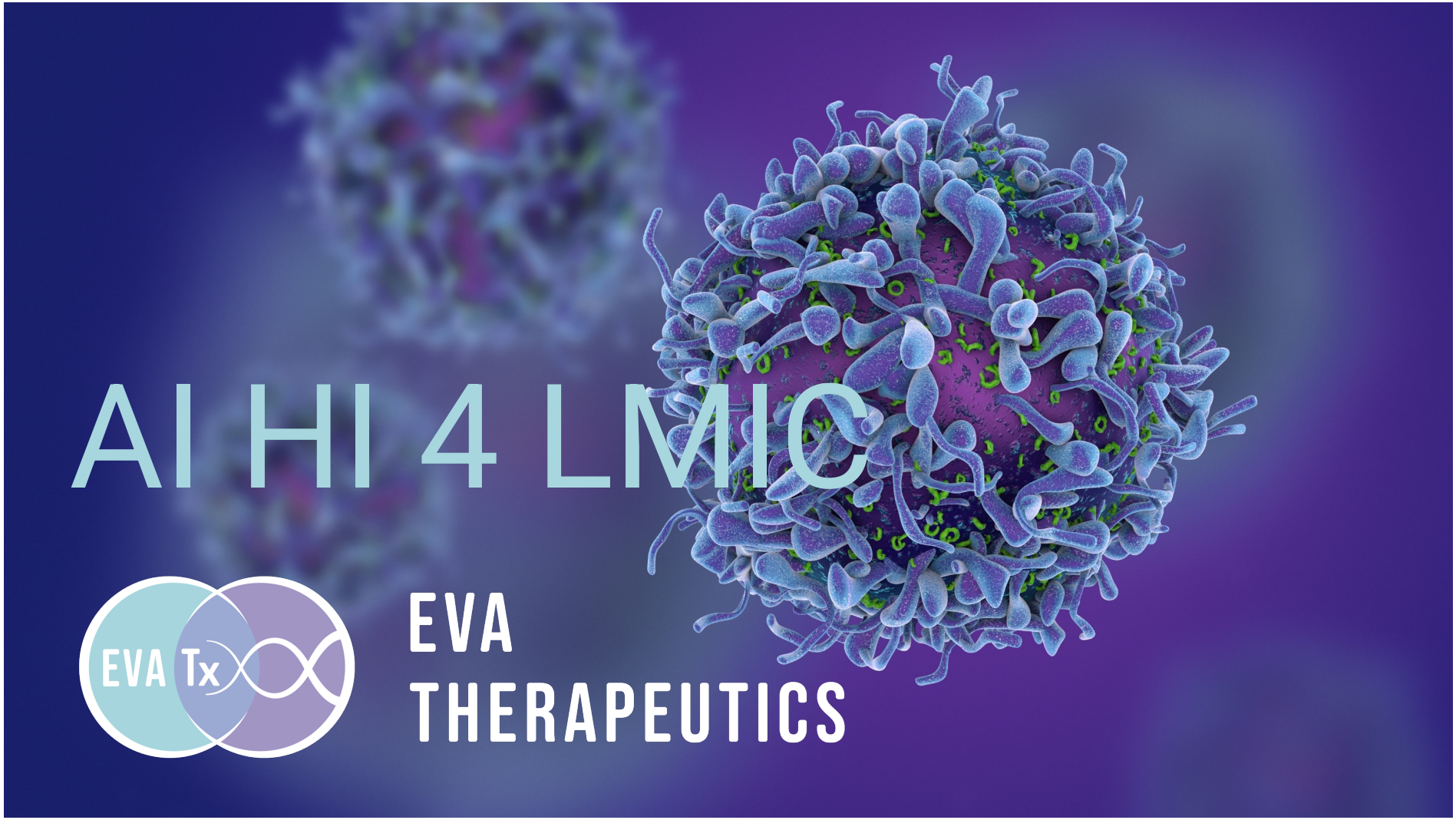
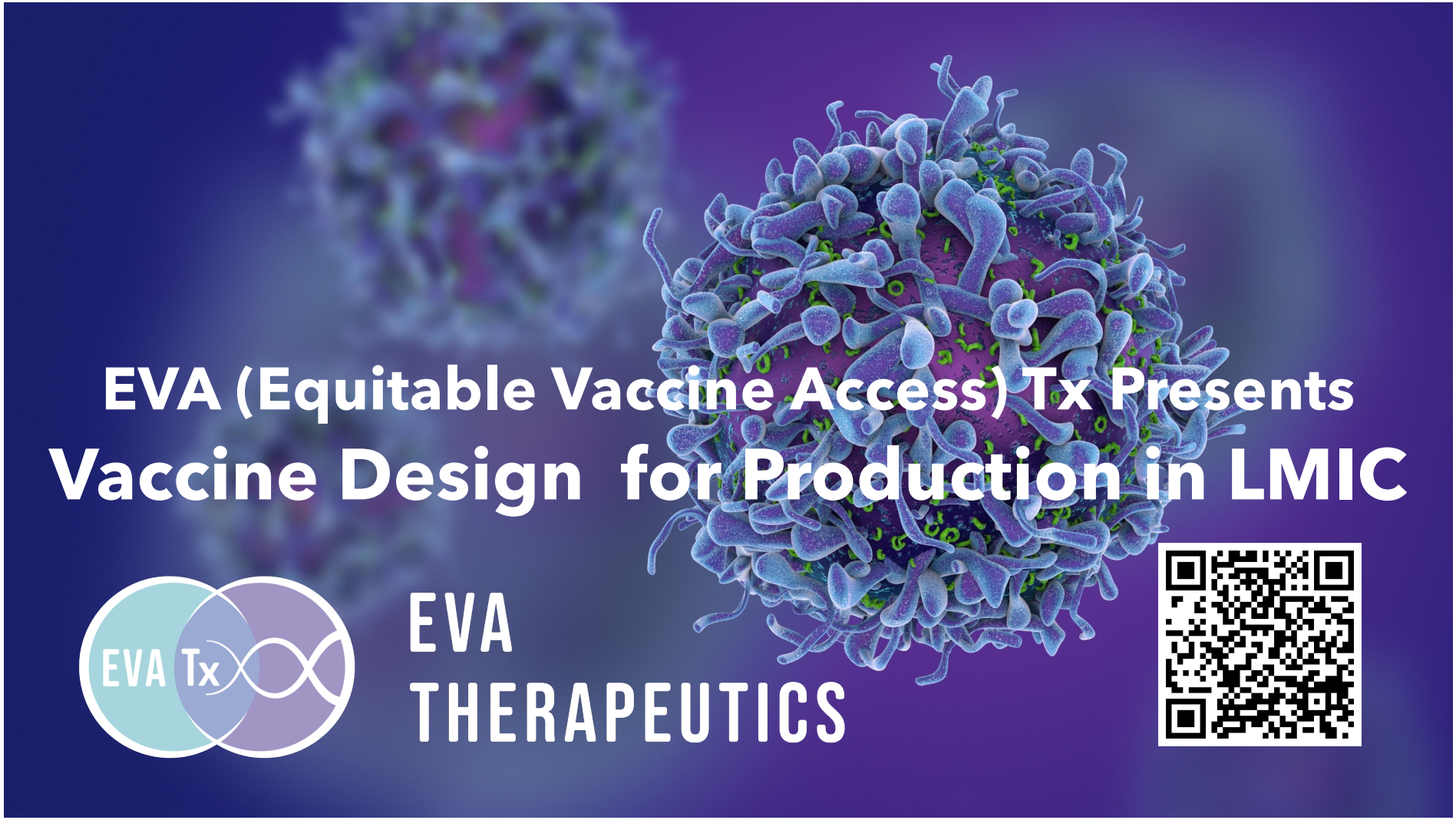

AI HI 4 LMIC
EVA Tx
EVA
THERAPEUTICS


EVA (Equitable Vaccine Access) Tx Presents
Vaccine Design for Production in LMIC
EVA Tx
EVA
THERAPEUTICS

Special Workshop 1: 11:00-13:00
Organized by *EVA Therapeutics, USA*

AI HI 4 LMIC
Artificial Intelligence Informed by Human Intelligence for Low-and Middle-Income Countries

11:00-11:10	**Welcome** ➢ EVA Therapeutics Mission and Vision **Jeffrey T. Safrit**, *CEO, EVA Therapeutics, USA*
11:10–11:25	**How LMIC Vaccine Developers can access Computational Vaccinology Tools at EVA Therapeutics** ➢ AI/HI Tools for Vaccine Design used by EVA Tx ➢ Current Equitable Vaccine Access Projects at EVA Tx **Annie De Groot**, *EVA Therapeutics, USA*
11:25-11:40	**Case study 1**: VennVax Mpox Vaccine Progress ➢ Development of an mRNA Mpox vaccine in Cape Town, South Africa **Hapiloe Maranyane-Tshililo**, *Afrigen Biologics, South Africa*
11:40-11:55	**Case study 2**: Universal Influenza Vaccine "UTIV" ➢ Development of a cross-conserved, universal T cell epitope-driven vaccine for influenza **Dan Hoft**, *Saint Louis University, USA*
11:55-12:00	**Questions / Closing Remarks** **Jeffrey T. Safrit**, *CEO, EVA Therapeutics, USA*
12:00–13:00	**LUNCH (SPONSORED BY EVA THERAPEUTICS)**

How LMIC vaccine developers can access Vaccine Design at EVA Tx

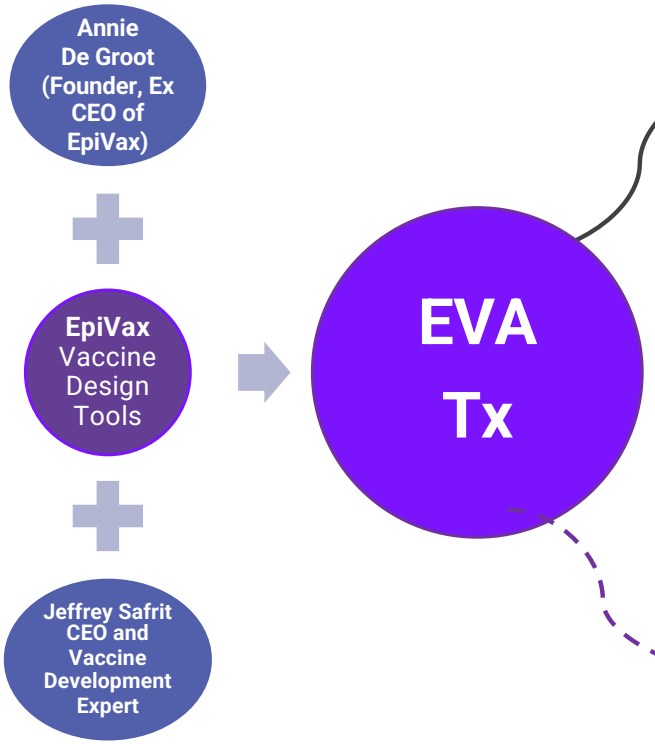
Annie S. De Groot, MD / President
Jeffrey T. Safrit, PhD / CEO



EVA THERAPEUTICS

EVA Therapeutics (EVA Tx)
EID Vaccine Design Expertise

EVA THERAPEUTICS



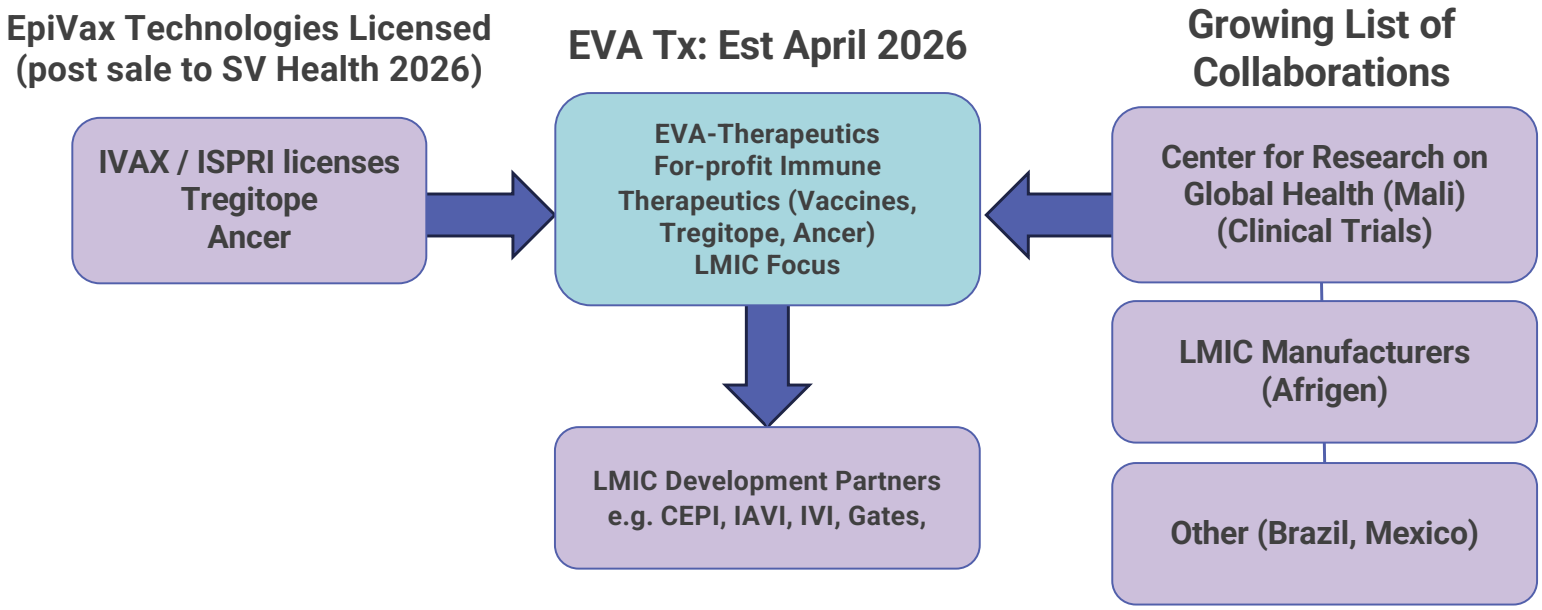
Current:

EVA Tx's Mission:
To design and advance vaccines and immunotherapies targeting diseases disproportionately affecting the LMIC population.And .. global access to personalized cancer vaccine design

Projects include
- Mpox (monkeypox) with Afrigen (SA)
- Bundibugyo immune engineering (with CRS Globale, Mali)
- Universal influenza vaccine (SLU, USA looking for partners)
- Patch delivery of tolerogenic peptides for allergy

Proposed:
Vaccine Design Partner to LMIC scientists

Eva Therapeutics Technology Flow



EVA Therapeutics Vaccine Design Tools

EVA THERAPEUTICS

iVAX Toolkit developed in 2009 with U19 funding from NIH

- Specifically focused on T cell Epitope Driven Vaccines (TDEV)
- Develops rapid, on-demand vaccines for infectious diseases.
- Includes **EpiMatrix, ClustiMer, EpiAssembler, JanusMatrix, VaccineCad, OptiMatrix** etc.
- In addition to accelerating vaccine design, these tools can **optimize antigen sequences** to enhance immune responses and vaccine efficacy.
- Used in multiple vaccine design projects over 30 years by EVA Tx founder, Annie De Groot (and EpiVax colleagues)

---

iVAX A safer, faster approach to vaccine design.

(ver. 1.0) | Contact

Home | Data Management | Conservation Analysis | Class I Analysis | Class II Analysis | OptiMatrix Analysis | NCBI BLAST Analysis | Homology Analysis | Vaccine Design | Ad Hoc Analysis | Batch Processing | Tutorial | Session

EVA Therapeutics Platfoms

EVA THERAPEUTICS

+ Ancer Personalized Cancer Vaccine Platform (est. 2017)

- **Input:** Patient mutanome and genome
- **Output:** Optimized multi-epitope vaccine for use as peptides or mRNA
- Specific for the HLA of the subject
- Both HLA class I (CTL) and class II (T helper) epitopes
- Tolerogenic epitopes removed using JanusMatrix
- Currently in use in two private cancer vaccine clinics

- Exclusive, Global License for use by EVA Therapeutics

Decades of collaborations in computational vaccine design*

EVA THERAPEUTICS



























































*** EpiVax Founder Annie De Groot has moved to EVA Therapeutics and has license to use EpiVax Vaccine design tools**

Recent EVA Tx Design Programs

EVA THERAPEUTICS

leidos / UNIVERSITY OF OXFORD — Genome-derived **Malaria vaccine** (USAID) (Leidos/Oxford)

intravacc innovating vaccines — **PanCoronavirus vaccine** with OMV delivery (CEPI)

SAINT LOUIS UNIVERSITY — T cell Epitope-Driven Universal **Flu A Vaccine** (SLU/NIAID)

Afrigen Biologics & Vaccines, An Avacare Health & IDC Company — Mpox Vaccine – **T cell epitope string (VennVax)** (CEPI)

NIH National Institute of Allergy and Infectious Diseases, Vaccine & Treatment Evaluation Units — **T cell epitope-driven COVID Vaccine** (Patch Delivery)

EVA Tx — Compassionate Use **Personalized Cancer Vaccine**

Vaccine design collaborations

Under the direction of Annie De Groot

Former CEO/CSO and founder of EpiVax, now at EVA Tx

Current Vaccine Project Collaborators
(Lassa Fever, Mpox)

EVA THERAPEUTICS

Vaccine Design
Project Management

Jeff Safrit
Annie De Groot
USA

Epitope Validation
(and Site for
Phase I Clinical Trials)

Ousmane Koita
CRS Globale
Mali

Afrigen
Biologics & Vaccines

Candidate Vaccine
Production/Manufacturing
Pre-Regulatory Discussions

Caryn Fenner
Rajen Nadoo
South Africa

Immunogenicity and
Challenge studies

Wendy Burgers
UCT
South Africa

Published Case Studies for TEDV POC

EVA THERAPEUTICS

- VennVax T cell epitope-based vaccine – 100% protection in challenge studies. (**now under development as an Mpox vaccine at Afrigen**)
- **H. pylori vaccine:** 100% cure in H. pylori infected mouse model
- **Tularemia Vaccine**: Protective against live challenge in murine model
- **Universal T cell epitope Driven Influenza Vaccine (UTIV)** (Dan Hoft, SLU) Immunogenic and protective, broadly conserved epitopes
- **Multi Epitope COVID-19 Vaccine**: Immunogenic in exposed, unexposed humans and HLA tg Mice
- **Lassa Fever Demonstration project** with MGH/VIC Mark Poznansky - DARPA



The Basic Concept –
Rapid design from pathogen to vaccine

EVA THERAPEUTICS

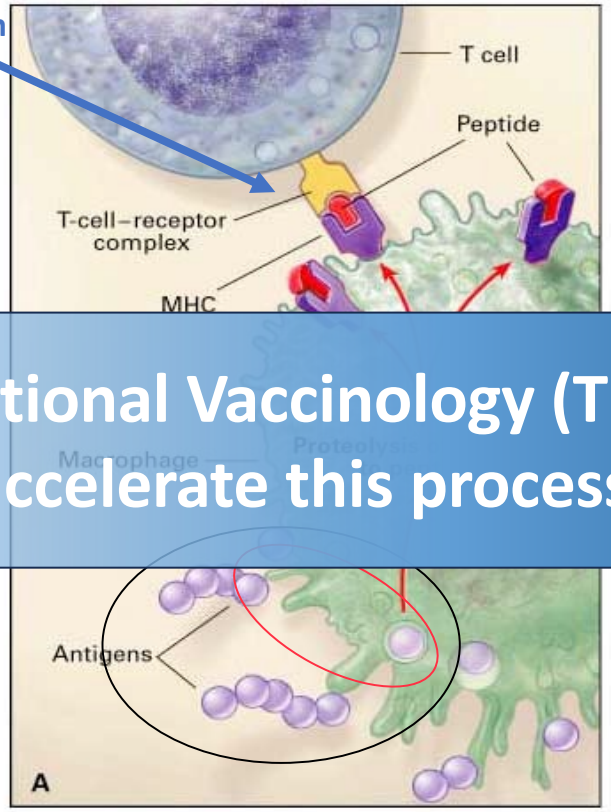
It's a long and tedious process to go from selecting an antigen to vaccine design.

Viruses

Bacteria

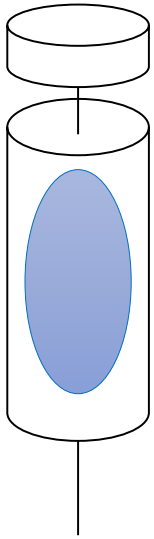
Parasites

Cancers



Computational Vaccinology (TEDV) can accelerate this process

Vaccine



EVA Tx Vaccine Approach (Tools)

EVA THERAPEUTICS

Predicting T cell epitope and evaluating antigens:

- **EpiMatrix** and the **Immunogenicity Scale**

Include B cell target (GPC) with broad T cell epitope coverage

- **EpiCC**

Finding conserved T cell epitopes (within LASV strains and related viruses)

- **Conservatrix, EpiMatrix, JanusMatrix**

Assemble T cell epitopes into multi-epitope string

- **EpiAssembler, VaccineCAD**

Vaccine production: mRNA, peptide strings on OMV, etc.

- Expertise of Afrigen and Intravacc among others

Antigenicity of vaccine is based on T cell epitope content

EVA THERAPEUTICS

Total T cell epitope content = Immunogenic potential



1 + 1 + 1 = Predicted Immunogenic Potential

De Groot A.S. and L. Moise. Prediction of immunogenicity for therapeutic proteins: State of the art. Current Opinions in Drug Development and Discovery. May 2007. 10(3):332-40.

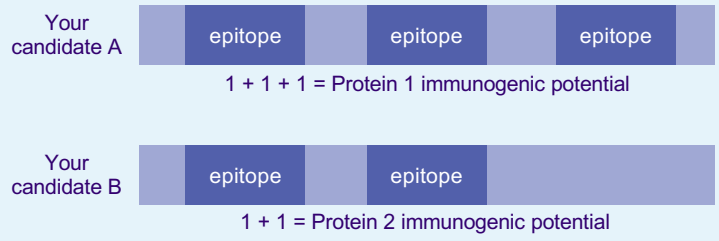
EpiMatrix Immunogenicity Scale

Ranking "global" immunogenicity of antigen candidates

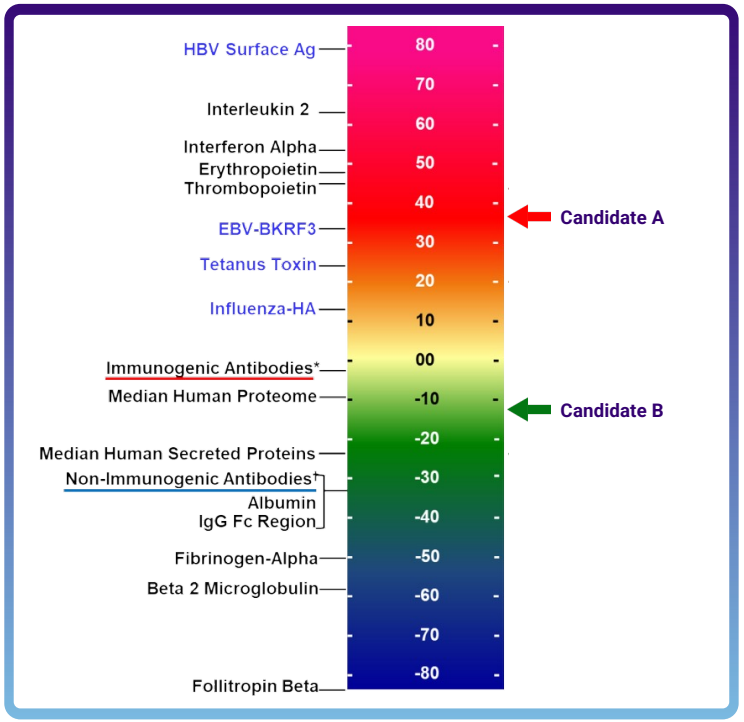
EVA THERAPEUTICS

The Immunogenicity Scale ranks proteins.

Total T cell epitope content = predicted immunogenic potential

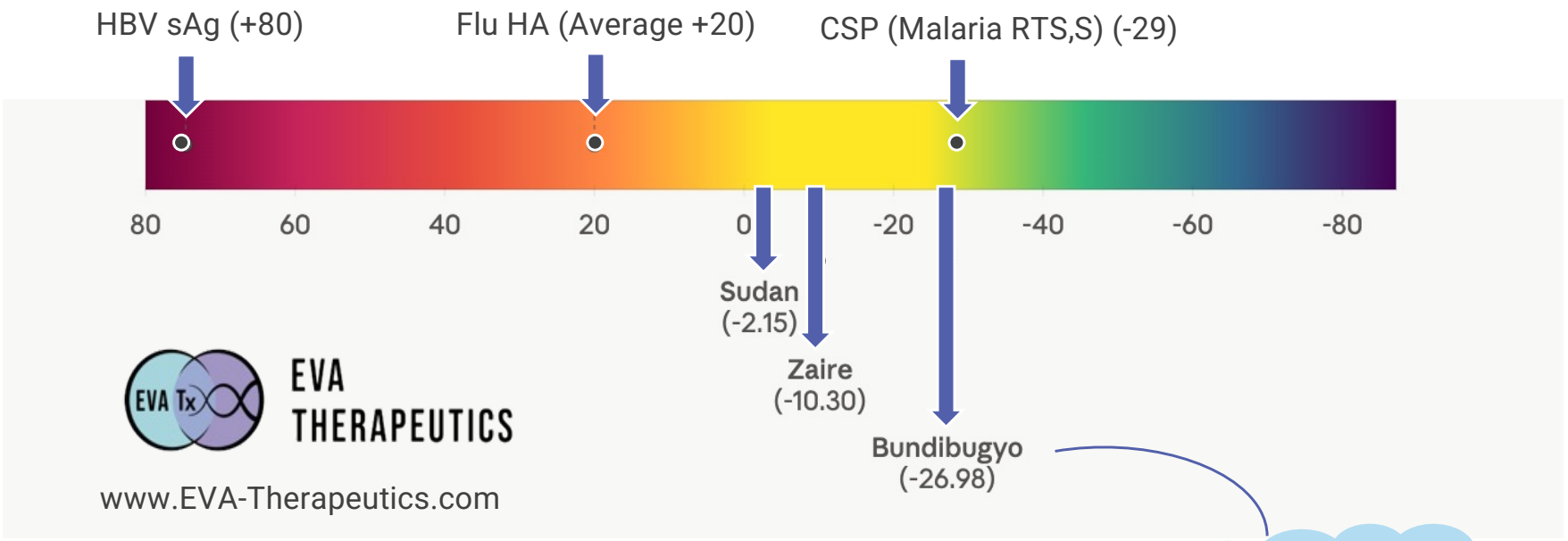


Normalized immunogenicity scores allow protein immunogenicity to be ranked.



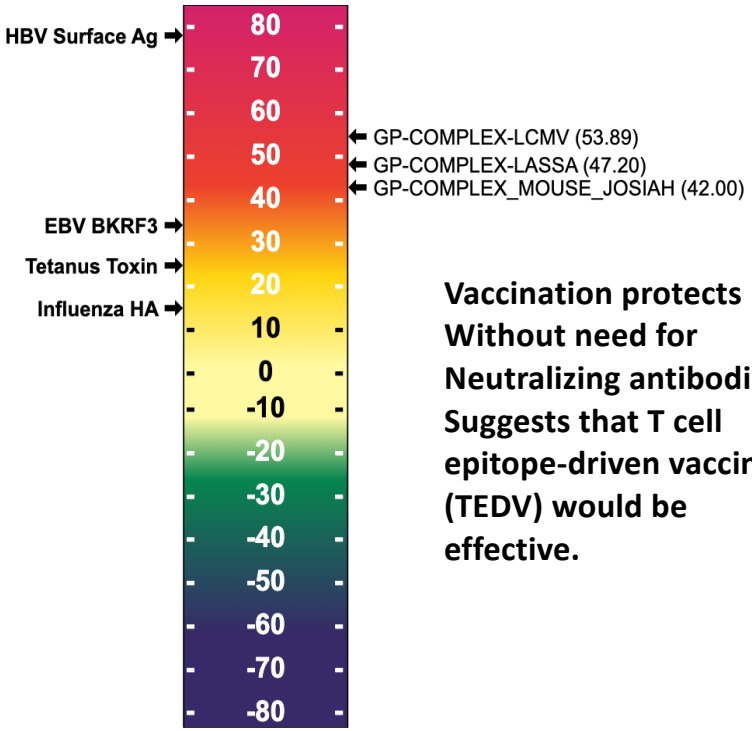
Example: Bundibugyo virus strain GP Antigenicity vs Benchmarks

EVA THERAPEUTICS



Lassa GP antigen is a good target

EVA THERAPEUTICS



Vaccination protects Without need for Neutralizing antibodies Suggests that T cell epitope-driven vaccine (TEDV) would be effective.

nature › nature communications › articles › article

Article | Open access | Published: 12 September 2023

A Lassa virus mRNA vaccine confers protection but does not require neutralizing antibody in a guinea pig model of infection

Adam J. Ronk, Nicole M. Lloyd, Min Zhang, Caroline Atyeo, Hailee R. Perrett, Chad E. Mire, Kathryn M. Hastie, Rogier W. Sanders, Philip J. M. Brouwer, Erica Olmann Saphire, Andrew B. Ward, Thomas G. Ksiazek, Juan Carlos Alvarez Moreno, Harshwardhan M. Thaker, Galit Alter, Sunny Himansu, Andrea Carfi ✉ & Alexander Bukreyev ✉

Nature Communications **14**, Article number: 5603 (2023) | Cite this article

15k Accesses | **37** Citations | **29** Altmetric | Metrics

Abstract

Lassa virus is a member of the *Arenaviridae* family, which causes human infections ranging from asymptomatic to severe hemorrhagic disease with a high case fatality rate. We have designed and generated lipid nanoparticle encapsulated, modified mRNA vaccines that encode for the wild-type Lassa virus strain Josiah glycoprotein complex or the prefusion stabilized conformation of the Lassa virus glycoprotein complex. Hartley

Focus on: T cell epitope clusters
EpiBar = Key driver of vaccine response

EVA THERAPEUTICS

Class I epitopes are also in these regions
Rank by Class I/II epitope content

MP-ICS-CLUSTERS-31-02A: Amino acid ABC transporter, periplasmic amino acid-binding protein

Frame Start	AA Sequence	Frame Stop	DRB1*0101 Z-Score	DRB1*0301 Z-Score	DRB1*0401 Z-Score	DRB1*0701 Z-Score	DRB1*0801 Z-Score	DRB1*1101 Z-Score	DRB1*1301 Z-Score	DRB1*1501 Z-Score	Hits
204	ASDFSSFLL	212									0
205	SDFSSFLLQ	213									0
206	DFSSFLLQA	214									0
207	FSSFLLQAQ	215			1.28		2	1.8		2.05	3
208	SSFLLQAQS	216									0
209	SFLLQAQSS	217	1.67		1.45		1.3	1.33		1.44	1
210	FLLQAQSSK	218	1.68		1.45		1.69	1.82	1.86		4
211	LLQAQSSKA	219	2.23	2.35	2.49	2.38	1.66	1.73	2.19	2.6	8
212	LQAQSSKAQ	220	2.15		2.34	2.21	2.12	2.34	2.09	1.85	7
213	QAQSSKAQI	221									0
214	AQSSKAQIL	222	1.61	1.76		2.06				1.44	2
215	QSSKAQILG	223									0
216	SSKAQILGL	224									0
217	SKAQILGLA	225									0

Total Assessments Performed: 112

Z score indicates the potential of a 9-mer frame to bind a given HLA allele; the strength of the score is indicated by the blue shading as shown below:

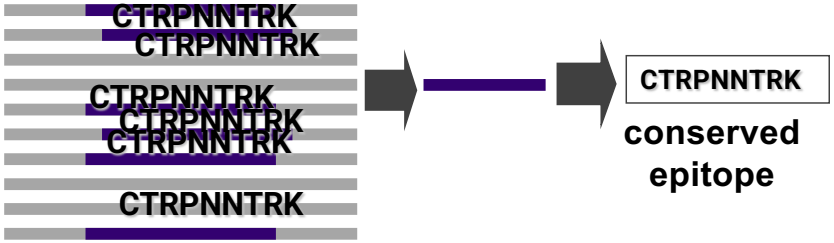
Cluster Regions Outlined | Top 1% | Top 5% | Top 10%

De Groot AS, Ardito M, Moise L, Gustafson EA, Spero D, Tejada G, Martin W. Immunogenic Consensus Sequence T helper Epitopes for a Pan-*Burkholderia* Biodefense Vaccine. Immunome Res. 2011 May;7(2):e7. doi: 10.4172/1745-7580.1000043. PMID: 25346775; PMCID: PMC4206550.

Immunogenic Consensus Sequence Vaccine Design
Overlapping conserved and immunogenic clusters

EVA THERAPEUTICS

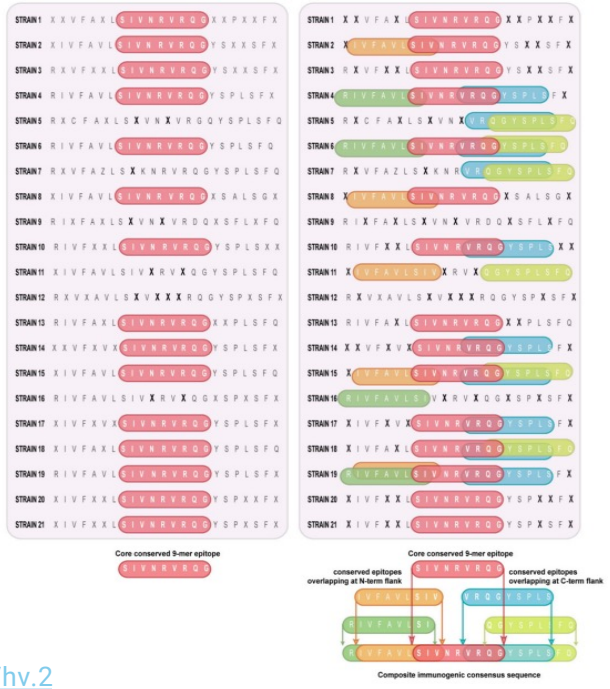
Conservatrix™
finds conserved 9-mers across multiple strains



Identifying the most conserved 9-mers allows for protection against more strains with fewer epitopes

EpiAssembler™
extends conserved epitopes across multiple strains

Clusters found in one strain,,,overlap with clusters found in others



Vaccine
Volume 30, Issue 52, 14 December 2012, Pages 7547-7560

Conservation of HIV-1 T cell epitopes across time and clades: Validation of immunogenic HLA-A2 epitopes selected for the GAIA HIV vaccine

Lauren Levitz [a], Ousmane A. Koita [d], Kotou Sangare [d], Matthew T. Ardito [a], Christine M. Boyle [a], John Rozehnal [b], Karamoko Tounkara [c], Sounkalo M. Dao [e], Youssouf Koné [c], Zoumana Koty [c], Soren Buus [f], Leonard Moise [a b], William D. Martin [a], Anne S. De Groot [a b c]

https://doi.org/10.1016/j.vaccine.2012.10.042

Confirmation of Immunogenic Consensus Sequence HIV-1 T-cell Epitopes in Bamako, Mali and Providence, Rhode Island

O.A. Koita, D. Dabitao, I. Mahamadou, M. Tall, S. Dao, A. Tounkara, H. Guiteye, C. Noumsi, O. Thiero, M. Kone, D. Rivera, J.A. McMurry, W. Martin & A.S. De Groot

To cite this article: O.A. Koita, D. Dabitao, I. Mahamadou, M. Tall, S. Dao, A. Tounkara, H. Guiteye, C. Noumsi, O. Thiero, M. Kone, D. Rivera, J.A. McMurry, W. Martin & A.S. De Groot (2006) Confirmation of Immunogenic Consensus Sequence HIV-1 T-cell Epitopes in Bamako, Mali and Providence, Rhode Island, Human Vaccines, 2:3, 119-128, DOI: 10.4161/hv.2869

To link to this article: https://doi.org/10.4161/hv.2869

https://www.tandfonline.com/doi/abs/10.4161/hv.2

Self vs. Foreign Epitopes
Better Ranking of Immunogenic Epitopes

EVA THERAPEUTICS

Epitopes highly conserved with the human genome may be tolerogenic

Immune Camouflage

Pathogens and tumors copy/paste epitopes that look like human Treg epitopes into their genomes

EXPERT REVIEW OF VACCINES, 2016
http://dx.doi.org/10.1586/14760584.2016.1123098

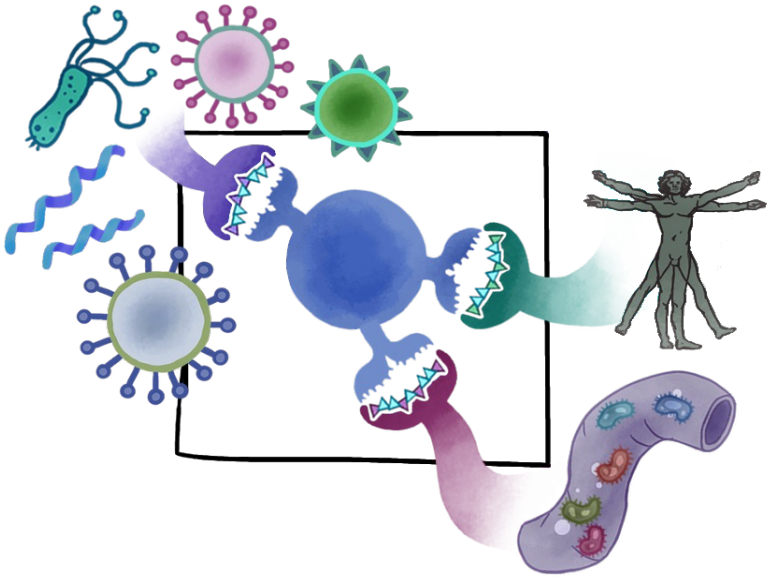
Taylor & Francis
Taylor & Francis Group

REVIEW

T cell epitope redundancy: cross-conservation of the TCR face between pathogens and self and its implications for vaccines and autoimmunity

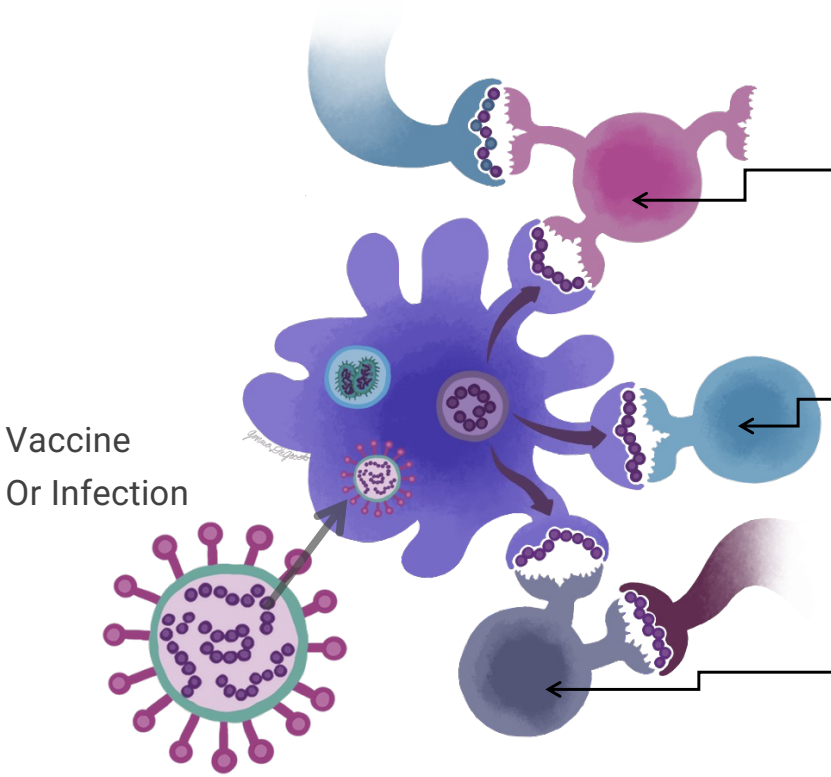
Leonard Moise[a,b], Sarah Beseme[a], Ryan Tassone[b], Rui Liu[b], Farzana Kibria[a], Frances Terry[a], William Martin[a] and Anne S. De Groot [a,b]

[a]EpiVax, Inc., Providence, RI, USA; [b]Institute for Immunology and Informatics, University of Rhode Island, Providence, RI, USA



How to define better T cell epitopes
Evaluate cross-conservation

EVA THERAPEUTICS



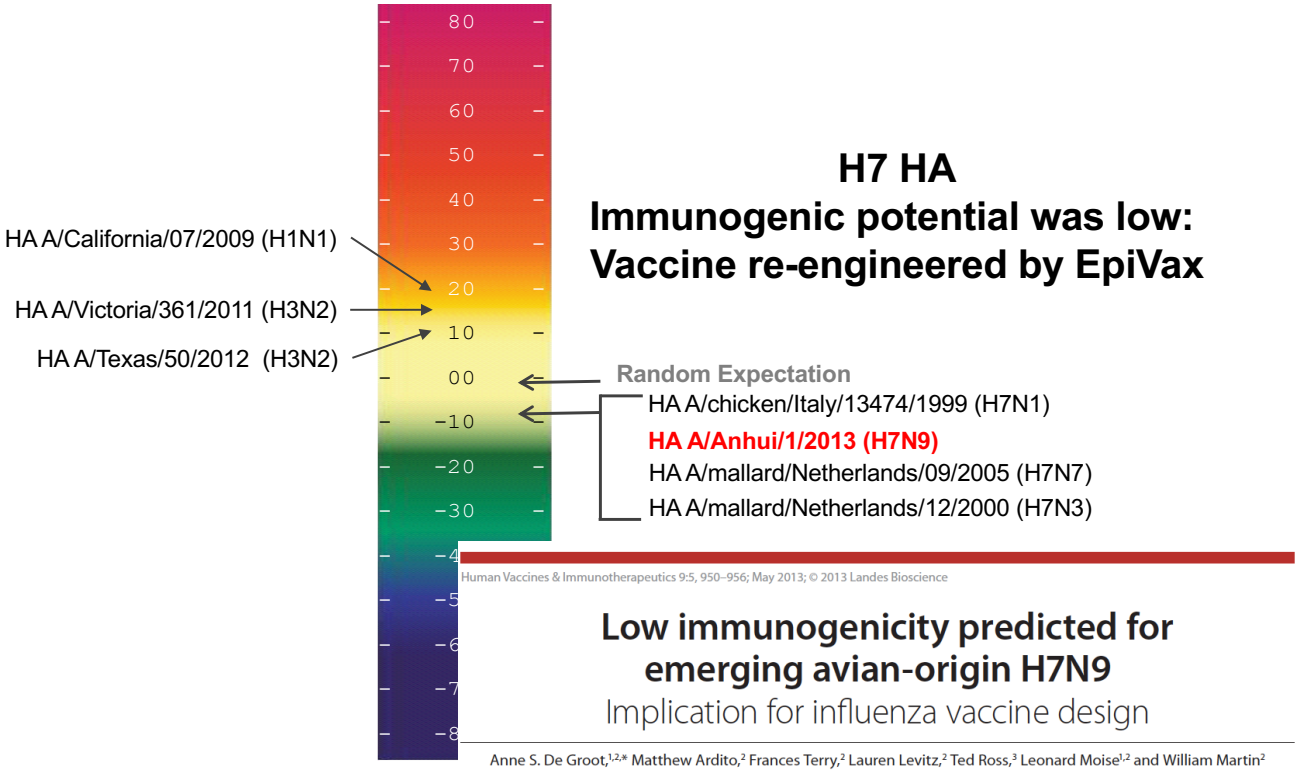
Remove: Extensive Cross-reactivity with "self (human proteome): Potential to be Treg

Unique sequence, limited cross-reactivity; **probable T effector epitope**

Include: Highly cross-reactive with other circulating virus (T memory) epitopes: Protective against next infection

Immune Engineering
H7N9 “Avian” influenza

EVA THERAPEUTICS



H7 HA
Immunogenic potential was low:
Vaccine re-engineered by EpiVax

Human Vaccines & Immunotherapeutics 9:5, 950–956; May 2013; © 2013 Landes Bioscience

Low immunogenicity predicted for emerging avian-origin H7N9

Implication for influenza vaccine design

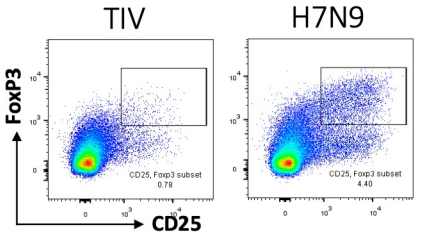
Anne S. De Groot,[1,2,*] Matthew Ardito,[2] Frances Terry,[2] Lauren Levitz,[2] Ted Ross,[3] Leonard Moise[1,2] and William Martin[2]

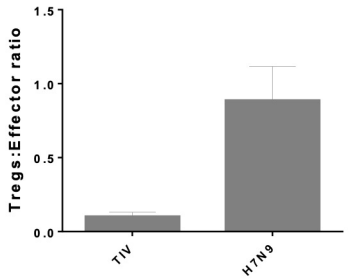
[1]Institute for Immunology and Informatics; University of Rhode Island; Providence, RI USA; [2]EpiVax, Inc.; Providence, RI USA; [3]Vaccine and Gene Therapy Institute of Florida; Port St. Lucie, FL USA

We predicted and confirmed presence of Treg epitopes in H7N9 HA

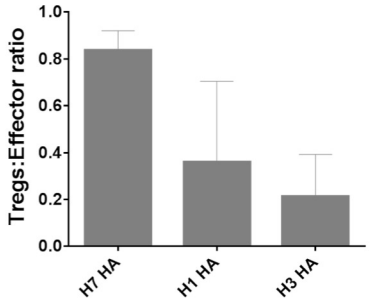
EVA THERAPEUTICS

The H7N9 vaccine candidate increases the expansion of T regulatory cells in comparison to TIV





H7N9 vaccine candidate increases the expansion of CD4 regulatory T cells when compared to the seasonal influenza vaccine TIV



Ratio of Tregs: T effector cells calculated from the total percent response for TIV and H7N9.

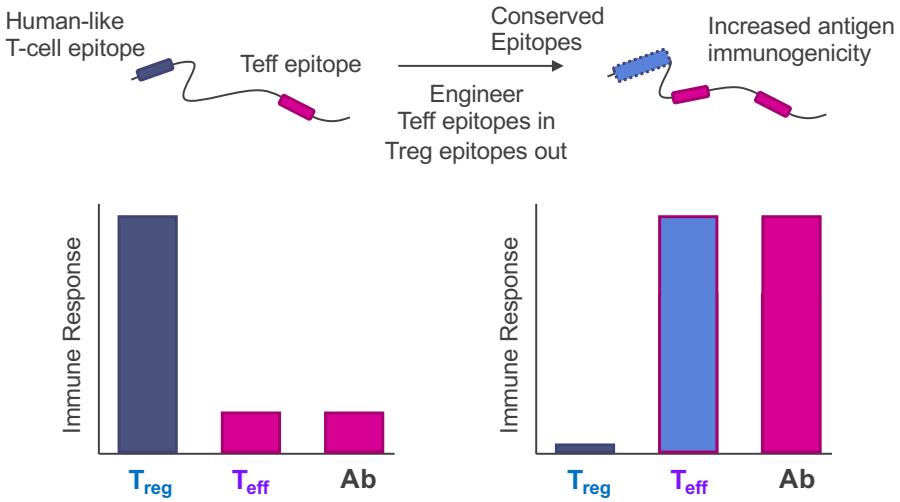
Tregs: $CD4^+Foxp3^+CD25^+$ and T effectors: $CD4^+CD154^+INFg^+TNFa^+$; *n=16*, bars represent the median ± S.D.

B cell targets: Carefully selected antigens recruit CD4 T cell memory

EVA THERAPEUTICS

Selecting Candidates by T cell epitope content

- **Identify promiscuous T helper epitopes with EpiMatrix, ClustiMer**
  - $CD4^+$ T_{eff} epitopes augment antibody production
- **Reduce T*reg* epitopes (JanusMatrix, OptiMatrix)**
  - Remove $CD4^+$ Treg responses that suppress protective antibody responses
- **Select Antigens that include highly cross-conserved epitopes (EpiCC)** (cross strain T memory epitopes)



Immune Engineering Vaccines – Avian Flu

Treg Epitope Discovered – 5 fold increase in Antibody Titer

EVA THERAPEUTICS

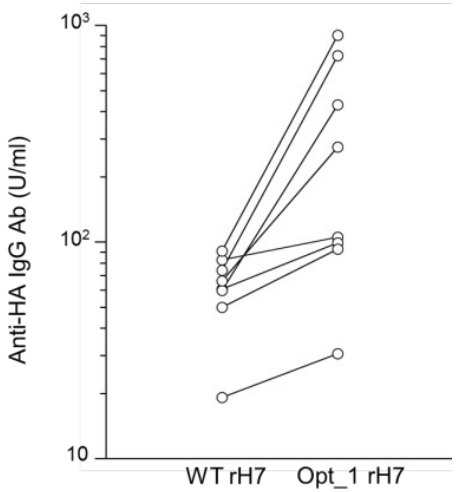
Immune-Engineered HA

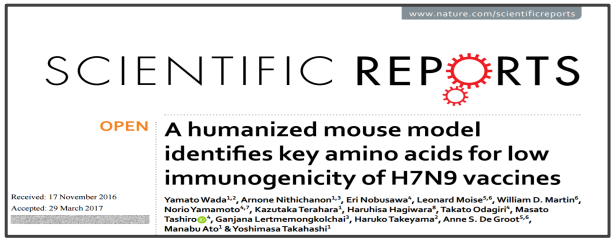
Remove Treg introduce Teff memory Epitope



	297										309	
H7-HA	P	R	Y	V	K	Q	R	S	L	L	L	A	T	Treg Epitope
	306										318	
H3-HA	P	R	Y	V	K	Q	N	T	L	K	L	A	T	T Eff$_m$ Epitope
							↓							
	297										309	
H7-HA-Opt1	P	R	Y	V	K	Q	N	T	L	K	L	A	T	T Eff$_m$ Epitope

Ab Titer Results




www.nature.com/scientificreports

SCIENTIFIC REPORTS

OPEN

A humanized mouse model identifies key amino acids for low immunogenicity of H7N9 vaccines

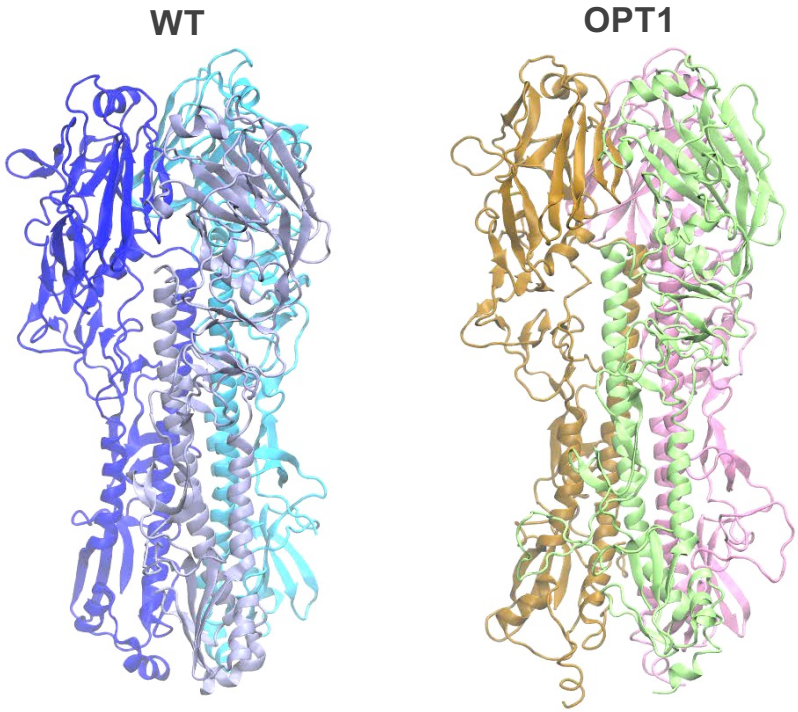
Received: 17 November 2016
Accepted: 29 March 2017

Yamato Wada[1,2], Arnone Nithichanon[1,3], Eri Nobusawa[4], Leonard Moise[5,6], William D. Martin[6], Norio Yamamoto[5,7], Kazutaka Terahara[1], Haruhisa Hagiwara[8], Takato Odagiri[9], Masato Tashiro[9,4], Ganjana Lertmemongkolchai[3], Haruko Takeyama[2], Anne S. De Groot[5,6], Manabu Ato[1] & Yoshimasa Takahashi[1]

Wada *et al. Sci Rep.* 2017; 7(1):1283

Immune Engineered H7N9 HA Containing 5 Seasonal Epitopes is Stable on Anhui/2013 and Guangdong/2016 Backgrounds

EVA THERAPEUTICS



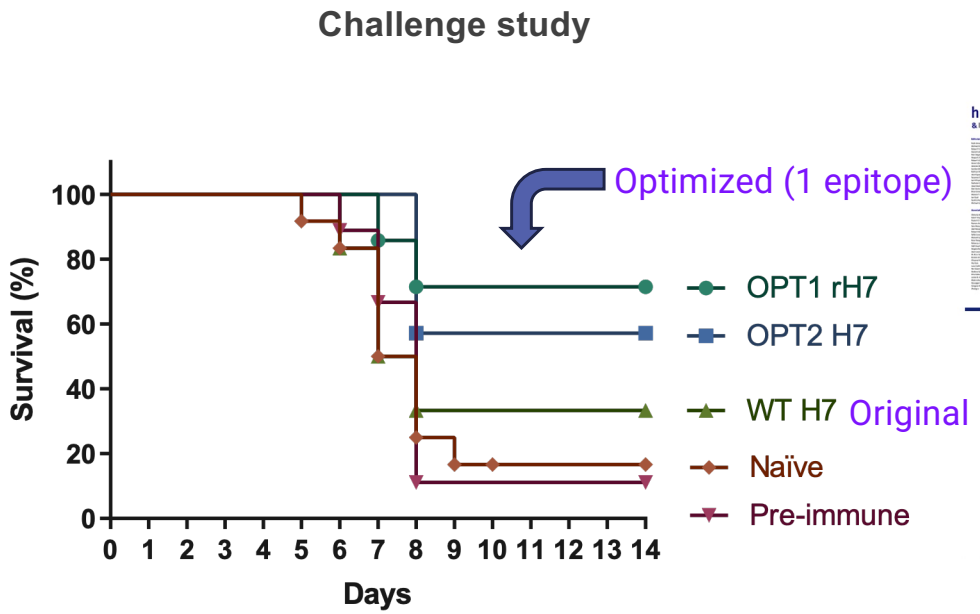
Anhui backbone shown

University of Massachusetts Medical School
UMASS

Immune-engineered H7N9 Vaccine

unadjuvanted Opt 1 vaccine protects > wild type

EVA THERAPEUTICS





Human Vaccines & Immunotherapeutics

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/khvi20

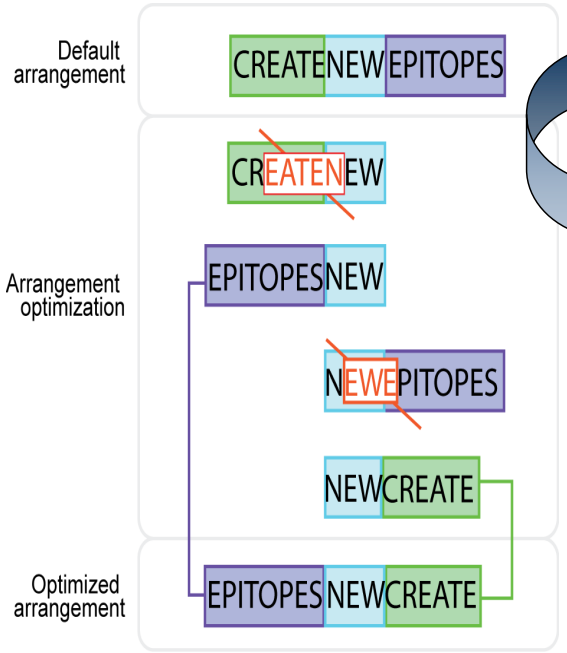
Immune-engineered H7N9 influenza hemagglutinin improves protection against viral influenza virus challenge

Hyesun Jang , Lauren M. Meyers , Christine Boyle , Anne S. De Groot , Lenny Moise & Ted M. Ross

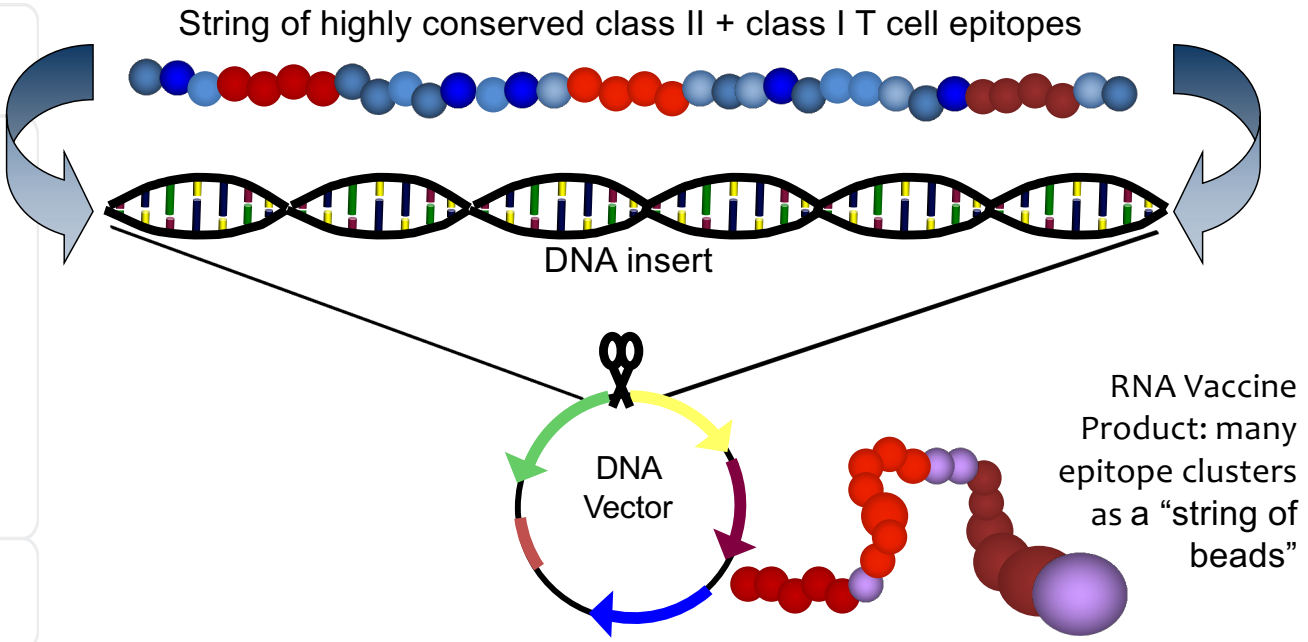
VaxCAD / RNA vaccine Design

EVA THERAPEUTICS

VaxCAD: Computationally Optimized String of Beads Design

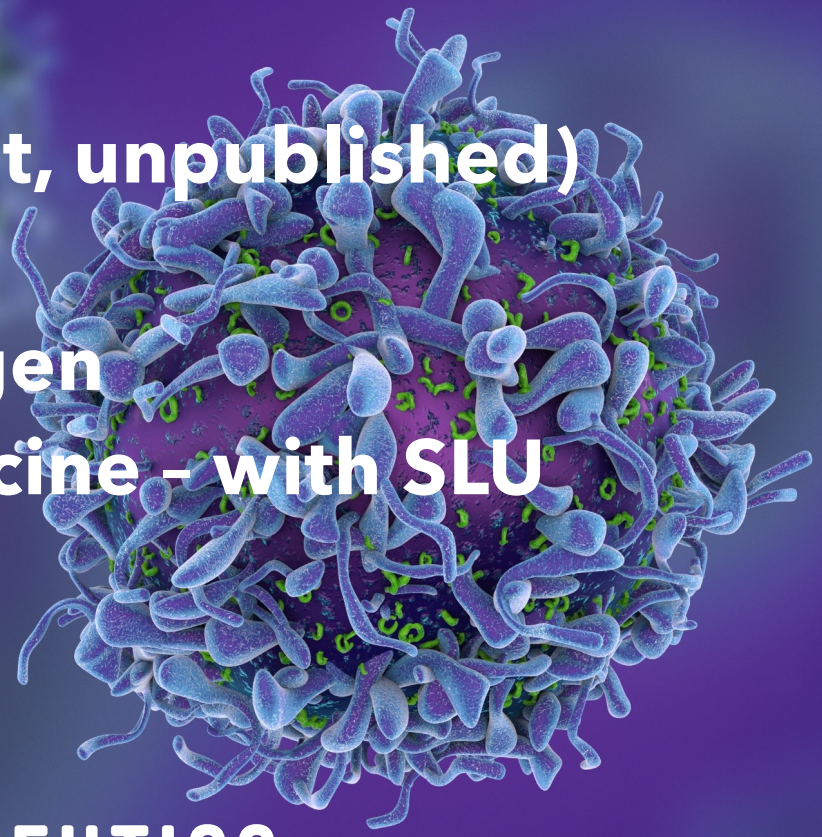


mRNA Vaccine Production: Construct expressing T cell epitopes as a string of beads insert



Case studies (Recent, unpublished)

- **Mpox – with Afrigen**
- **Universal Flu Vaccine – with SLU**



EVA THERAPEUTICS

Case study: Mpox

EVA THERAPEUTICS

Current project: Mpox (Afrigen)

EVA THERAPEUTICS

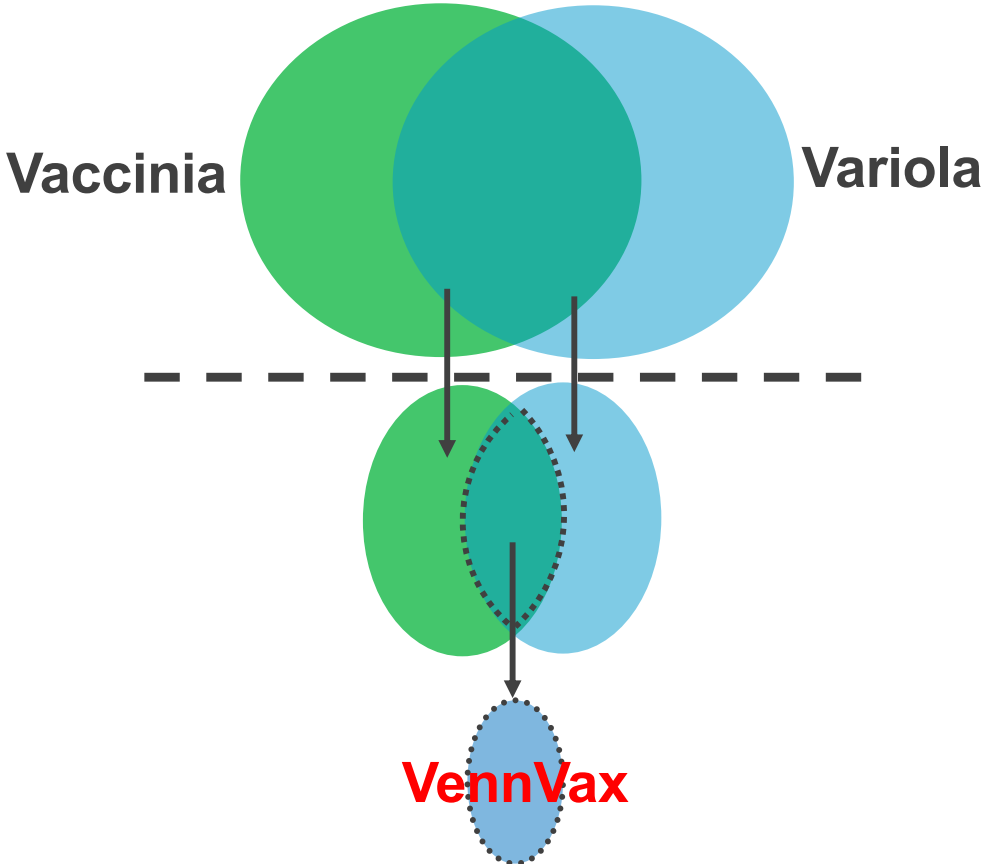
Genomes

iVAX

Immunogenic and conserved
T Cell Epitopes

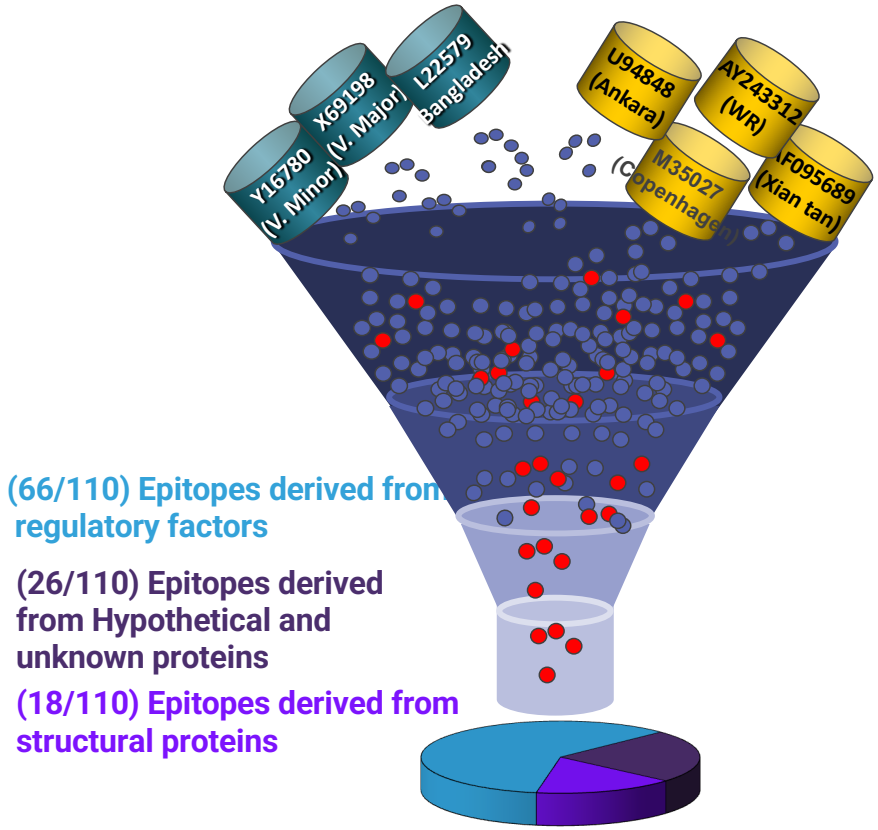
iVAX

Vaccine



Comprehensive search for conserved and immunogenic VennVax epitopes

EVA THERAPEUTICS



1. Downloaded 7 complete genomes from GenBank.

2. Identified highly conserved 9-mers

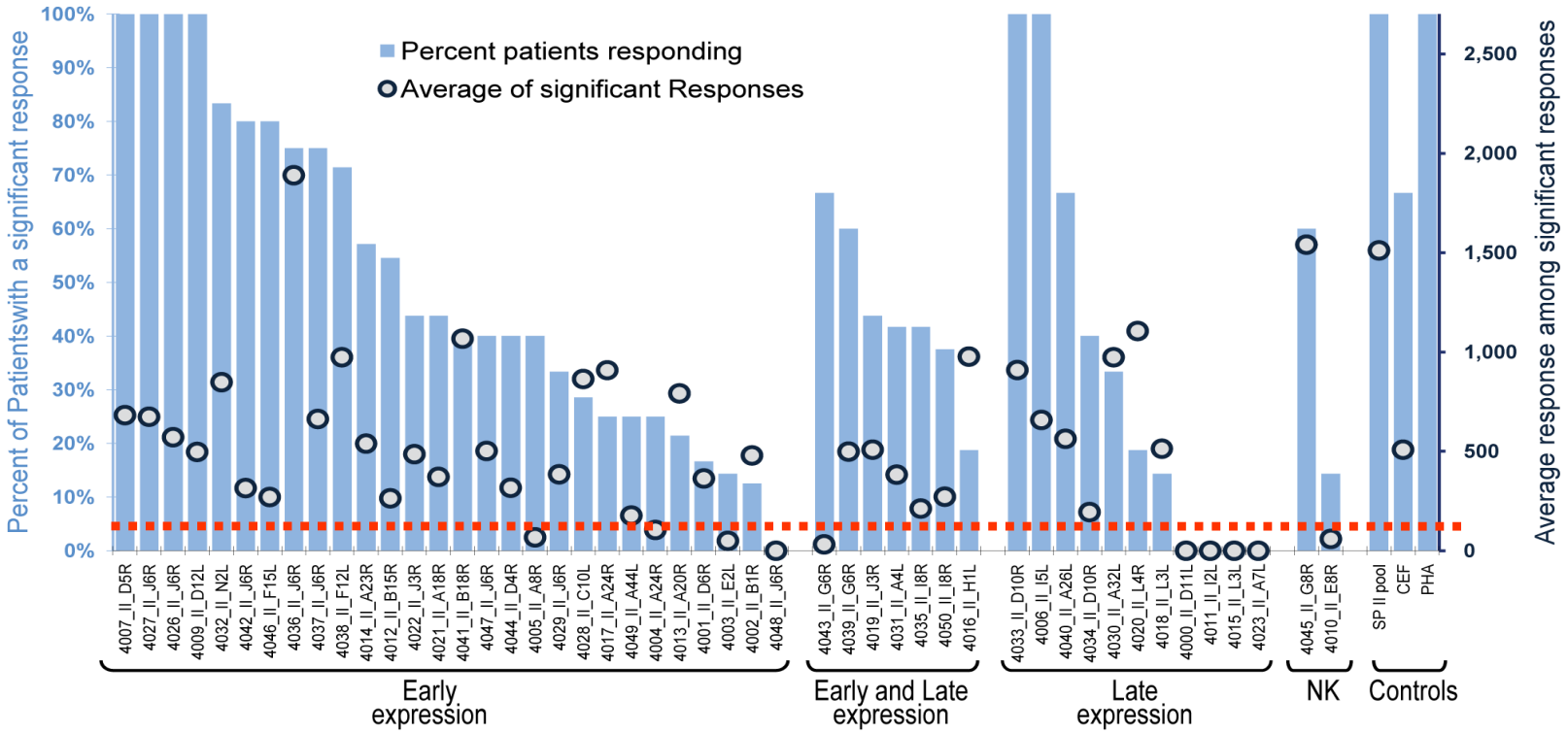
3. Identified promiscuous Class II T cell epitopes and Class I epitopes

4. Eliminated human-like epitopes

Vaccine. 2009;27:6471-9

HLA class II VennVax epitopes are recognized by exposed humans - by T cells from "Dryvax" vaccinees

EVA THERAPEUTICS

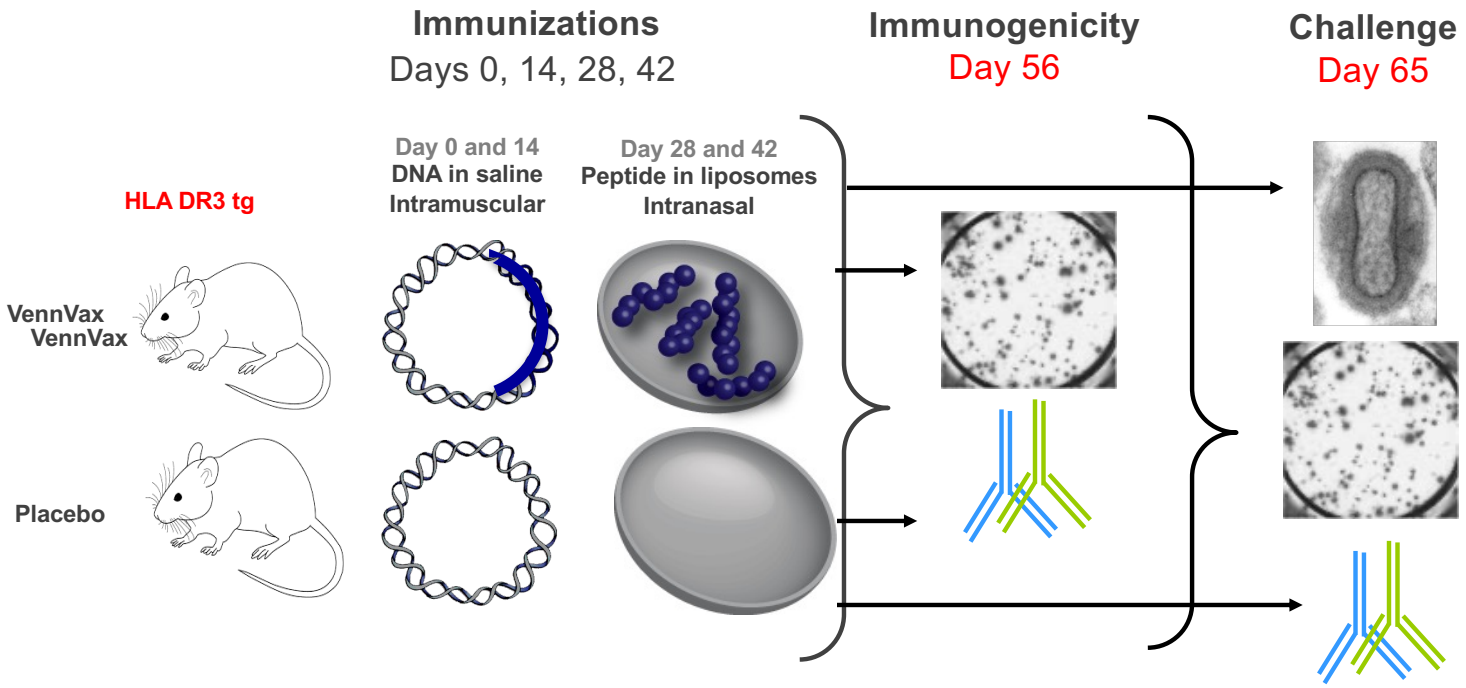


88% of predicted T cell epitopes confirmed in vitro using human PBMC

Vaccine. 2009;27:6471-9

VennVax vaccine challenge study design

EVA THERAPEUTICS

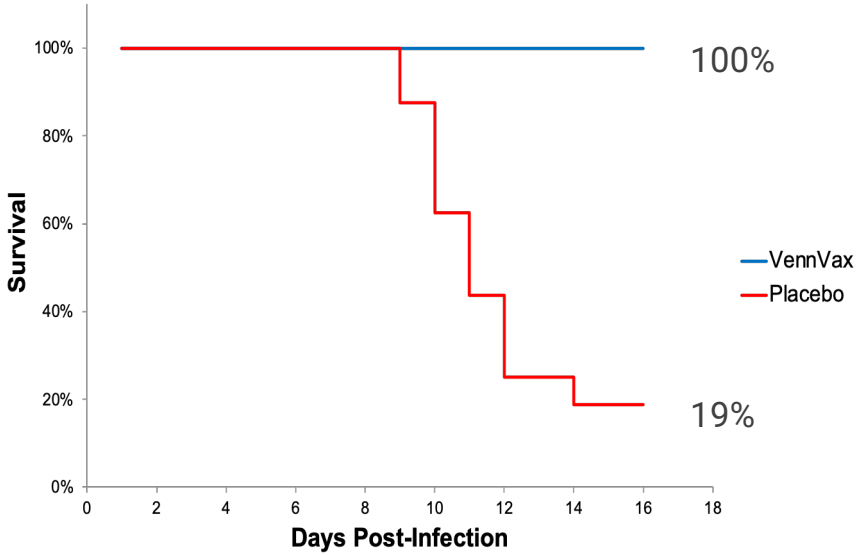


Vaccine. 2011;29:501-11

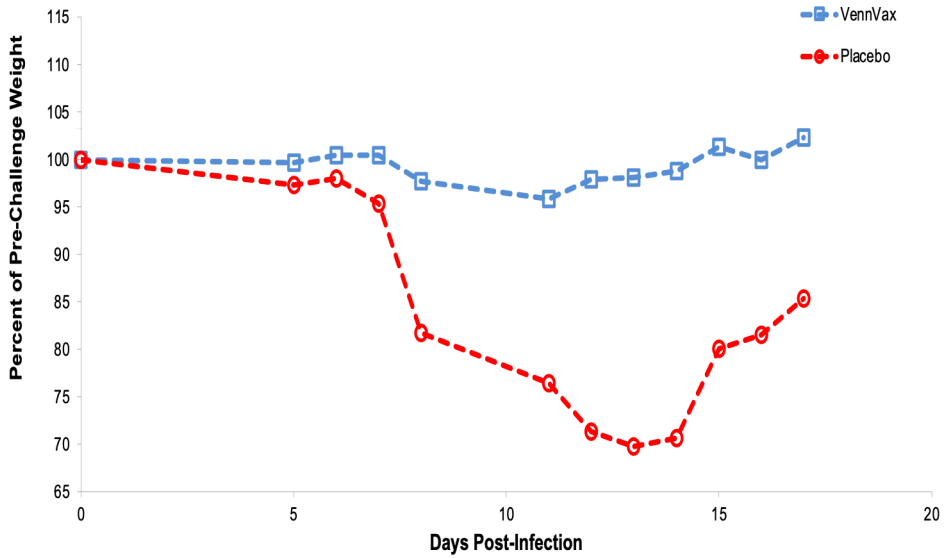
VennVax protects against severe disease and death

EVA THERAPEUTICS

Survival



Morbidity



Vaccinia Western Reserve
10X LD_{50}
Intranasal

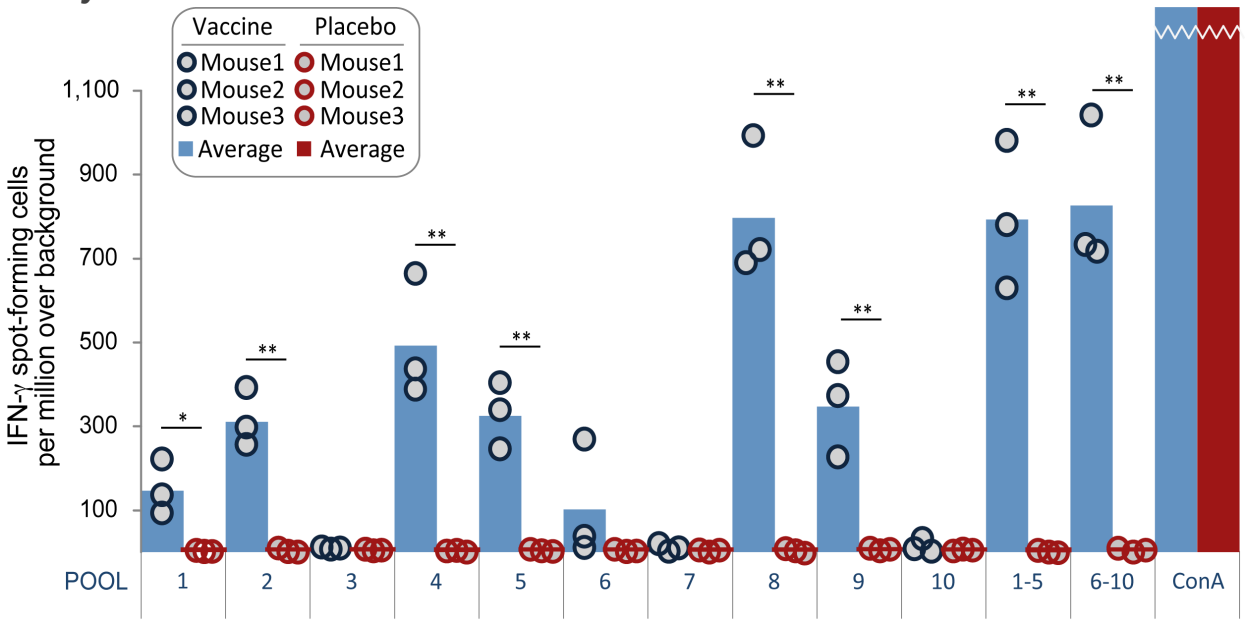
VennVax vaccinated mice N=18; Placebo N=16

Vaccine. 2011;29:501-11

Vaccinated mice: VennVax stimulates strong T cell response ... 50 Epitopes – 10 pools of 5 epitopes

EVA THERAPEUTICS

HLA DR3 tg mice
Day 56



- HLA class II epitope-specific Th1 cytokine and chemokine responses
  - IFNγ
  - IL-2
  - MIP-1α
  - MIP-1β
- Immunogenic promiscuous epitopes
  - DR3 tg
  - DR1 tg

Vaccine. 2011;29:501-11

Case study:
Universal Flu Vaccine (Dan Hoft)

EVA THERAPEUTICS

Thank you !

EVA THERAPEUTICS

Selected published human validation (*ex vivo* & humanized models)

EVA THERAPEUTICS

CD4 T cell epitopes prospective studies

Disease/Target	Publication
Malaria	Noe et al. Front Immunol., 2021 12:689920
SARS-CoV-2	Meyers et al. npj Vaccines, 2021 6(1):71
Q Fever	Scholzen et al., Infect Immun. 2019 19;87(10):e00213-19
Q fever	Scholzen A et al. Front Immunol. 2019;10:207
IFN-α	Mufarrege EF et al. Clin Immunol. 2017;176:31-41
Mesothelioma	Hoffmann PR et al. Hum Vaccin Immunother. 2015;11(7):1585-95
HCC	Tomimaru Y et al. Vaccine. 2015;33(10):1256-66
H. pylori	Zhang S et al. PLoS One. 2014;9(4):e94974
HFMD	Wei R et al. PLoS One. 2012;7(12):e51957
H1N1 influenza	Schanen BC et al. Vaccine. 2011 Apr 12;29(17):3299-309
Smallpox	Moise L et al. Vaccine. 2009; 27(46):6471-9
Tularemia	McMurry JA et al. Vaccine. 2007;25(16):3179-91

T cell epitope prediction / validation retrospective analyses

Disease/Target	Publication
Pompe disease	De Groot et al. Front Immunol., 2021, 12:636731
Bladder cancer	Richard et al. Sci Rep. 2021 11;11(1):9983
Malaria	Khan et al. Hum Vaccin Immunother. 2020;16(2):214-227
Pompe disease	De Groot AS et al. Clin Immunol. 2019;200:66-70

CD8 T cell epitopes prospective studies

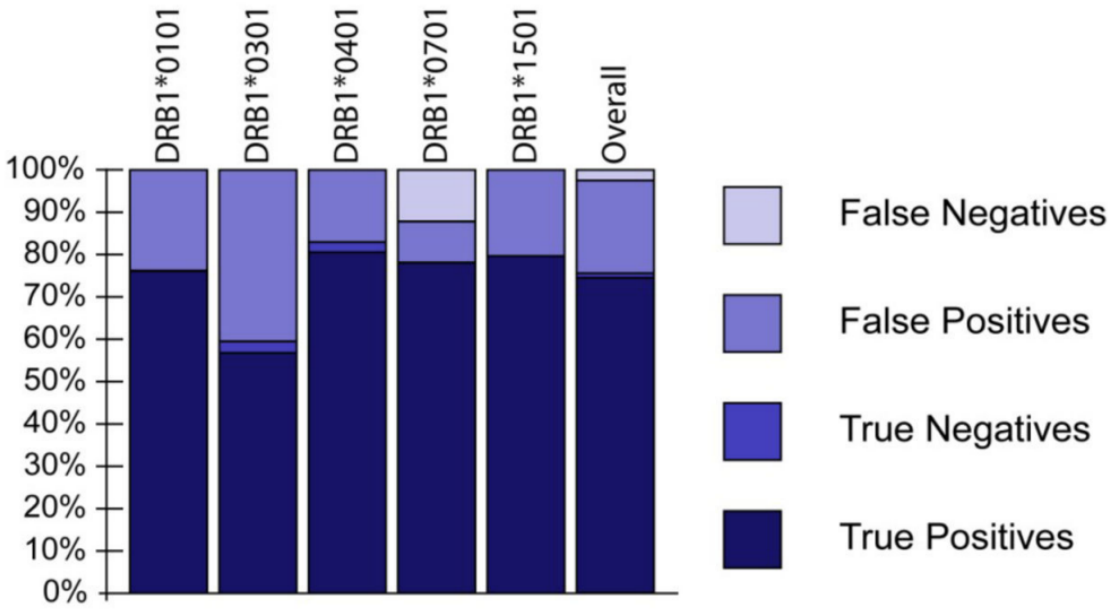
Disease/Target	Publication
Malaria	Tucker et al. Front Immunol., 2021 12:684116
SARS-CoV-2	Meyers et al. npj Vaccines, 2021 6(1):71
Mesothelioma	Hoffmann et al. Hum Vaccin Immunother. 2015;11(7):1585-95
HCC	Tomimaru Y et al. Vaccine. 2015;33(10):1256-66
Smallpox	Moise L et al. Vaccine. 2009;27(46):6471-9
Tularemia	McMurry JA et al. Vaccine. 2007;25(16):3179-91

Treg epitope validation studies

Disease/Target	Publication
SARS-CoV-2	Miah et al. Front Immunol., 2023;14:1290688
Factor V	De Groot et al., Clin Immunol., 2021 224:108661
H7N9	Wada Y et al. Sci Rep. 2017;7(1):1283
H7N9	Liu R et al. Hum Vaccin Immunother. 2015;11(9):2241-52
HCV	Losikoff PT et al. J Hepatol. 2015;62(1):48-55
IgG	Hui DJ et al. Mol Ther. 2013;21(9):1727-37
IgG	De Groot AS et al. Blood. 2008;112(8):3303-11

Class II HLA Binding: from in silico to in vitro
>90% correlation with in vitro data

EVA THERAPEUTICS



De Groot AS, Ardito M, Moise L, Gustafson EA, Spero D, Tejada G, Martin W. Immunogenic Consensus Sequence T helper Epitopes for a Pan-*Burkholderia* Biodefense Vaccine. Immunome Res. 2011 May;7(2):e7. doi: 10.4172/1745-7580.1000043. PMID: 25346775; PMCID: PMC4206550.

Published: 'Immunogenic Consensus Sequence Epitopes are more cross-protective

EVA THERAPEUTICS

Go to Vaccine on ScienceDirect

ELSEVIER

Vaccine

Volume 37, Issue 36, 23 August 2019, Pages 5371-5381

Highly conserved influenza T cell epitopes induce broadly protective immunity

Christopher S. Eickhoff [a], Frances E. Terry [c], Linda Peng [a], Krystal A. Meza [a], Isaac G. Sakala [a], Daniel Van Aartsen [a], Leonard Moise [c d], William D. Martin [c], Jill Schriewer [b], R. Mark Buller [b], Anne S. De Groot [c d], Daniel F. Hoft [a b]

Influenza

Universal T Cell Epitope-driven Influenza Vaccine
Preclinical and progressing to clinic

frontiers | Frontiers in Immunology

SAINT LOUIS UNIVERSITY

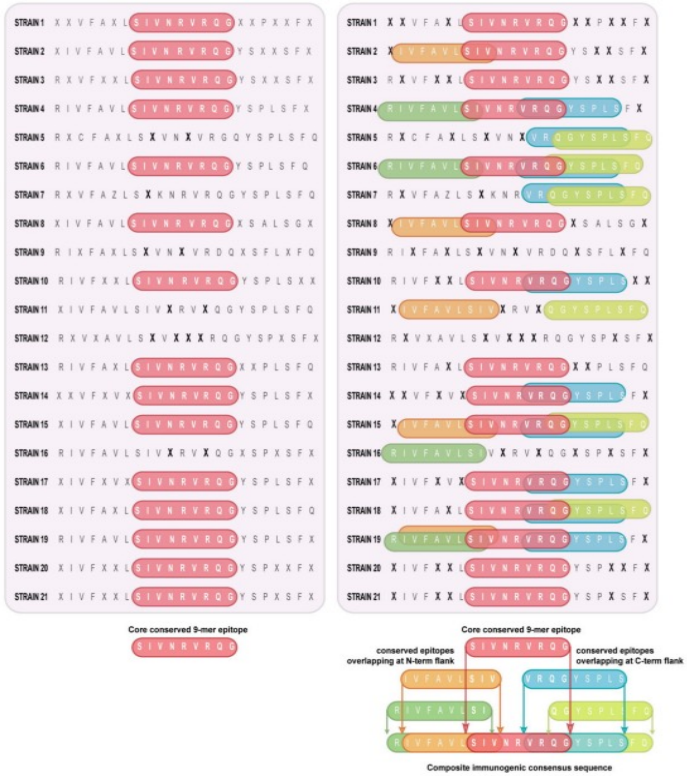
Identification of immunodominant T cell epitopes induced by natural Zika virus infection

Christopher S. Eickhoff[1], Krystal A. Meza[1], Frances E. Terry[2], Chase G. Colbert[1], Azra Blazevic[1], Andres H. Gutiérrez[2], E. Taylor Stone[3], James D. Brien[3], Amelia K. Pinto[3], Hana M. El Sahly[4], Mark J. Mulligan[5], Nadine Rouphael[6], Maria L. Alcaide[7], Kay M. Tomashek[8], Chris Focht[9], William D. Martin[2], Leonard Moise[2], Anne S. De Groot[2,10] and Daniel F. Hoft[1,3]*

Validation of Immunogenic Consensus Sequence
Overlapping immunogenic clusters

EVA THERAPEUTICS

Clusters found in one strain…overlap with clusters found in others



frontiers | Frontiers in Immunology

TYPE Original Research
PUBLISHED 29 August 2023
DOI 10.3389/fimmu.2023.1247876

SAINT LOUIS UNIVERSITY

Check for updates

OPEN ACCESS

EDITED BY
Erez Bar-Haim,
Israel Institute for Biological Research (IIBR), Israel

REVIEWED BY
Anat Zvi,
Israel Institute for Biological Research (IIBR), Israel
Victoria Adeleke,
University of KwaZulu-Natal, South Africa
Simone Gonçalves Fonseca,
Universidade Federal de Goiás, Brazil

*CORRESPONDENCE
Daniel F. Hoft
Daniel.Hoft@health.slu.edu

RECEIVED 26 June 2023
ACCEPTED 07 August 2023

Identification of immunodominant T cell epitopes induced by natural Zika virus infection

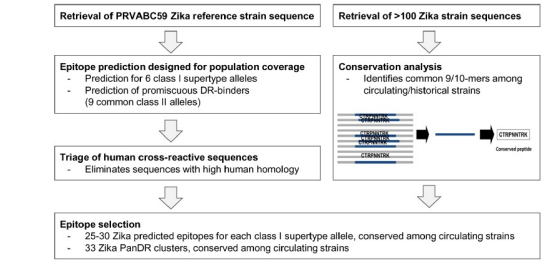
Christopher S. Eickhoff[1], Krystal A. Meza[1], Frances E. Terry[2], Chase G. Colbert[1], Azra Blazevic[1], Andres H. Gutiérrez[2], E. Taylor Stone[3], James D. Brien[3], Amelia K. Pinto[3], Hana M. El Sahly[4], Mark J. Mulligan[5], Nadine Rouphael[6], Maria L. Alcaide[7], Kay M. Tomashek[8], Chris Focht[9], William D. Martin[2], Leonard Moise[2], Anne S. De Groot[2,10] and Daniel F. Hoft[1,3]*

Validation of approach – Zika Epitopes *outperformed* "standard"

EVA THERAPEUTICS

Identification of immunodominant T cell epitopes induced by natural Zika virus infection

A



B

EpiMatrix Cluster Detail Report

Sequence: DR1 - NS5 cluster 2917-2934

Frame start	Amino acid sequence	Frame stop	DRB1*0101 Z-score	DRB1*0301 Z-score	DRB1*0401 Z-score	DRB1*0701 Z-score	DRB1*0801 Z-score	DRB1*0901 Z-score	DRB1*1101 Z-score	DRB1*1301 Z-score	DRB1*1501 Z-score	Hits
2917	EEFFINKVR	2925	-0.12	-0.89	0.03	-0.44	0.34	0.14	-0.32	0.57	0.41	0
2918	EFFINKVRS	2926	0.54	0.6	0.45	-0.73	0.53	-0.01	1.05	0.93	0.54	0
2919	FFINKVRSN	2927	0.66	-0.2	0.63	0.39	0.67	0.04	1.06	-0.64	-0.88	0
2920	FINKVRSNA	2928	1.14	1.99	0.36	1.4	2.34	1.4	2.05	2.31	0.88	4
2921	INKVRSNAA	2929	2.3	2.29	2.47	2.76	1.63	2.38	2.58	1.68	2.67	8
2922	NKVRSNAAL	2930	1.09	0.75	0.7	0.47	0.73	0.67	0.82	1.04	0.52	0
2923	KVRSNAALG	2931	1.78	1.65	1.76	0.67	1.46	2.03	1.84	1.51	1.07	5
2924	VRSNAALGA	2932	1.99	2.01	2.3	1.65	1.5	1.94	2.26	2.13	1.97	8
2925	RSNAALGAT	2933	-0.72	1.14	-1.23	0.08	-0.17	1.19	-0.7	0.02	1.09	0
2926	SNAALGATF	2934	0.69	0.86	0.98	0.53	0.4	1.59	0.38	1.04	0.29	0
Summarized Results			**DRB1*0101**	**DRB1*0301**	**DRB1*0401**	**DRB1*0701**	**DRB1*0801**	**DRB1*0901**	**DRB1*1101**	**DRB1*1301**	**DRB1*1501**	**Total**
Maximum single Z-score			2.3	2.29	2.47	2.76	2.34	2.38	2.58	2.31	2.67	--
Sum of significant Z-scores			6.07	7.94	6.53	4.41	2.34	6.35	8.73	6.12	4.64	53.13
Count of significant Z-scores			3	4	3	2	1	3	4	3	2	25
Total assessments performed: 90			**EpiMatrix Cluster Score (w/o flanks): 48.49**								Top 10%	Top 5%	Top 1%

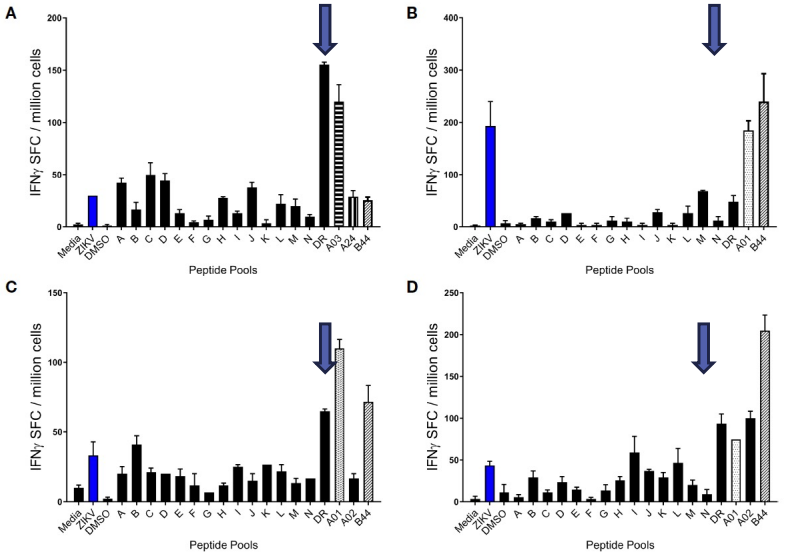


FIGURE 2

Human T cell responses induced by ZIKV infection. PBMC from four different participants **(A–D)** previously infected with ZIKV were studied in overnight IFN-γ ELISPOT assays. Each sample was stimulated with live ZIKV or media control, overlapping peptide pools A-N, predicted promiscuous panDR clusters (DR), or pools of ZIKV peptides predicted to bind MHC I supertypes. While all sets of PBMC were stimulated with live ZIKV, overlapping peptide pools, and the MHC II pool (DR), participant PBMC were only stimulated with MHC I peptide pools matched to the participant HLA type. Shown are the means + SE of the numbers of IFN-γ spot forming cells (SFC) per million PBMC from 4 different Zika-infected participants.