

Peptide Vaccine for Infectious Disease

M2 Toyama

2020/5/11

Contents

1. Introduction

2. Example of Peptide Vaccine

3. Peptide Vaccine for SARS-CoV-2

4. Summary

Vaccine

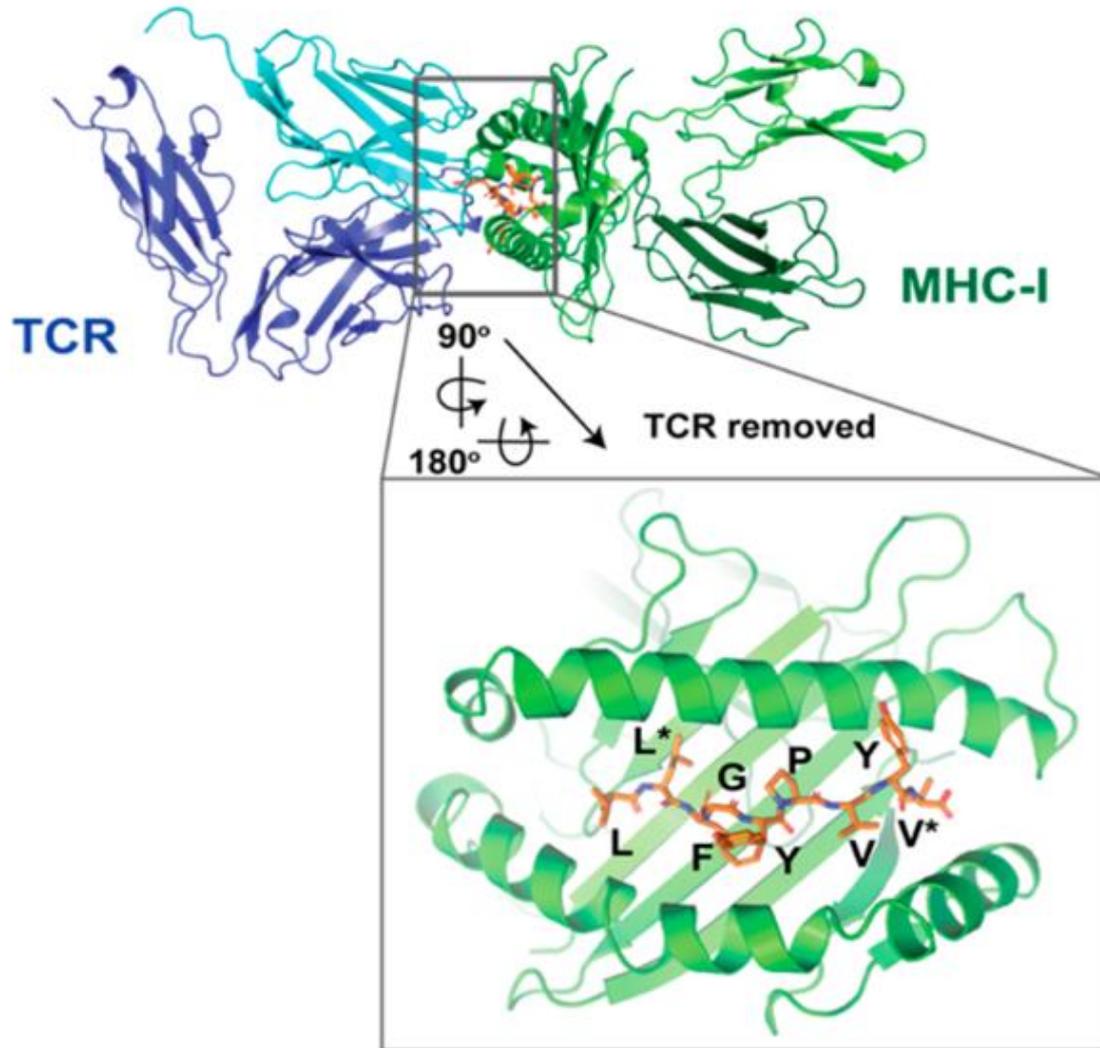


- Vaccines stimulate immune system and prevent infectious disease.
- Vaccination prevents 2~3 million death every year.
- Development of some vaccines remains challenging. (e.g. HIV, influenza virus)

Nat. Med., **2005**, *11*, 45.

Nat. Rev. Immunol., **2006**, *6*, 148.

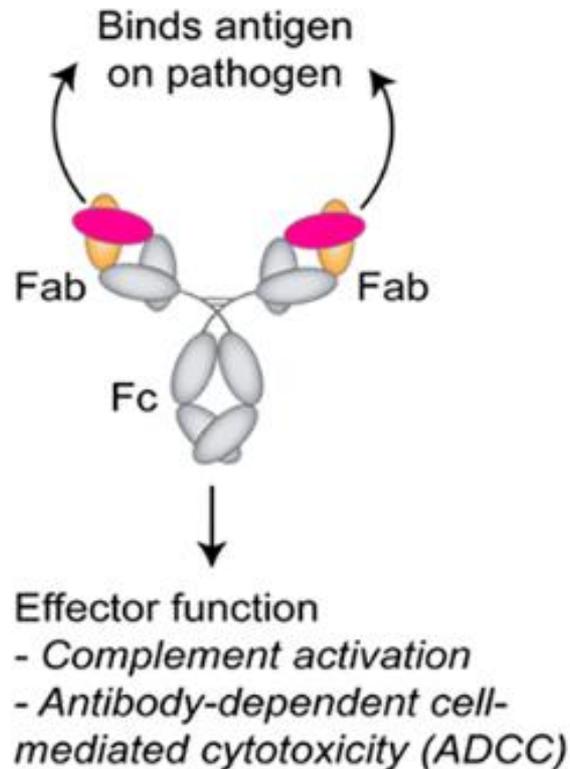
T-cell Stimulation



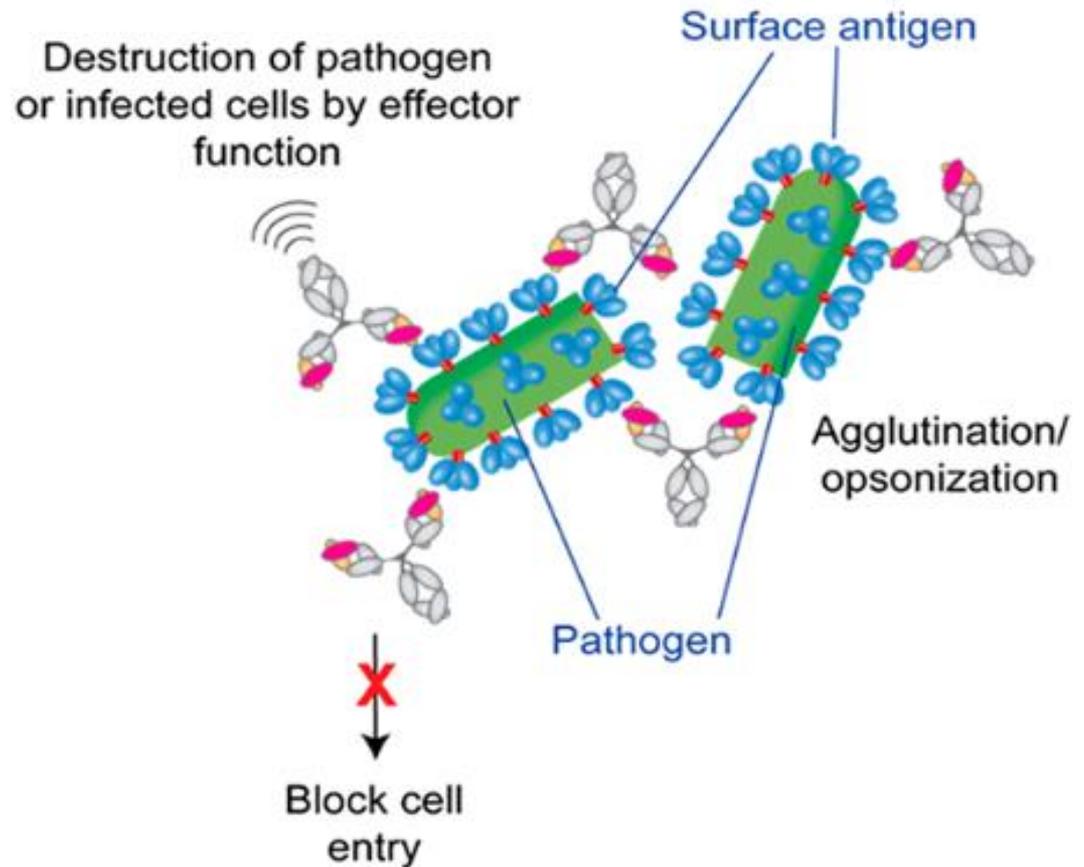
- Antigen is presented on MHCs.
- MHC-I : 8-11 residues
- MHC-II : 11-30 residues
- TCR recognizes the epitope and activate immune response.

B-cell Stimulation

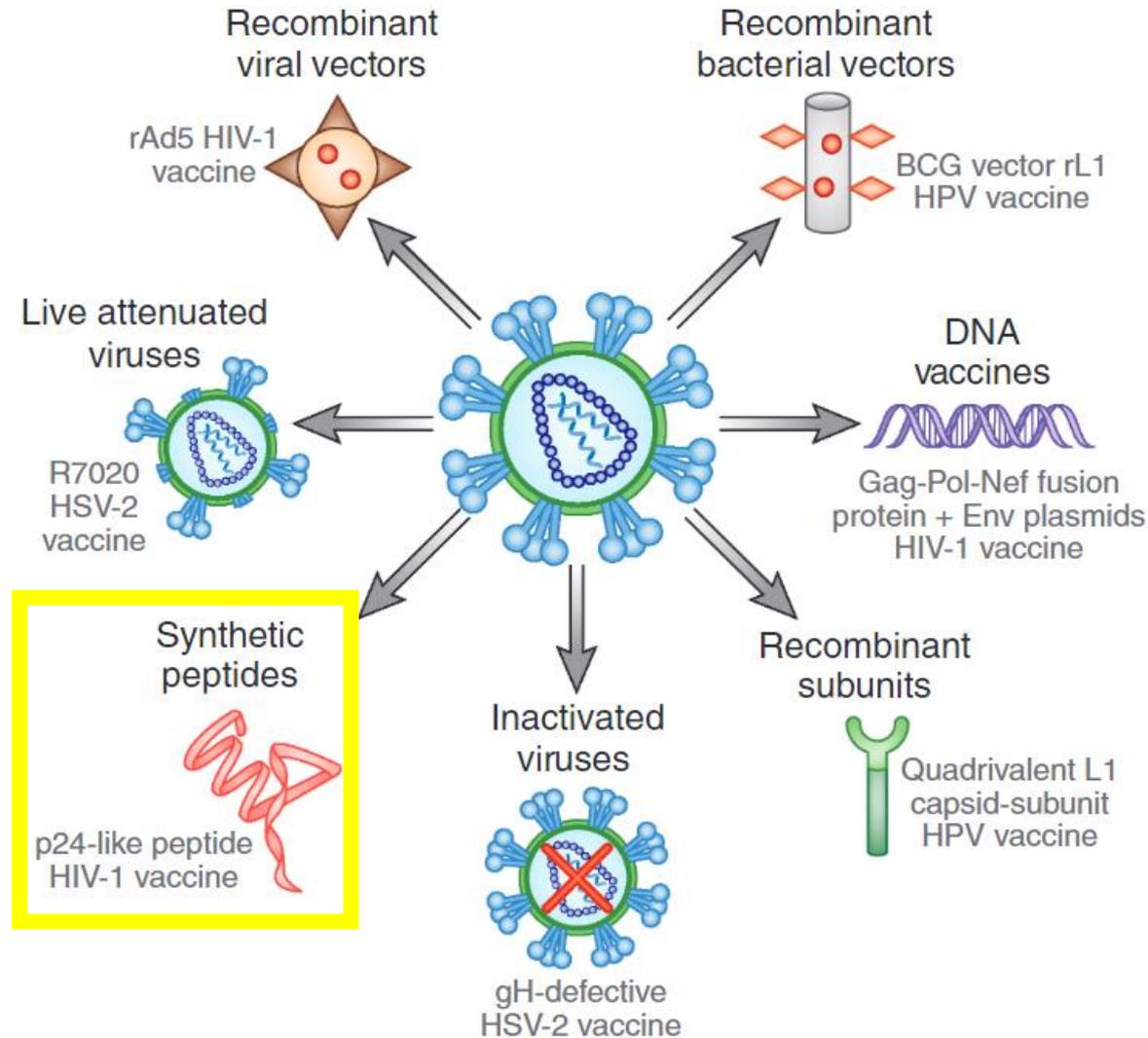
Antibody



Mechanisms of antibody function



Types of Vaccines



Contents

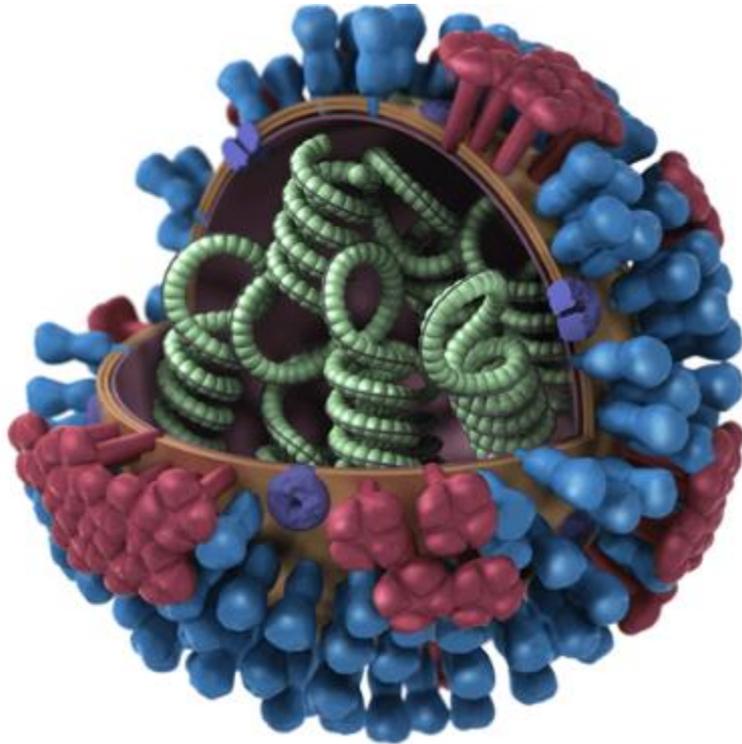
1. Introduction

2. Example of Peptide Vaccine

3. Peptide Vaccine for SARS-CoV-2

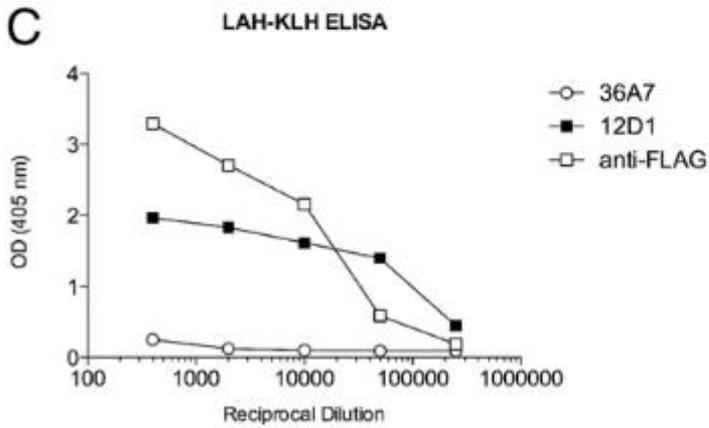
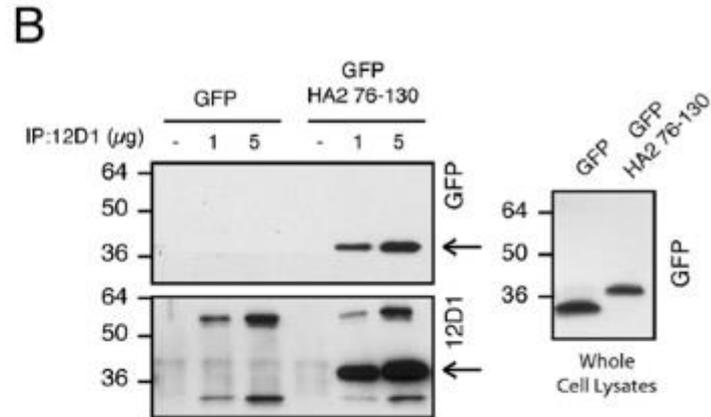
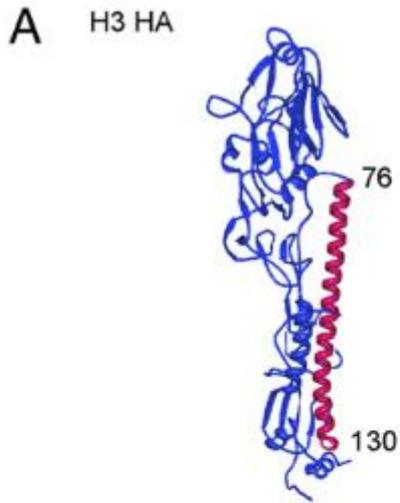
4. Summary

Target: Influenza Virus



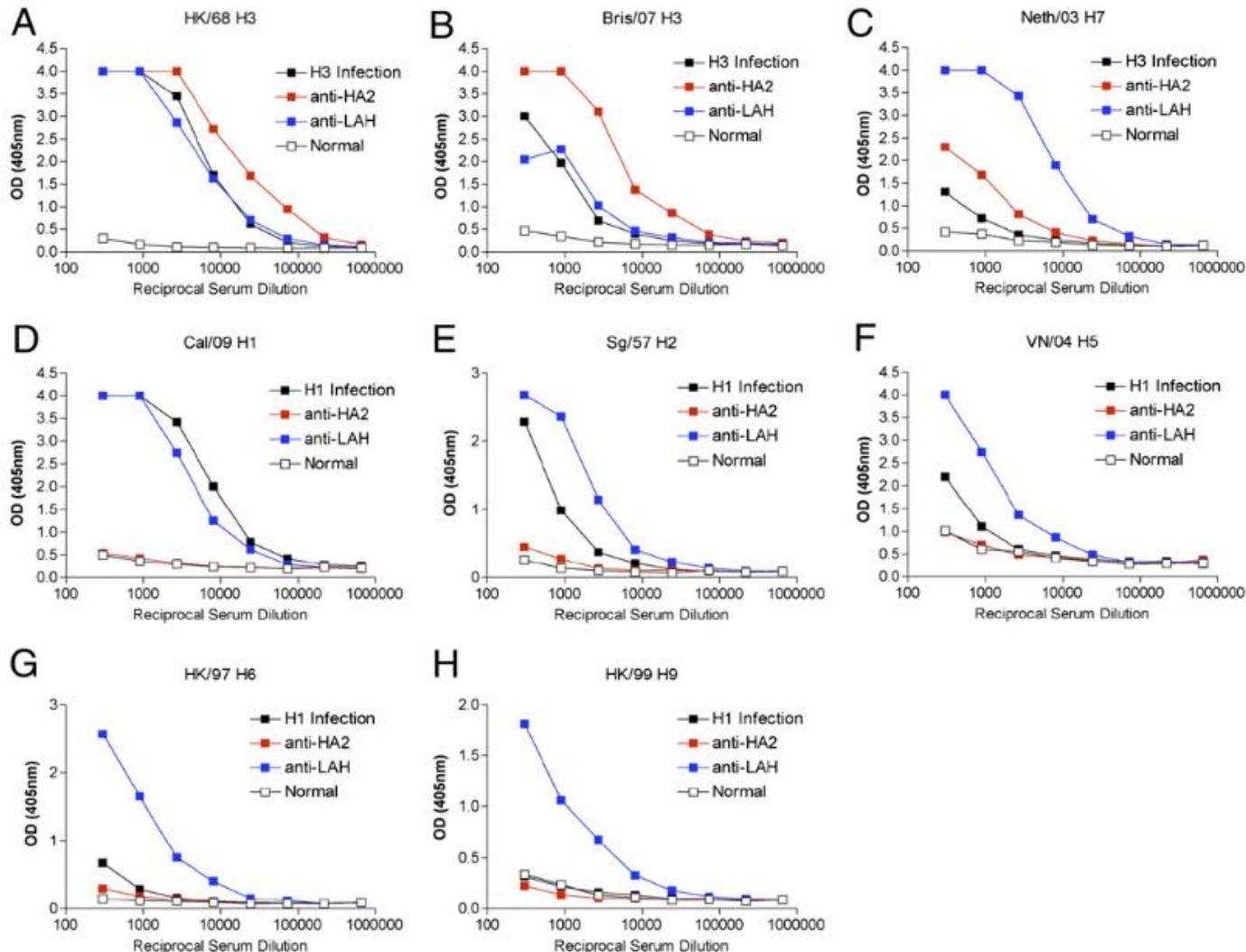
- ~10 million people are infected every year in Japan.
- Very rapid mutation
- Hemagglutinin (HA) is the major target of vaccine.

LAH-KLH Peptide



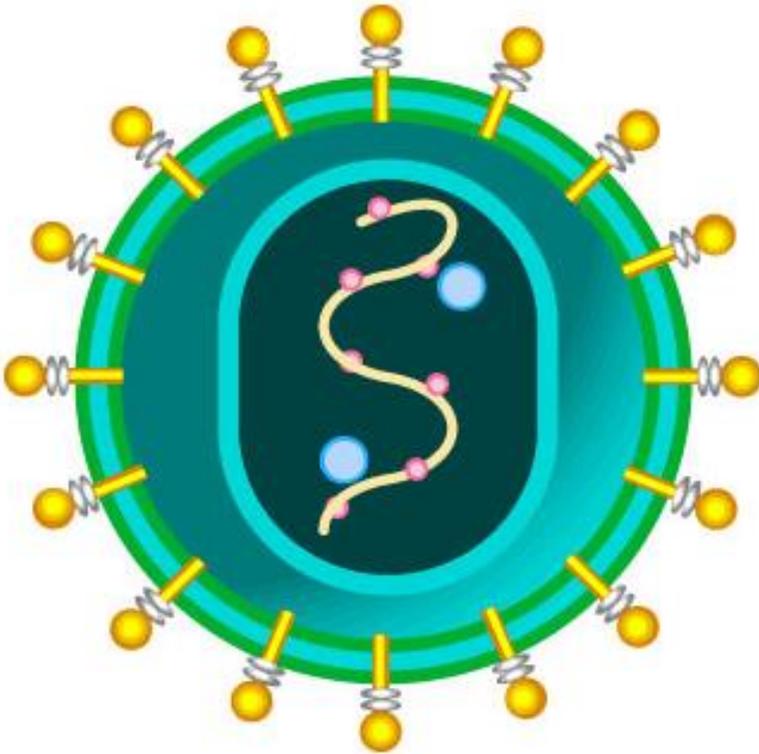
- mAb 12D1 reacts with LAH of HA2.
- LAH-KLH was synthesized and used as a peptide vaccine.

Activity of Peptide Vaccine



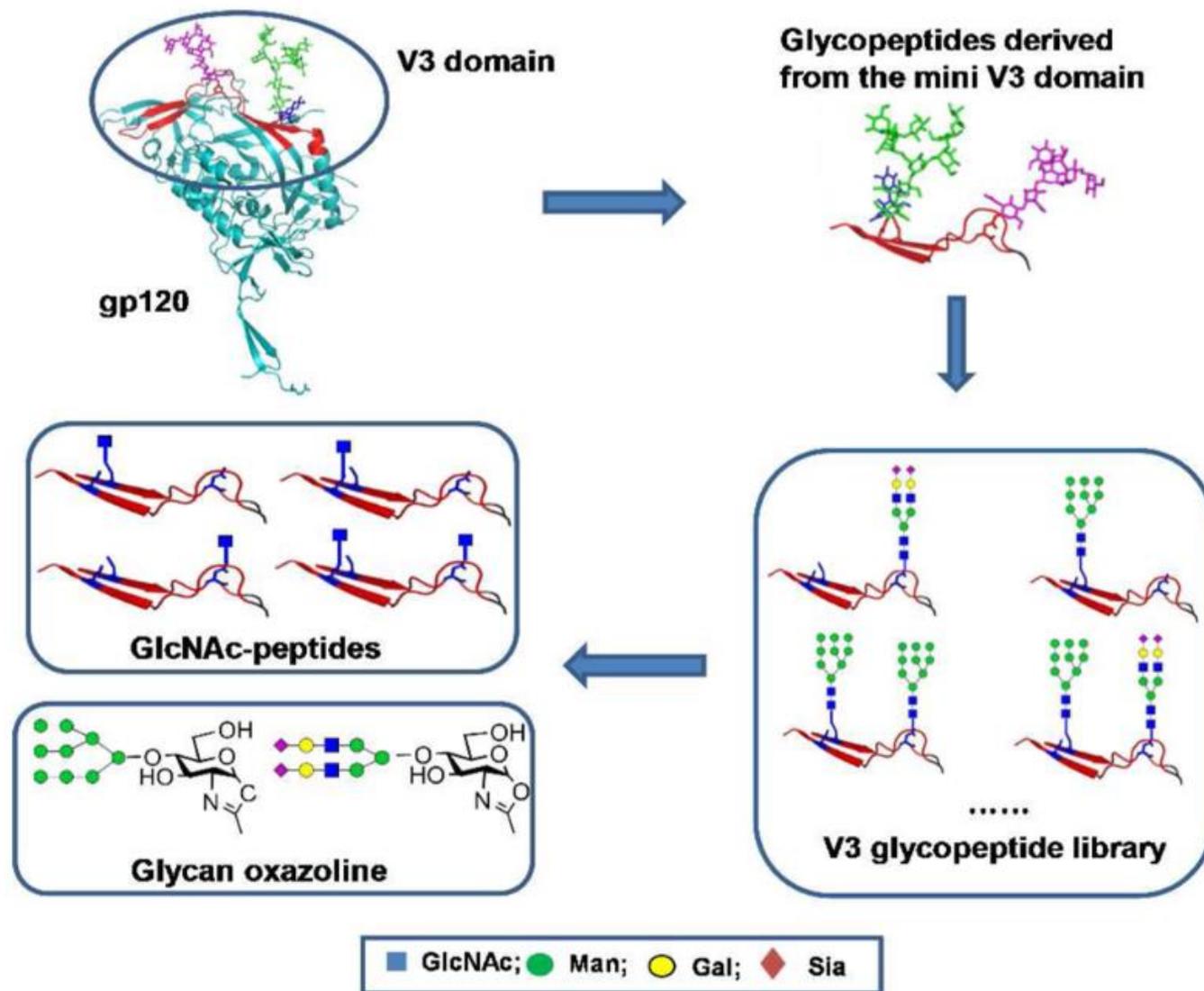
Proc. Natl. Acad. Sci. U. S. A., 2010, 107, 18979.

Target: HIV

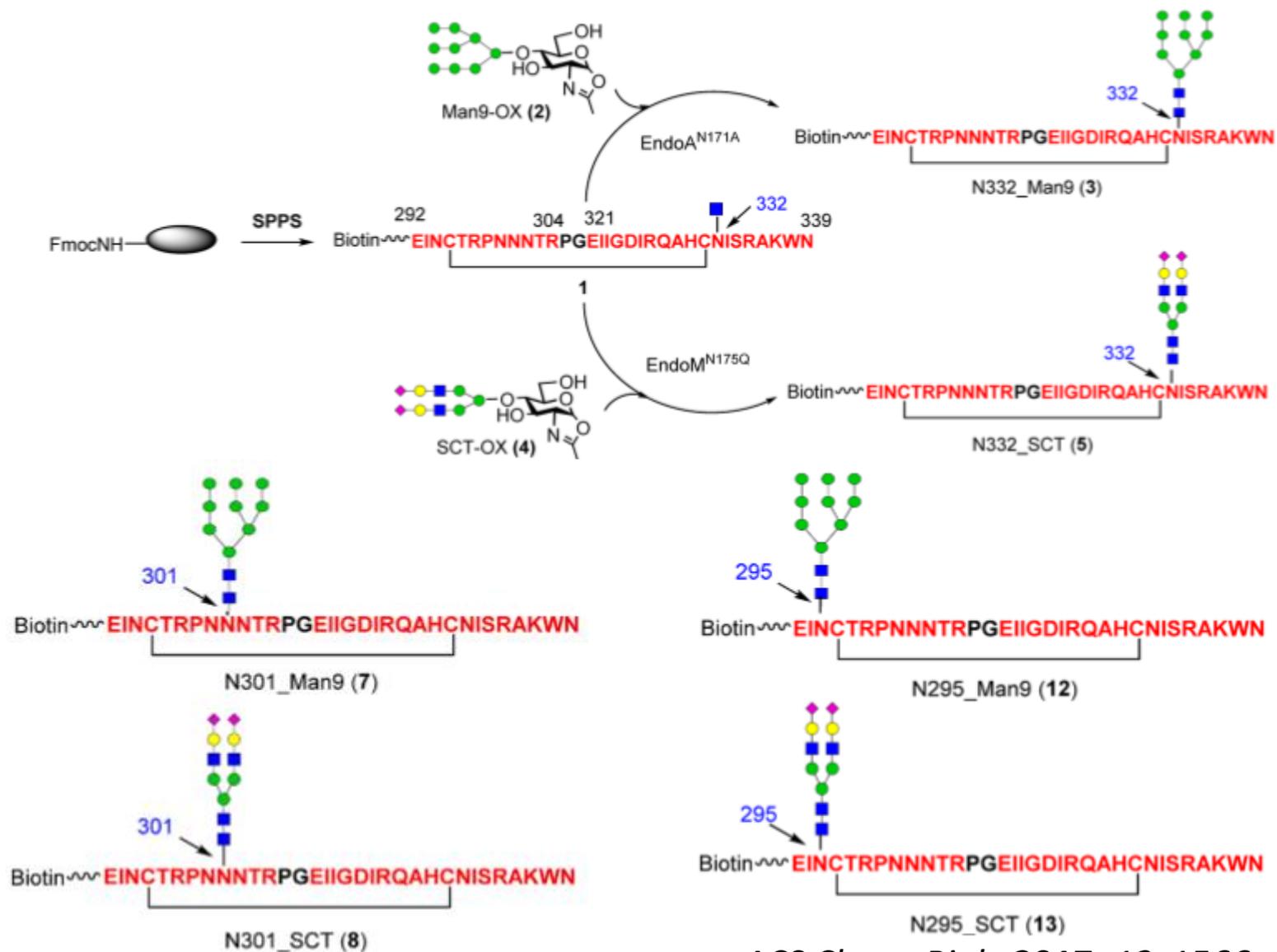


- After long incubation (~10 years), immune system is destroyed.
- 30,000 patients in Japan
- There exist many types of virus.
- Non-human animals do not catch virus.

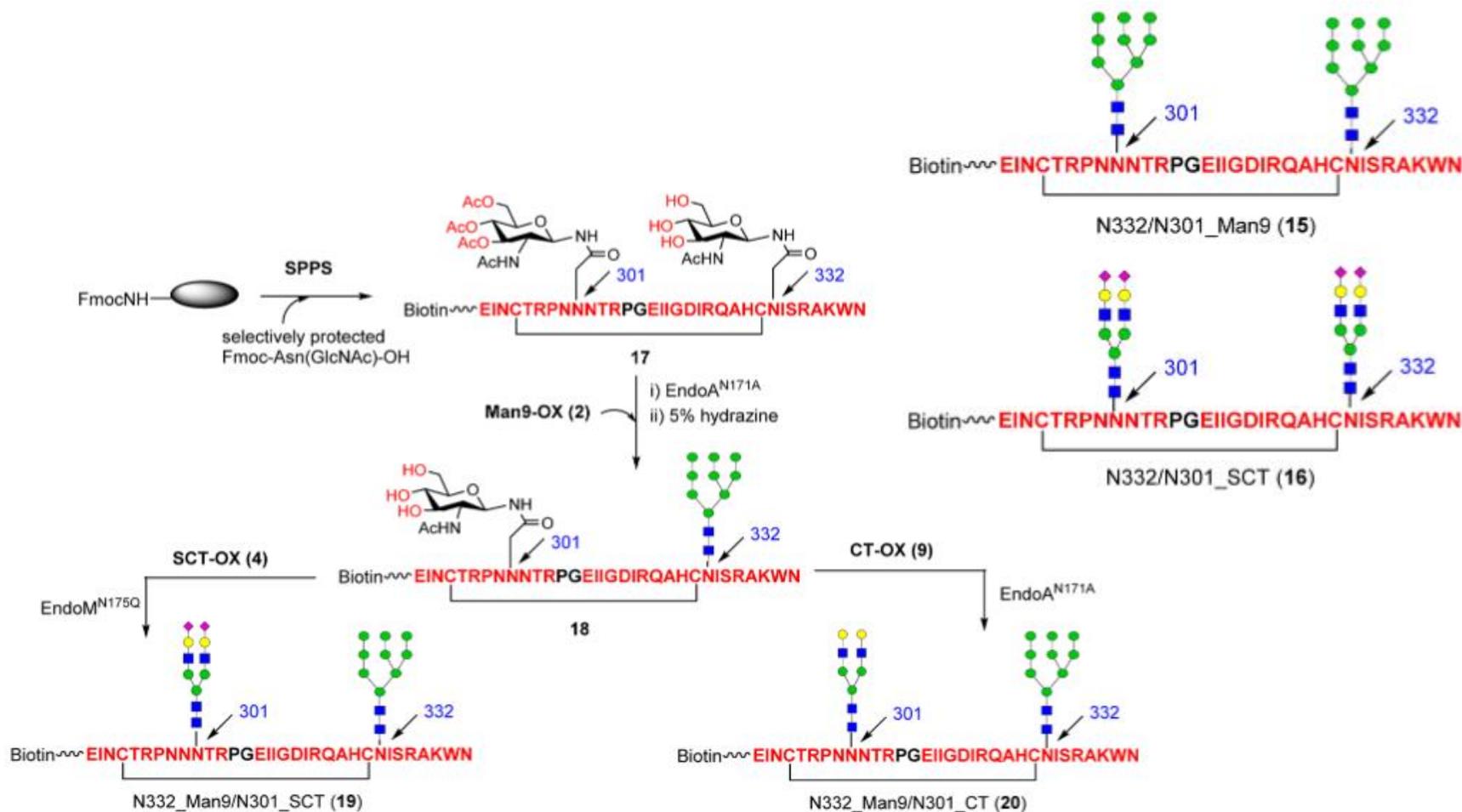
Retrosynthetic Study



Synthesized Peptide (1st Generation)

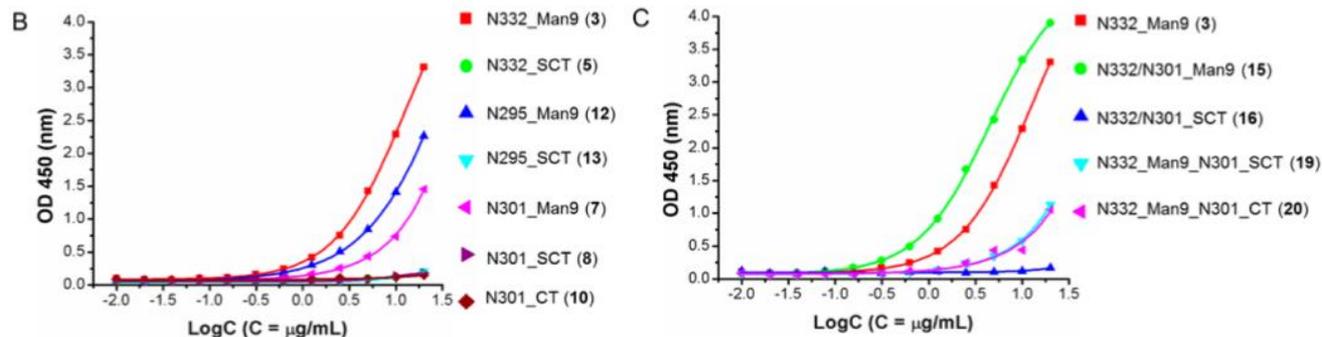


Synthesized Peptide (1st Generation)

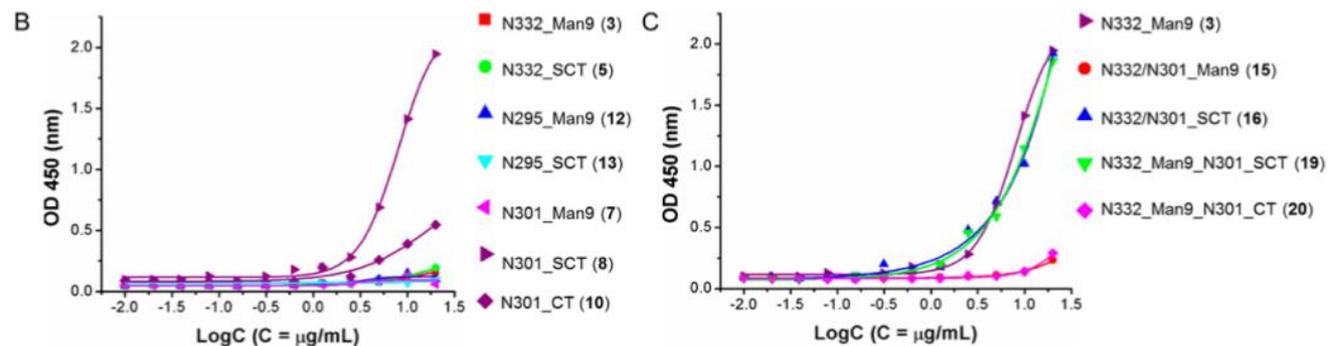


ELISA Study

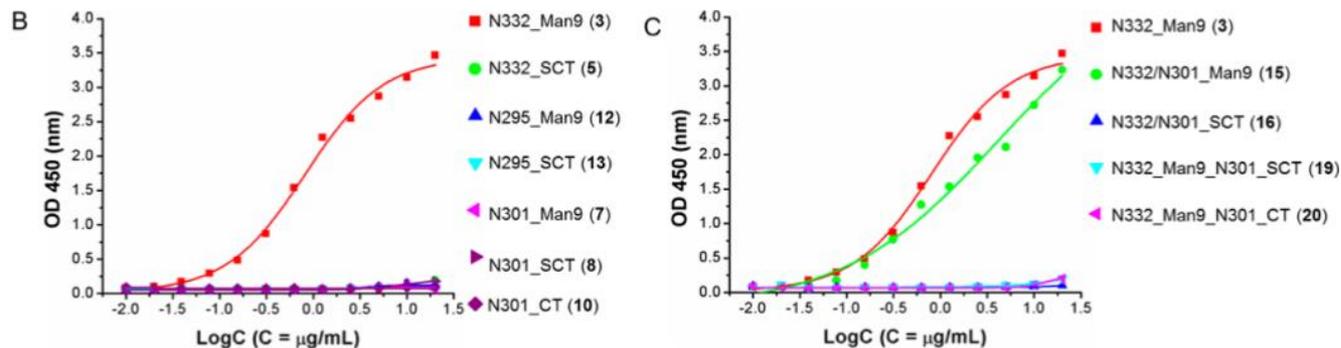
PGT128



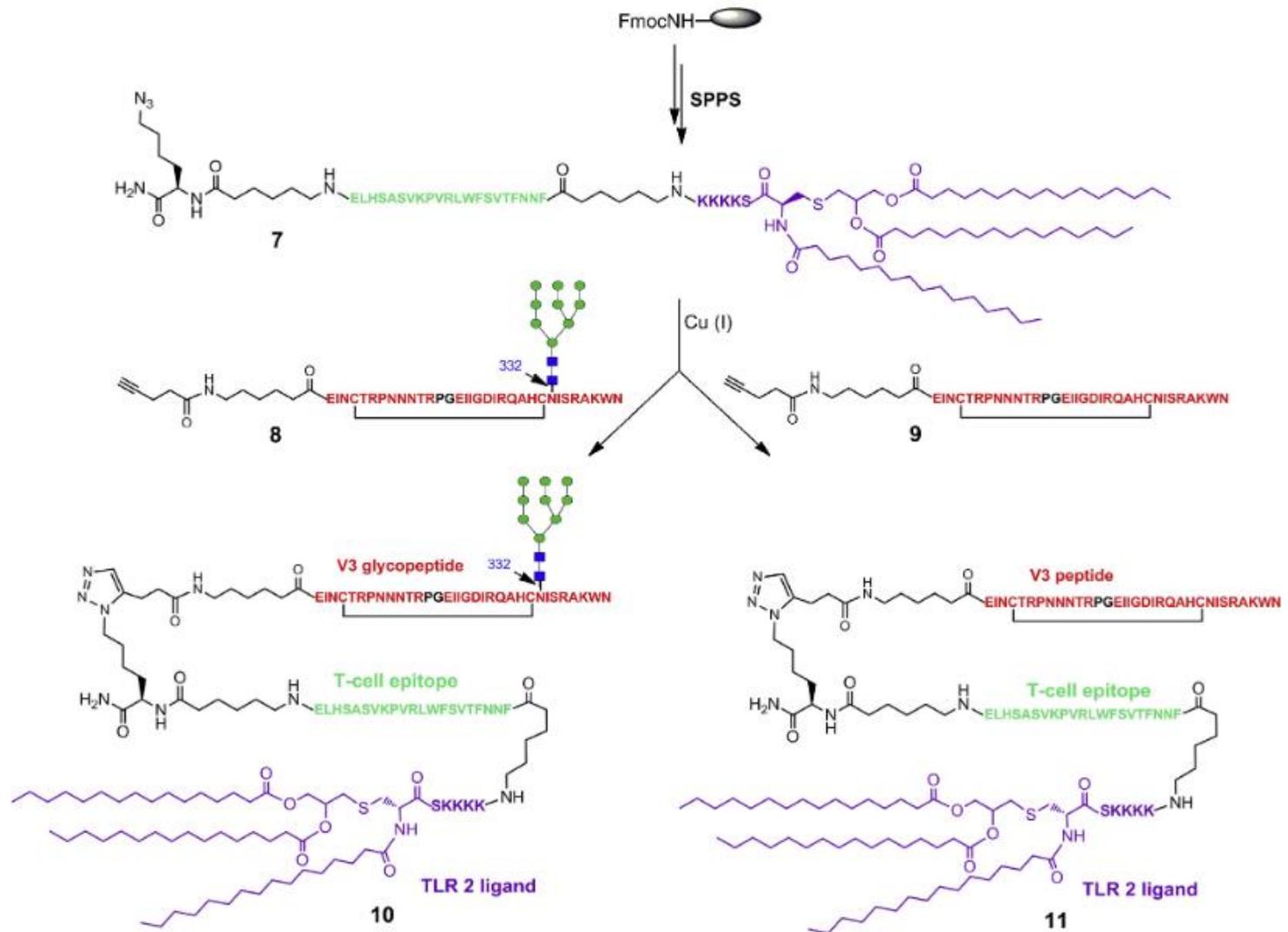
PGT121



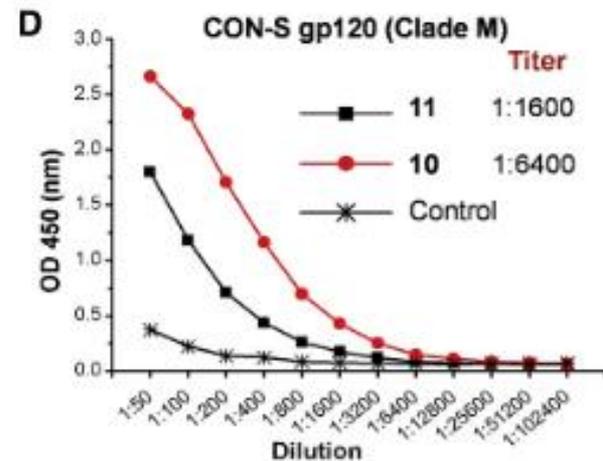
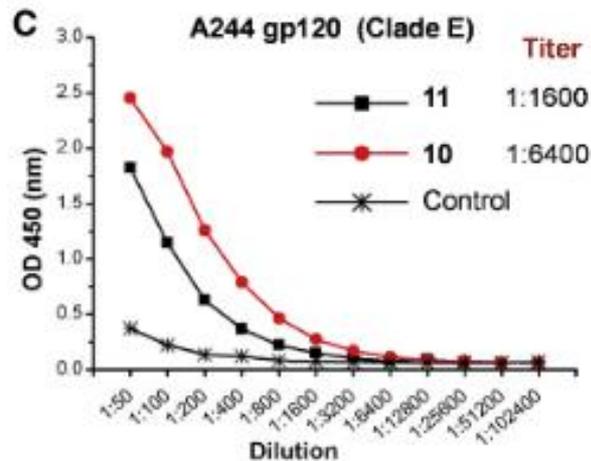
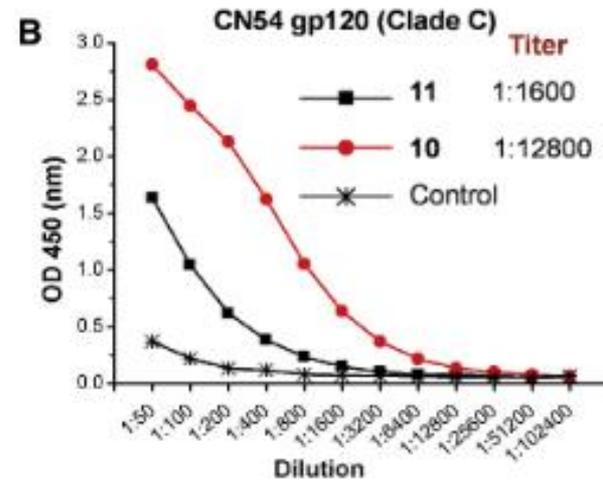
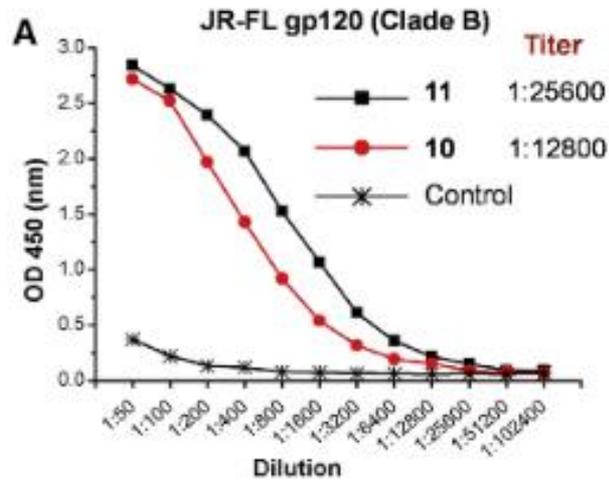
10-1074



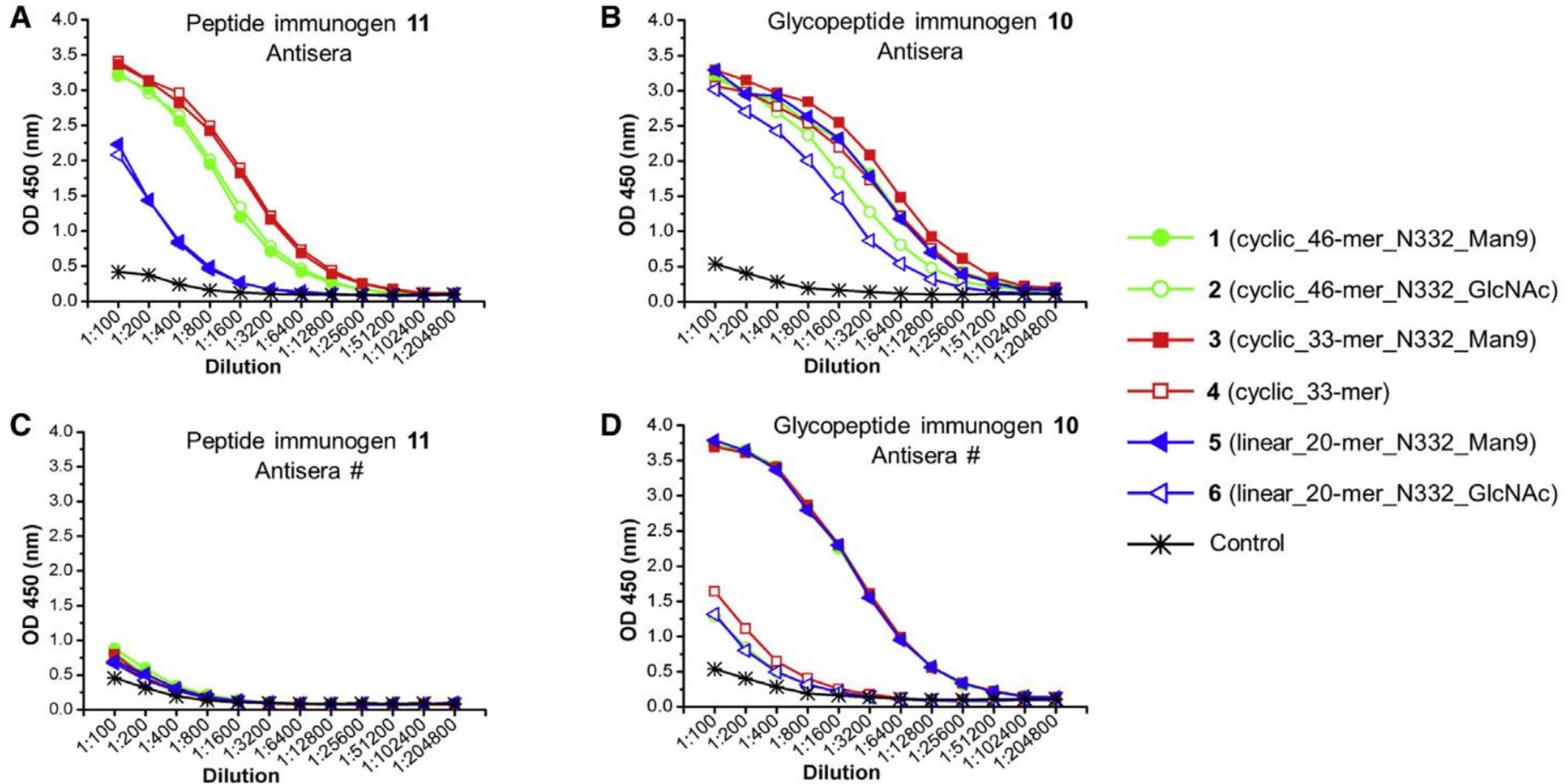
Synthesized Peptide (2nd Generation)



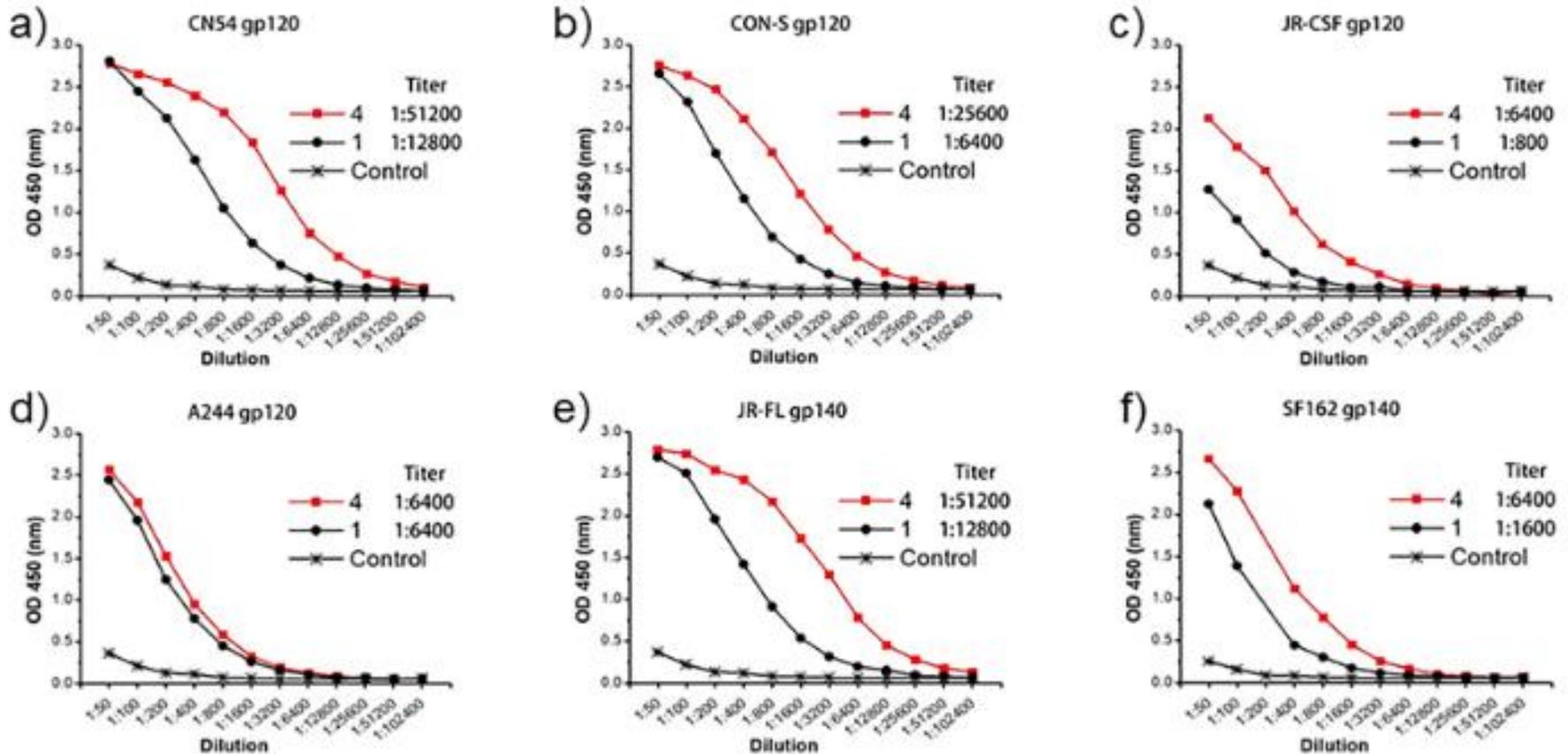
Activity of 2nd Generation Peptide Vaccine



Antisera Binding to Various V3 mimic

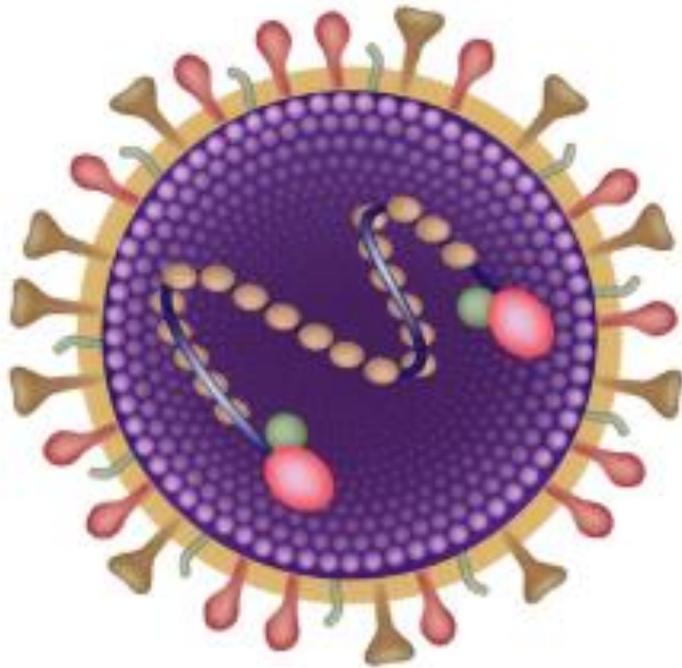


Activity of 3rd Generation Peptide Vaccine



Target: Respiratory Syncytial Virus (RSV)

Respiratory Syncytial Virus



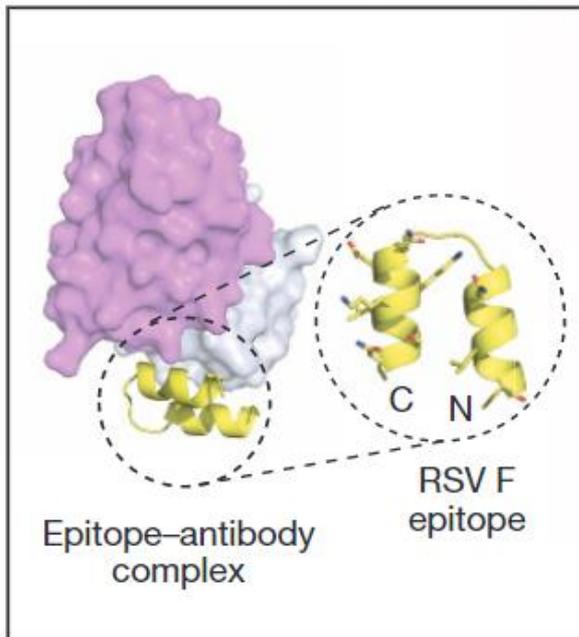
- Infection mainly in infants
- Symptoms include bronchiolitis and pneumonia.
- Cause of 6.7% of all deaths in children of ages 1 month to 1 year
- Neutralizing antibody Pali and Mota

Lancet, **2010**, 375, 1545.

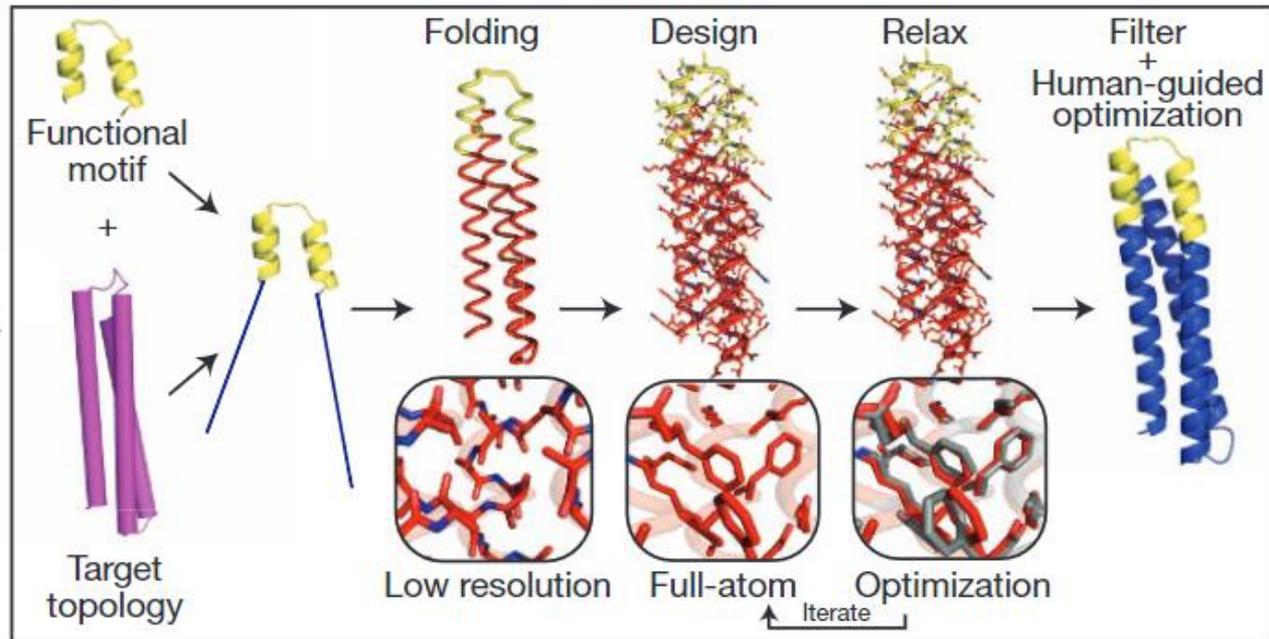
Nature, **2014**, 507, 201.

Computational Method

Neutralization epitope



Rosetta FFL

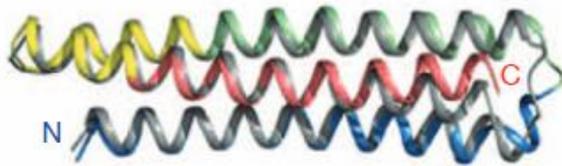


Fold From Loops (FFL) procedure

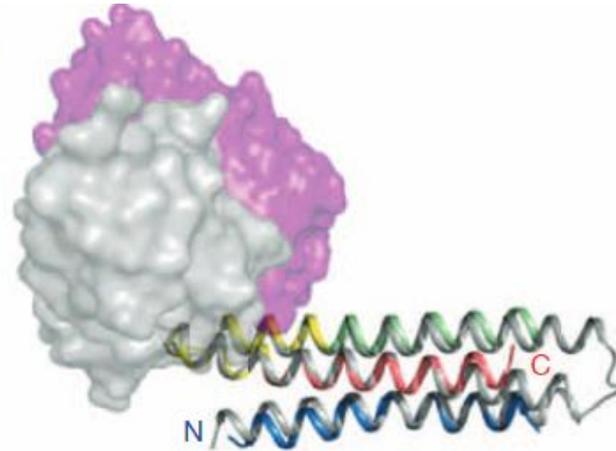
- (1) Selection of the functional motif
- (2) Folding to build diverse conformation
- (3) Sequence design and structural relaxation
- (4) Filtering and human guided optimization

Structural Characterization of FFL-001

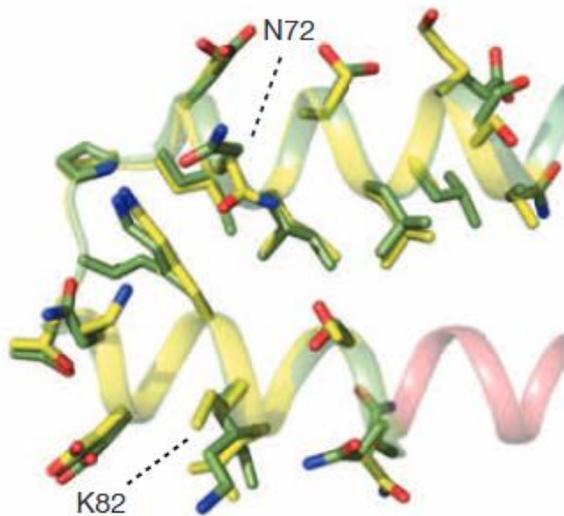
e



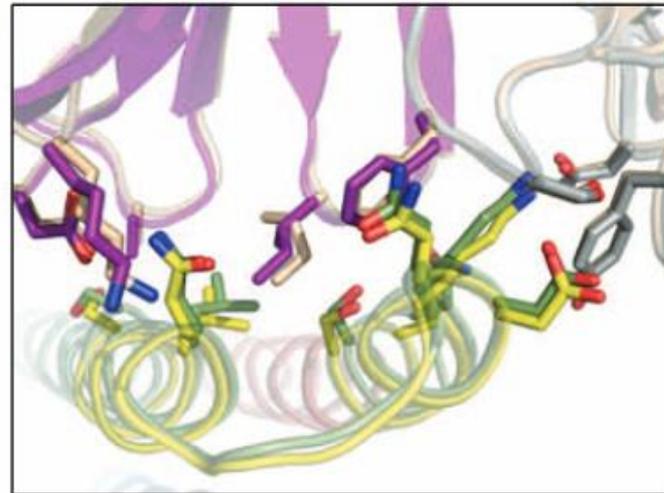
f



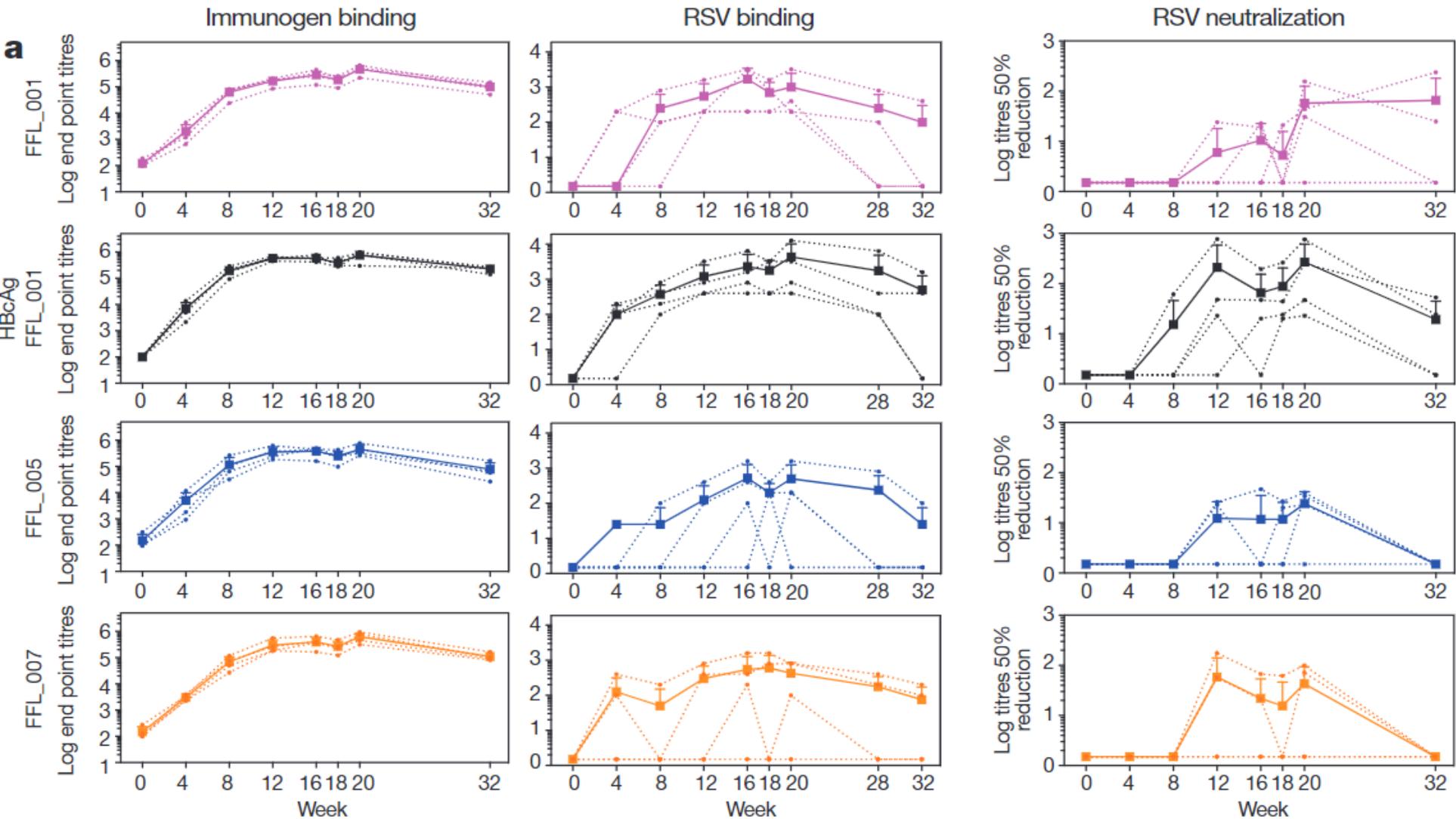
g



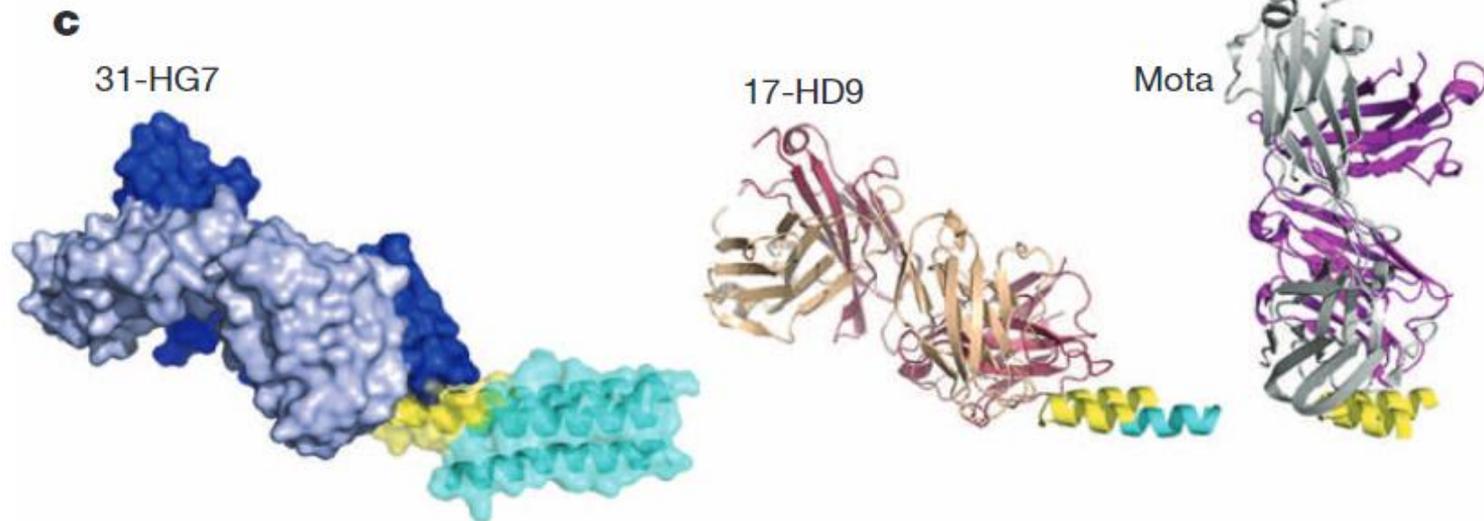
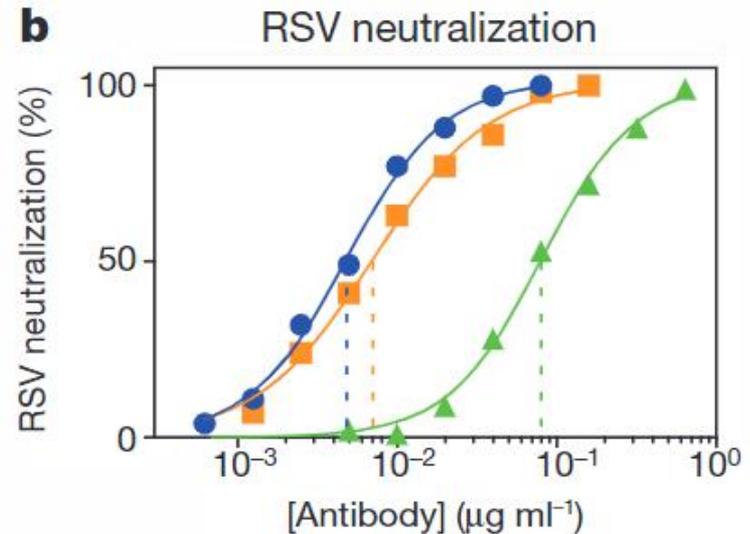
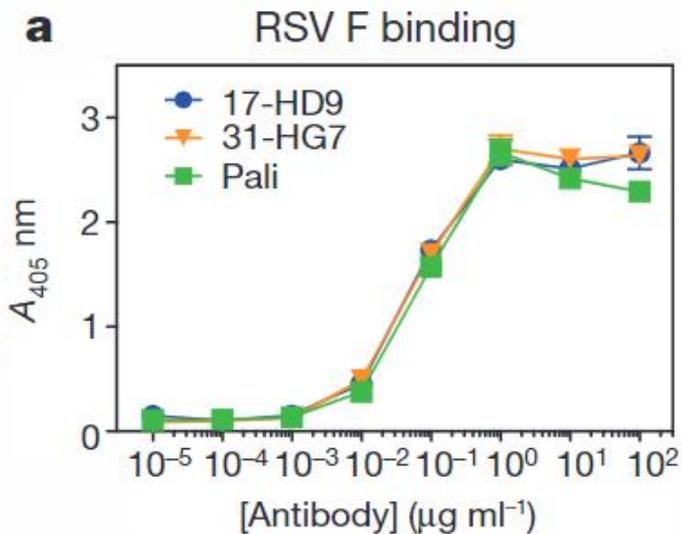
h



Serological Analysis



Analysis of Produced mAbs



Contents

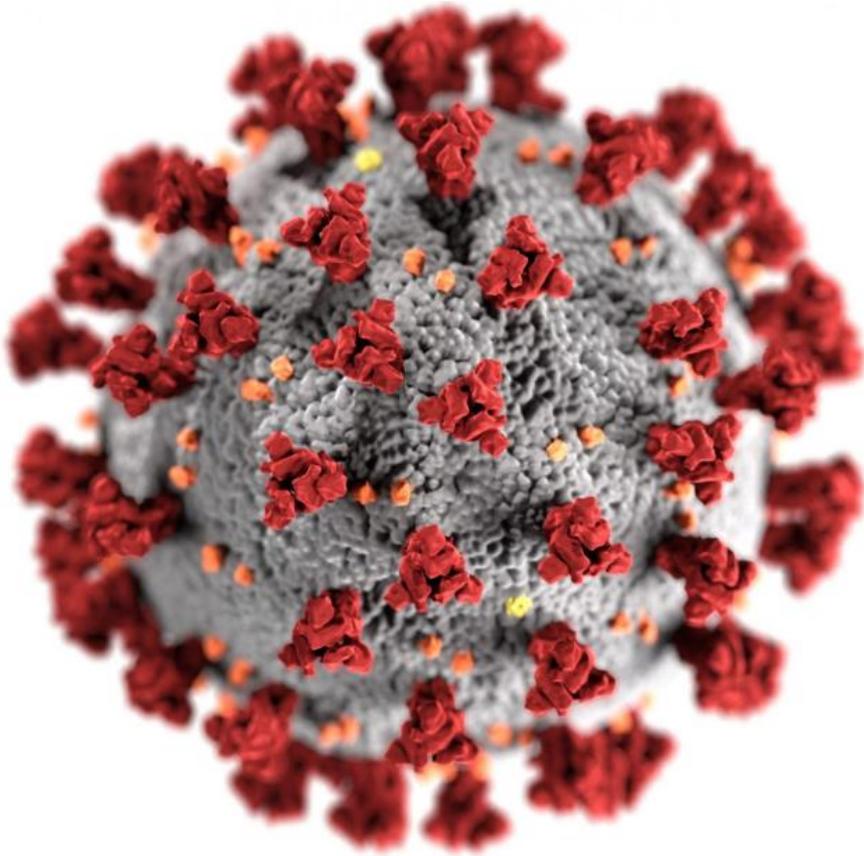
1. Introduction

2. Example of Peptide Vaccine

3. Peptide Vaccine for SARS-CoV-2

4. Summary

Target: SARS-CoV-2



- More than xx cases and yy deaths in the world (2020/5/10)
- S protein binds to human ACE2 receptor to cause infection.
- DNA, mRNA, inactivated virus vaccines are under development.

Latest Vaccine Development

Israel Claims 'Terrific Breakthrough' In COVID-19 Treatment! Isolates Key Antibody

The Defence Ministry of the country had earlier reported to an Israel newspaper Haaretz, about the similar kind of progress about the antibody in March.

The Logical Indian Crew

India | 5 May 2020 / Updated : 5 Hrs ago

Writer : [Devyani Madaik](#) | Editor : [Prateek Gautam](#) | Creatives : [Abhishek M](#)



Peptide Vaccine for SARS-CoV

Table 1. Amino acid sequences of the six synthetic peptides.^a

Peptide	Amino acid positions	Amino acid sequence	No. of amino acids	Molecular mass, Da	pI
S1	75–96	TFGNPVIKFDGIYFAATEKSN	22	2416.6	6.74
S2	229–251	TNFRILATFSPAQDIWGTSAAA	23	2409.5	6.51
S3	573–593	ISPCSFQGVSVITPGTNASSE	21	2010.1	3.25
S4	1120–1140	YDPLQPELDSFKEELDKYFKN	21	2618.8	4.10
S5	788–820	LPDPLKPTKRSFIEDLLFNKVTLDAGFMKQYG	33	3754.2	9.53
S6	1002–1030	ASANLAATKMSECVLGQSKRVDFCGKGYH	29	3072.4	9.05

^a Provisional patent application number 60/487,396 (filing date July 14, 2003).

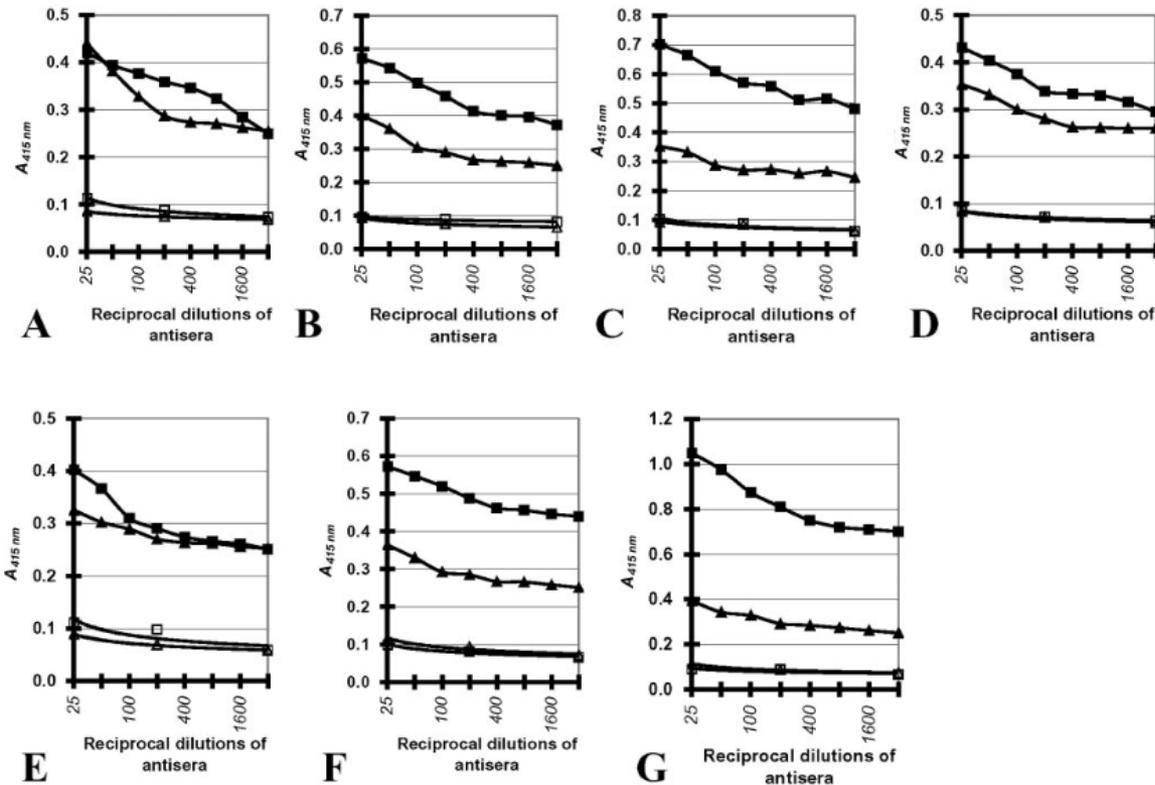


Table 2. Results of immunofluorescent confocal microscopy.

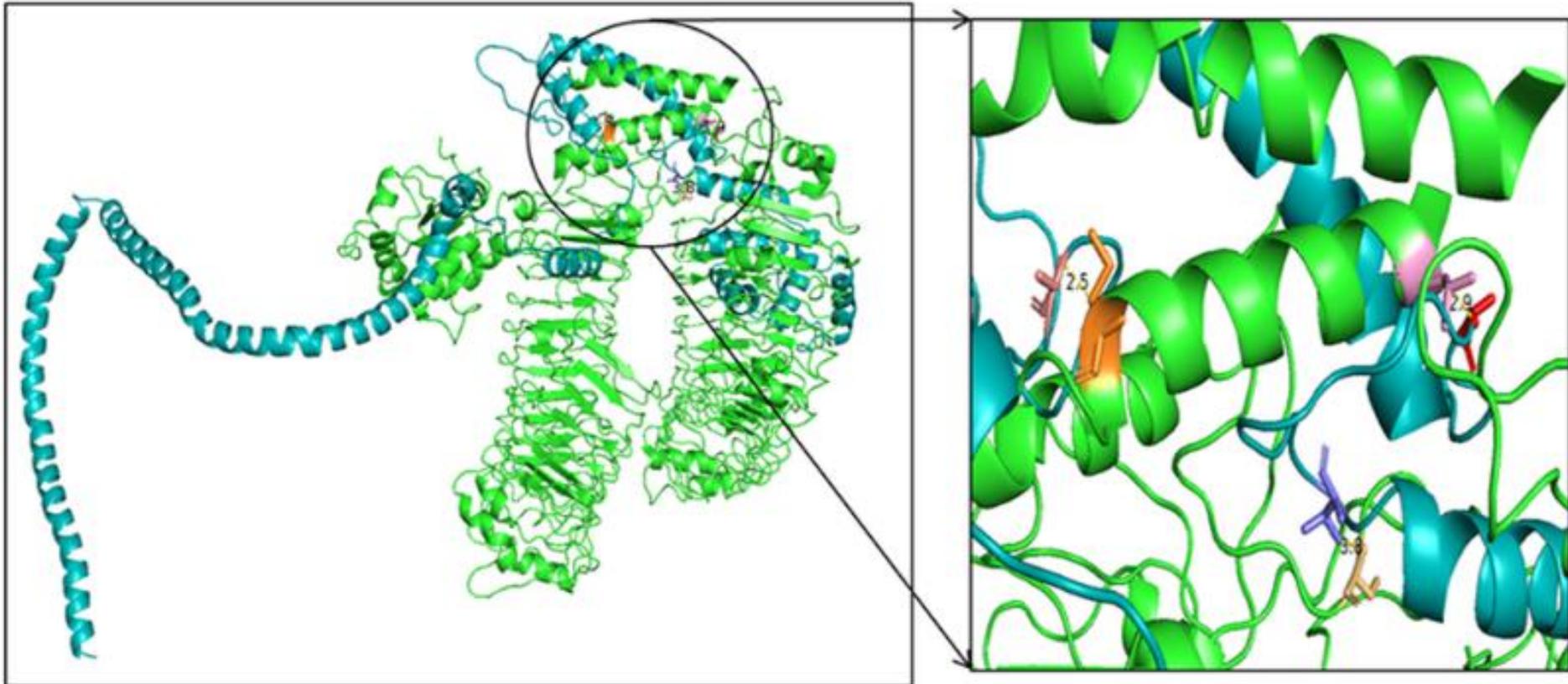
Antigen used for immunization	Immunization in rabbits		Immunization in monkeys	
	Antiserum	Result of confocal microscopy	Antiserum	Result of confocal microscopy
S1 peptide	R_S1	–	M_S1	–
S1-KLH conjugate	R_S1_KLH	–	M_S1_KLH	–
S2 peptide	R_S2	–	M_S2	–
S2-KLH conjugate	R_S2_KLH	+	M_S2_KLH	–
S3 peptide	R_S3	–	M_S3	+
S3-KLH conjugate	R_S3_KLH	–	M_S3_KLH	–
S4 peptide	R_S4	–	M_S4	–
S4-KLH conjugate	R_S4_KLH	–	M_S4_KLH	–
S5 peptide	R_S5	+	M_S5	–
S5-KLH conjugate	R_S5_KLH	+	M_S5_KLH	–
S6 peptide	R_S6	–	M_S6	+
S6-KLH conjugate	R_S6_KLH	+	M_S6_KLH	+
Mix peptide ^a	R_MIX	–	M_MIX	+
Mix-KLH conjugate ^a	R_MIX_KLH	–	M_MIX_KLH	+

^a Mix peptide and Mix-KLH conjugate were prepared by mixing the six synthetic peptides (S1, S2, S3, S4, S5, and S6) in equal amounts.

Epitope Conservation among Coronaviruses

Bt-CoV	K	L	H	Q	L	T	Y	L	L									
MERS-CoV	K	L	Q	P	L	T	F	L	L									
SARS-CoV	Y	L	K	P	T	T	F	M	L									
2019_nCoV	Y	L	Q	P	R	T	F	L	L									
Bt-CoV	G	F	V	V	R	I	G	A	A									
MERS-CoV	G	F	V	V	R	I	G	A	A									
SARS-CoV	G	I	Y	F	A	A	T	E	K									
2019_nCoV	G	V	Y	F	A	S	T	E	K									
Bt-CoV	A	V	N	A	N	A	Q	A	L									
MERS-CoV	A	V	N	N	N	A	Q	A	L									
SARS-CoV	V	V	N	Q	N	A	Q	A	L									
2019_nCoV	V	V	N	Q	N	A	Q	A	L									
Bt-CoV	W	A	A	F	Y	V	Y	K	L									
MERS-CoV	W	A	A	F	Y	V	Y	K	L									
SARS-CoV	W	G	T	S	A	A	A	Y	F									
2019_nCoV	W	T	A	G	A	A	A	Y	Y									
Bt-CoV	C	L	E	S	Q	V	D	A	A	A	F	S	K	L	M	W		
MERS-CoV	C	I	E	V	D	I	Q	Q	T	F	F	D	K	T	W	P		
SARS-CoV	C	T	T	F	D	D	V	Q	A	P	N	Y	T	Q	H	T		
2019_nCoV	C	V	N	L	T	T	R	T	Q	L	P	P	A	Y	T	N		
Bt-CoV	D	L	G	S	Q	Y	L	Y	S	V	S	H	A	V	G	H		
MERS-CoV	D	H	G	D	M	Y	V	Y	S	A	G	H	A	T	G	T		
SARS-CoV	N	V	T	G	F	H	T	I	N	H	T	F	G	N	P	V		
2019_nCoV	N	V	T	W	F	H	A	I	H	V	S	G	T	N	G	T		
Bt-CoV	A	V	D	E	F	S	C	N	G	I	S	P	D	S	I	A	R	G
MERS-CoV	S	V	N	D	F	T	C	S	Q	I	S	P	A	A	I	A	S	N
SARS-CoV	F	F	S	T	F	K	C	Y	G	V	S	A	T	K	L	N	D	L
2019_nCoV	S	F	S	T	F	K	C	Y	G	V	S	P	T	K	L	N	D	L

Computational Peptide Vaccine Design



Contents

1. Introduction

2. Example of Peptide Vaccine

3. Peptide Vaccine for SARS-CoV-2

4. Summary

Summary

- Vaccines rescue millions of people every year.
- Peptide vaccines are less allergenic.
- LAH of HA2 is effective as immunogenic epitope. (influenza virus)
- 3 component peptide induces antibody against gp120. (HIV)
- Computationally designed peptide induce better neutralizing antibodies than existing antibody drug. (RSV)
- Vaccine study of SARS-CoV may help develop vaccine against SARS-CoV-2.