VACCINE EFFICACY OF FMD VIRUS-LIKE PARTICLES PRODUCED BY THE BACULOVIRUS EXPRESSION SYSTEM

Erwin van den Born

MSD Animal Health

Acknowledgements

Pirbright Institute, UK
Bryan Charleston
Claudine Porta
Eva Perez

University of Oxford, UK
Dave Stuart
Abhay Kotecha
Elizabeth Fry

University of Reading, UK
Ian Jones
Silvia Loureiro

MSD Animal Health, Netherlands
Ruud Segers
Amaya Serrano García
Alexandra Jiménez-Melsió
Holger Hönemann

This work was supported by the Wellcome Trust grant number 101122/Z/13/Z

Background

MSD Animal Health

There is a need for novel innovative FMD vaccines

- Vaccination is the only method available to control FMD in low and middle income countries.

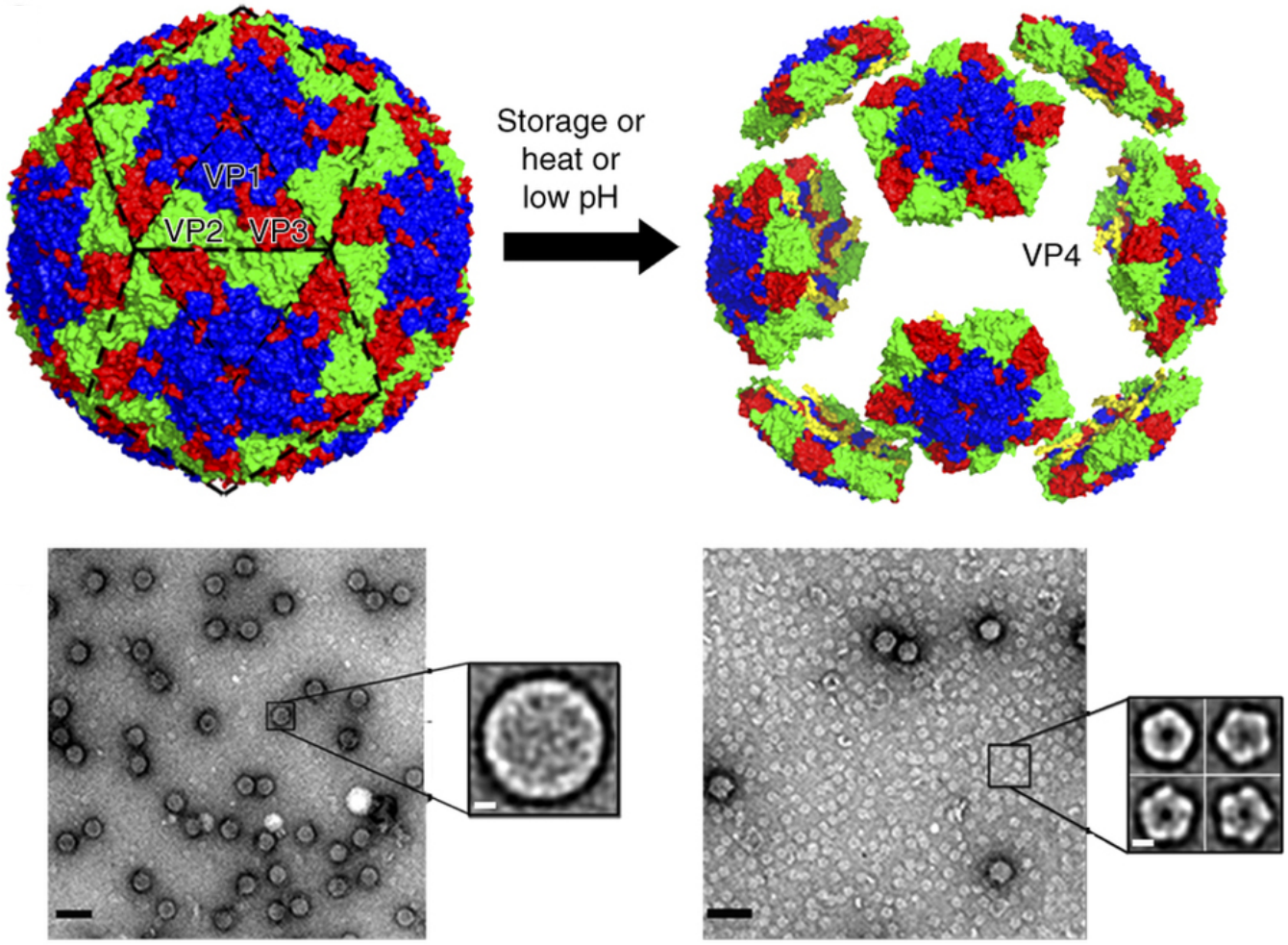
- Availability of vaccines is poor, most strikingly in Africa.

- Current ‘killed virus’ vaccines:
  - High potency vaccines ($6PD_{50}$) provide sufficient protection
  - Live virus production in high containment facilities
  - Require expensive cold chains to deliver effective products

Decivac FMD DOE

MSD Animal Health

There is a need for novel innovative FMD vaccines



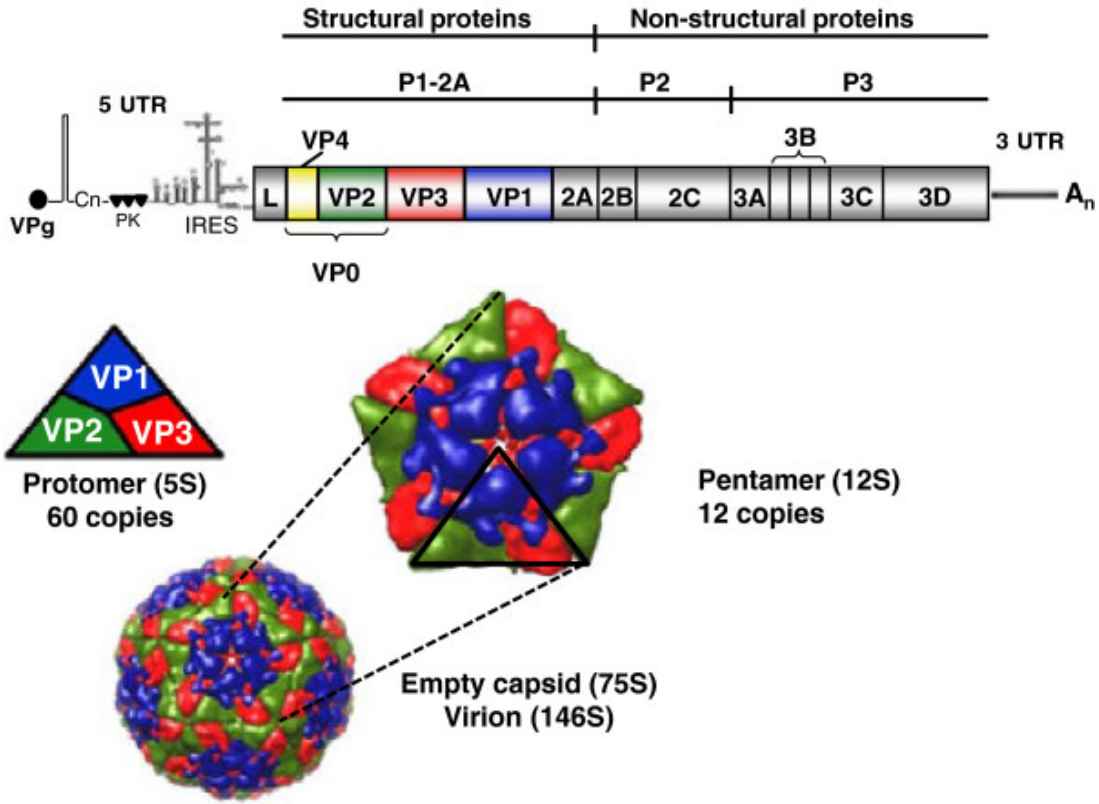
Kotecha *et al.* (2015) *Nat Struct Mol Biol*

MSD Animal Health

Virus-like particles are promising alternative antigens

Virus-like particles (VLPs):

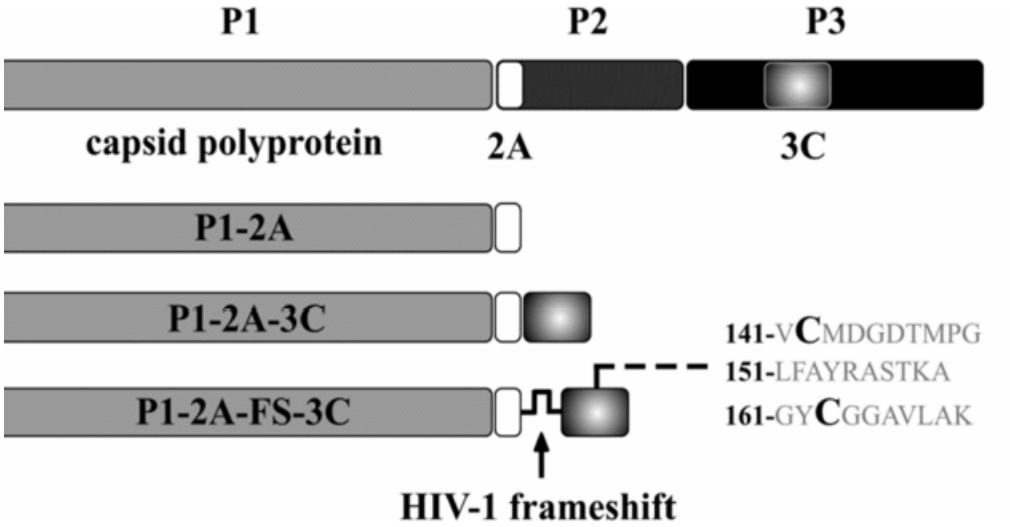
- If vaccines contain 75S particles, sufficient protection is anticipated
- Vaccine production in standard facilities (baculovirus expression)
- Stability/antigenicity can be improved (e.g. stabilizing mutations)

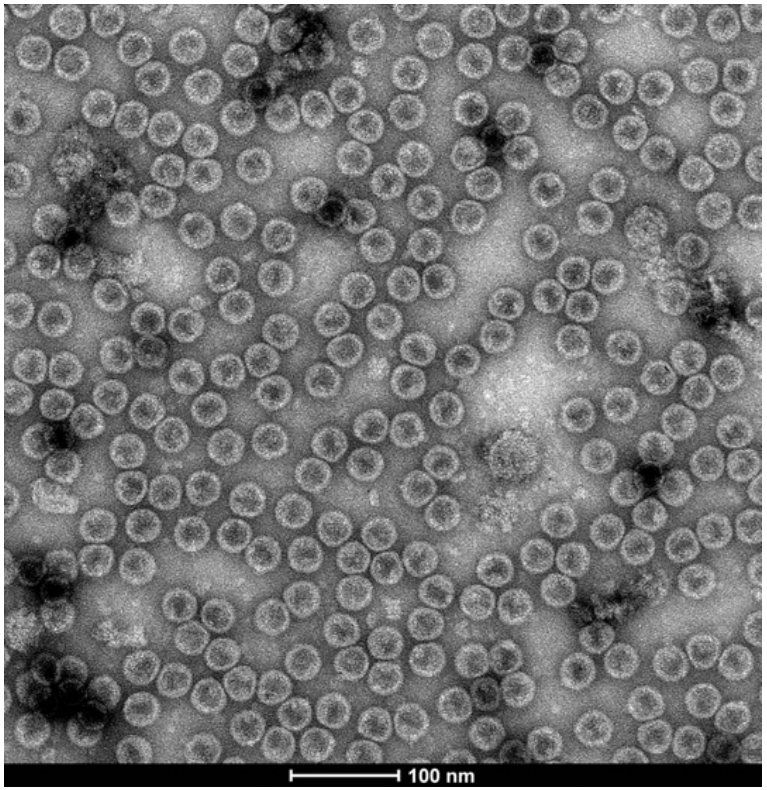


Jamal and Belsham (2013) *Vet Res*

MSD Animal Health

VLP production in baculovirus expression system



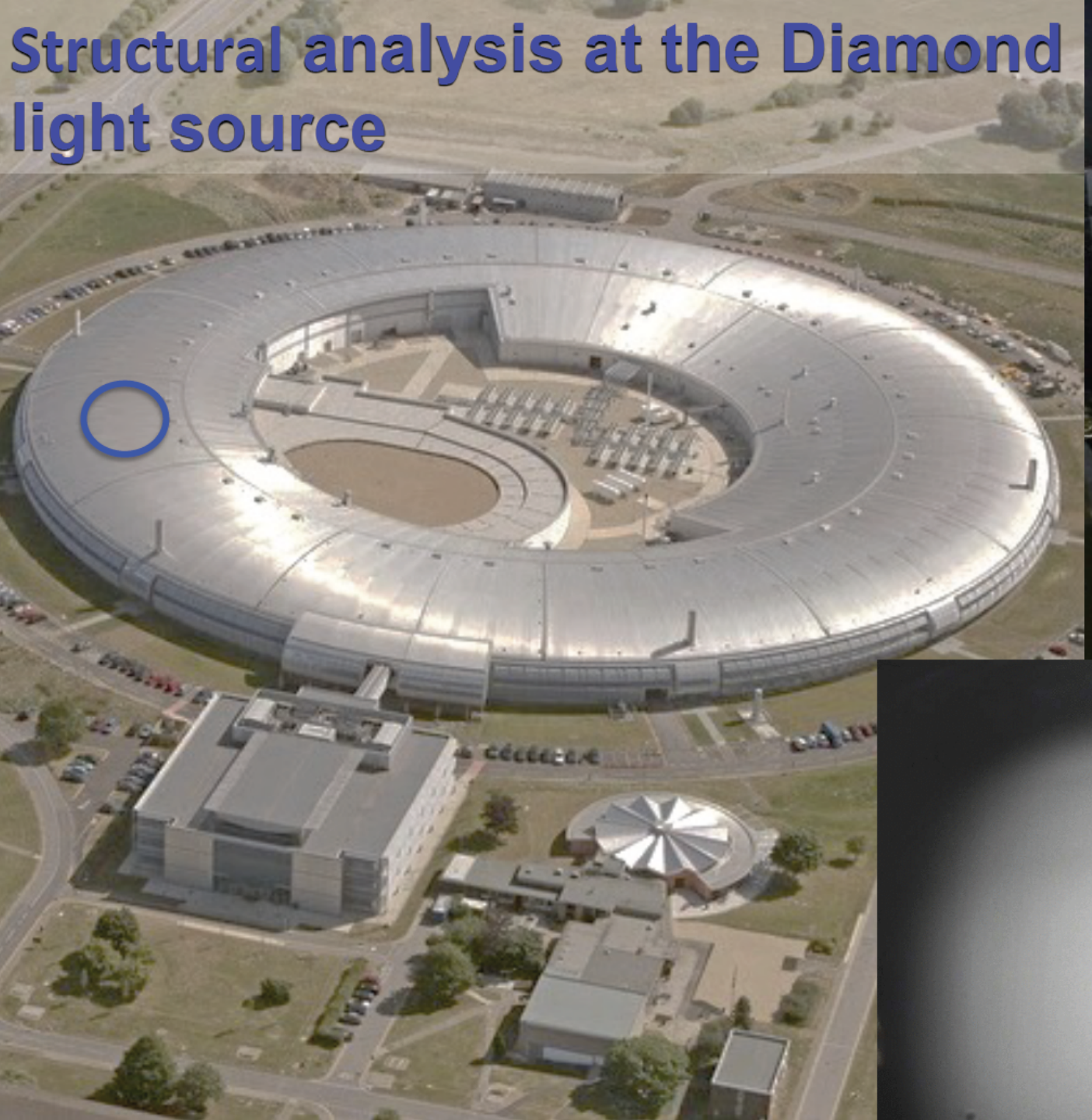


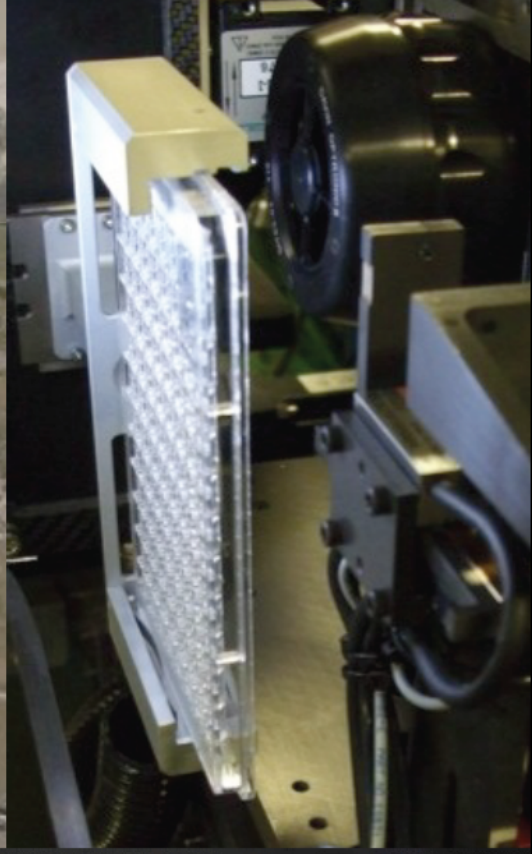
A22 75S particles

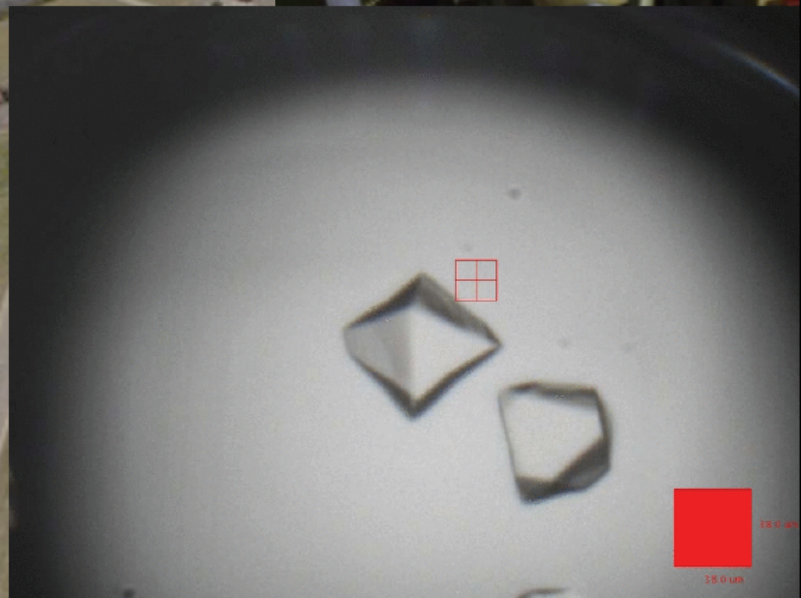
Porta *et al.* (2013) *J Virol Met*

MSD Animal Health

Structural analysis at the Diamond light source

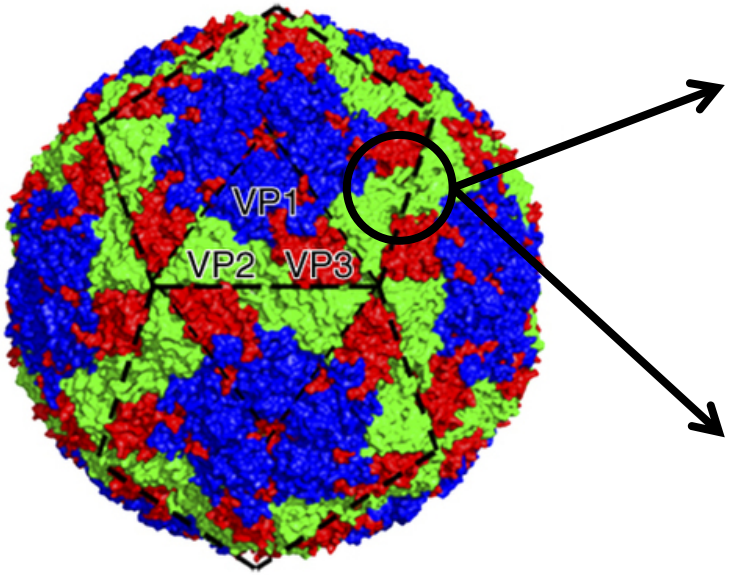


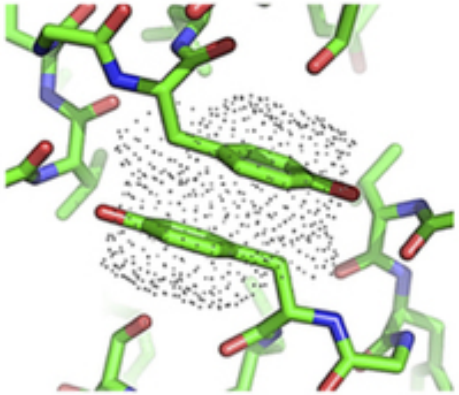




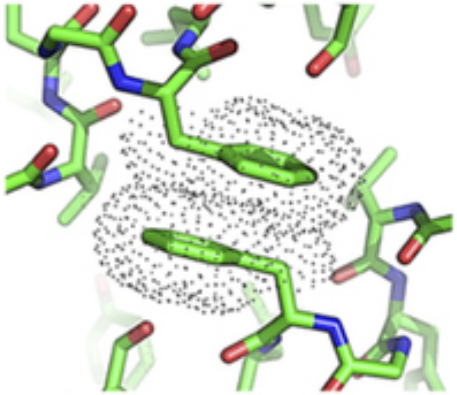
Capsid stabilization through mutations in VP2

Stabilization of the
VP2-VP2 interface

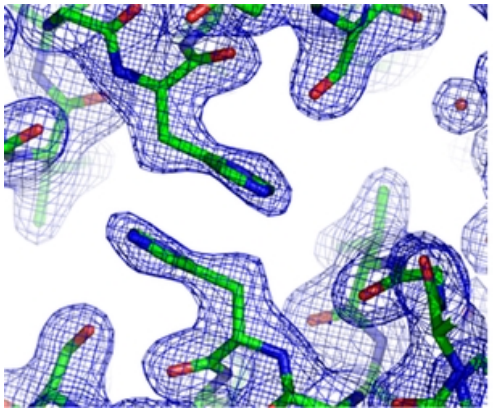




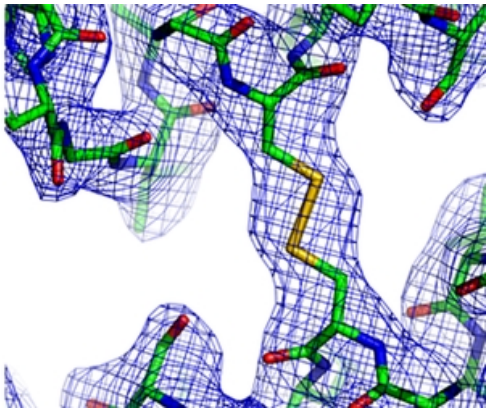
O1Manisa VP2-S93Y



O1Manisa VP2-S93F



93His



93Cys

MSD Animal Health

Kotecha *et al.* (2015) *Nat Struct Mol Biol*

Production & characterization of VLPs

MSD Animal Health

Optimization of VLP production

- Baculovirus expression system

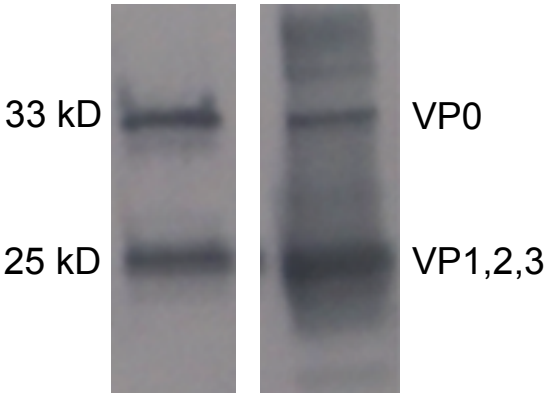
- High yield of VLPs important

- Optimization parameters:
  - Type of insect cells
  - Type of baculovirus vector
  - Time of harvest after infection
  - Translation initiation site of expression cassette
  - Codon optimization of expression cassette
  - Harvest method
  - Downstream process

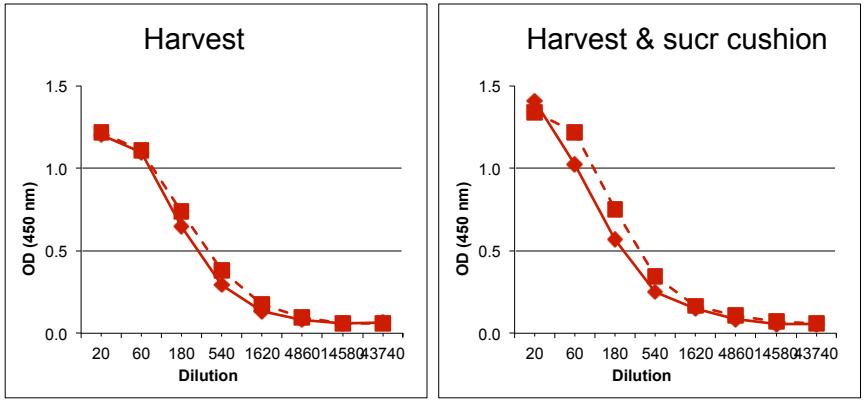
- Yield of FMDV protein increased up to 10^2 fold

Analysis of VLPs by several techniques (A/IRN H93C)

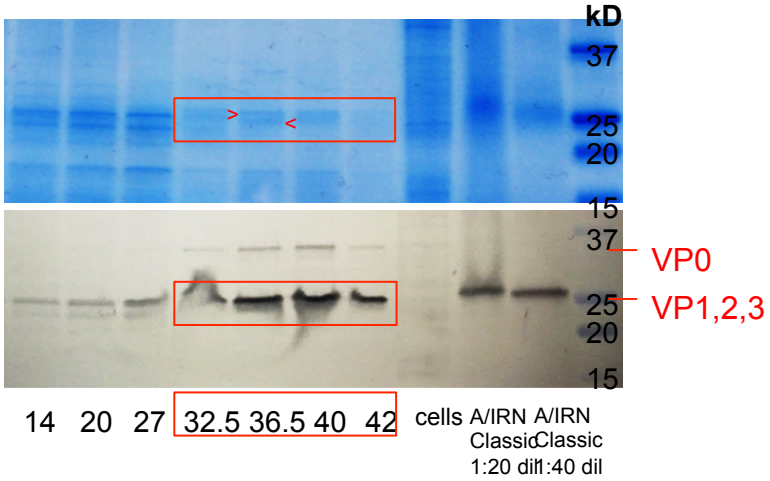
Western blotting with cattle serum



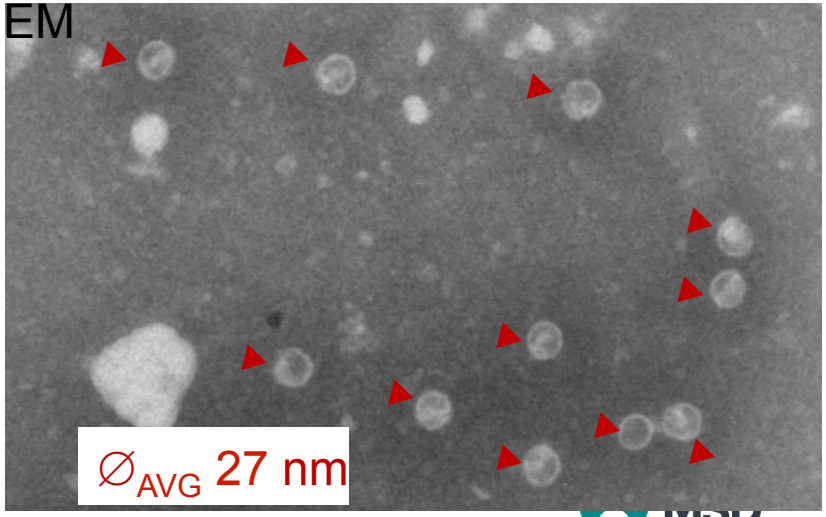
ELISA



Sucrose cushion centrifugation



EM

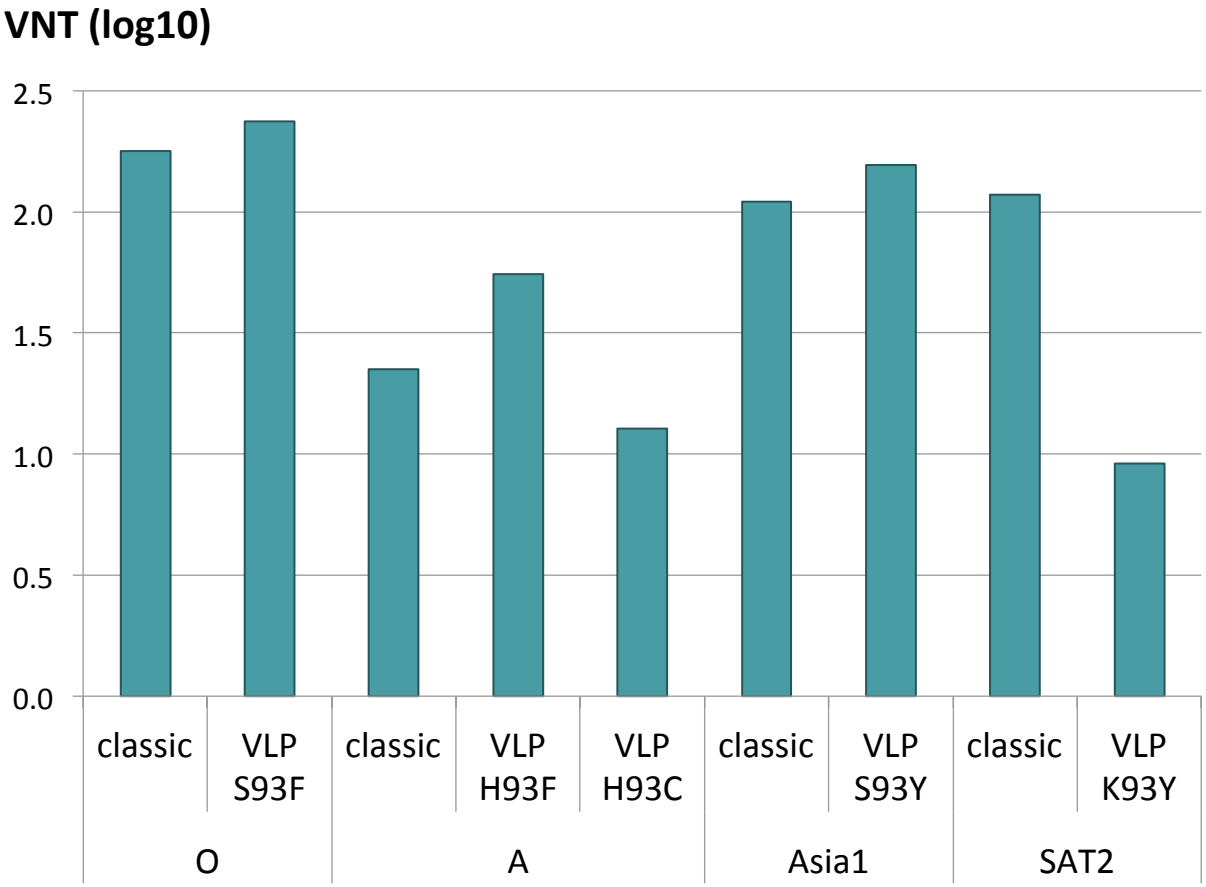


MSD Animal Health

Immunogenicity: virus neutralizing titres in guinea pigs

Study design
- Vaccines contain fixed volume of antigen
- 4 serotypes included
- 5 animals/group
- Blood sample at 4 wpv
- VN assay on serum

Note: strain in VN assay not always optimal for classic antigen and/or VLP



Cattle vaccination/challenge trial planned

MSD Animal Health

Conclusions & Summary

MSD Animal Health

- Virus-like particles (i.e. 75S capsids) can be produced in the baculovirus expression system
- Yield and quality of capsids were significantly improved
- Amino acid position 93 of VP2 can be mutated to stabilize the capsids
- Virus neutralizing titres induced in guinea pigs by VLPs are comparable to that of classic antigen

→ *Virus-like particles have the potential to be a commercially viable alternative to conventional killed vaccines*