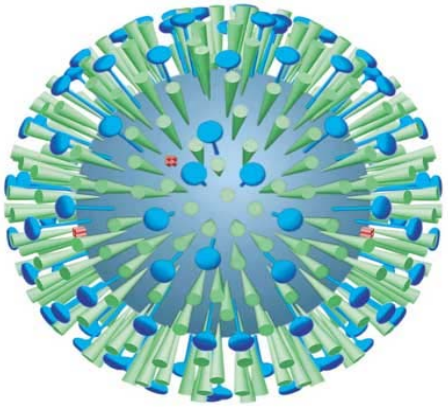
Nanoparticulate Vaccine Design: The VesiVax® System



Gary Fujii, Ph.D.
President and CEO
Molecular Express, Inc.

May 16, 2006
Orlando, Florida

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Influenza

- ***Each year up to 20% of the world's population contracts influenza***
- ***250,000 to 500,000 people die annually from influenza-associated complications***
- ***Pacific Bridge Life Sciences estimates the associated cost of influenza at $5.2B in 2004***
- ***"Avian influenza" mortality rates greater than 50%***

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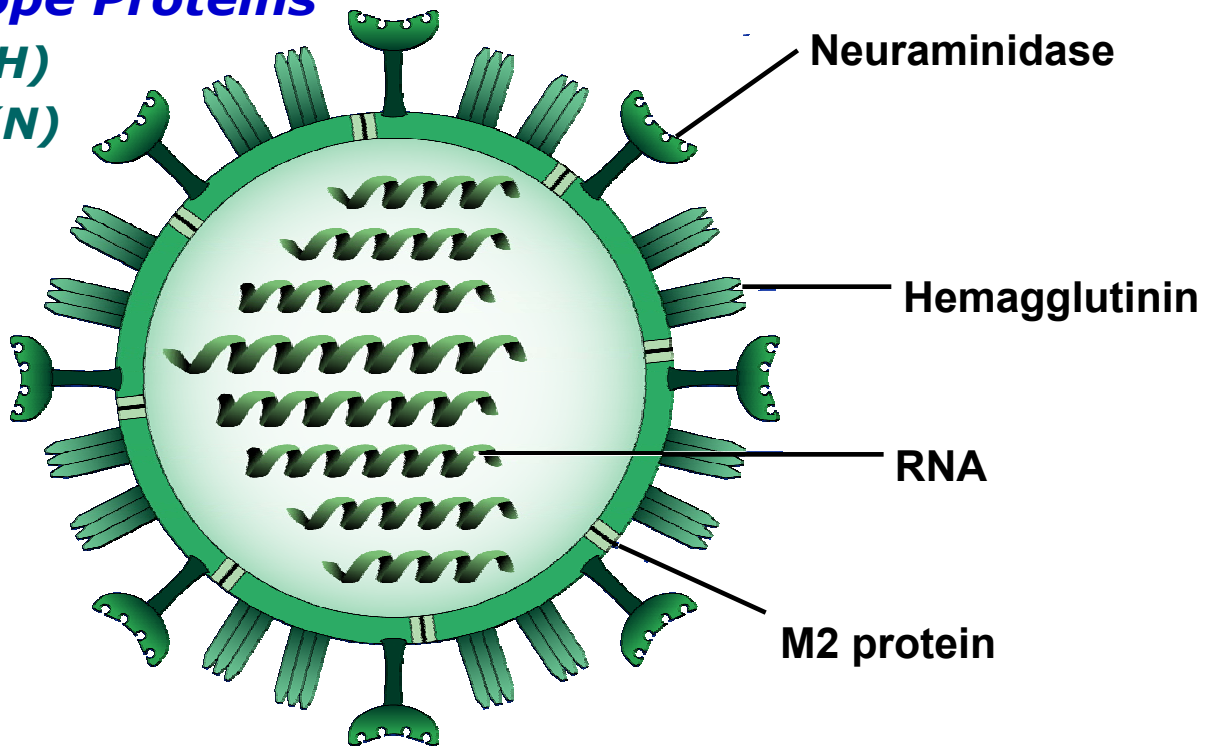
Influenza Virus Type A

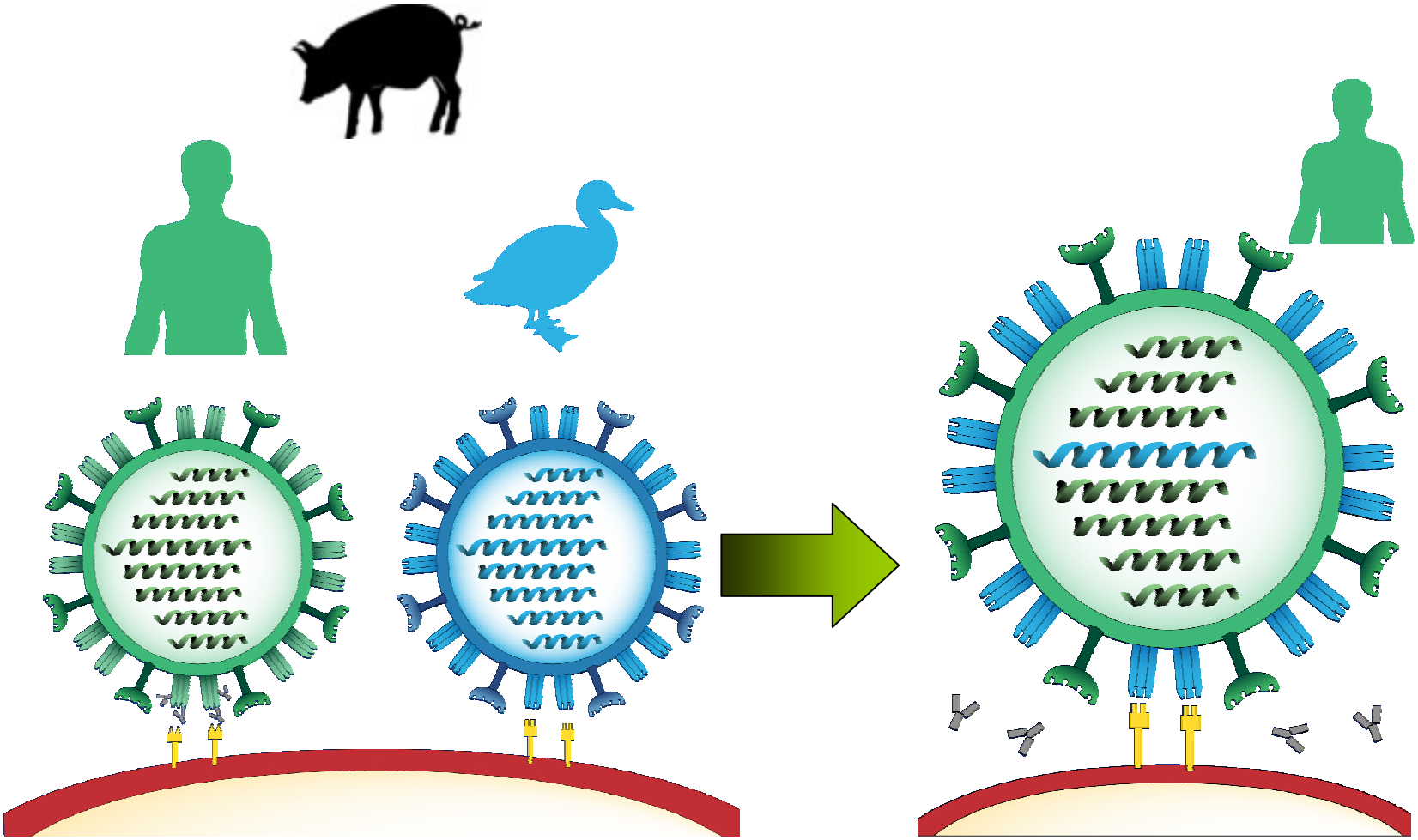
- *Enveloped RNA Virus*
- *Genome encodes 10 proteins*
- *Major Viral Envelope Proteins*
  - *Hemagglutinin (H)*
  - *Neuraminidase (N)*



Survival Strategies Employed by the Influenza Virus

- ***Antigenic Drift***
  - ***High mutation rates***
  - ***RNA viruses lack proofreading capabilities***
    - ***Often one mutation per genome copy***
    - ***Evolutionary advantage***
    - ***Active response to changes in environment and drug regimen***
- ***Antigenic Shift***
  - ***Shuffling of viral genes gives rise to "reassortants"***
  - ***Recombination of H and N creates new strains***
- ***Infective for multiple hosts***
  - ***Humans, pigs, birds, horses, dogs, mice***
- ***Hardy***
  - ***Able to survive and retain virulence for up to 48 hours on hard non-porous surfaces***

Antigenic Shift



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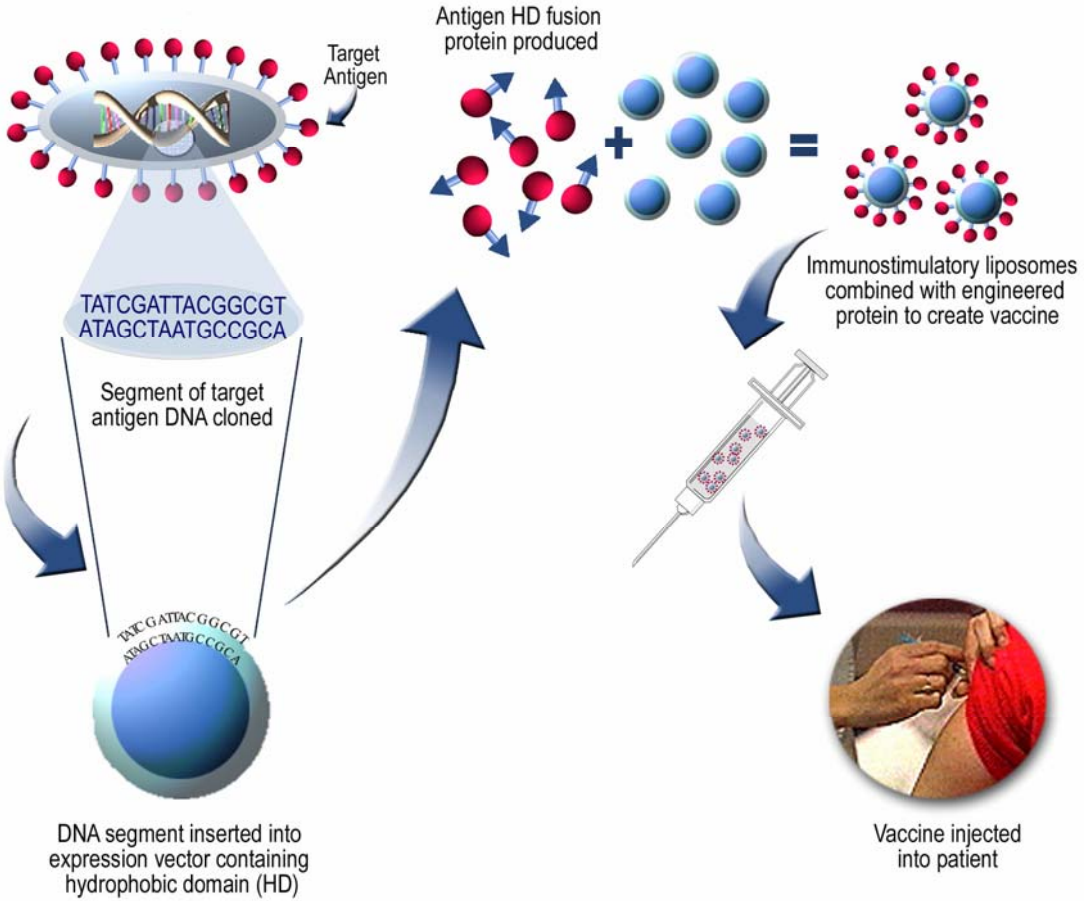
Influenza Vaccines

Time-intensive production process

- Generates inefficiencies that gives the virus an advantage
- Specific strains and virulence must be forecasted and produced well in advance of each flu season
- There is no feedback loop in this process, when the forecasts are inaccurate, supply chain is already committed, and course corrections can not be made
- Because the influenza virus changes constantly, clinical evaluation of new vaccines is impractical

The VesiVax® System

Designed to facilitate rapid vaccine development -



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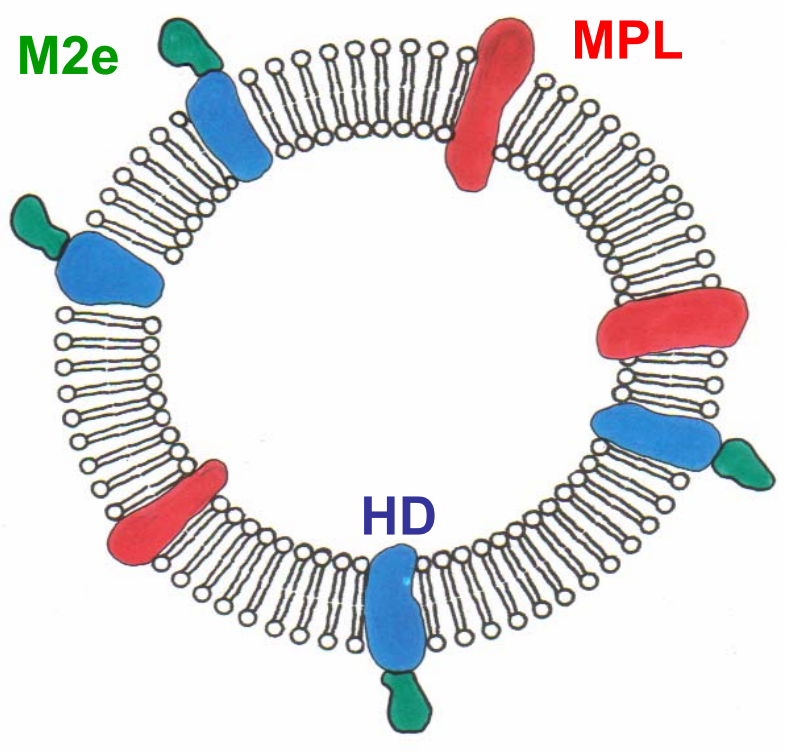
VesiVax® Influenza Vaccine

VesiVax® influenza vaccine targets the highly conserved M2 ectodomain segment (M2e)



HD = Hydrophobic domain

M2e = Antigen (~100/Liposome)

MPL = Adjuvant (~2500/Liposome)

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VesiVax® Influenza Vaccine

Vaccine Design

Influenza type A M2e sequences

Subtype	M2eA Sequence	Year
H1N1	MSLLTEVETPTRNEWGCRCNDSSD	1918 – "Spanish"
H1N1	MSLLTEVETPIRNEWGCRCNGSSD	1934 – PR/8
H2N2	MSLLTEVETPIRNEWGCRCNDSSD	1957 – "Asian"
H3N2	MSLLTEVETPIRNEWGCRCNDSSD	1968 – "Hong Kong"
H5N1	MSLLTEVETLTRNGWECKCRDSSD	1997 – "Avian"
H9N2	MSLLTEVETPTRNGWECKCNDSSD	1999 – "Avian"
H5N1	MSLLTEVETPTRNEWECRCSDSSD	2004 – "Avian"
H6N2	MSLLTEVETPIRNEWGCRCNDSSD	X-88

H5N1- First evidence of influenza virus transmitted from birds to humans. It is important to note that the majority of Influenza type A strains have high sequence homology for M2e. The conserved nature of M2e allows for the potential to create a vaccine that is effective against all strains.

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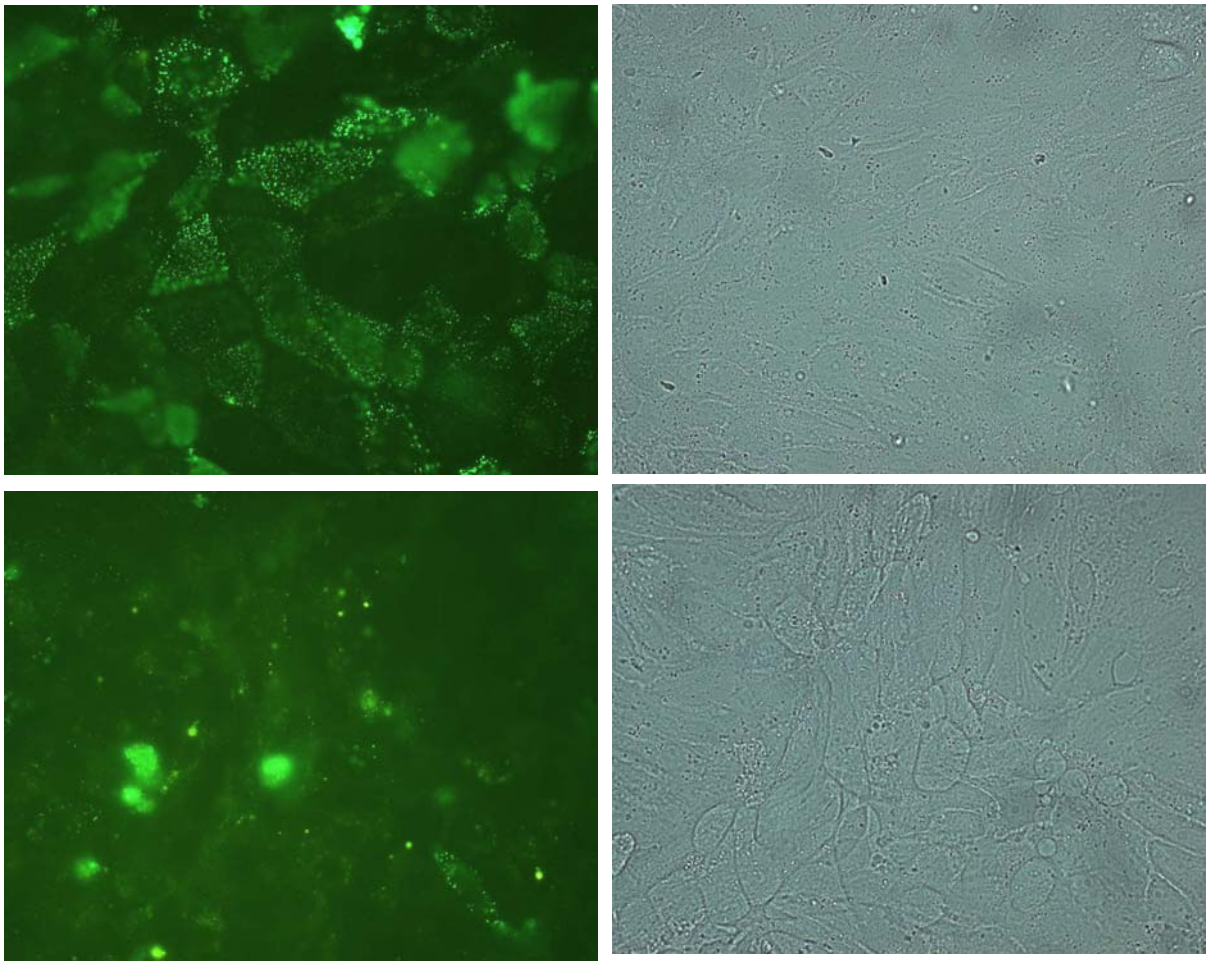
VesiVax® Influenza Vaccine

Virally Infected Cells Display M2e



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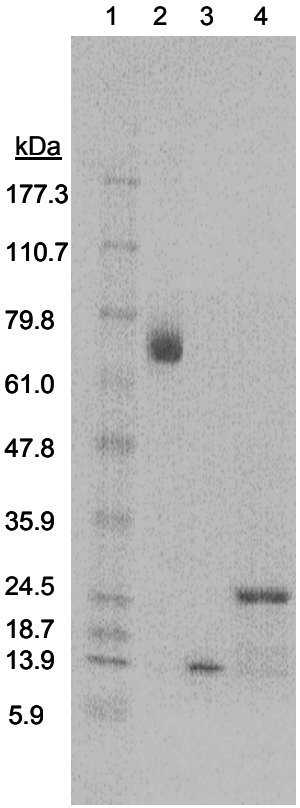
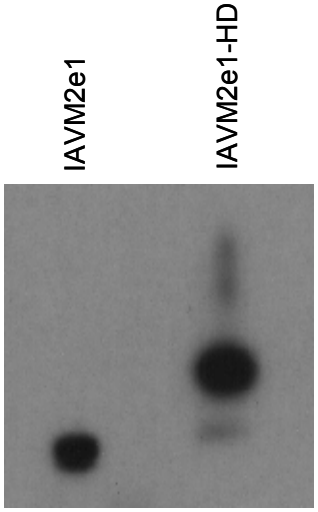
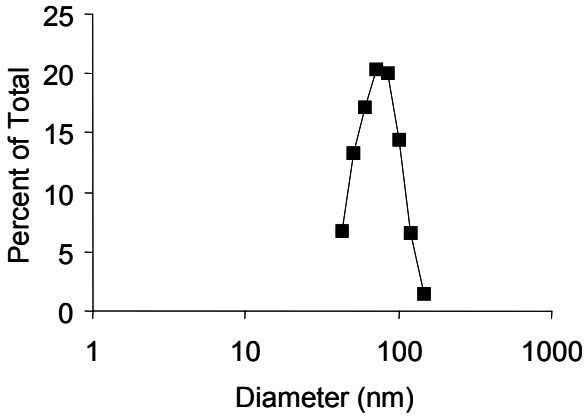
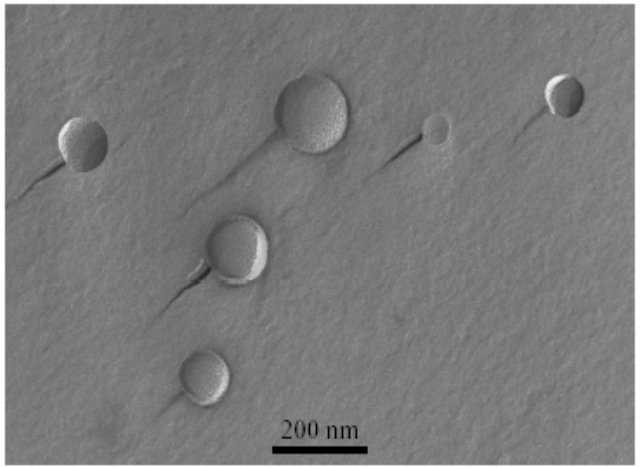
Preparation of L-M2e-HD









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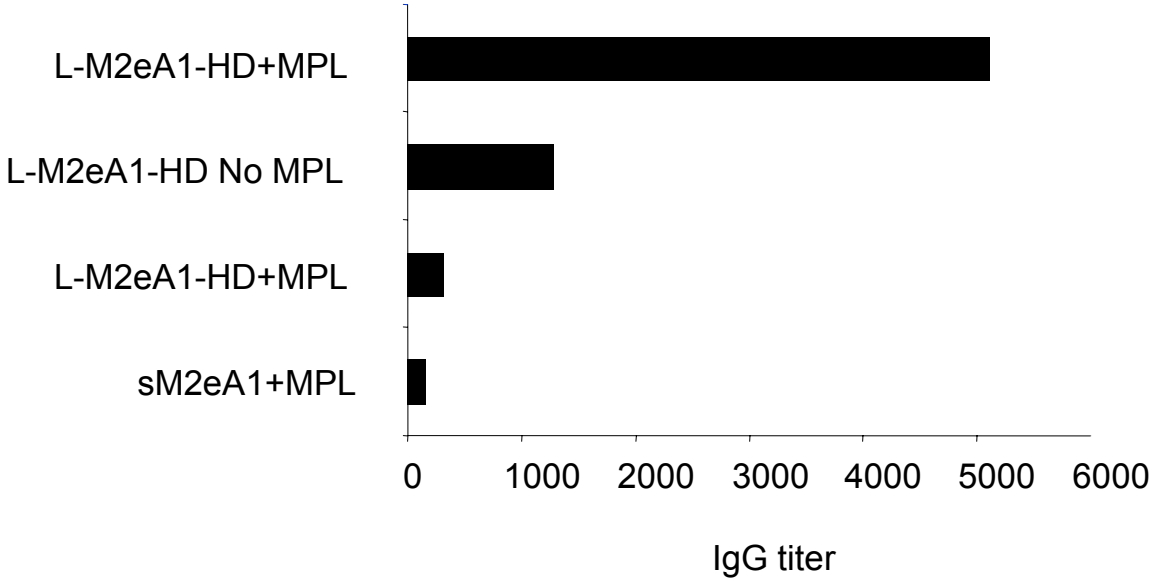
VesiVax® Influenza Vaccine

Preliminary Formulation Screen



BALB/c mice (n=5)
Immunized twice (SubQ/IN)

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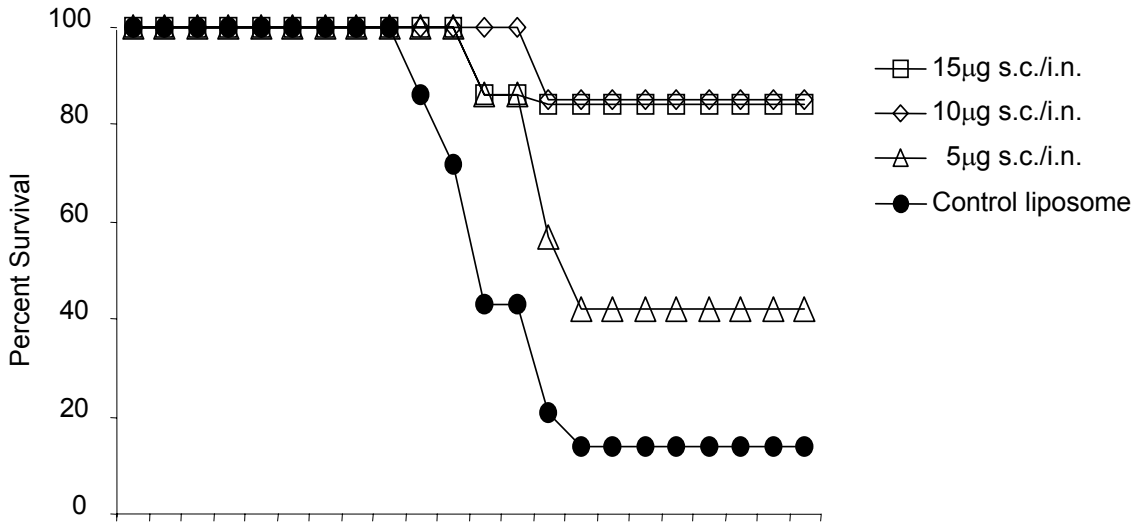
Dose Ranging Study



BALB/c mice (n=7)
Immunized twice (SubQ/IN)
Challenged with 10X LD50

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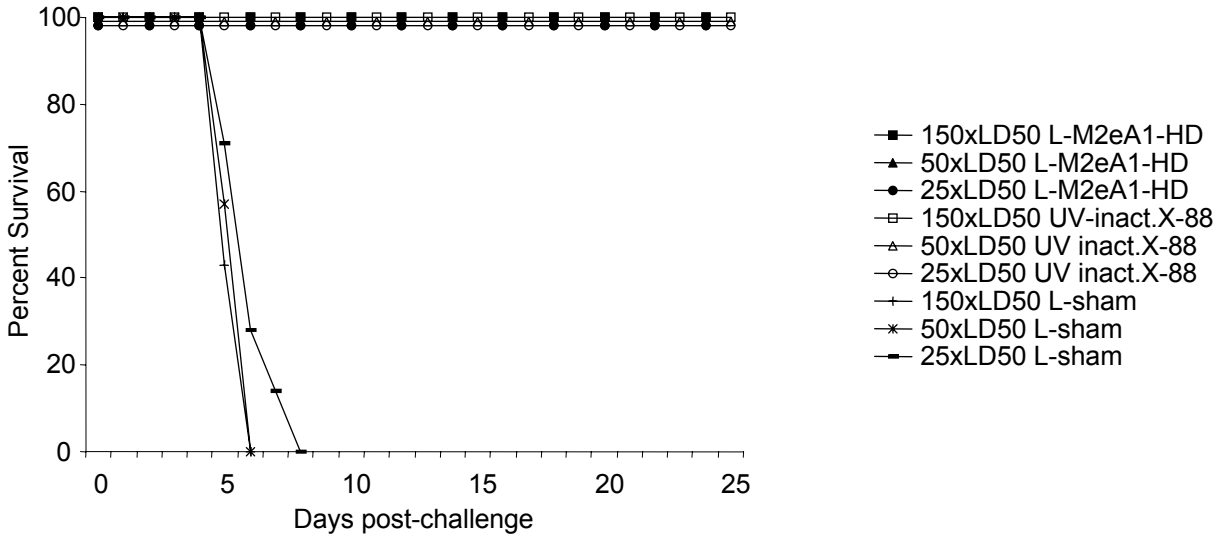
VesiVax® Influenza Vaccine

Maximal Viral Challenge



BALB/c mice (n=7)
Immunized twice (SubQ/IN)
Challenged with X-88

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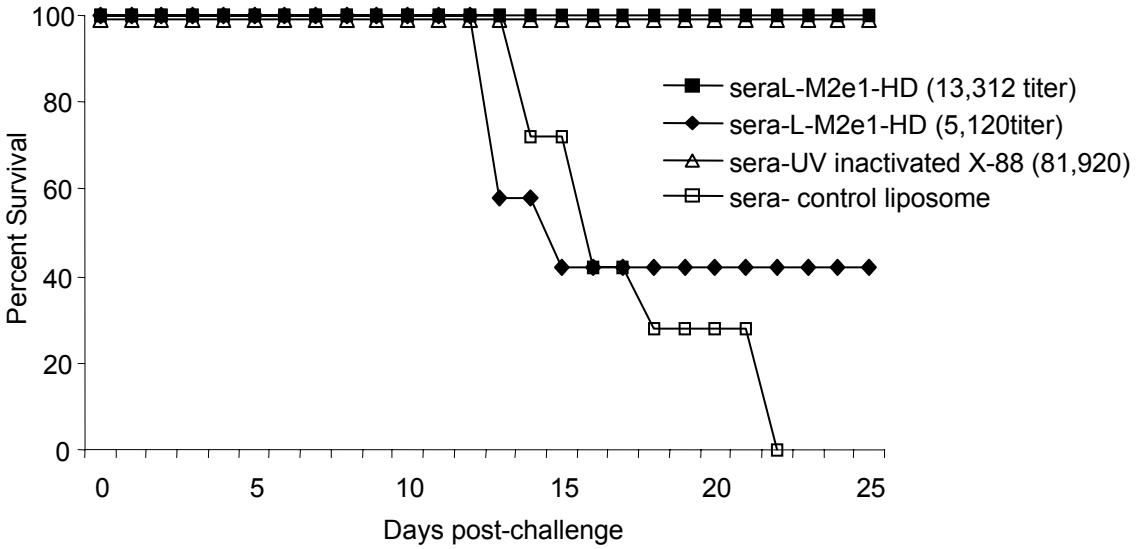
VesiVax® Influenza Vaccine

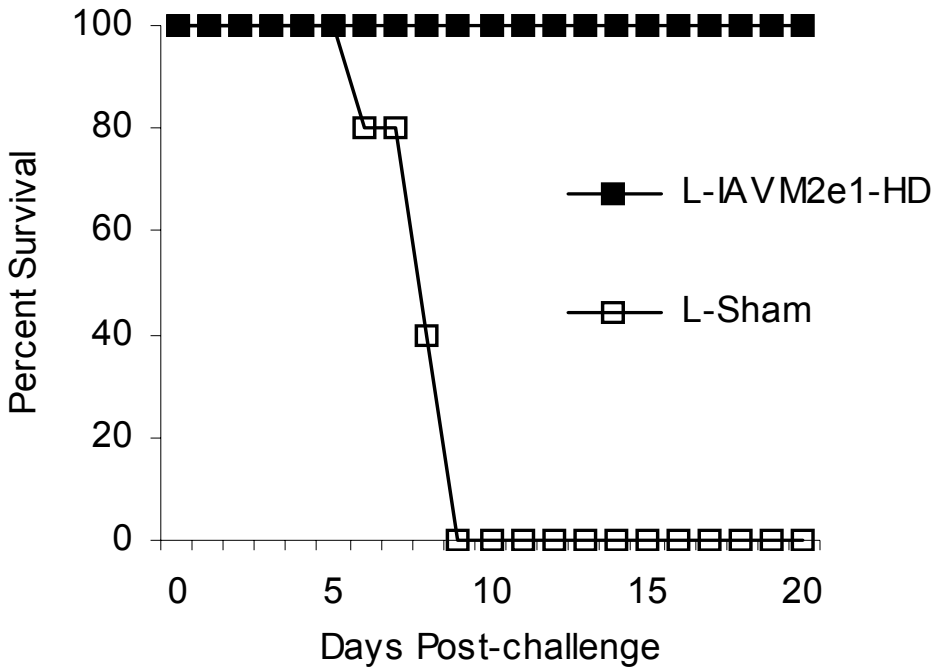
Passive Transfer of Immunity



Immunized Mouse Sera	Coating Antigen	IgG Titer
L-IAVM2e1-HD	IAVM2e1	13,312
L-IAVM2e1-HD	IAVM2e1	5,120
Sham-L	IAVM2e1	0
UV Irradiated IAV	1:32 Irr. IAV	81,920
UV Irradiated IAV	IAVM2e1	256
PBS	1:32 Irr. IAV	0
PBS	IAVM2e1	0

VesiVax® Influenza Vaccine

Cross-Protection of M2e



VesiVax® Influenza Vaccine

Reduction of Viral Burden

Immunization	M2e1	M2e2	M2e3
Challenge	H1N1	H5N1	H9N2
N-fold Reduction	>300	>10	>50

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VesiVax® Influenza Vaccine

M2 as a target for vaccine development

- Evolutionarily conserved
- Not as susceptible to the high mutation and reassortment rates observed with the H and N epitopes
- Present on the surface of viruses and infected cells

Is M2 a good flu vaccine target?

- Significant protection observed for epidemic and pandemic strains of influenza
- Cross protection against strains with the same M2 demonstrated
- The data suggests that M2 mediated immunity is antibody dependent
- M2 specific antibodies recognize M2 on the surface of infected cells and on the virus

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VesiVax® Vaccination Studies

Protection from severe infection observed

Against viral and bacterial pathogens
In different species and strains of animals
In both sexes
In short and long term studies
In adults and young animals
Through different routes of vaccination

Assays of immunological response parameters demonstrate

Antibody titers increase >30x over placebo
Antigen specific proliferation of immune cells increase >10x
Key cytokine levels increase by >10x over placebo

No significant side effects observed

The VesiVax® Advantage

VesiVax® Influenza Vaccine

- Recombinant DNA system allows "cut & paste" design of M2e antigens
- Flexible design facilitates rapid engineering of new influenza vaccines
- Routine scale-up procedure
- Production simplified
- Minimal biohazard (BL1)
- Selective antigen display (M2e)
- Reduced possibility of side effects
- No risk of infection

Influenza Virus Vaccine

- Pathogen-based vaccines are not amenable to rapid development
- Time and labor intensive manufacturing process
- Complex production procedures (eggs)
- Biohazard requirements (BL2-BL4)
- Non-selective antigen display
- Inflammation at the site of injection
- Increased possibility of clinical complications

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Implications

VesiVax® technology

- ***Represents a leap forward in vaccine development and production***
- ***Demonstrated efficacy with Influenza***
- ***Demonstrated efficacy with HSV2***
  - ***Significantly shortens time of vaccine production***
  - ***Can potentially respond to new pathogens in weeks, not months***

Acknowledgements

Centers for Disease Control and Prevention (CDC)
National Institute of Allergy and Infectious Diseases (NIAID)
California State Polytechnic University, Pomona (CSPUP)

William A. Ernst, Ph.D. – Molecular Express
Airan Alvarado – Molecular Express
Terrence Tumpey, Ph.D. - CDC
Jill Adler-Moore, Ph.D. – CSPUP
Jon A. Olson, M.S. – CSPUP

Alex Kim
Vivi Tran
Shauna Avalos
Adam Rosenthal
Matt Reid
Luciana Song
Shireen Dejbaksh
Dena Johnson
Wendy Tai
Roya Masoud
David Gibbs

Supported by NIH grants: 1R43AI44579-01; 1R43AI056890-01

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Questions