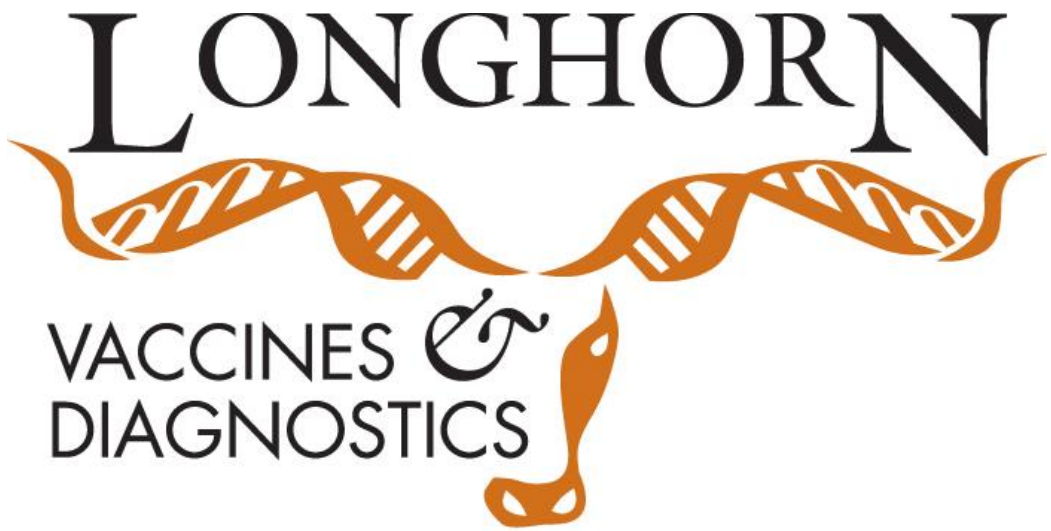

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Composite Peptide Conjugate Vaccines Induced Broadly Reactive Serum and Monoclonal Antibodies to Influenza

PRESENTED BY CLARA J. SEI

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TUESDAY, NOVEMBER 13TH, 2018

INTERNATIONAL SOCIETY FOR INFLUENZA AND OTHER RESPIRATORY VIRUS DISEASES

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Background

- Emergence of influenza variants that escape vaccines and are resistant to antiviral therapeutics.
- Seasonal and pandemic influenza management challenges.
- Small composite peptide vaccines were produced utilizing conserved Hemagglutinin (HA), Neuraminidase (NA), and Matrix ectodomain (M2e) influenza proteins.
- Our preliminary studies evaluate both vaccine and therapeutic approaches against Influenza viruses.

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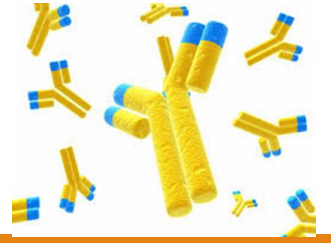
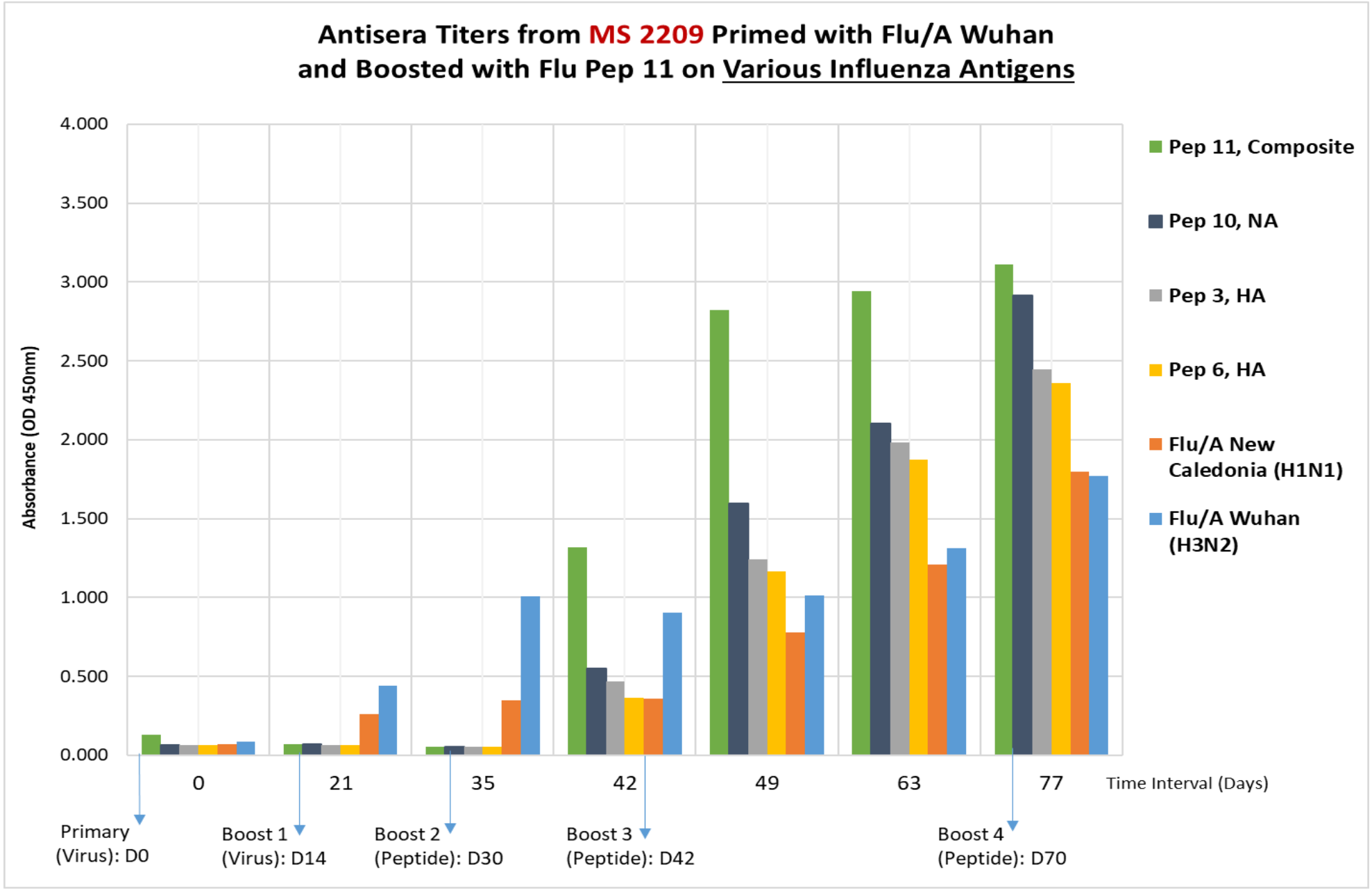
Methods

- Mice were immunized with the composite peptide conjugate vaccines and their humoral responses evaluated in the Antisera ELISA.
- Monoclonal antibodies (mAbs) were developed from mouse spleen fusions.
- Ability of mAbs to bind across a diverse set of influenza strains was evaluated in the Binding ELISA.
- Presence of cross-neutralizing antibodies against H3N2 and H1N1 was evaluated in the Microneutralization assay.

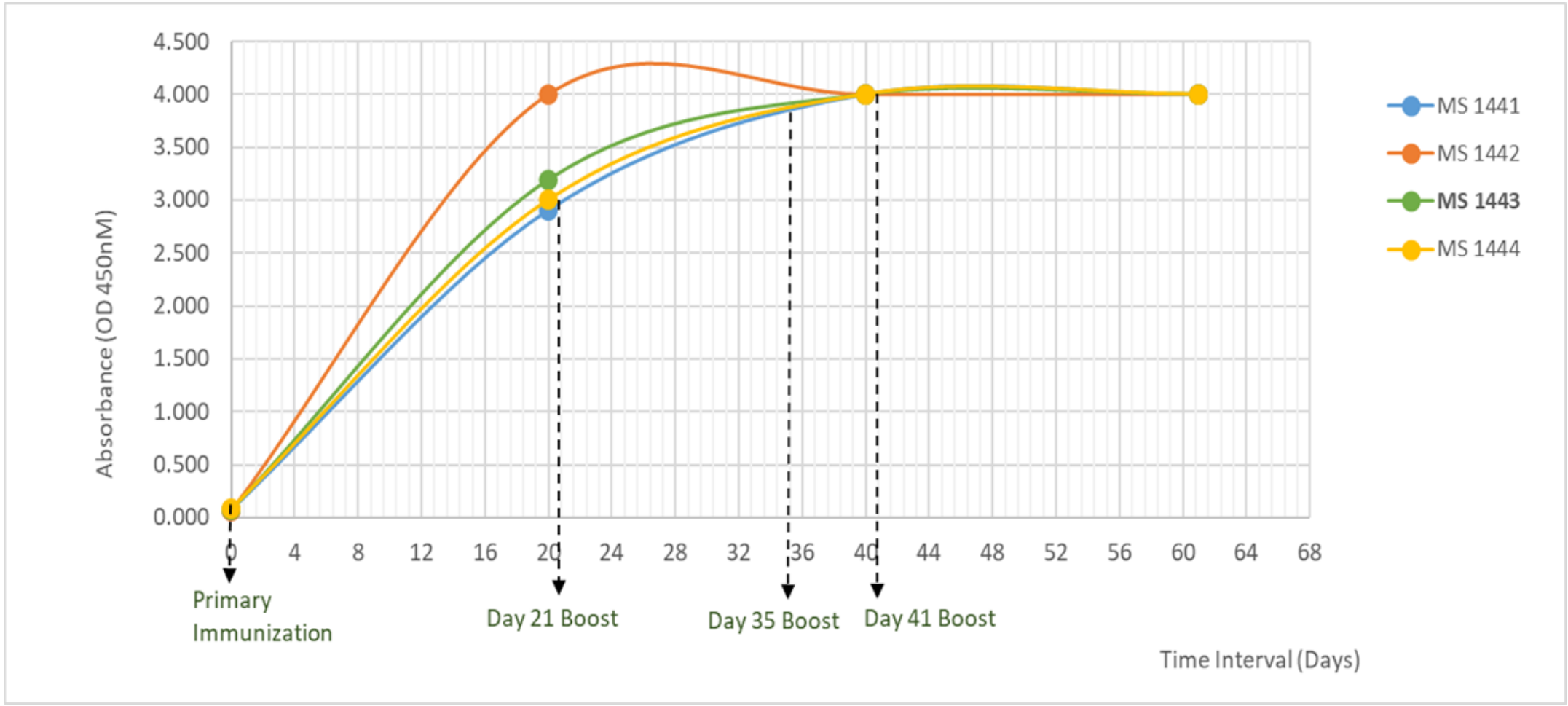


Peptide Conjugate Vaccines

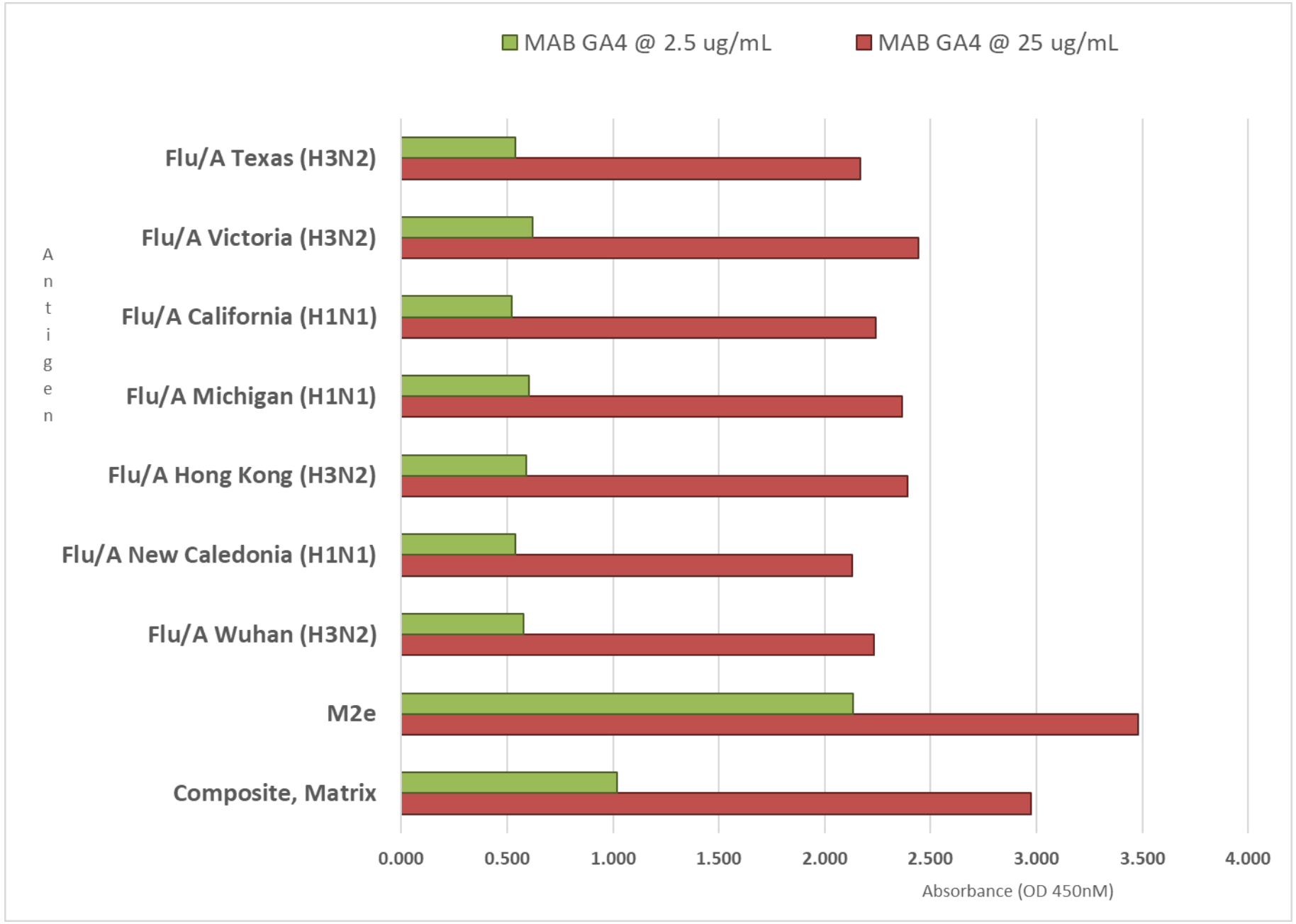
PEPTIDE	SEQUENCE	CONJUGATE	ADJUVANT	DOSE & REGIMEN	MODE OF ADMIN	PEPTIDE SOURCE PROTEIN	MOUSE, MAB & ISOTYPE
Pep 11 composite	GNLFIAPWGVIHHP HYEECSCY	CRM	TITERMAX GOLD	H3N2, 10^6 Pep: 20 ug D0, 14, 30, 42, 70	H3N2: IM Pep: SQ	Hemagglutinin Neuraminidase	MS 2209 Many MABs under development
Pep 5906 composite	SLLTEVETPIRNENE WGLLTEVETPIRQYI KANSKFIGITE	CRM	FREUNDS	50 ug D0, 21, 35, 41	SQ	Matrix Ectodomain (M2e)	MS 1443 MAB GA4 (IgG1)


Antisera Titers from MS 2209 Primed with Flu/A Wuhan
and Boosted with Flu Pep 11 on Various Influenza Antigens
Absorbance (OD 450nm)
4.000
3.500
3.000
2.500
2.000
1.500
1.000
0.500
0.000
0
21
35
42
49
63
77
Time Interval (Days)
Pep 11, Composite
Pep 10, NA
Pep 3, HA
Pep 6, HA
Flu/A New Caledonia (H1N1)
Flu/A Wuhan (H3N2)
Primary (Virus): D0
Boost 1 (Virus): D14
Boost 2 (Peptide): D30
Boost 3 (Peptide): D42
Boost 4 (Peptide): D70

MS 1443 Antisera Titers on Matrix (Peptide 5906)



Purified MAB GA4 Binding Activity



Cross-Neutralizing Antibodies

- MS 1441-1444 pooled sera from D63 bleed.
- MS 1443 MAB GA4

- Presence of cross-neutralizing antibodies in Serum and MAB produced from the composite matrix conjugate vaccine.

	Neutralizing Titers	
	M1441-1444 Pooled Serum	MS 1443 MAB GA4 (ug/mL)
Flu/A Michigan, H1N1	81920	11
Flu/A Texas, H3N2	40960	22

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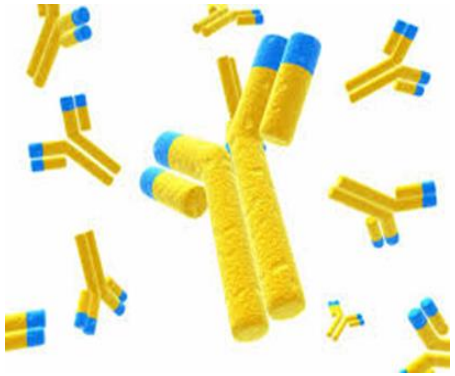
Conclusions

- Composite peptide vaccines were highly immunogenic with strong humoral responses.
- Broadly reactive serum antibodies against peptide and live influenza virus were detected.
- mAbs were identified that bind to target epitopes on live influenza.
- Presence of cross-neutralizing antibodies against H3N2 and H1N1.



- **Current and future studies…**
  - ADCC activity of anti-influenza MAB GA4.
  - Anti-influenza MABs (against HA & NA) are being characterized, *in vitro*.
  - *In vivo* protection studies are being designed.

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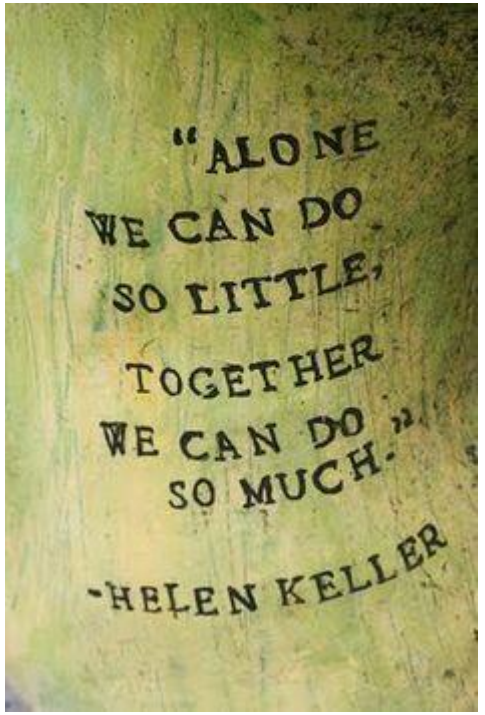

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