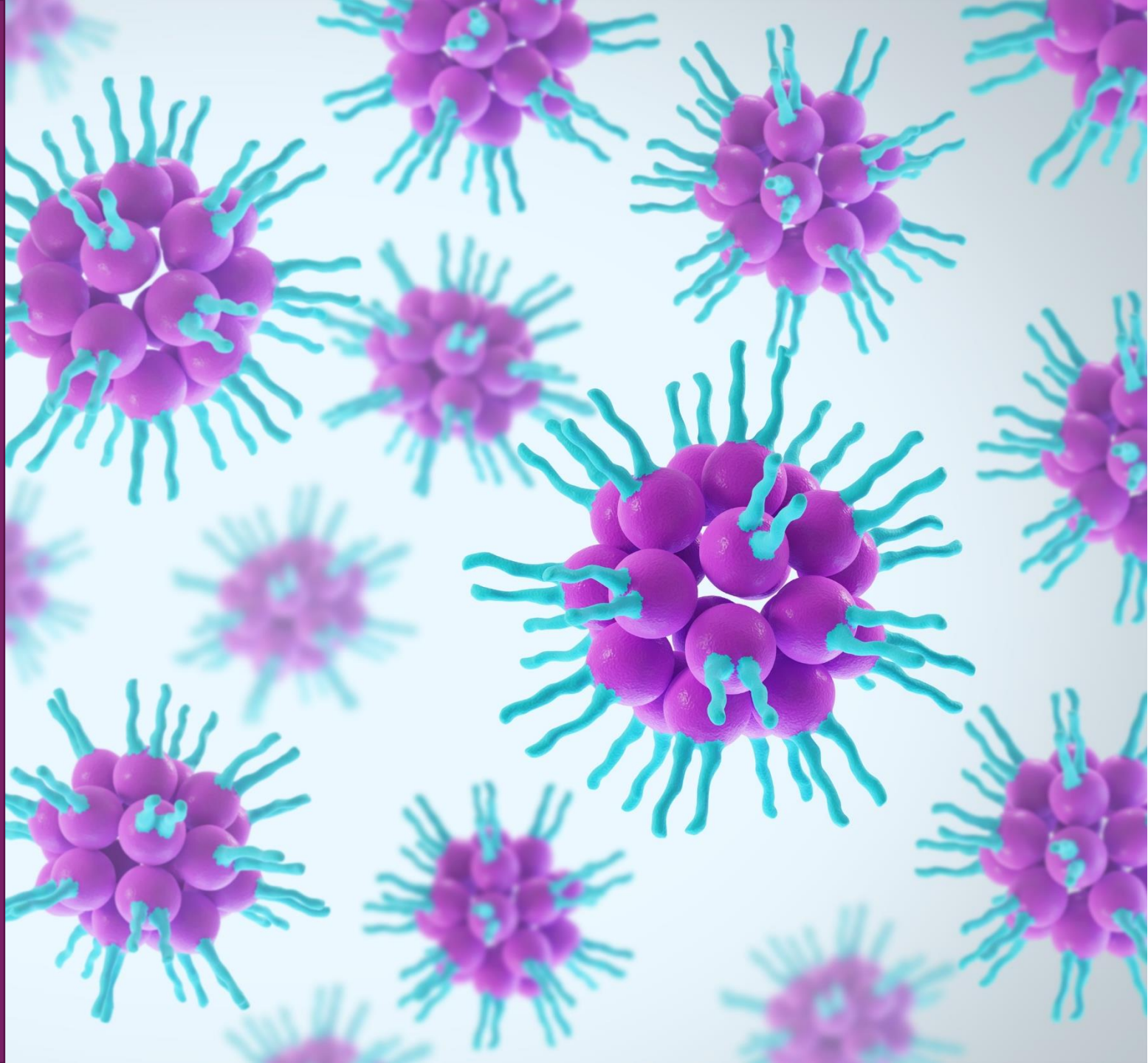


Evaluation of the
therapeutic potential
of antibody and T cell
targeted immune
responses towards
RSV small
hydrophobic protein

Dr. Genevieve Weir

RespiDART

November 29-30, 2018



Disclosures – Genevieve Weir

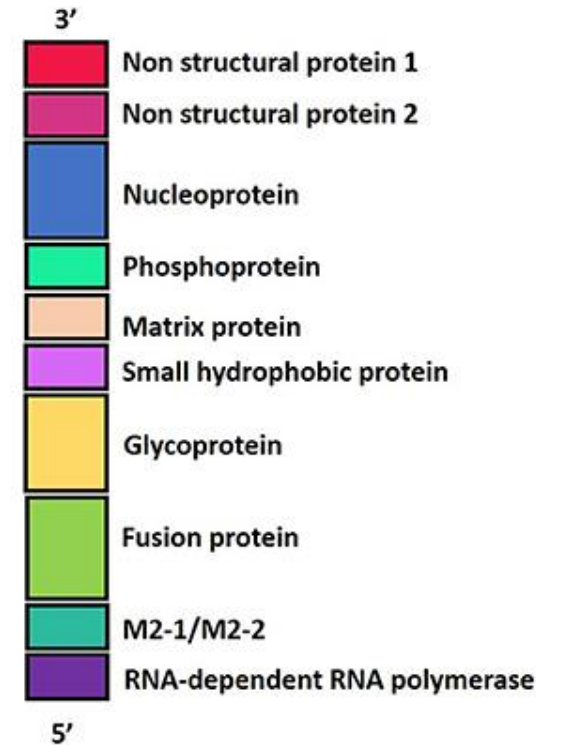
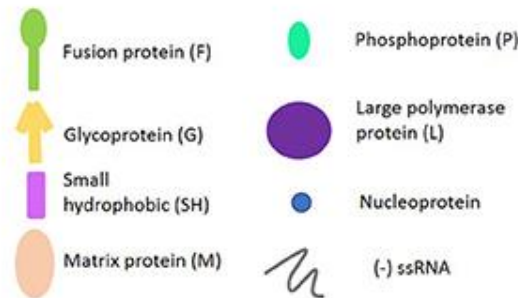
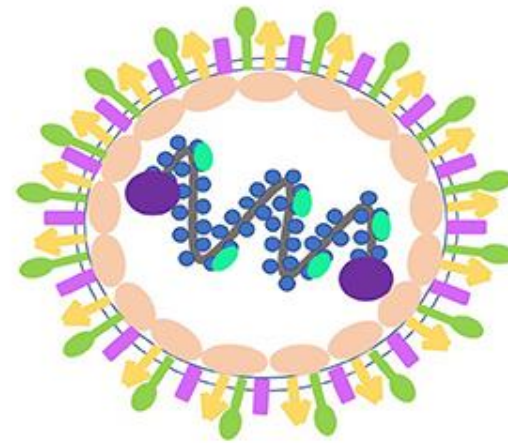
- Employee and stock shareholder of IMV Inc.

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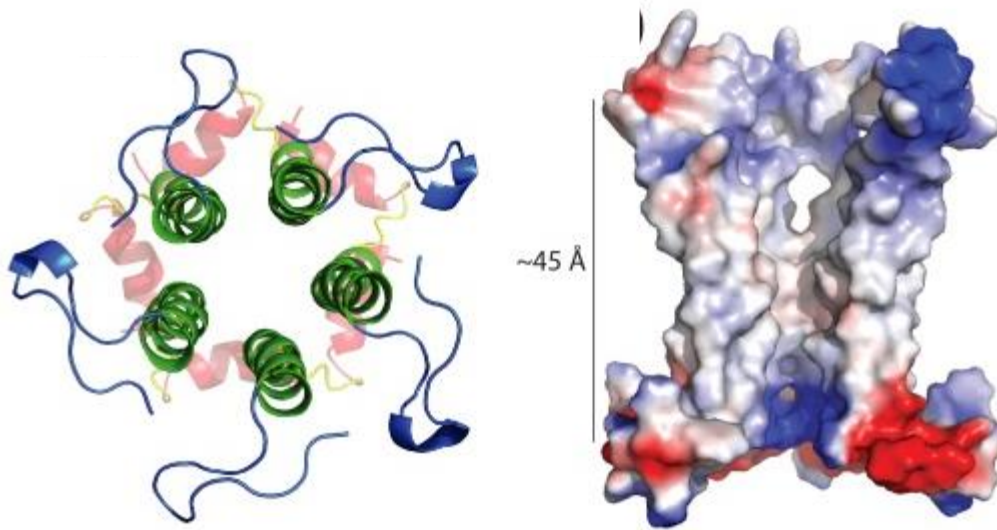
RSV Vaccination in the Elderly

- Highly prevalent disease of lower respiratory tract
- Ubiquitous pathogen that can re-infect throughout life
 - Several immune evasion mechanisms prevent development of immune memory
 - Significant cause of hospitalizations in the elderly
- Subunit vaccine approaches target F or G protein to neutralize virus

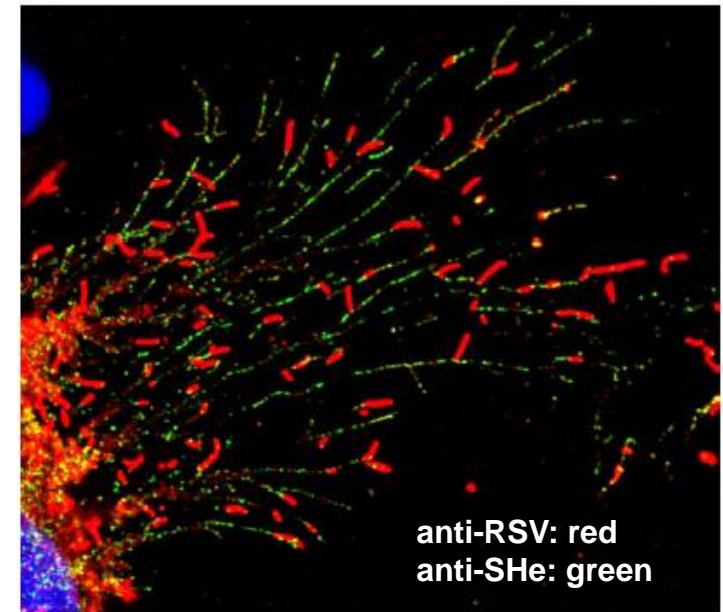


Canedo-Marroquin *et al*, *Front Cell Infect Microbiol*, 2017

Small Hydrophobic Protein Ectodomain (SHe)

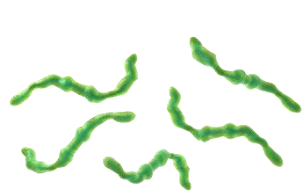


Gan *et al.*, *JBC*, 2012

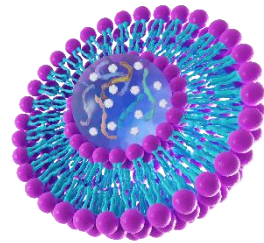


Schepens *et al.*, *EMBO Mol Med*, 2014

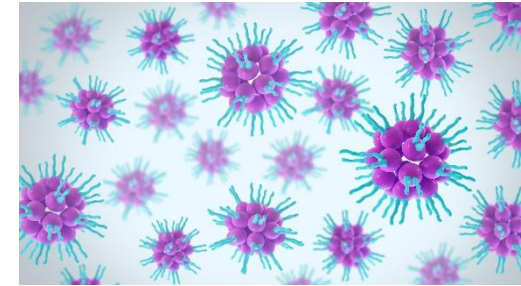
DPX Technology



Active Ingredients

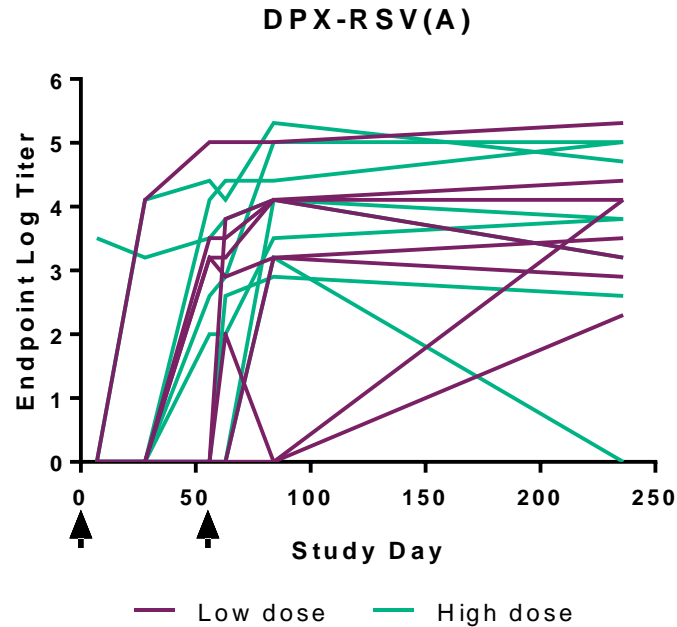


Lipid Nanoparticle



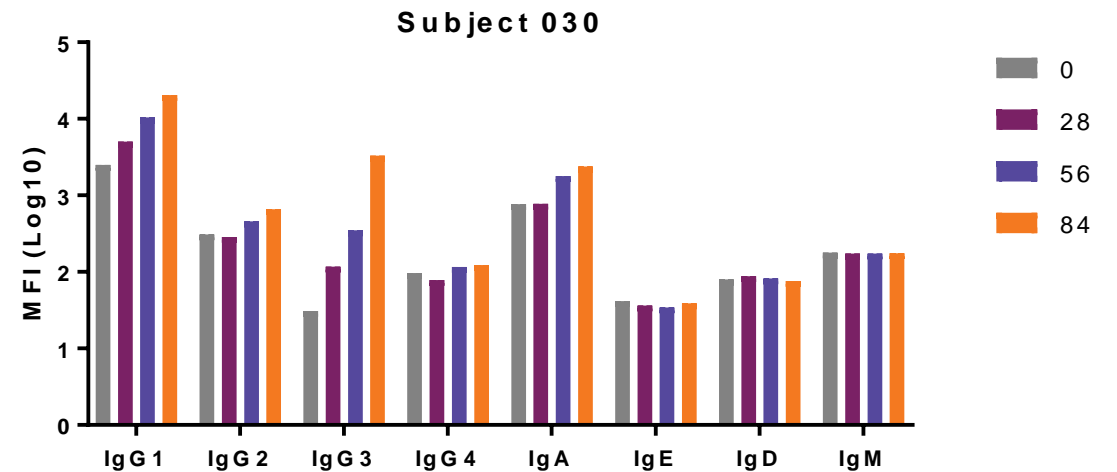
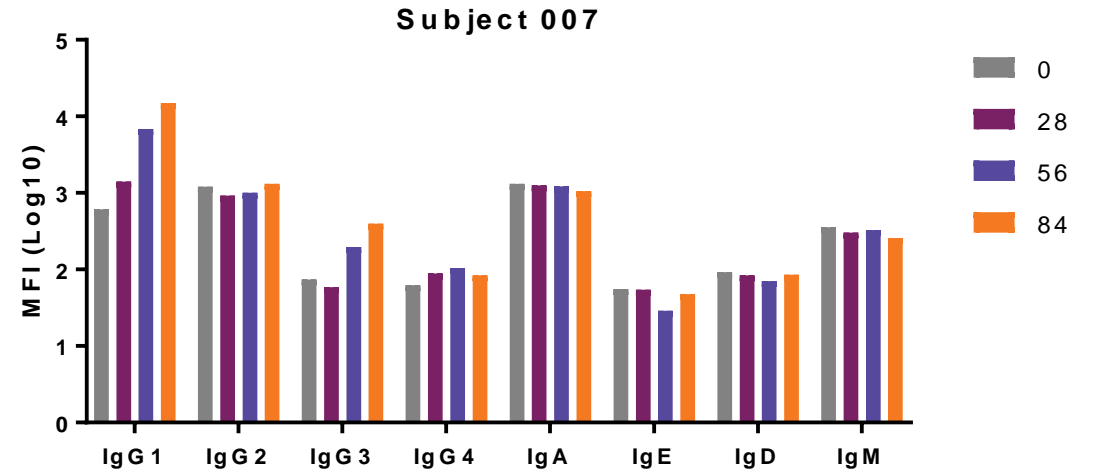
- Lipid nanoparticle delivery platform with new “No release” mechanism of action (DPX)
- Forcing an active uptake and in vivo delivery of active ingredients into immune cells
- MOA can be leveraged to program and generate new types of T and B cell therapeutic capabilities bypassing conventional immune responses and their inherent limitations
- Multiple manufacturing advantages; fully synthetic; hydrophilic and hydrophobic compounds, wide-range of applications (peptides, small-molecules, RNA/DNA, antibodies...), long term stability & low cost of goods
- > 200 patents and patents filed to cover technology and multiple applications

Clinical Evaluation of DPX-RSV(A)

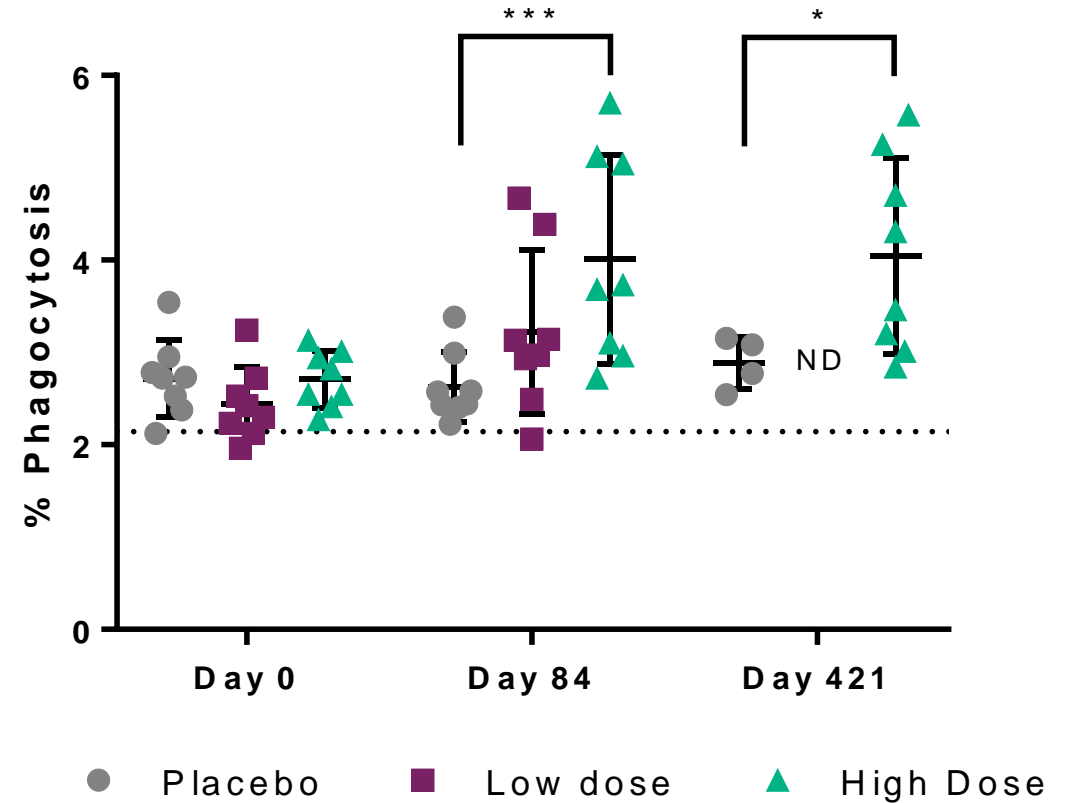
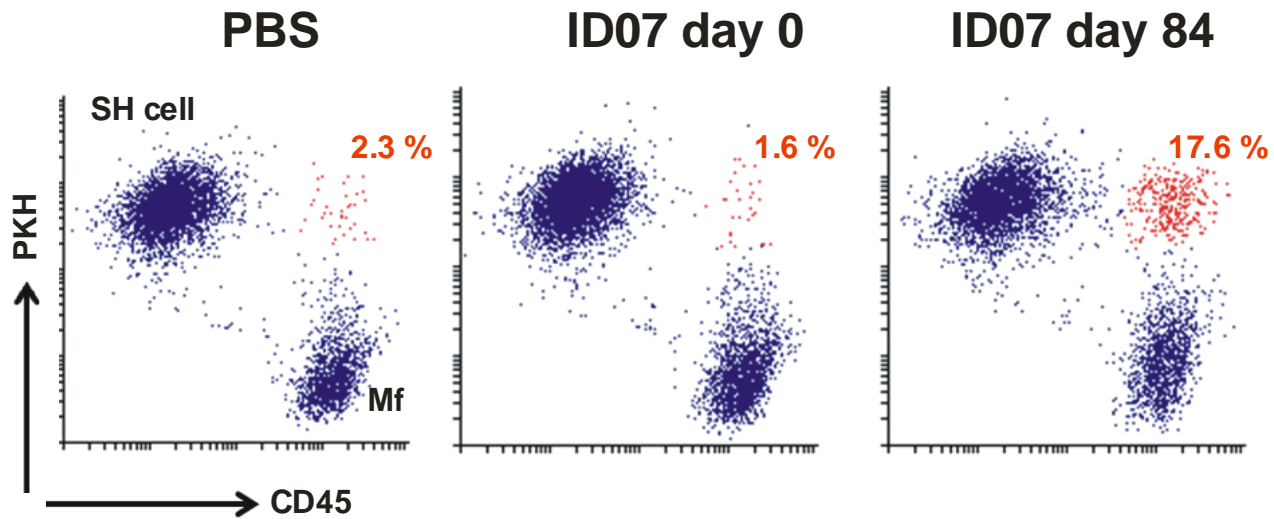


- Healthy adults 50-64 years of age
- DPX-RSV(A) administered at 2 SHe dose levels:
 - Low dose: 10 μ g
 - High dose: 25 μ g
- Day 0 and 56

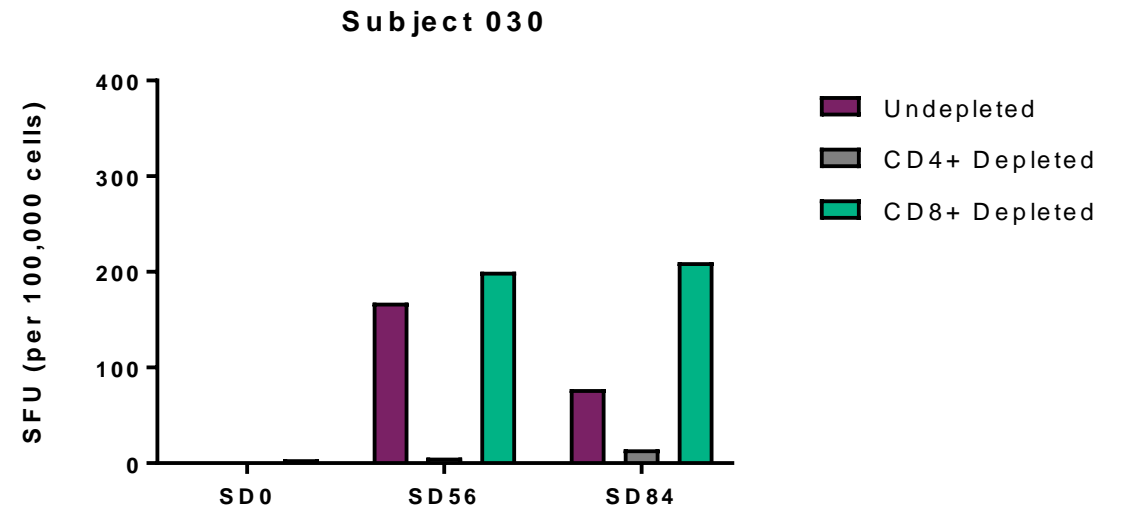
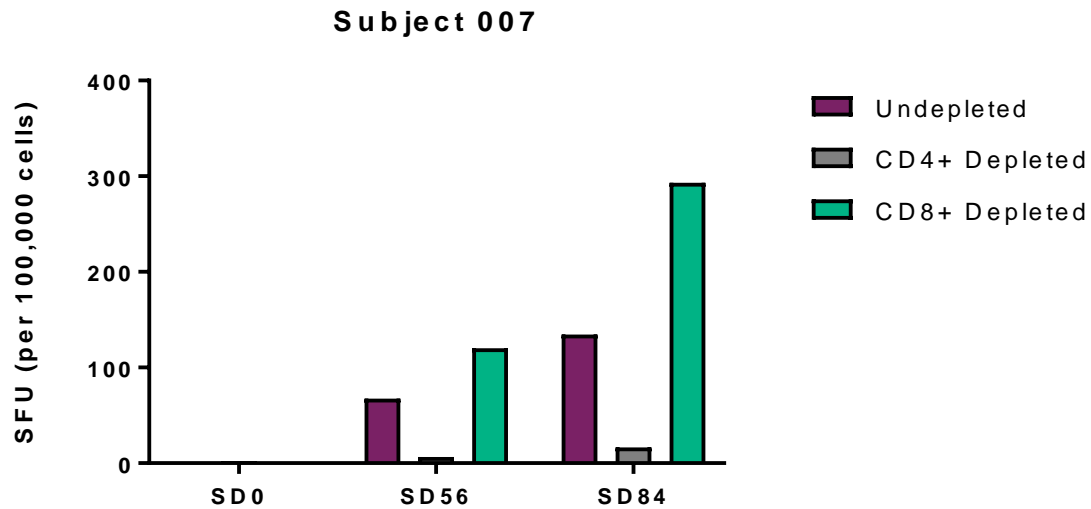
Langley et al, J Infect Dis 2018



Vaccine induced RSV SHe-specific serum IgG promotes Ab-dependent phagocytosis



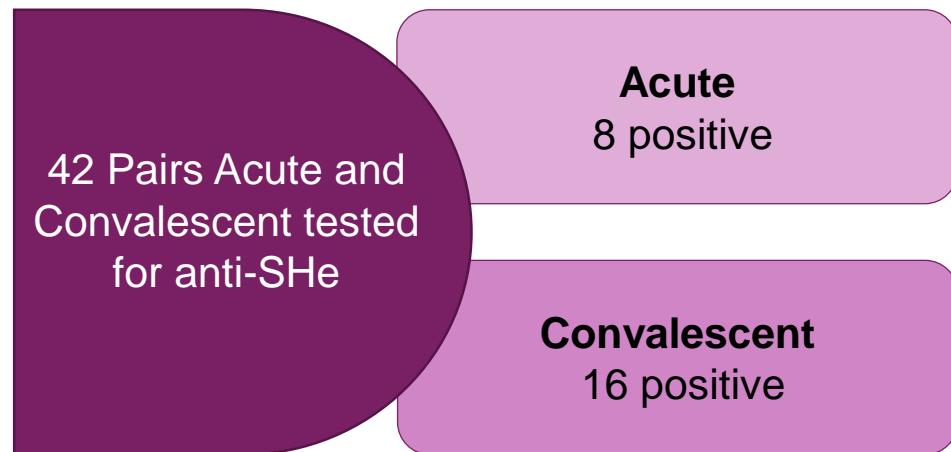
DPX-RSV(A) induces CD4⁺ T cell response



- Using PBMCs collected prior to day 0 and 56 injections of DPX-RSV(A) and 84
- IFN- γ ELISPOT with whole PBMCs or CD4⁺/CD8⁺ depleted
- Stimulation with SHe antigen

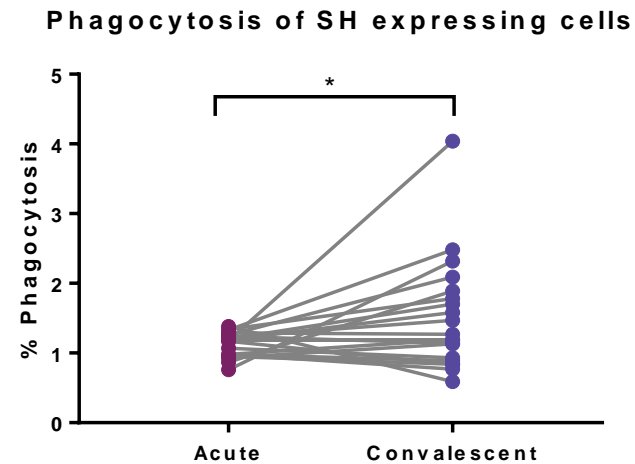
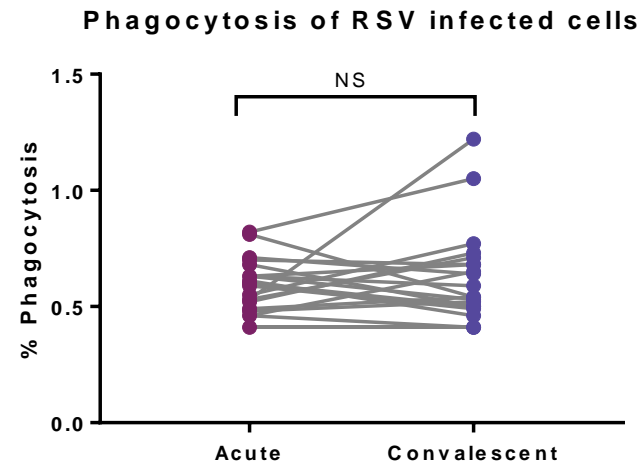
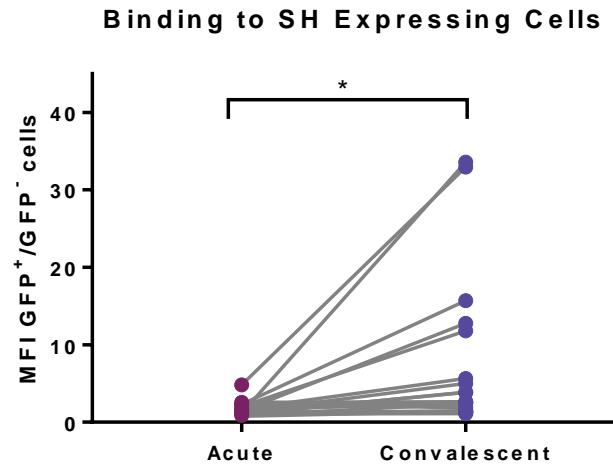
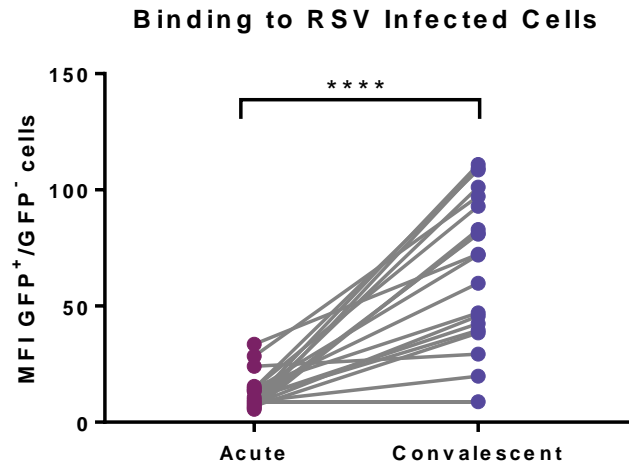
Anti-SHe titres induced by natural infection

- 42 subjects with confirmed RSV infection
- Serum collected at time of illness (acute) and 4-6 weeks later (convalescent)
- No apparent correlation with clinical presentation
- Rise in anti-SHe at convalescent phase was most likely to occur in subjects with anti-SHe detected in acute phase ($p < 0.013$)



Age	Average 76 (58-91)
Sex	24 male, 18 female
COPD	18
Diabetes	13
Congestive heart failure	11

Anti-SHe IgG developed during infection are functional



Summary

- DPX-RSV(A) induces potent antibody and CD4⁺ T cell mediated immune response directed towards SH antigen
 - Anti-SHe antibodies can bind RSV infected cells and mediate phagocytosis
- Anti-SHe antibodies can also be induced by natural infection and may play a role in disease resolution

Abstract # 105

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Thank You

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