QUILT Immunotherapy Trials - 2020

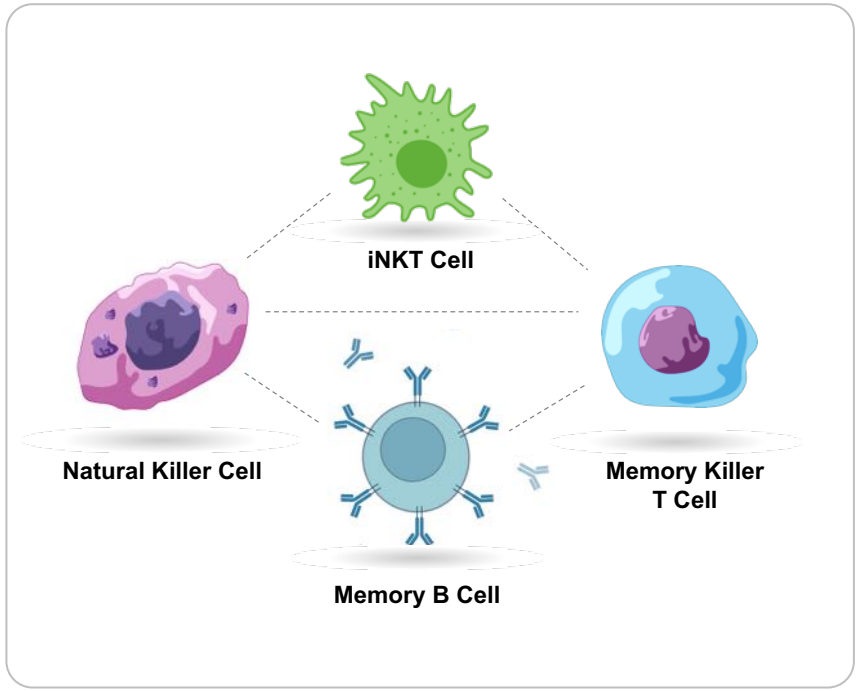
U.S. National Library of Medicine
ClinicalTrials.gov

Find Studies ▾ About Studies ▾ Submit Studies ▾ Resources ▾ About Site ▾ PRS Login

Home > Search Results > Study Record Detail Save this study Saved Studies (22)

QUILT-3.055: A Study of Combination Immunotherapies in Patients Who Have Previously Received Treatment With Immune Checkpoint Inhibitors

ClinicalTrials.gov Identifier: NCT03228667



Infectious Disease

HIV - 2009

Novel Adenovirus type 5 vaccine platform induces cellular immunity against HIV-1 Gag, Pol, Nef despite the presence of Ad5 immunity

H1N1 Pandemic - 2009

Contents lists available at ScienceDirect
Vaccine
journal homepage: www.elsevier.com/locate/vaccine

Prevention of influenza virus shedding and protection from lethal H1N1 challenge using a consensus 2009 H1N1 HA and NA adenovirus vector vaccine

SIV - 2011

NIH Public Access
Author Manuscript
Vaccine. Author manuscript; available in PMC 2013 November 26.

Induction and Comparison of SIV immunity in Ad5 Naïve and Ad5 Immune Non-human Primates using an Ad5 [E1-, E2b-] based vaccine

Lassa Fever - 2019

Contents lists available at ScienceDirect
Vaccine
journal homepage: www.elsevier.com/locate/vaccine

Adenoviral vector-based vaccine is fully protective against lethal Lassa fever challenge in Hartley guinea pigs

COVID - 2021

ORIGINAL RESEARCH article
Front. Immunol., 16 September 2021 | https://doi.org/10.3389/fimmu.2021.729837
frontiers in Immunology

Dual-Antigen COVID-19 Vaccine Subcutaneous Prime Delivery With Oral Boosts Protects NHP Against SARS-CoV-2 Challenge

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- IL-15 Fusion Proteins

Late Stage Clinical Trial Update

- Bladder Cancer
- Lung Cancer
- Pancreatic Cancer
- 2nd Gen COVID Vaccine

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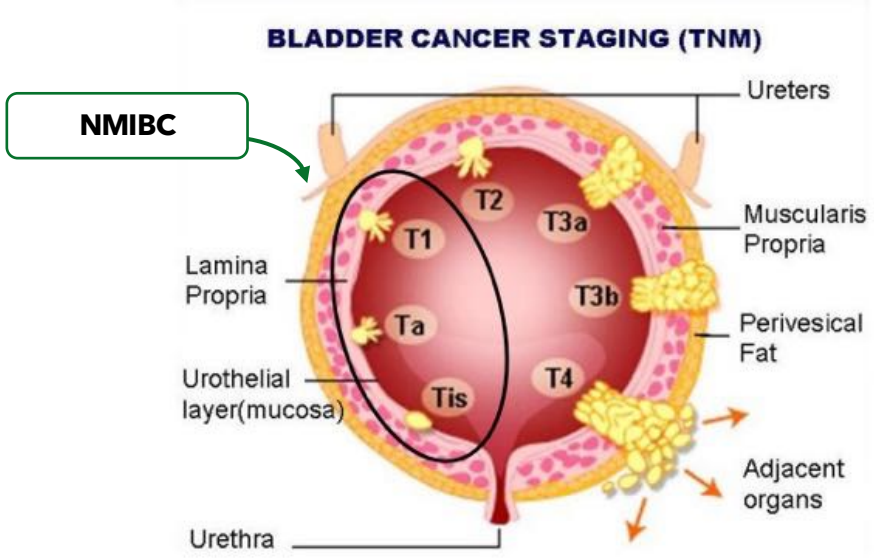
Registrational Trial in Bladder Cancer

Bladder Cancer Epidemiology

- Bladder cancer is the 6th most common cancer in the U.S.
- Approximately 80,000 new diagnoses and 18,000 deaths in 2019
- Prevalence about 600,000 patients
- **75% of bladder cancer in the U.S. is Non-Muscle Invasive Bladder Cancer (NMIBC)**



Reprinted from Shah A, Lamke E. J Ady Pract Oncol. 2018; 9:316-320.

NMIBC Current Standard of Care

First Line Standard of Care for CIS +/- Papillary Disease

CIS ± papillary disease (Ta/T1) → **Transurethral Resection** → **BCG induction + maintenance therapy for up to 3 years**

BCG-Unresponsive CIS is at especially high risk of progression to muscle invasive disease and metastasis

- **Radical cystectomy** (curative intent)
- **BCG-unresponsive CIS (± papillary)**
  - **Valrubicin** Approved 1998 — CR: 19%
  - **Pembro** Approved Jan 2020 — CR: 41%
  - **Investigational Agent** e.g. Anktiva (N-803) — CR: 72%

→ **Radical cystectomy**

Phase 1: Bladder Cancer – Complete Response in 9 of 9 Patients

N-803 + BCG in High-Risk NMIBC – Phase 1 Results
Durable Complete Responses (CR) or No Recurrence (NR) in 9 out of 9 Patients

Dose (intravesicular instillation)	Patient	Stage	Response Assessments							
			W12	6M	9M	12M	15M	18M	21M	24M
100 µg	1	Pap T1	CR*	CR	CR	CR	CR	CR	CR	CR
	2	Pap Ta	CR*	CR	CR	CR	CR	CR	CR	CR
	3	Pap T1	CR*	CR	CR	CR	CR	CR	CR	CR
200 µg	4	Pap T1	IC	CR*	CR	CR	CR	CR	CR	CR
	5	CIS	IC	IC	IC	CR	CR	CR	CR	CR
	6	Pap T1	CR*	CR	CR	CR	CR	CR	CR	CR
400 µg	7	Pap T1	CR*	CR	CR	CR	CR	CR	CR	CR
	8	CIS	CR*	CR	CR	CR	CR	CR	CR	CR**
	9	Pap Ta	CR*	CR	CR	CR	CR	CR	CR	CR

9 of 9 (100%) Patients Disease-Free at 24 Months

BCG naïve alone (SoC): Historical response rate is 55-75% at 3-6 months post BCG alone

Based on this data, FDA granted Fast Track Designation to the Pivotal Trial

*CR termed as No Recurrence (NR) in Papillary Disease **Negative Cystoscopy Inconclusive Cytology


Original Research

Safety, Tolerability, and Long-Term Clinical Outcomes of an IL-15 analogue (N-803) Admixed with Bacillus Calmette-Guérin (BCG) for the Treatment of Bladder Cancer

Charles J. Rosser, Sergei Tikhonenkov, Jeffrey W. Nix, Owen T.M. Chan, Irina Ianculescu, Sandeep Reddy & ...show all

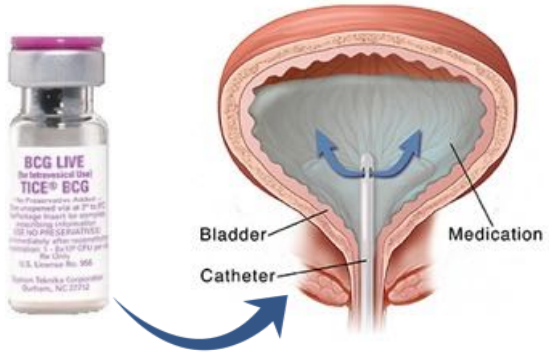
Article: 1912885 | Received 03 Mar 2021, Accepted 31 Mar 2021, Published online: 03 May 2021

https://doi.org/10.1080/2162402X.2021.1912885

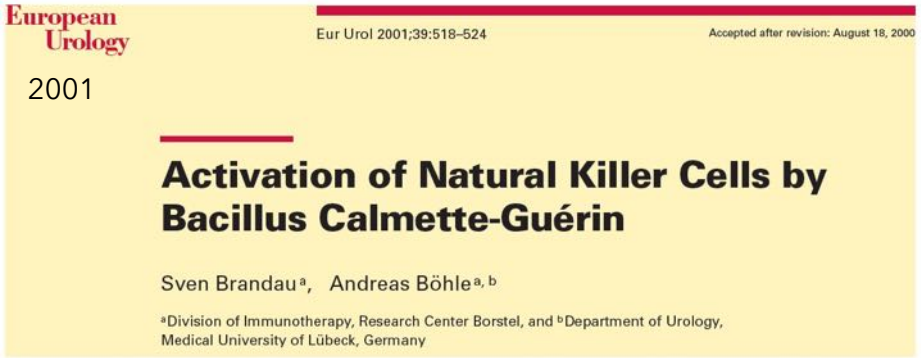
QUILT 3.032: NMIBC Trial Rationale

Anktiva Synergistic with BCG: Enhances Proliferation of NK and T Cells

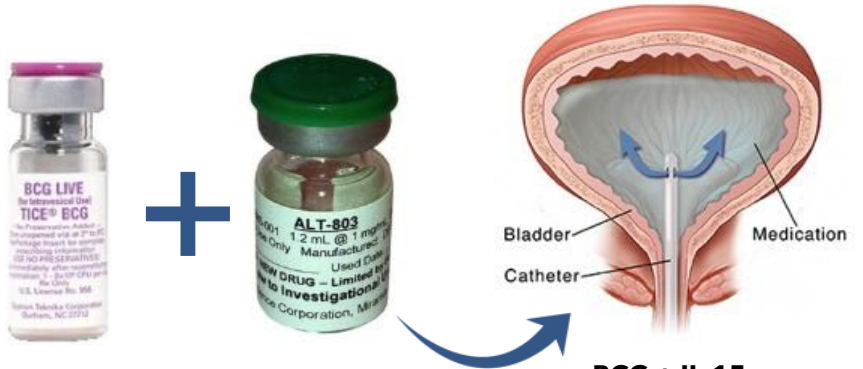
Prime: BCG Activates Natural Killer Cells



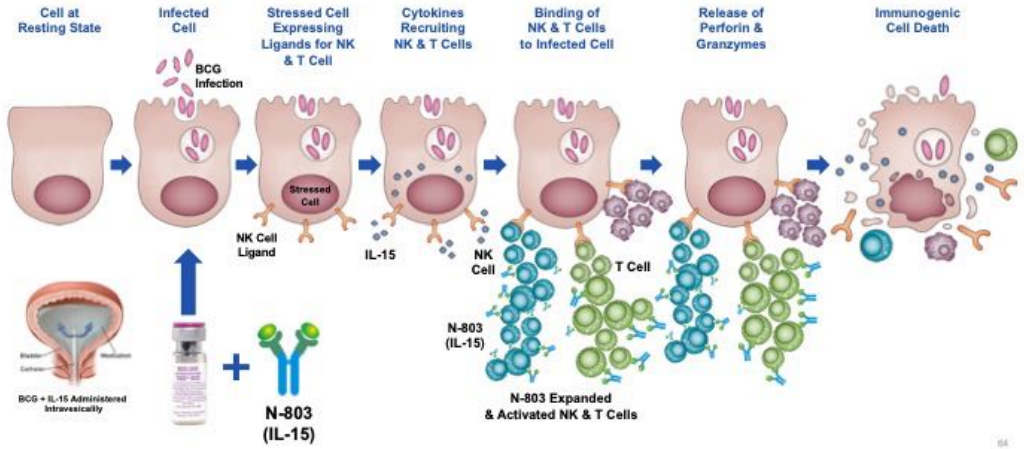
BCG **BCG Administered Intravesically**



Boost: Anktiva IL-15 Proliferates Natural Killer Cells & T Cells



BCG **Anktiva** **BCG + IL-15 Administered Intravesically**



QUILT 3.032: Primary Endpoint Met in CIS and Papillary

For primary endpoint to be met, the lower limit of the 95% confidence interval should be >20%.

BCG Unresponsive CIS NMIBC

Primary Endpoint	Results
Complete Response Rate at Any Time (3 or 6 months) – All Subjects	• 58/81 72% (95% CI: 60.5, 81.1)
Subjects Not Re-inducted (early responders)	• 44/57 77% (95% CI: 64.2, 87.3)

BCG Unresponsive Papillary NMIBC

Primary Endpoint	Results
Disease-Free Survival Rate at 12 months	• 57.1% 95% CI (43.7%, 68.5%)

Data Extraction: September 2021

Durable Response with High Cystectomy Avoidance and Overall Survival

BCG Unresponsive CIS NMIBC

Durable Progression Free Survival

Endpoint	Results
Progression-Free Survival Rate	• 12 months: 88% 95% CI (78.0%, 93.5%) • 18 months: 88% 95% CI (78.0%, 93.5%) • 24 months: 85% 95% CI (73.5%, 92.0%)

Cystectomy Avoidance

Endpoint	Results
Cystectomy-Free Rate	• 12 months: 89% 95% CI (80.1%, 94.6%) • 18 months: 88% 95% CI (77.4%, 93.4%) • 24 months: 85% 95% CI (72.7%, 91.8%)

Overall Survival

Endpoint	Results
Bladder Cancer Specific Survival Rate	• 12 months: 100.0% 95% CI (100.0, 100.0) • 18 months: 100.0% 95% CI (100.0, 100.0) • 24 months: 100.0% 95% CI (100.0, 100.0)

Data Extraction: September 2021, Data Analyzed by Kaplan Meyer Method

High Benefit Risk Ratio:
No Treatment Related SAEs or Deaths

Safety Analysis in BCG Unresponsive NMIBC (CIS & Papillary)

	CIS	Papillary	CIS
Parameter	**Cohort A (N=81)**	**Cohort B (N=73)**	**Cohort C (N=11)**
Treatment-related grade 3-5 AE	2 (2%)	2 (3%)	0 (0%)
Treatment-related SAE	0 (0%)	0 (0%)	0 (0%)
Treatment-related Deaths	0 (0%)	0 (0%)	0 (0%)
Treatment-related AE Causing Discontinuation	2 (2%)	1 (1%)	0 (0%)

Data Extraction: September 2021

Comparison: Merck & ImmunityBio
Immune Related SAEs

	Merck	ImmunityBio
	KEYNOTE-057 Cohort A n (%)	QUILT 3.032 All Cohorts n (%)
Subjects in the Population	102	165
Any Adverse Immune Mediated Events	21 (20.6%)	0 (0%)
Hypothyroidism	8 (7.8%)	0 (0%)
Hyperthyroidism	5 (4.9%)	0 (0%)
Pneumonitis	3 (2.9%)	0 (0%)
Adrenal Insufficiency	1 (1.0%)	0 (0%)
Colitis	1 (1.0%)	0 (0%)
Hepatitis	1 (1.0%)	0 (0%)
Hypophysitis	1 (1.0%)	0 (0%)
Nephritis	1 (1.0%)	0 (0%)
Type 1 Diabetes Mellitus	1 (1.0%)	0 (0%)
Severe Skin Reaction	1 (1.0%)	0 (0%)
Uveitis	1 (1.0%)	0 (0%)

https://www.fda.gov/media/133542/download
Table 17: KEYNOTE-057 AEOSIs by Decreasing Frequency (APaT Population)

Data Extraction: September 2021

Safety & Efficacy Comparison: Merck & ImmunityBio

ENDPOINT	KEYNOTE-057	QUILT 3.032
	N=97	N=81
CR Rate (95% CI)	41% (31%, 52%)	72% (61%, 81%)
Median Duration of CR in Months (range)	16.2 (0.0+ – 26.8)	19.9 (7.9, 26.6)
% Cystectomy Free	63%	88%
Median Duration of Follow-up	24.1 months	21.3 months
Treatment Related SAEs	5%	0%

Data Extraction: September 2021

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Late Stage Clinical Trial Update

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Median Overall Survival of Anktiva Compared to Any Therapy in Patients Who Progressed on Checkpoint Inhibitor

Additional Therapy Following Checkpoint Inhibitor Progression

Median OS: 6.1 Months

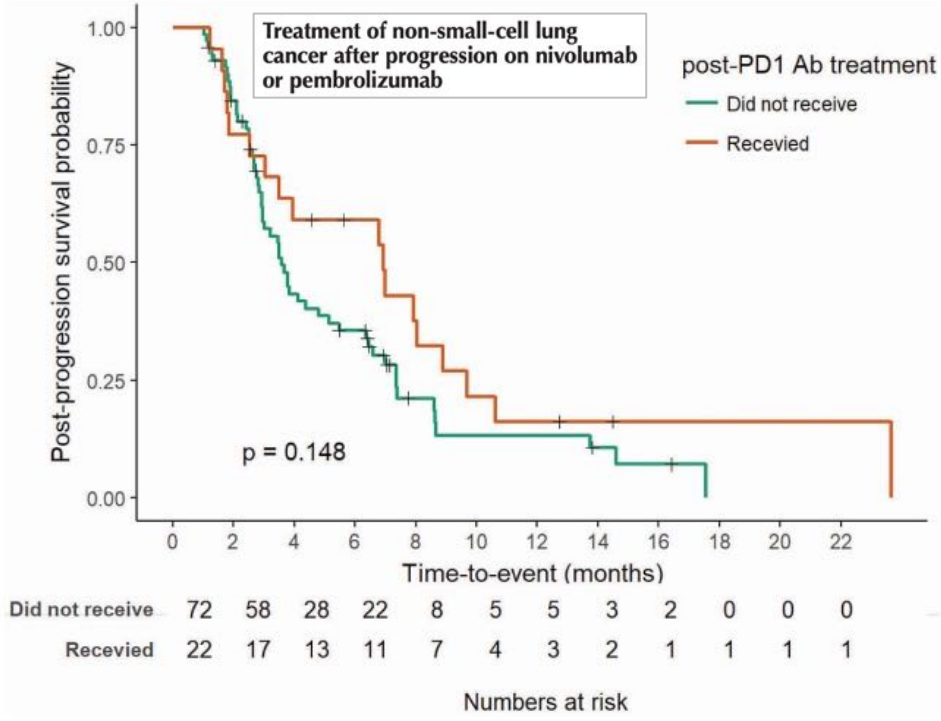
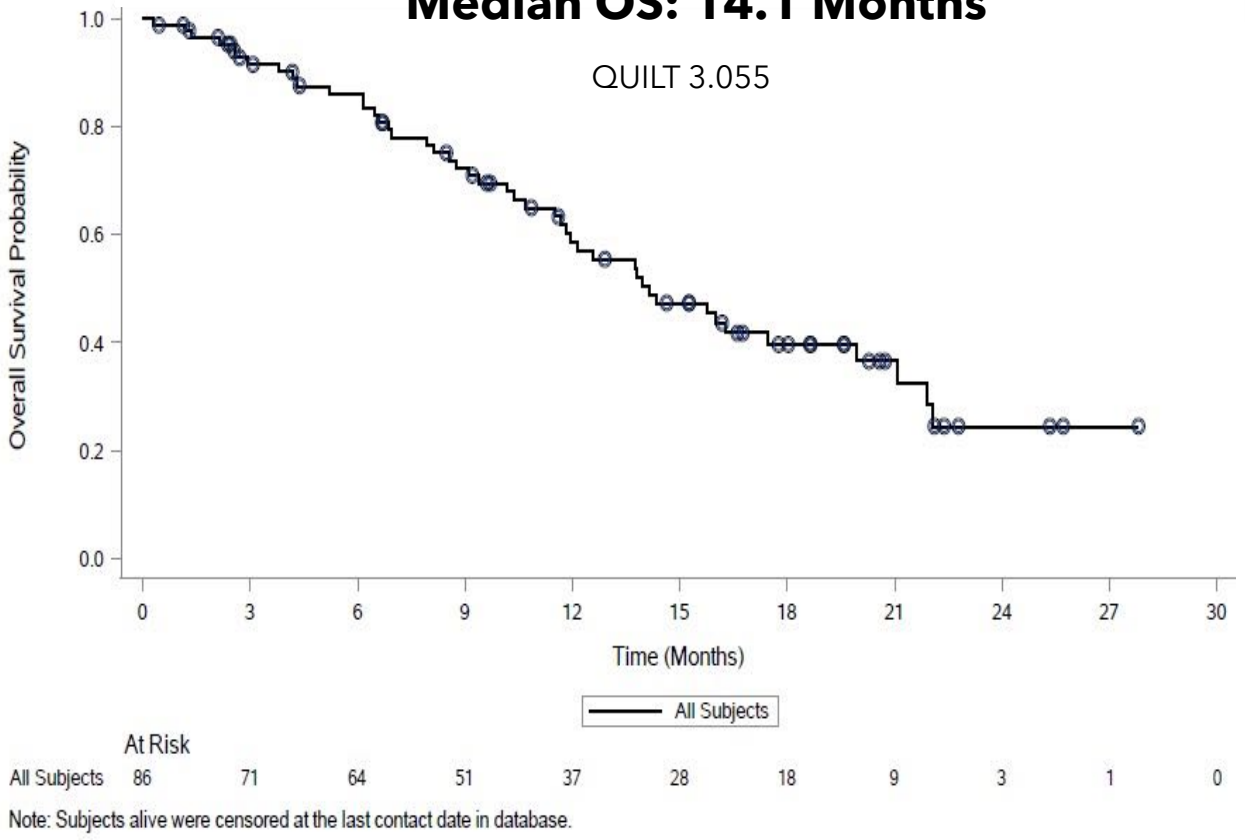


FIGURE 3 Post-progression survival after cessation of PD-1 monoclonal antibody (Ab) in 22 patients who received post-progression therapy and 72 patients who did not within 30 days of PD-1 Ab cessation.

doi: 10.3747/co.27.5495

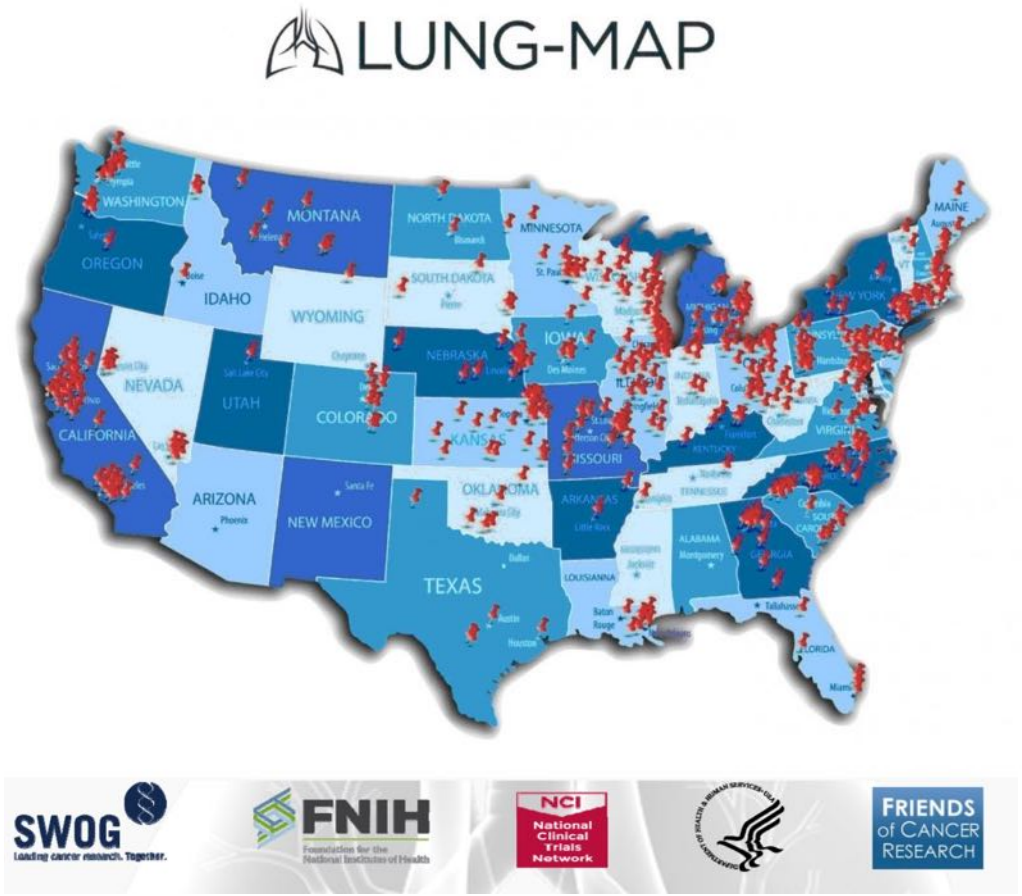
Anktiva IL-15 Therapy Following Checkpoint Inhibitor Progression

Median OS: 14.1 Months



Note: Subjects alive were censored at the last contact date in database.

Anktiva Selected by LUNG-MAP for 2nd Line Patients who Progressed on Checkpoint Therapy



National Cancer Institute Selects ImmunityBio's N-803 IL-15 Receptor Agonist to Combine with Keytruda in 700-Site Lung-MAP Clinical Trial of a Chemo-Free Therapy

October 4, 2021

- ImmunityBio's study will test its IL-15 receptor superagonist complex N-803 (Anktiva) in combination with Merck's pembrolizumab (Keytruda) in up to 478 second-line patients with tumors that are not targetable with a drug, which accounts for the majority of NSCLC cases.
- The study is one of the National Cancer Institute's largest lung cancer clinical trials with more than 700 sites and enrollment is anticipated to begin in Q4 2021.

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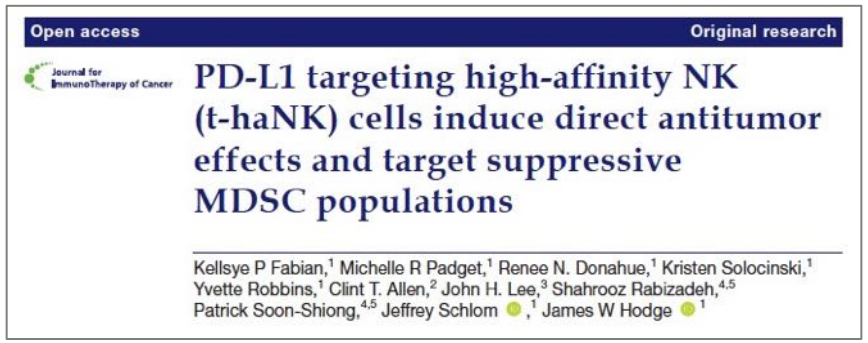
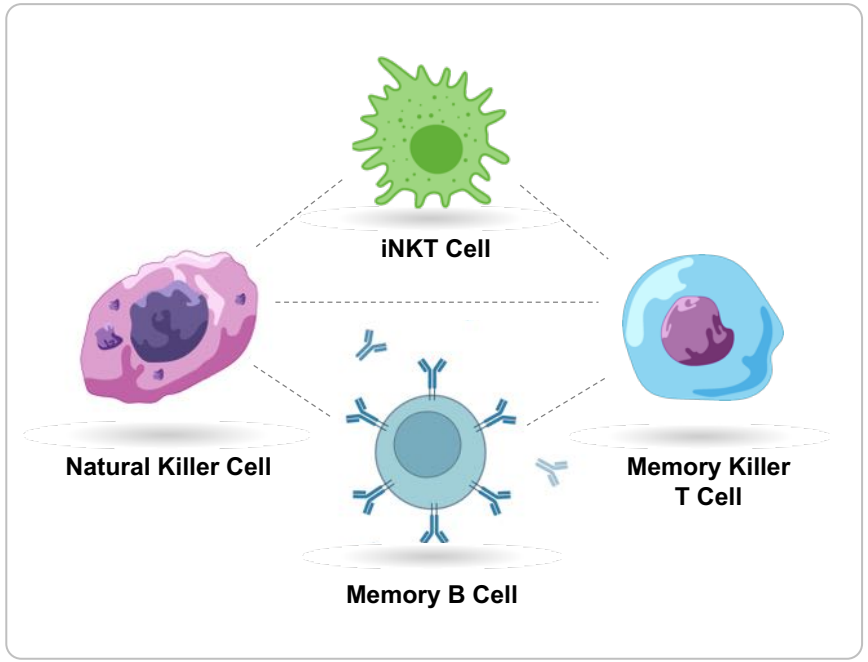
Exploratory Trial of PD-L1 t-haNK and Anktiva in Combination with Chemo Modulation in Metastatic Pancreatic Cancer

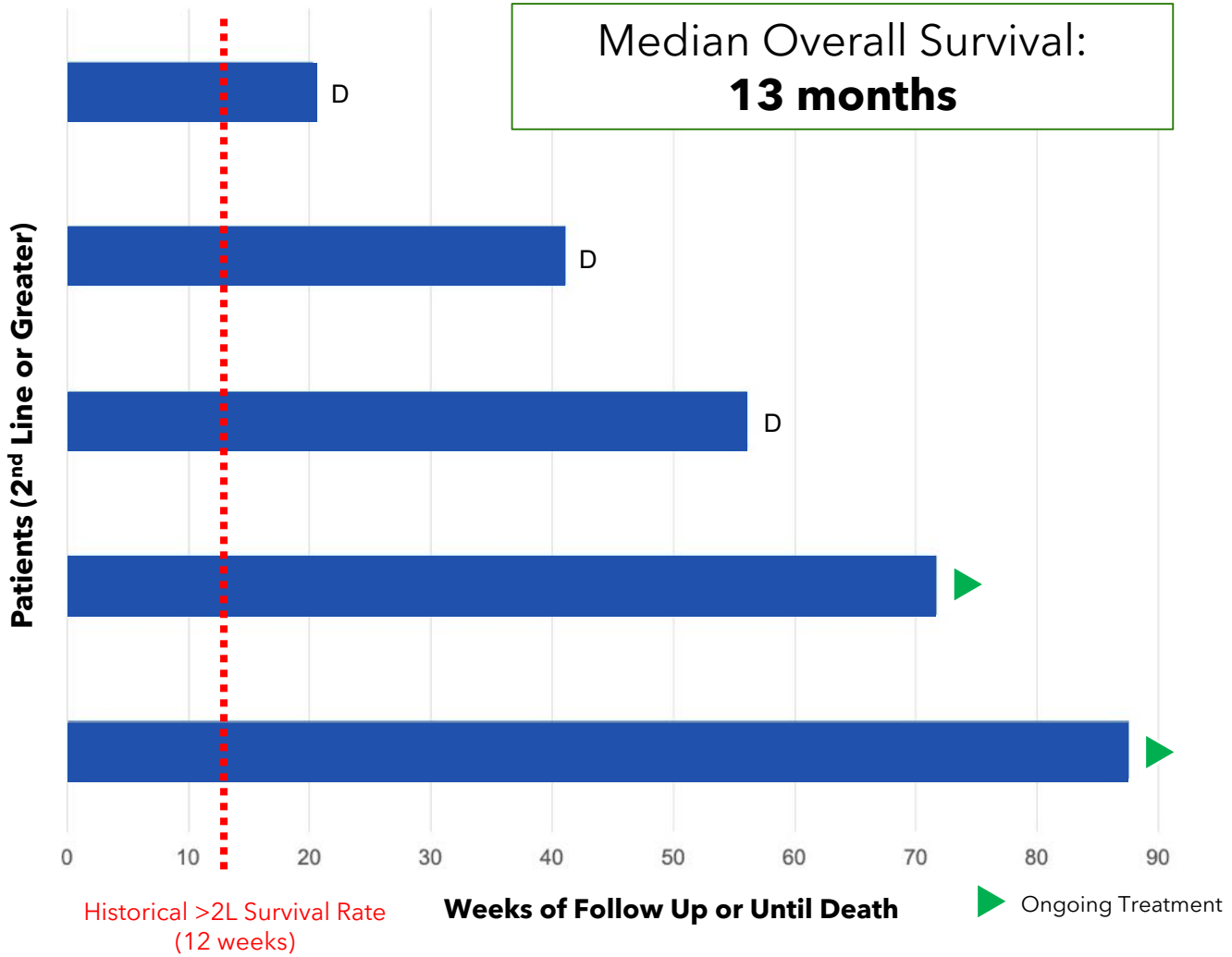

Open access Original research

Journal for ImmunoTherapy of Cancer

PD-L1 targeting high-affinity NK (t-haNK) cells induce direct antitumor effects and target suppressive MDSC populations

Kellsye P Fabian,[1] Michelle R Padget,[1] Renee N. Donahue,[1] Kristen Solocinski,[1] Yvette Robbins,[1] Clint T. Allen,[2] John H. Lee,[3] Shahrooz Rabizadeh,[4,5] Patrick Soon-Shiong,[4,5] Jeffrey Schlom ,[1] James W Hodge [1]



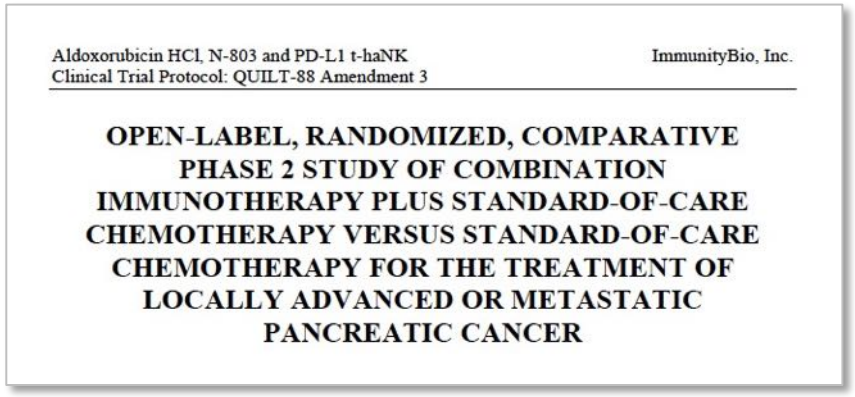


Pancreatic Cancer: An Unmet Need

Actively Enrolling

Phase 2 Trial of PD-L1 t-haNK and Anktiva in Combination with Chemo Immunomodulation in Advanced Metastatic Pancreatic Cancer

NCT04390399 (QUILT-88) N=248


Aldoxorubicin HCl, N-803 and PD-L1 t-haNK
Clinical Trial Protocol: QUILT-88 Amendment 3
ImmunityBio, Inc.

OPEN-LABEL, RANDOMIZED, COMPARATIVE PHASE 2 STUDY OF COMBINATION IMMUNOTHERAPY PLUS STANDARD-OF-CARE CHEMOTHERAPY VERSUS STANDARD-OF-CARE CHEMOTHERAPY FOR THE TREATMENT OF LOCALLY ADVANCED OR METASTATIC PANCREATIC CANCER

Status:
- Enrolling • **Cohort A** 1st Line therapy (Randomized)
- Enrolling • **Cohort B** 2nd Line therapy (Randomized)
- Enrolling • **Cohort C** 3rd Line or greater therapy (Single-Arm)

ImmunityBio Completes Enrollment in Phase 2 Study of Nant Cancer Vaccine for 3rd Line or Greater Metastatic Pancreatic Cancer Patients—90% of Patients Have Exceeded Historical Survival Rates to Date

October 13, 2021

- More than 50 participants in third-line cohort of QUILT 88 trial have received the Nant Cancer Vaccine, which includes ImmunityBio's off-the-shelf, targeted natural killer cells (PD-L1 t-haNK), IL-15 receptor agonist Anktiva (N-803), and Aldoxorubicin, plus low-dose chemotherapy.
- Of the evaluable patients in the study's third cohort (third-line or greater disease state), 90% (43/48) have exceeded the historical survival rates of approximately two months with standard-of-care chemotherapy.
- Of the 48 evaluable patients, approximately half had extremely advanced disease upon enrollment (i.e. had progressed after three to six prior lines of therapy) and, of these patients, 87% (20/23) have exceeded historical survival rates.
- Mature data is expected in Q1 2022 and the company plans to meet with the FDA in 2022 to discuss the path for the approval of combination therapies for pancreatic cancer.

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Next Generation Platforms for Accessible, Durable, and Broadly Protective Coronavirus Vaccines

The Universal COVID Vaccine with Cross Reactivity to Memory B & T Cells

Current COVID-19 Vaccine Challenges

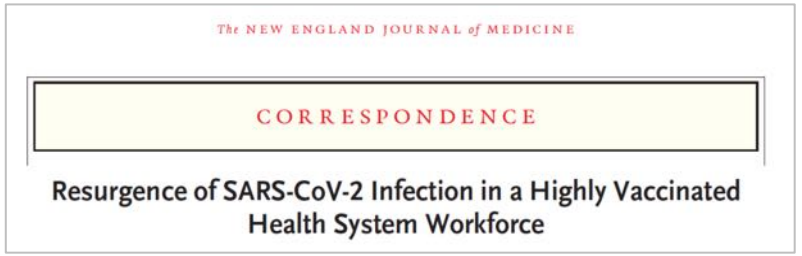
Access

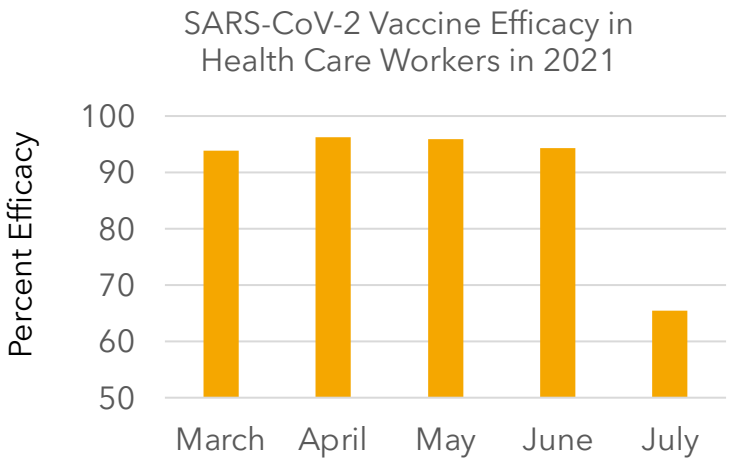
Requirement for deep cold storage of mRNA vaccines

Vaccine hesitancy in the US has left nearly half the population unvaccinated

Durability

Immune protection may wane after several months with current vaccine candidates, necessitating regular boosters

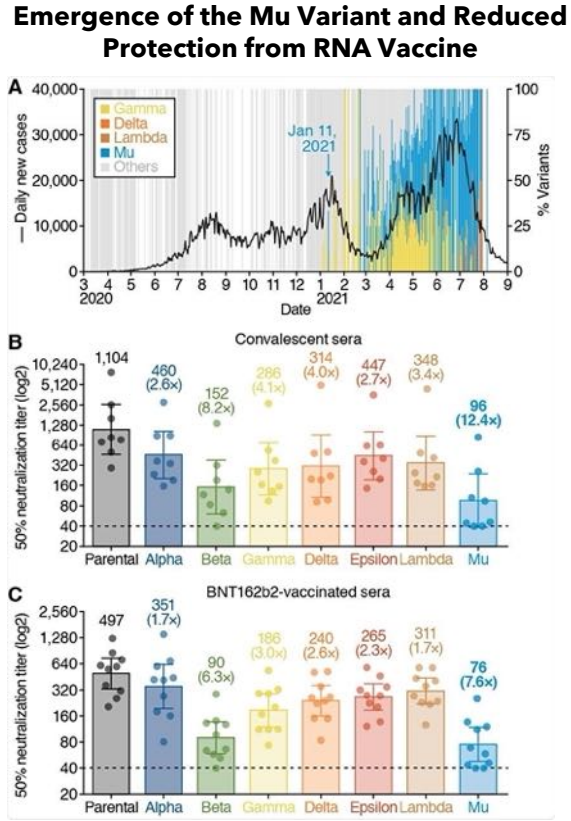




Keehner J, NEJM 2021

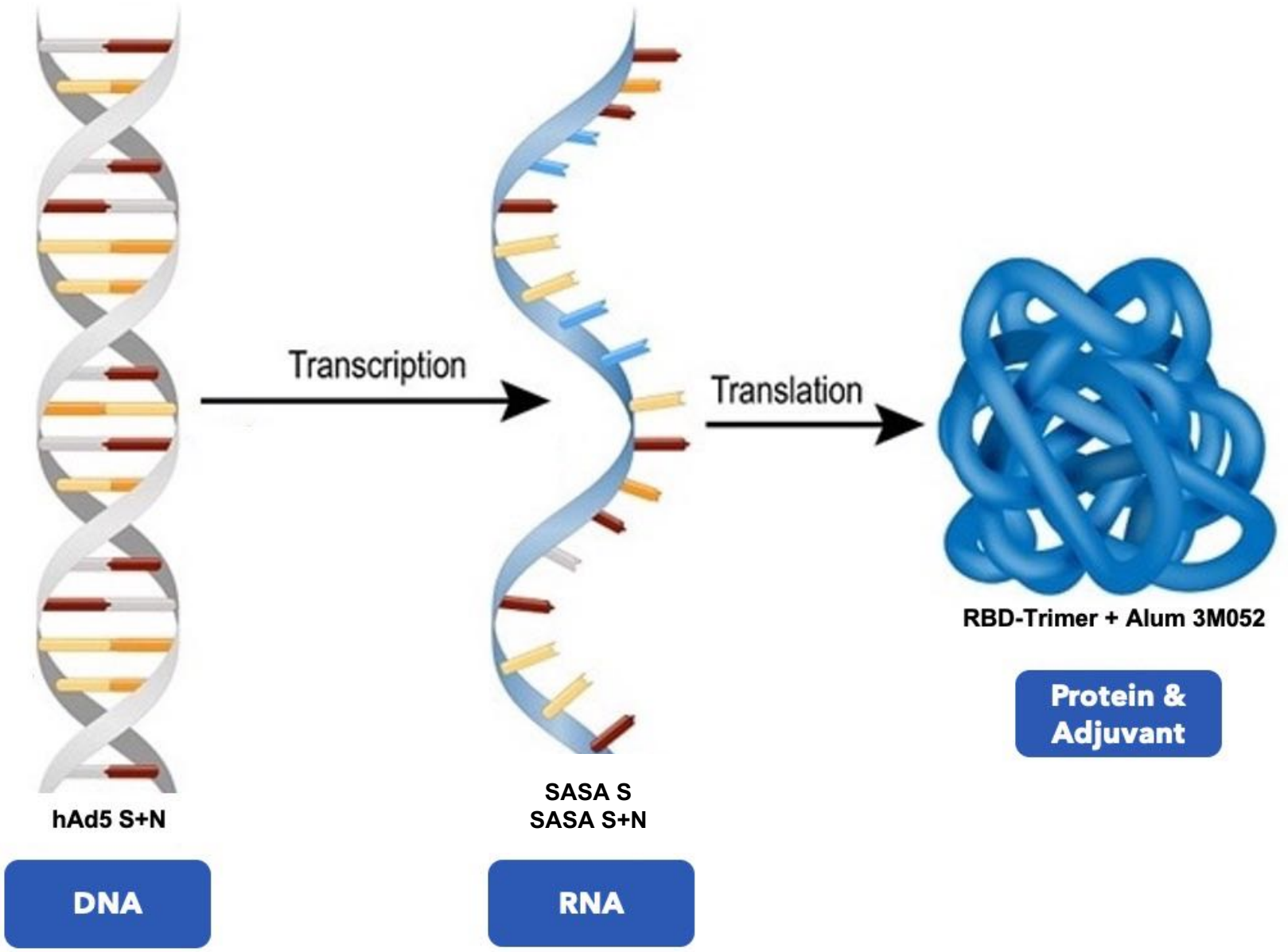
Breadth

Preliminary results show that the efficacy of all currently authorized COVID vaccines is markedly reduced against emerging viral variants.

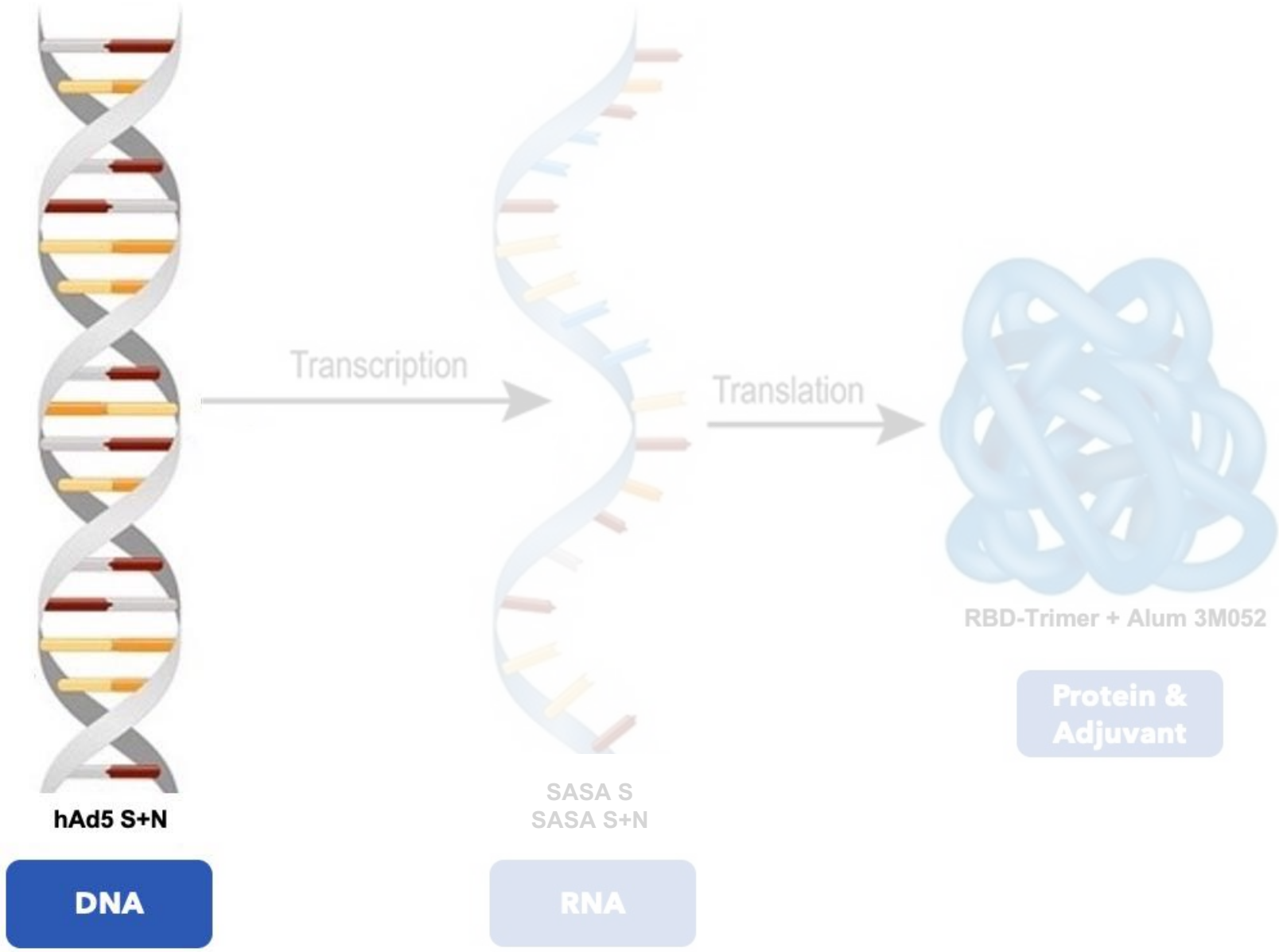


Sato K, et al. *bioRxiv*, 2021.

Next Generation Vaccine Platforms



Next Generation Vaccine Platforms

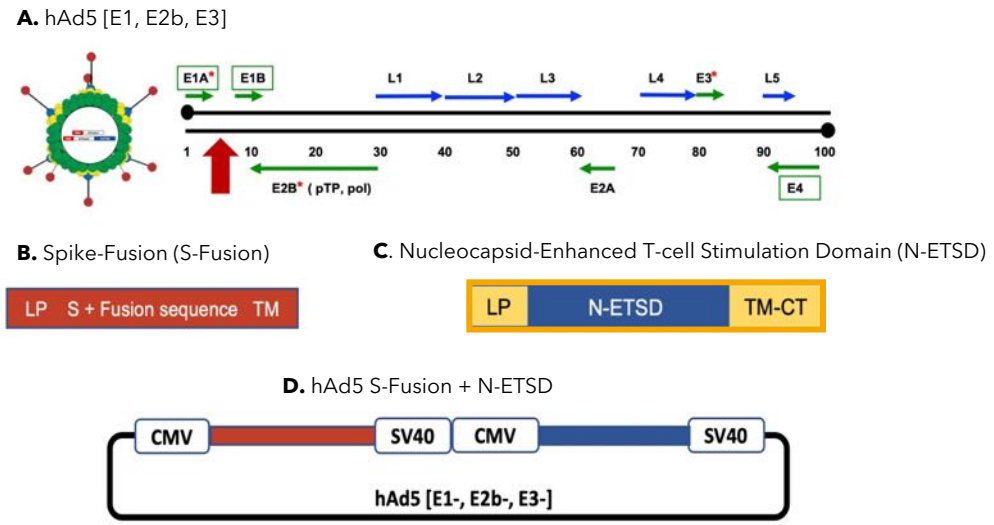


hAd5 S+N: Harnessing T & B Cell Memory and Nucleocapsid Antigen

DNA Vaccine

Adenovirus (hAd5)

hAd5 S-Fusion + N-ETSD



Investigational Agent Name:

hAd5 S-Fusion+N-ETSD

- Unique and only clinically available human Adenovirus (hAd5) vector technology without adenoviral fiber production (E1-, E2b-, E3- Deleted): **potent, long-lasting protein production for maximal cellular and humoral immunity.**
- **Proven safety profile** of hAd5 in 13 Phase I / II clinical trials in over 125 elderly and immuno-compromised cancer patients.
- Proven antigen specific $CD4^+$ and CD8+ T cell generation in patients **even with previous adenoviral immunity.**
- Unique vaccine construct maximizing cell mediated immunogenicity and **reducing the risk of antibody dependent enhancement**.
- Established cell line: **high yields, scalable, fully industrialized**. GMP plant activated.
- **Stable at simple refrigeration** (2-8°C).

The Significance of Nucleocapsid (N) in Vaccine Design

Memory T Cells with 17 Year Protection Against SARS-CoV

July 2020

Article

SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls

https://doi.org/10.1038/s41586-020-2550-z
Received: 20 May 2020
Accepted: 7 July 2020
Published online: 15 July 2020
Check for updates

Nina Le Bert[1,9], Anthony T. Tan[1,9], Kamini Kunasegaran[1], Christine Y. L. Tham[1], Morteza Hafezi[1], Adeline Chia[1], Melissa Hui Yen Chng[1], Meiyin Lin[1,2], Nicole Tan[1], Martin Linster[1], Wan Ni Chia[1], Mark I-Cheng Chen[3], Lin-Fa Wang[1], Eng Eong Ooi[1], Shirin Kalimuddin[4], Paul Anantharajah Tambyah[5,6], Jenny Guek-Hong Low[1,4], Yee-Joo Tan[2,7] & Antonio Bertoletti[1,8]

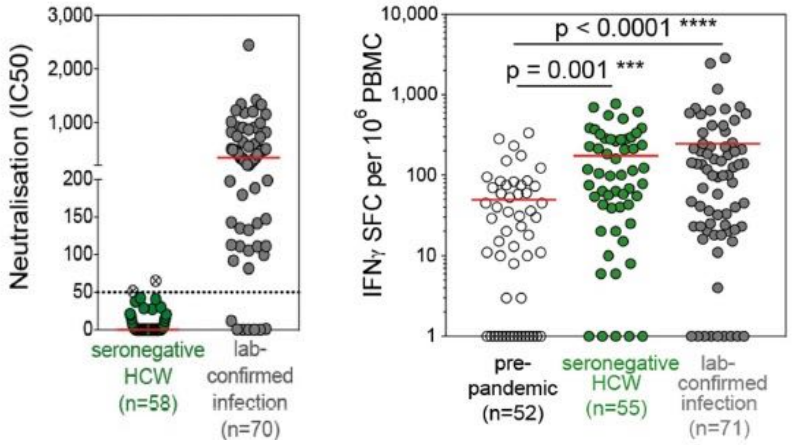
Memory T cells induced by previous pathogens can shape susceptibility to, and the clinical severity of, subsequent infections[1]. Little is known about the presence in humans of pre-existing memory T cells that have the potential to recognize severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Here we studied T cell responses against the structural (nucleocapsid (N) protein) and non-structural (NSP7 and NSP13 of *ORF1*) regions of SARS-CoV-2 in individuals convalescing from coronavirus disease 2019 (COVID-19) ($n = 36$). In all of these individuals, we found CD4 and CD8 T cells that recognized multiple regions of the N protein. Next, we showed that patients ($n = 23$) who recovered from SARS (the disease associated with SARS-CoV infection) possess long-lasting memory T cells that are reactive to the N protein of SARS-CoV 17 years after the outbreak of SARS in 2003; these T cells displayed robust cross-reactivity to the N protein of SARS-CoV-2. We also detected SARS-CoV-2-specific T cells in individuals with no history of SARS, COVID-19 or contact with individuals who had SARS and/or COVID-19 ($n = 37$). SARS-CoV-2-specific T cells in uninfected donors exhibited a different pattern of immunodominance, and frequently targeted NSP7 and NSP13 as well as the N protein. Epitope characterization of NSP7-specific T cells showed the recognition of protein fragments that are conserved among animal betacoronaviruses but have low homology to 'common cold' human-associated coronaviruses. Thus, infection with betacoronaviruses induces multi-specific and long-lasting T cell immunity against the structural N protein. Understanding how pre-existing N- and ORF1-specific T cells that are present in the general population affect the susceptibility to and pathogenesis of SARS-CoV-2 infection is important for the management of the current COVID-19 pandemic.

T Cell Viral Protection in the Absence of Antibodies

November 2021

nature
https://doi.org/10.1038/s41586-021-04186-8
Accelerated Article Preview

Pre-existing polymerase-specific T cells expand in abortive seronegative SARS-CoV-2



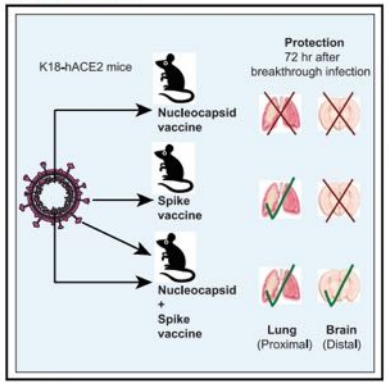
Nucleocapsid Protein Prevents Breakthrough Infection in Brain

September 2021

Cell Reports
Report

Combining spike- and nucleocapsid-based vaccines improves distal control of SARS-CoV-2

Graphical abstract



Authors
Tanushree Dangi, Jacob Class, Nicole Palacio, Justin M. Richner, Pablo Penaloza MacMaster

Correspondence
richner@uic.edu (J.M.R.), ppm@northwestern.edu (P.P.M.)

In brief
Most SARS-CoV-2 vaccines are based on the spike antigen alone, and it is unknown whether including other viral antigens improves protection. Dangi et al. show that combining a spike vaccine with a nucleocapsid vaccine improves the control of a SARS-CoV-2 infection, warranting the inclusion of nucleocapsid in next-generation SARS-CoV-2 vaccines.

Highlights

- SARS-CoV-2 vaccines do not prevent breakthrough infection in K18-ACE2 mice
- A spike vaccine confers better protection than a nucleocapsid vaccine
- A spike vaccine confers acute protection in lung, but not in brain
- Combining spike and nucleocapsid vaccines improves distal protection in brain

The Important Revelation of Memory B & T Cell Cross Reactivity for a Universal COVID Vaccine

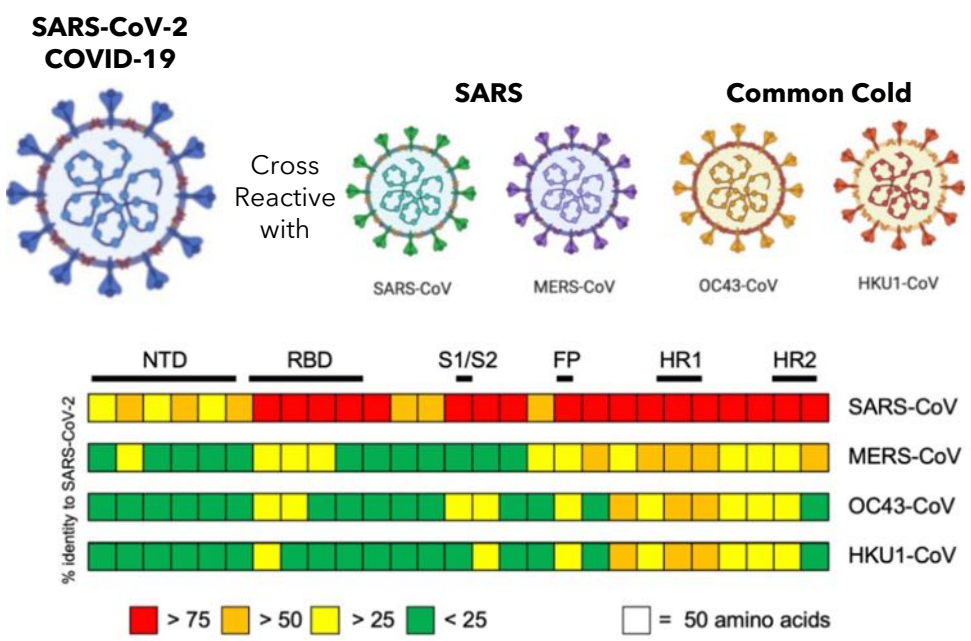
Cross Reactive Memory B Cells

June 2020

medRxiv. 2020 Jun 23;2020.06.22.20137695. doi: 10.1101/2020.06.22.20137695. Preprint

Serologic cross-reactivity of SARS-CoV-2 with endemic and seasonal Betacoronaviruses

Jennifer Hicks [1 2], Carleen Klumpp-Thomas [3 2], Heather Kalish [1 2],

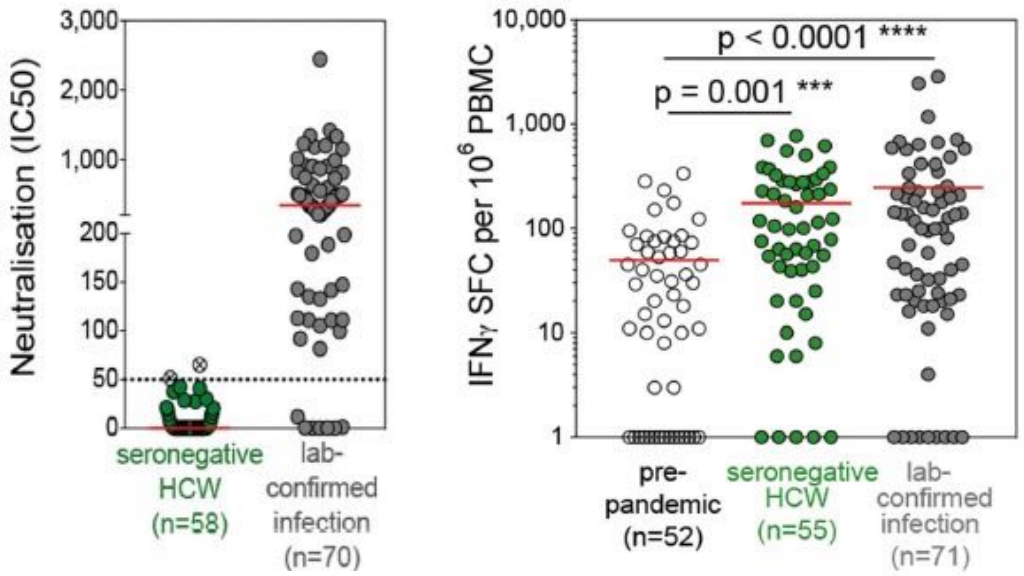


Cross Reactive Memory T Cells

June 2021

nature
https://doi.org/10.1038/s41586-021-04186-8
Accelerated Article Preview

Pre-existing polymerase-specific T cells expand in abortive seronegative SARS-CoV-2



hAd5 S+N Vaccine Generates Cross Reactive Memory B Cell in Healthy Volunteers: The Potential for a Universal COVID Vaccine

B Cells From Common Cold Coronavirus Cross Reacts with SARS-CoV-2

June 2020

> medRxiv. 2020 Jun 23;2020.06.22.20137695. doi: 10.1101/2020.06.22.20137695. Preprint

Serologic cross-reactivity of SARS-CoV-2 with endemic and seasonal Betacoronaviruses

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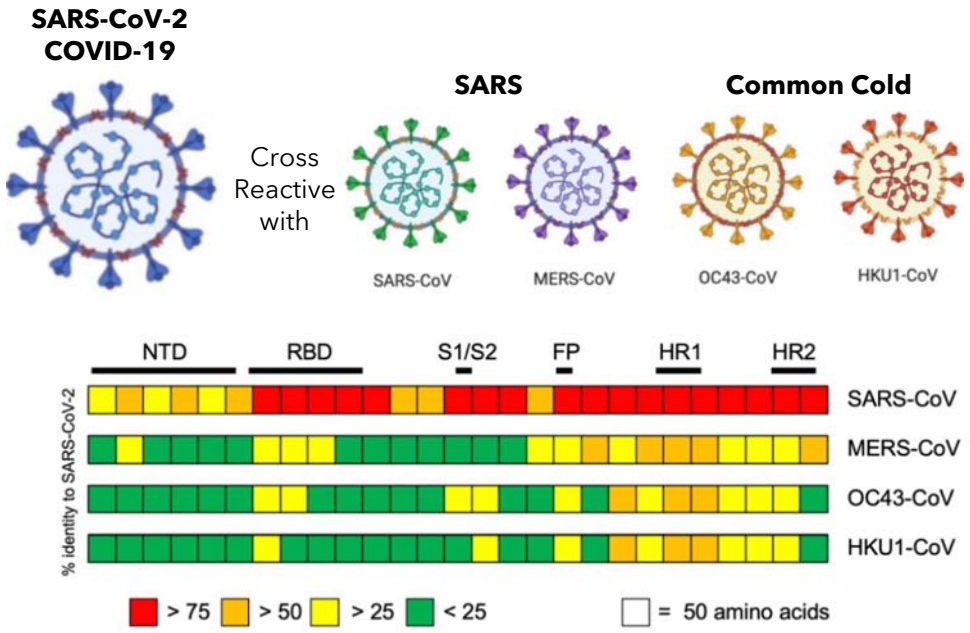
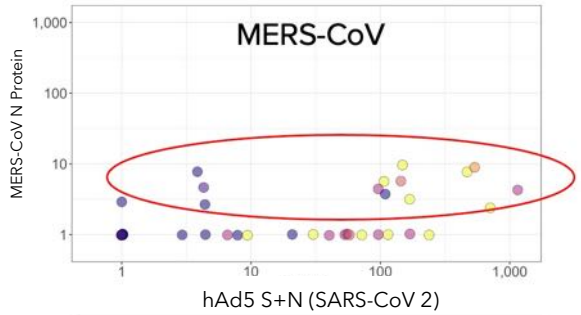
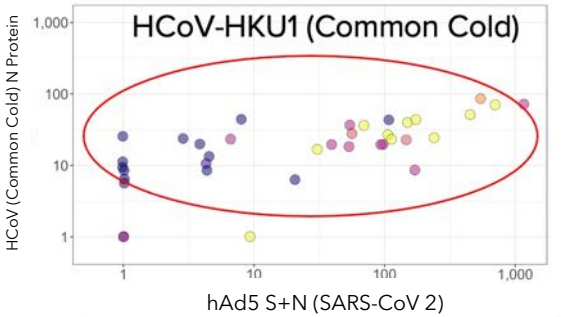
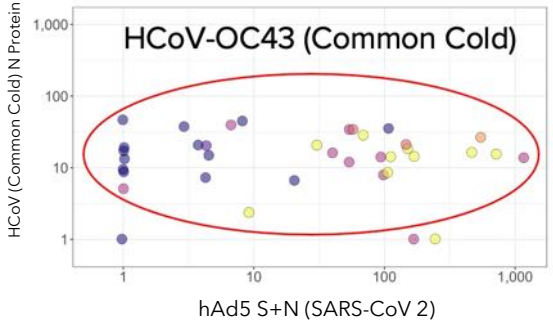


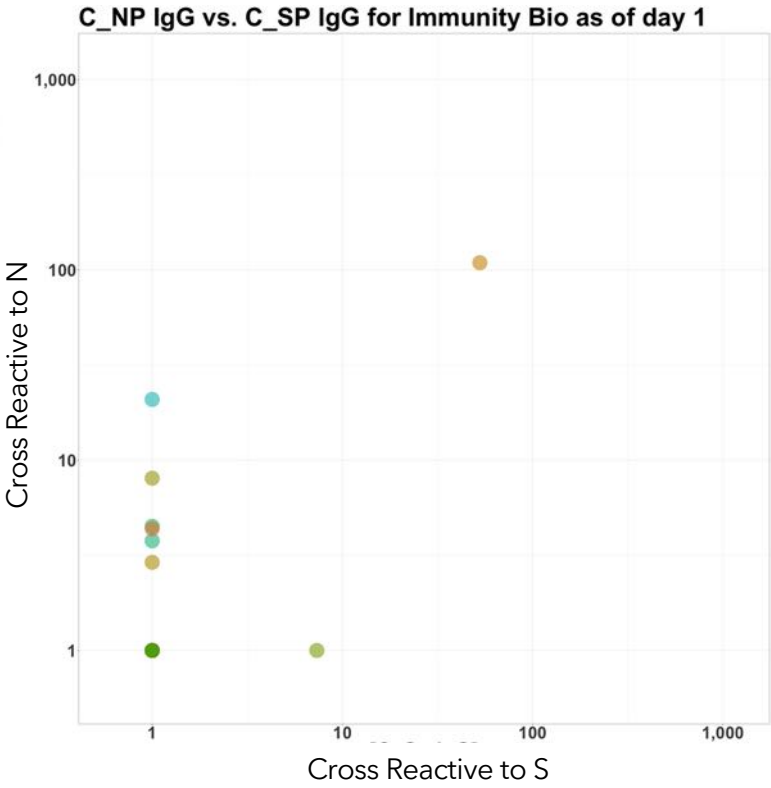
hAd5 S+N Generates Antibodies that Cross React with MERS-CoV and Common Coronaviruses

December 2021 (Unpublished)







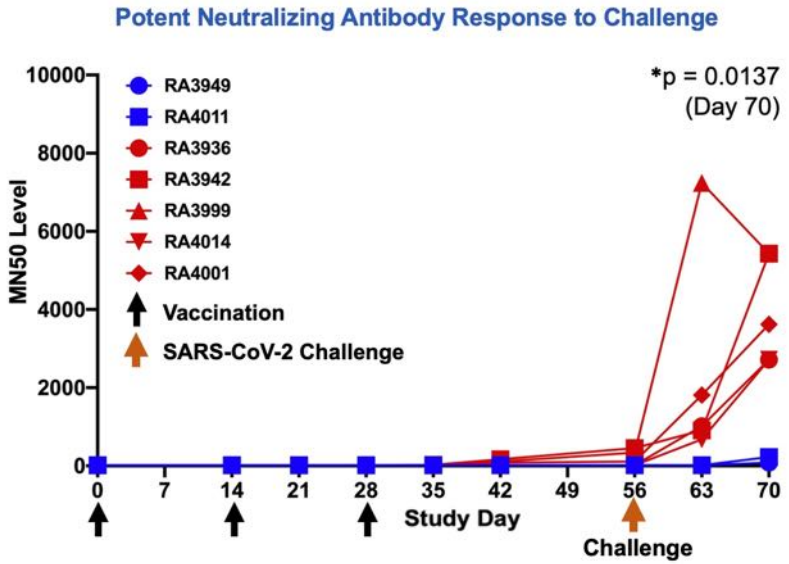


hAd5 S+N Vaccine Generates Cross Reactive Memory B Cell in NHP Studies and in Healthy Volunteers

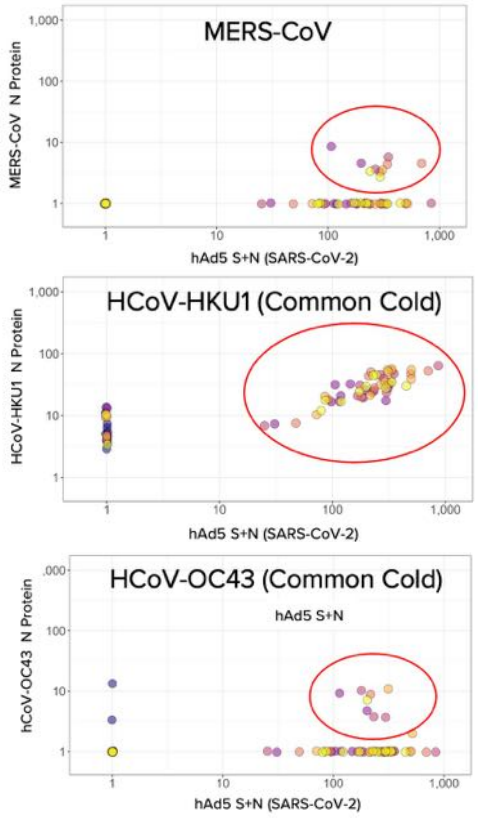
Cross Reactive B Cells in NHP

hAd5 S+N Induces Cross Reactive Memory B Cells to N of SARS-CoV-2

September 2021



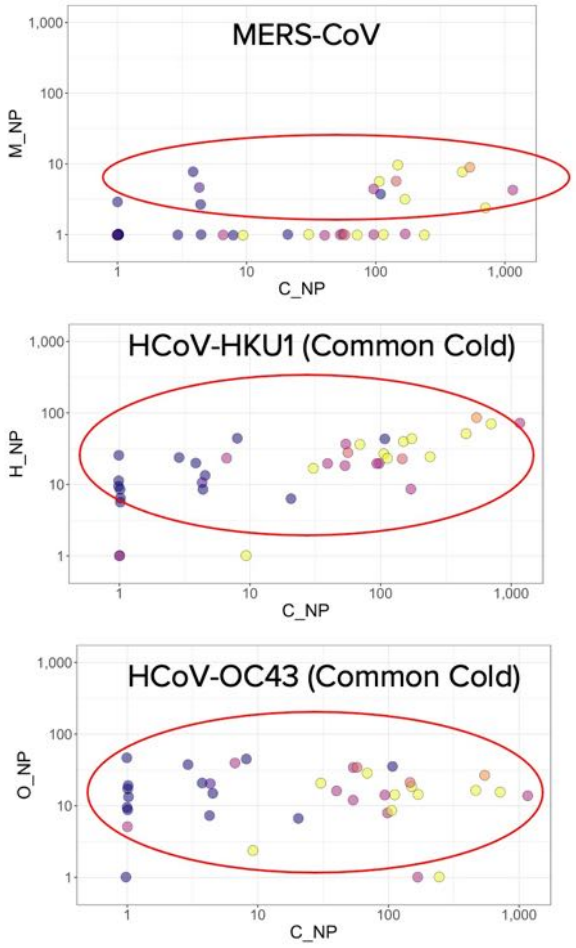
November 2021 (Unpublished)



Cross Reactive B Cells in Healthy Subjects Phase 1

hAd5 S+N Induces Cross Reactive Memory B Cells to N of SARS-CoV-2

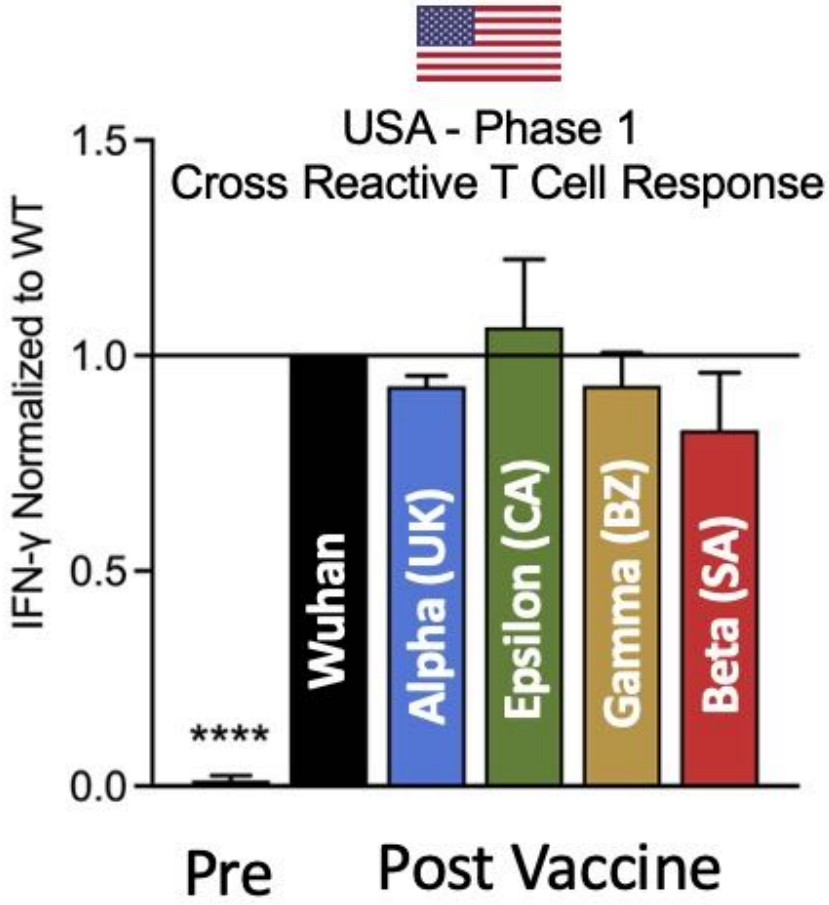
November 2021 (Unpublished)



hAd5 S+N Vaccine Generates Cross Reactive Memory T Cell in Phase 1 Studies and in Healthy Volunteers

Cross Reactive Memory T Cells in Healthy Subjects Phase 1

November 2021 (Unpublished)



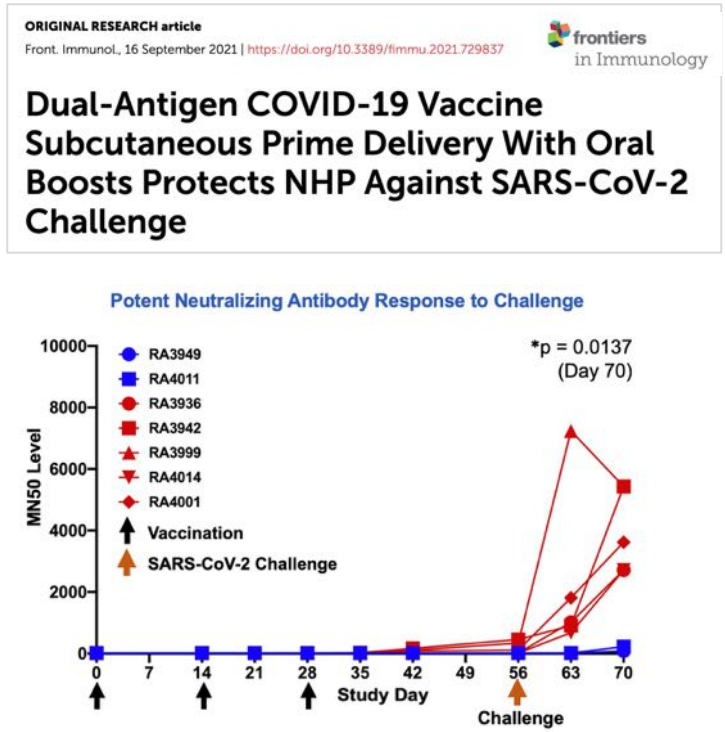
Summary: A 2nd Generation SARS-CoV-2 Vaccine Generating Memory B & T Cells Which Are Cross Reactive to MERS and Common Cold Coronaviruses

The Potential for a Universal COVID Vaccine

hAd5 Induced Memory B Cells

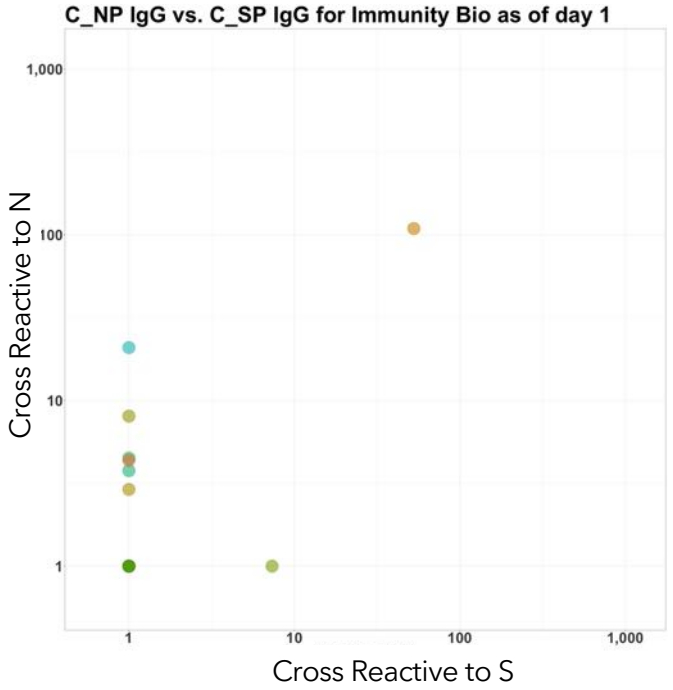
September 2021

hAd5 S + N vaccination induces memory B cells with complete protection following viral challenge in NHP



November 2021 (Unpublished)

hAd5 vaccine induces cross reactive memory B cells to S & N following vaccination in healthy subjects

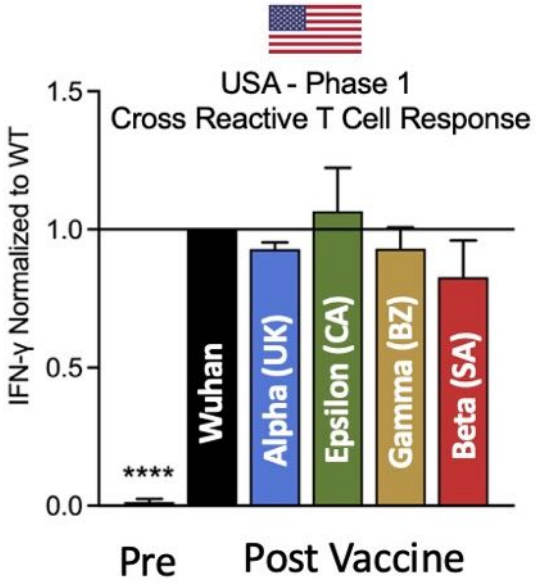


hAd5 Induced Memory T Cells

November 2021 (Unpublished)

hAd5 S + N vaccination induces both memory T cell and cross reactive memory B cells in healthy subjects

Cross Reactive Memory T Cells



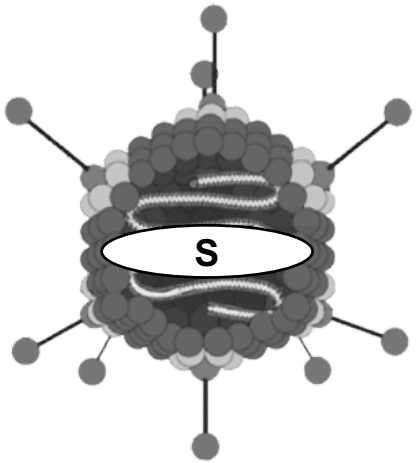
Heterologous DNA / DNA Prime/Boost

SISONKE BOOST TRIAL (Phase I / II / III)

PRIME IM

DNA Vaccine

Adenovirus Type 26 (Ad26)
with Spike (S)

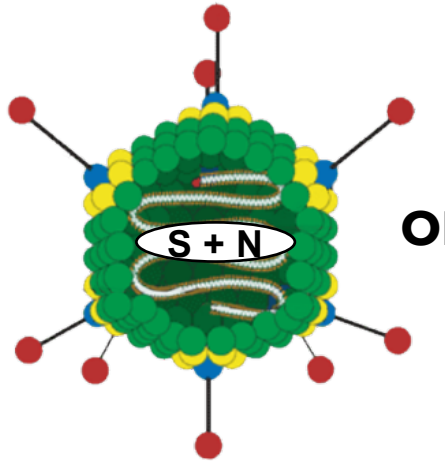


+

BOOST SC

DNA Vaccine

Human Adenovirus Type 5 (hAd5)
with S-Fusion + N-ETSD

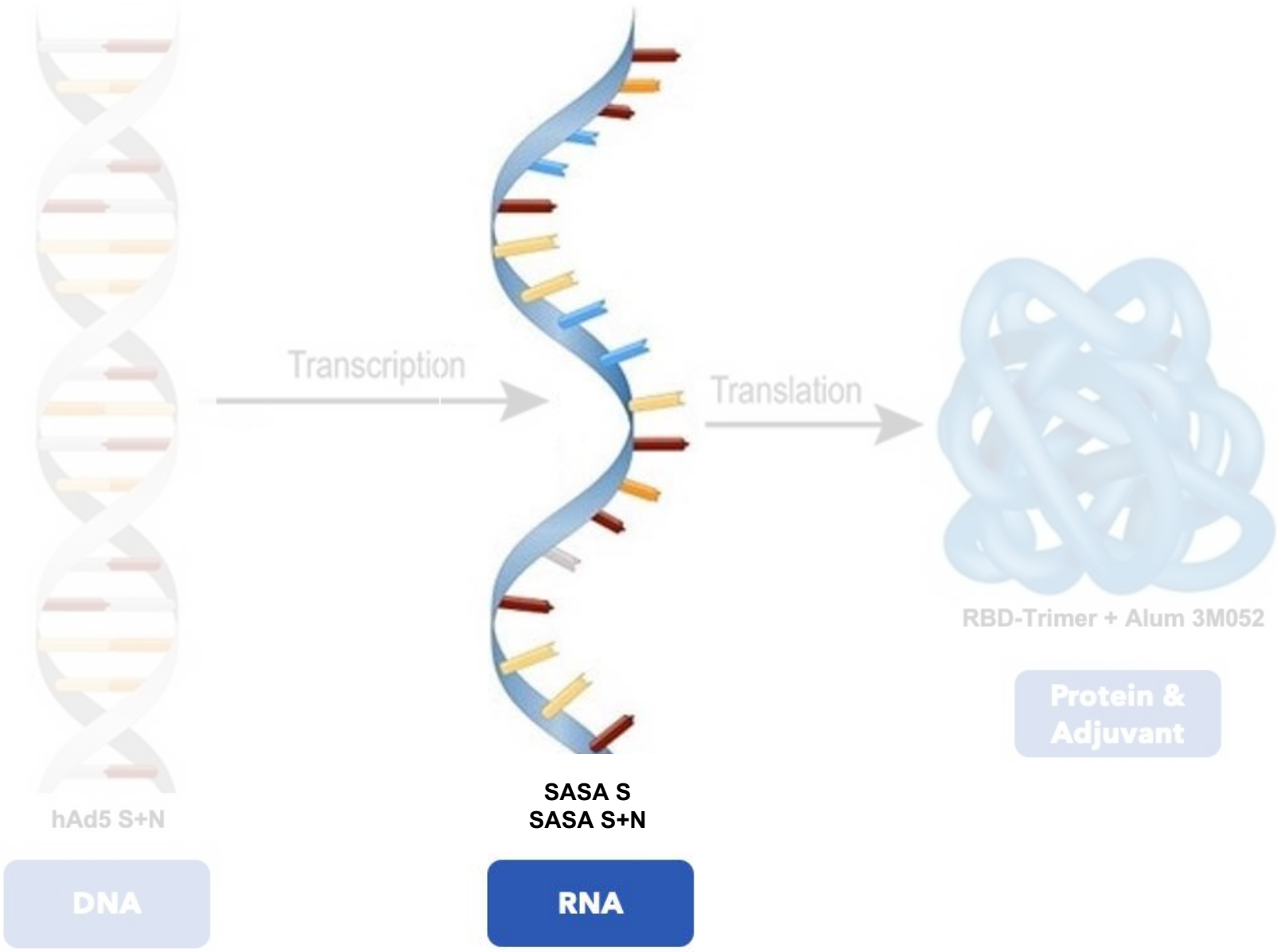


OR Placebo =

Phase I & II Enrollment Completed

N = 60

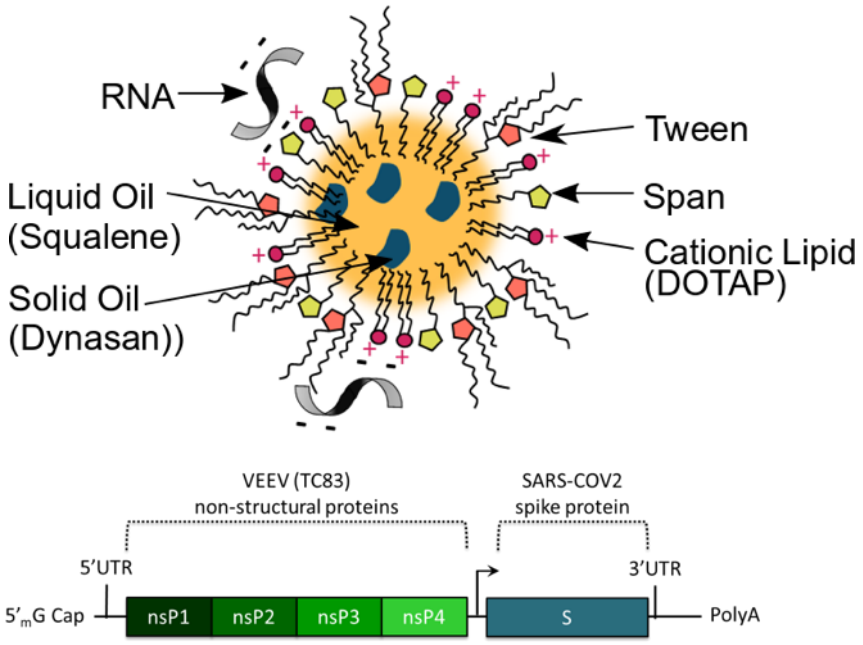
Next Generation Vaccine Platforms



RNA Prime Overcomes Current Vaccine Challenges and Leads to Strong Antibody and Cellular (CD4) Responses

SASA Vaccine

Self-Amplifying Self-Adjuvant RNA (SASA)
Nanoparticle Lipid Carrier (NLC) with Spike (S)



Investigational Agent Name:

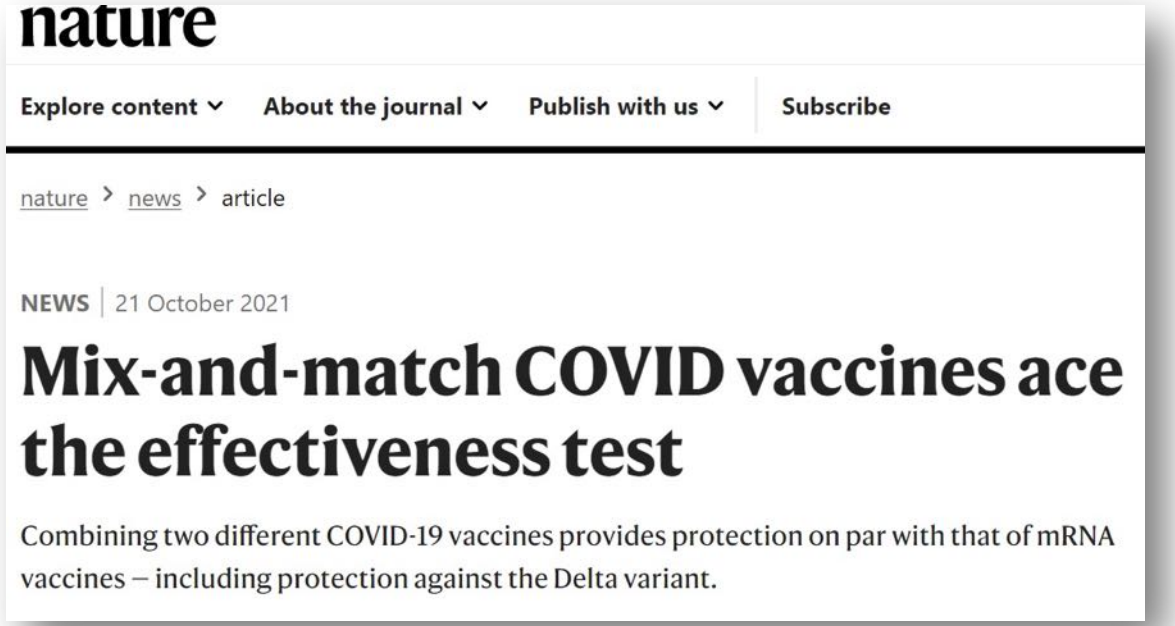
SASA

Self-Amplifying Self Adjuvant

Limitation	Current RNA Vaccines	ImmunityBio RNA Vaccines
Storage / Distribution	Requirement for deep-cold chain.	**NLC formulation** allows for storage at room temperature for years
Potency	Elicit immunity at levels similar to recovered patients, which may allow re-infection.	**Self replicating RNA** allows for increased potency, allowing for potential single shot protection
Duration of Immunity	Modest immunogenicity may be associated with short durability	**Self-Adjuvanting RNA vaccine platform** may increase duration and breadth of immunity
Protection against mutant SARS-CoV-2 strains	RNA sequence encapsulated within delivery vehicle making adaptations to new strains challenging	**RNA decorated on outside of NLC**, allowing for easy swapping of genetic sequence. Demonstrated ability to vaccinate with multivalent strains

RNA + DNA: “Mix and Match”

- Heterologous prime boost (“Mix and Match”) has been shown to elicit some of the strongest and potentially most durable immune responses to COVID
  - “Prime” with RNA vaccine leads to strong antibody response
  - “Boost” with adenovirus vaccine makes strong cellular immune responses
- IBRX has both technologies together ready for commercial-scale manufacturing and global distribution


nature

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NEWS | 21 October 2021

Mix-and-match COVID vaccines ace the effectiveness test

Combining two different COVID-19 vaccines provides protection on par with that of mRNA vaccines — including protection against the Delta variant.

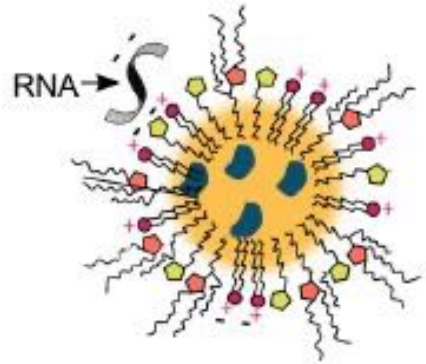
Heterologous RNA / DNA Prime/Boost

THEMBA TRIAL (Pending)

PRIME (Day 1) IM + **BOOST (Day 22) SC** =

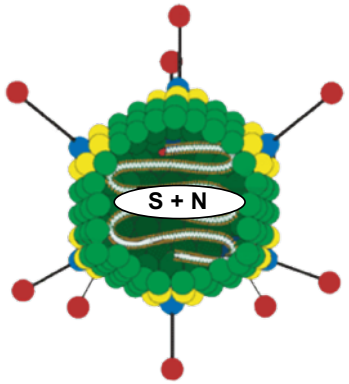
SASA Vaccine

Self-Amplifying Self-Adjuvating (SASA) RNA with Spike (S) and Nucleocapsid (N)



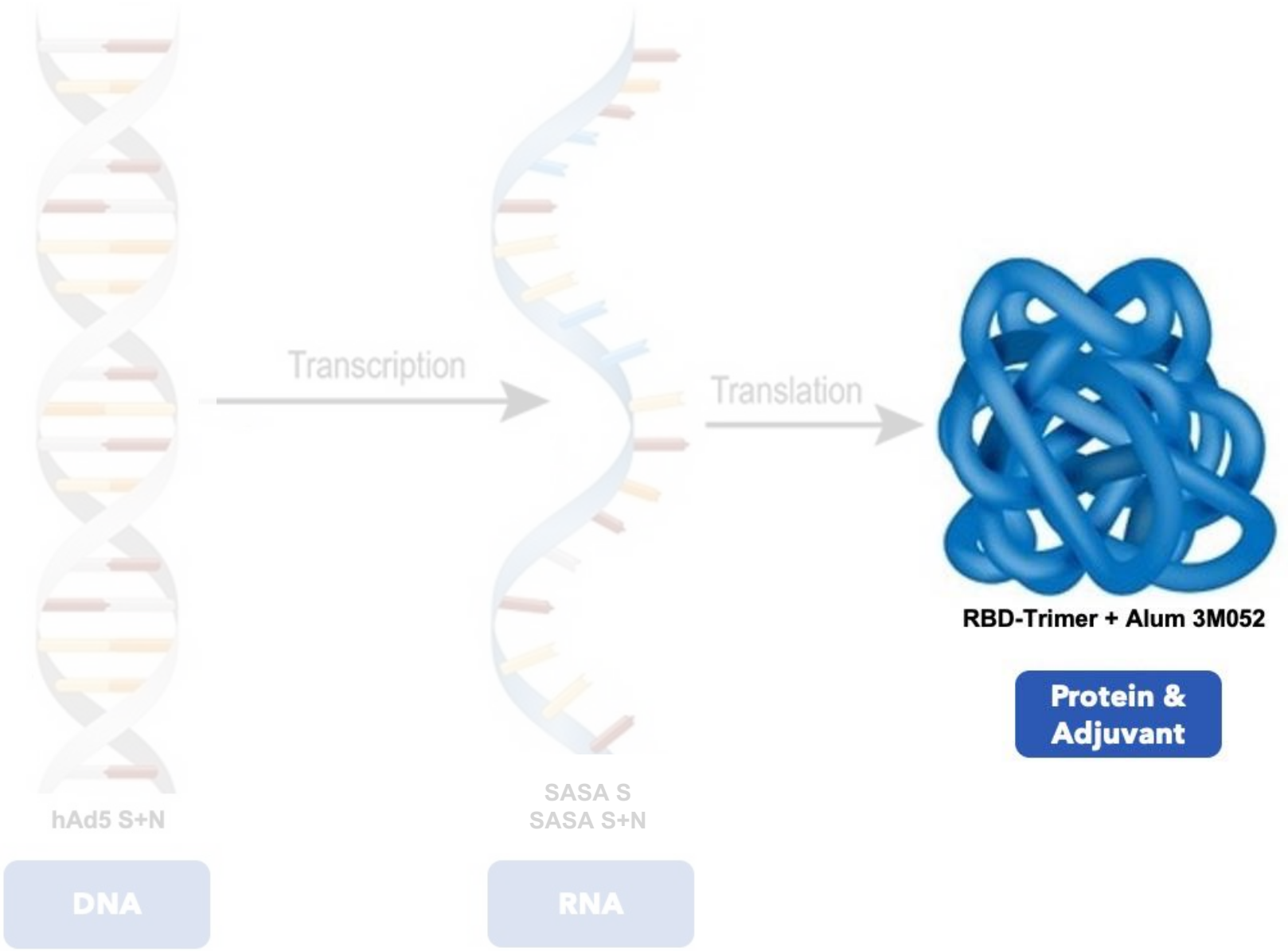
DNA Vaccine

Human Adenovirus Type 5 (hAd5) with S-Fusion + N-ETSD



- Strong Antibody Response: Potent Th1 Antibodies to **Both Wildtype and Beta Variant**
- Strong Immune Cell Response: Potent CD8+ T Cells to **Both S and N for Wildtype and Beta Variant**
- Potent CD4+ T Cells to **Both S and N for Wildtype and Beta Variant**

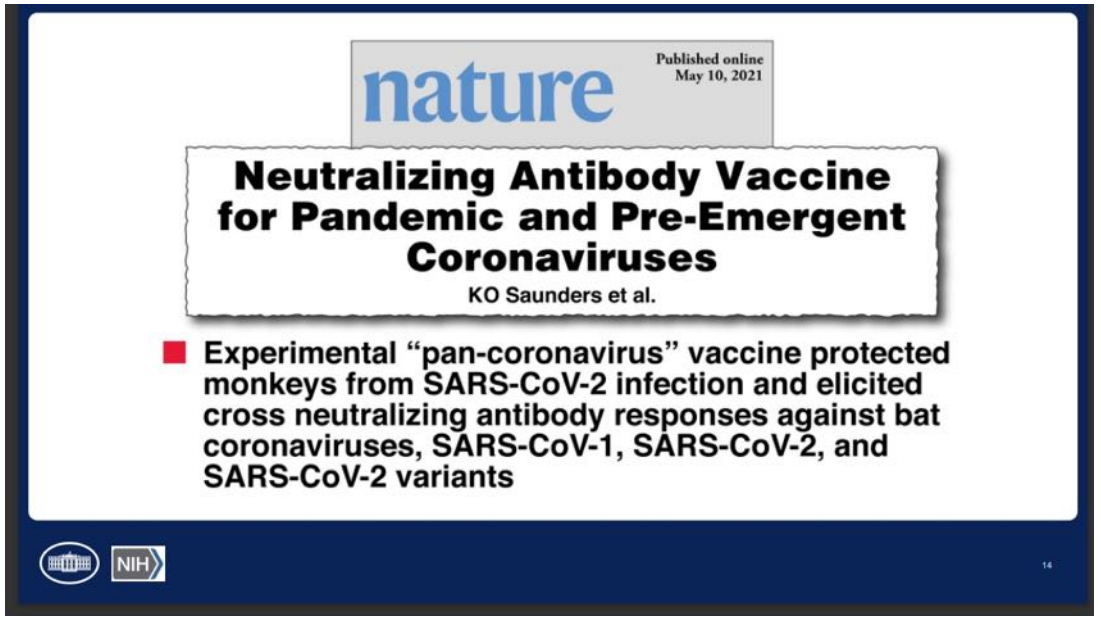
Next Generation Vaccine Platforms



3M-052-Alum Adjuvant Formulation Shows Potential for Durable, Broad, and Potent Protection from COVID Variants

- Adjuvant: a molecule that enhances the body's immune response to a vaccination.
- Adjuvant formulation, 3M-052-Alum, developed by IDRI and 3M, was used in Duke's experimental "pan-coronavirus" vaccine.
- Preliminary studies show that vaccines combining 3M-052 adjuvant formulation with coronavirus proteins:
  - provide protection against SARS-CoV-1, SARS-CoV-2 (and variants of concern), and animal coronaviruses.
  - generate higher antibody levels against a wide range of COVID strains compared with mRNA vaccines.
  - protect lab animals from COVID infection and pathology (e.g., damage to lung tissue).

A Potential Pan-Coronavirus Vaccine



Subunit Protein with Adjuvant (THEMBA 2)

July 2021

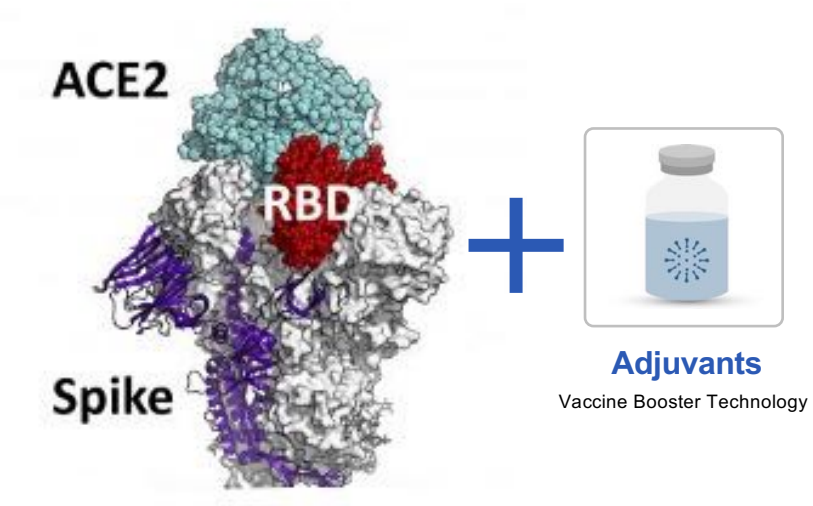
SCIENCE IMMUNOLOGY | RESEARCH ARTICLE

CORONAVIRUS

A yeast-expressed RBD-based SARS-CoV-2 vaccine formulated with 3M-052-alum adjuvant promotes protective efficacy in non-human primates

RBD Subunit Protein

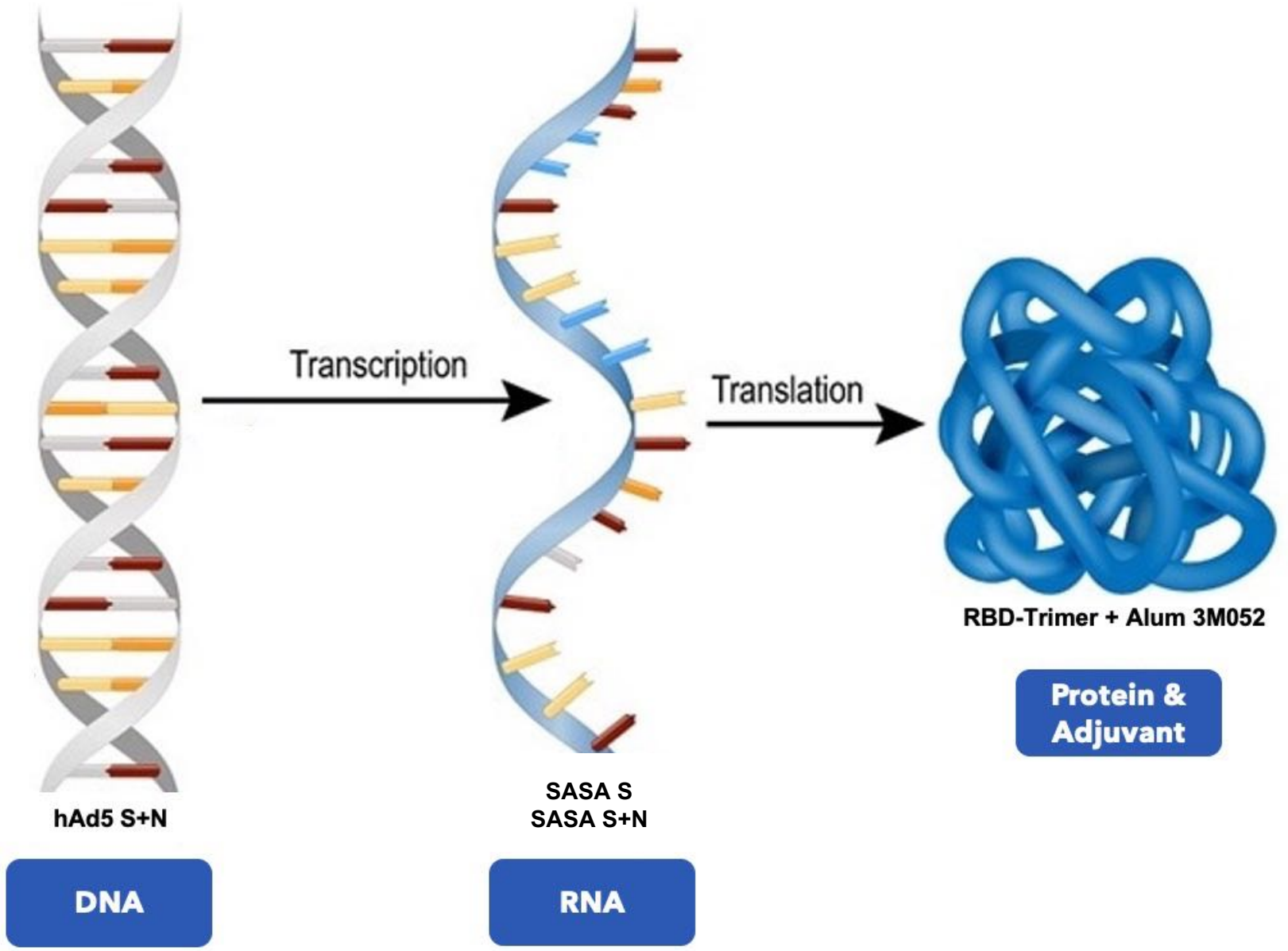
with 3M-052 Adjuvant



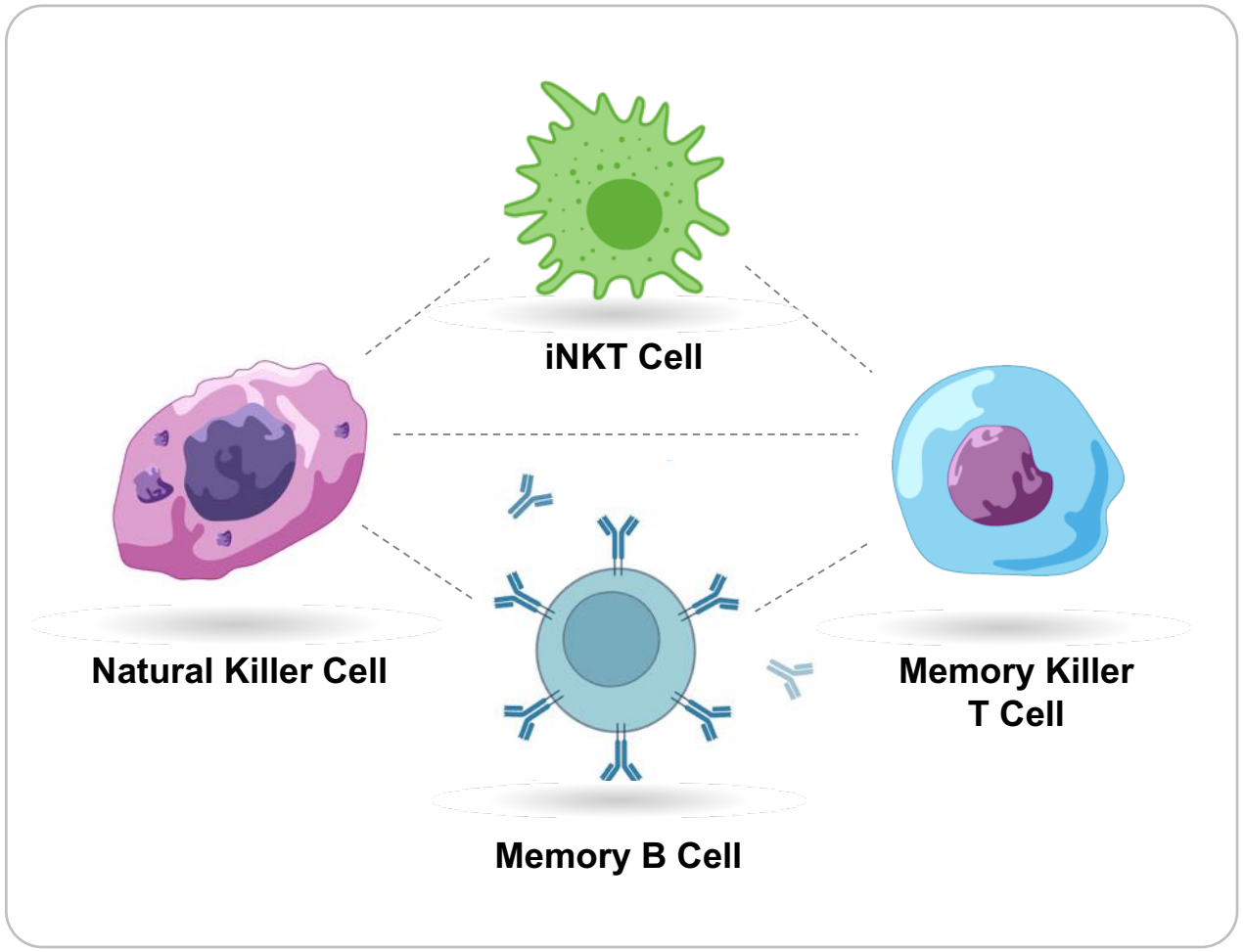
In collaboration with Baylor and IDRI

"THEMBA 2" COVID-19 Vaccine Clinical Trial Pending – South Africa

Next Generation Vaccine Platforms



First-in-Class Immunotherapy Platforms



Natural Killer Cells

- NK-92 Off-the-Shelf
- Autologous m-ceNK
- iNKT Cells

Memory B & T Cells

- Adenovirus
- Yeast
- Toll Receptor Activators
- saRNA

NK + T Cells

- IL-15 Fusion Proteins

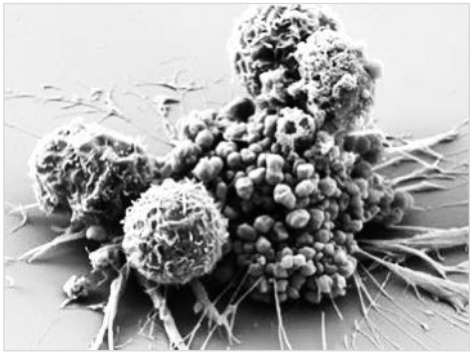
ImmunityBio: A Leading Immunotherapy Company

ImmunityBio

NASDAQ: IBRX

20

Actively Recruiting Clinical Trials



1,800+

Patients Studied

13

Active Phase II / III Clinical Trials

17

First in Human Immunotherapy Molecules and cells

Antibody Cytokine Fusion Proteins

Chemo Immuno Modulators

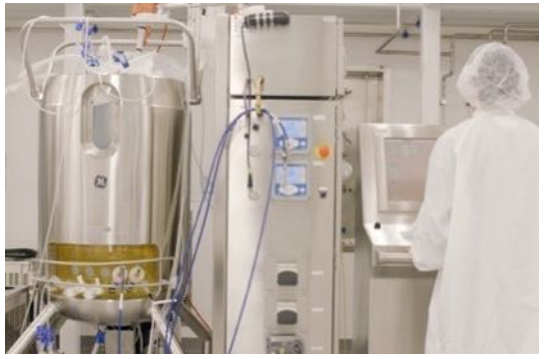
Vaccine Technologies

Natural Killer Cells

A Leading Immunotherapy Platform in Oncology & Infectious Diseases

2038+

Worldwide Patents Extending to 2035 and Beyond



400,000

Square Feet of Manufacturing and R&D Facilities

>5 Trillion

Over 5 Trillion Natural Killer Cells Manufactured to Date