Improving the duration of immunity for FMD vaccines

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Challenges for FMD control in endemic settings through vaccination

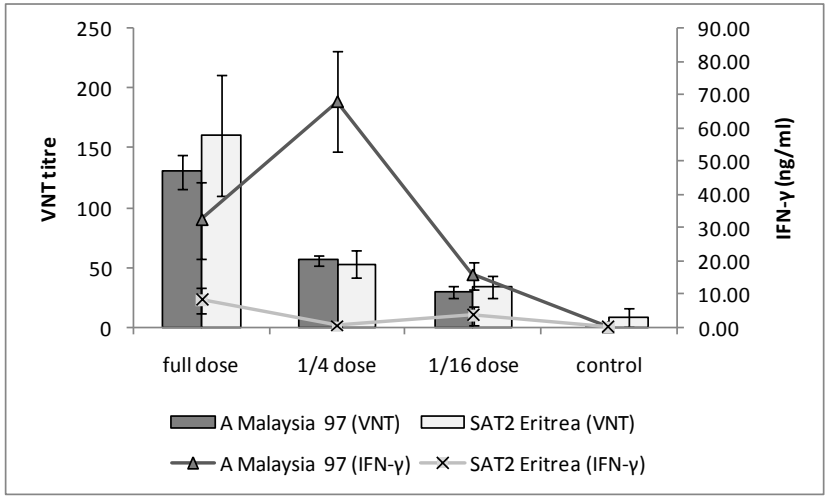
Killed inactivated oil adjuvanted vaccines are in use.

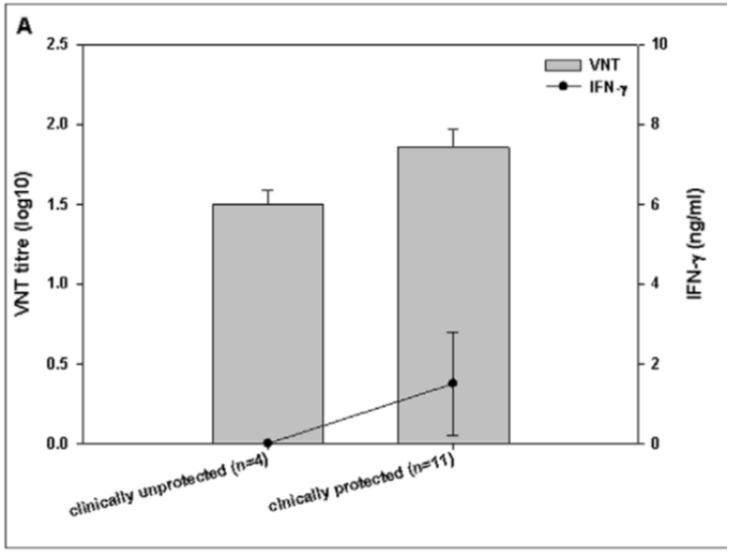
Biannual vaccinations (3 PD50 vaccines) are practised to control the disease in endemic settings

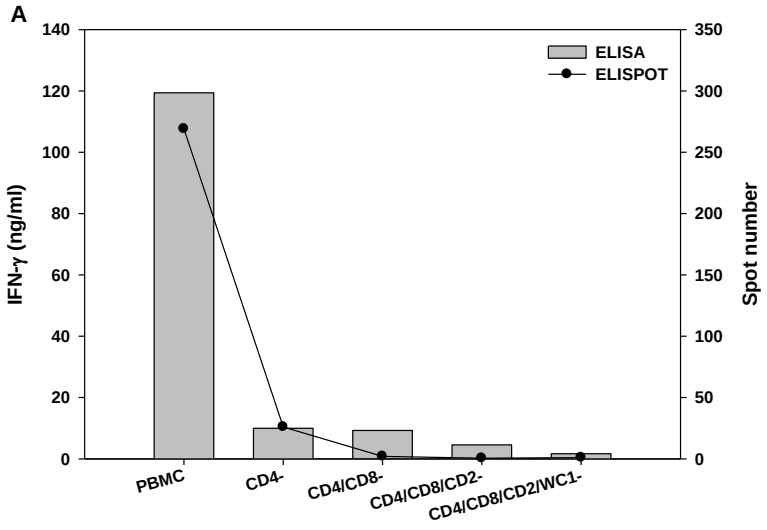
One of the major challenges- short lived immunity (~3 to 4 months max) which allows at least 2 month window for bringing back the disease before 2nd vaccination.

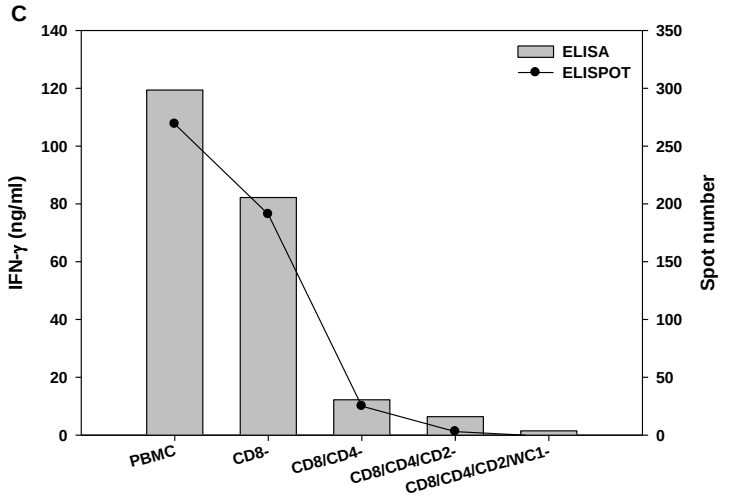
Main aim: To increase the duration of immunity, at least to cover the window between biannual vaccination

VNT and IFN-γ responses in serotype A and SAT2 vaccinated cattle on 21dpv





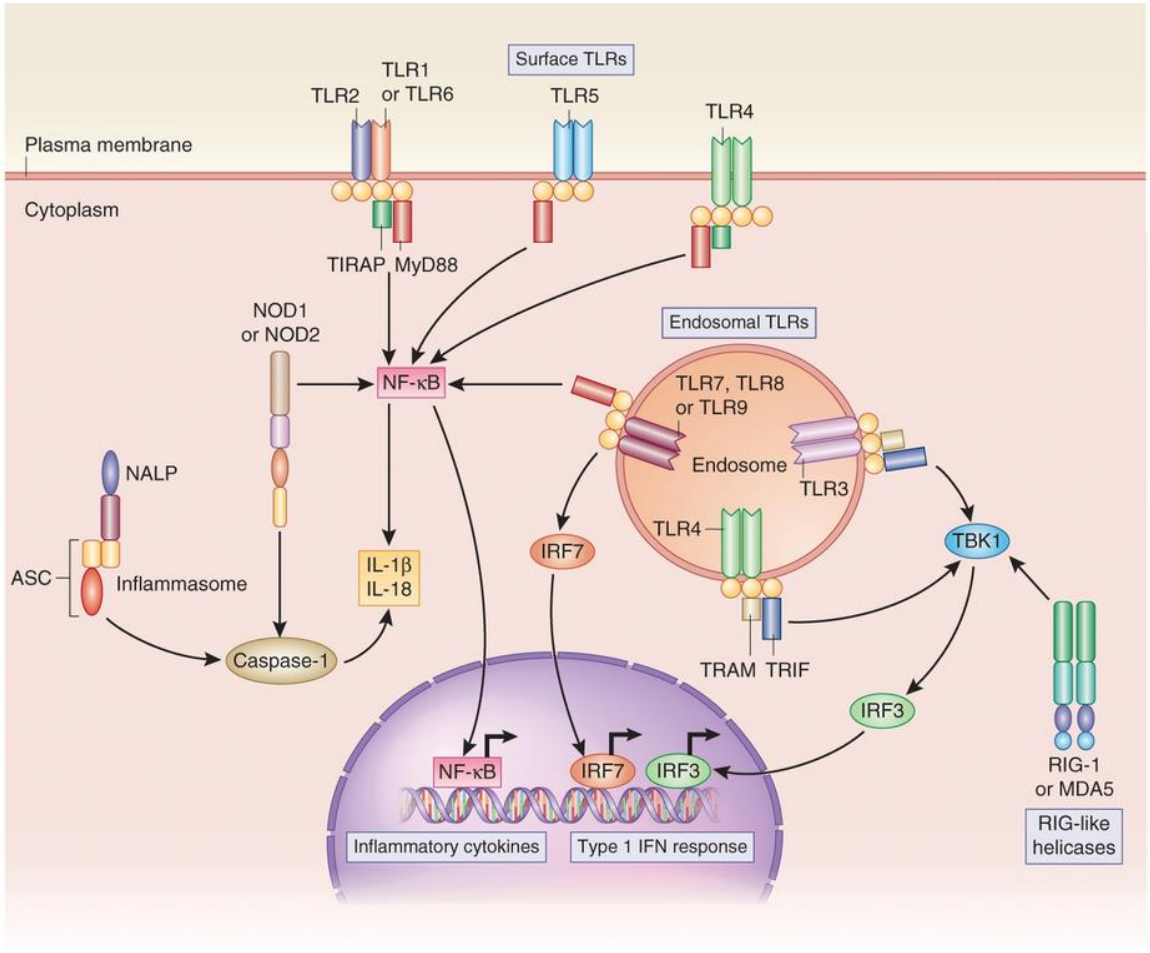




Oh et al 2012

How does the new generation adjuvants help?

- Activate the innate immune system via ligand binding to PRR
- Enhance the anti-viral environment
- Enhance the adaptive response (CMI and humoral)
- Improve memory responses



Screening of potent adjuvants-I Type O antigen (sub-optimal dose) in cattle

	Groups	No of animals	Details of vaccine	FMD antigen	Adjuvant/ISA 206	Protected/Total	Percent protectic
*	1	4*	FMD antigen + Abisco 300 + ISA 206	5 µg	1 mg + 1 ml	3/3	100
	2	4*	FMD antigen + CpG + Emulsigen + ISA 206	5 µg	0.25 mg + 1 ml + 1ml	1/3	33
	3	4	FMD antigen + ISA 70V	5 µg	1 ml	2/4	50
*	4	4	FMD antigen + ISA 206 + Poly I:C	5 µg	1 ml + 0.4 mg	3/4	75
*	5	4	FMD antigen + ISA 206 + Imiquimod	5 µg	1 ml + 0.4 mg	3/4	75
*	6	4	FMD antigen + ISA 206 + MPL-A	5 µg	1 ml + 0.4 mg	3/4	75

Screening of potent adjuvants- II Type O antigen (sub-optimal dose): cattle

Groups	No of animals	Details of vaccine	FMD antigen	Adjuvant/ISA 206	Protected/Total	Percent protectic
7	4	FMD antigen + Liposome	5 µg	0.2 ml	1/4	25
8	4	FMD antigen + ISA 206	5 µg	1 ml	2/4	50
9	4	FMD antigen + ISA 206	10 µg	1 ml	4/4	100
10	2	PBS alone without FMD antigens	Nil	Nil	0/2	0

*,one animal died (non- specific) before the day of challenge (21 dpv). Animals were vaccinated intramuscularly on one occasion and challenged by the intradermolingual route with log10^4 $CCID_{50}$ dose of FMDV O/IND/R2/75, 3 weeks later.

Final screening of potent adjuvants using Type A antigen (sub-optimal dose) in cattle

Group	No of animals	Vaccine details	A22 FMD antigen	Protected / Total	Percentage of protection
1	2	None	None	0/2	0
2	5	A22 FMD antigen+ISA-206	2 µg	0/5	0
3	5	A22 FMD antigen+ISA206 +AbISCO®300	2 µg	5/5	100
4	5	A22 FMD antigen+ISA-206 +Poly(I:C)	2 µg	5/5	100
5	5	A22 FMD antigen+ISA-206 +MPLA	2 µg	4/5	80
6	5	A22 FMD antigen+ISA-206 +R848	2 µg	2/5	40
7	5	A22 FMD antigen+ISA-206 +MPLA+R848	2 µg	1/5	20

Serotype A Vaccine Trial Design

A22 Iraq+ ISA-206 control

A22 Iraq+ ISA-206 **+ poly (I:C) adjuvant**

A22 Iraq+ ISA-206 **+ AbISCO adjuvant**

A22 Iraq+ ISA-206 **+ R848 adjuvant**

A22 Iraq+ ISA-206 **+ MPLA adjuvant**

A22 Iraq+ ISA-206 **+ R848+ MPLA adjuvant**

Non-Vaccinates control

A22 Iraq Vaccination (sub-optimal dose)

A22 Iraq Challenge

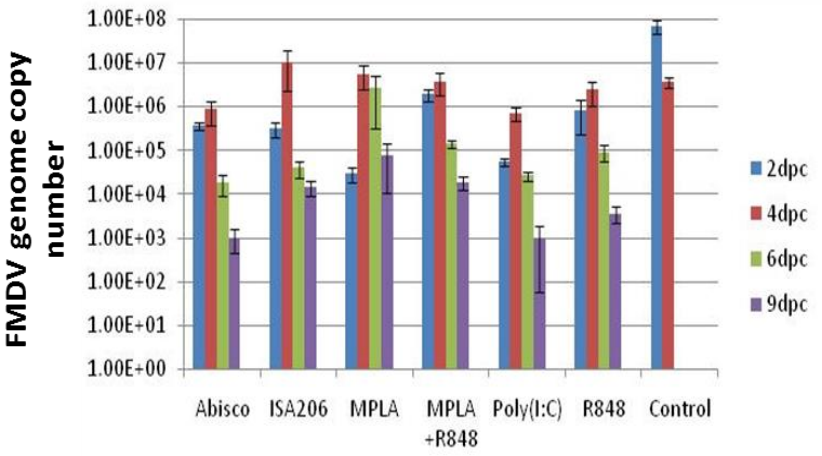
Cull

Sampling
Daily Rectal Temp
Swabs
Clotted blood
Heparinized blood

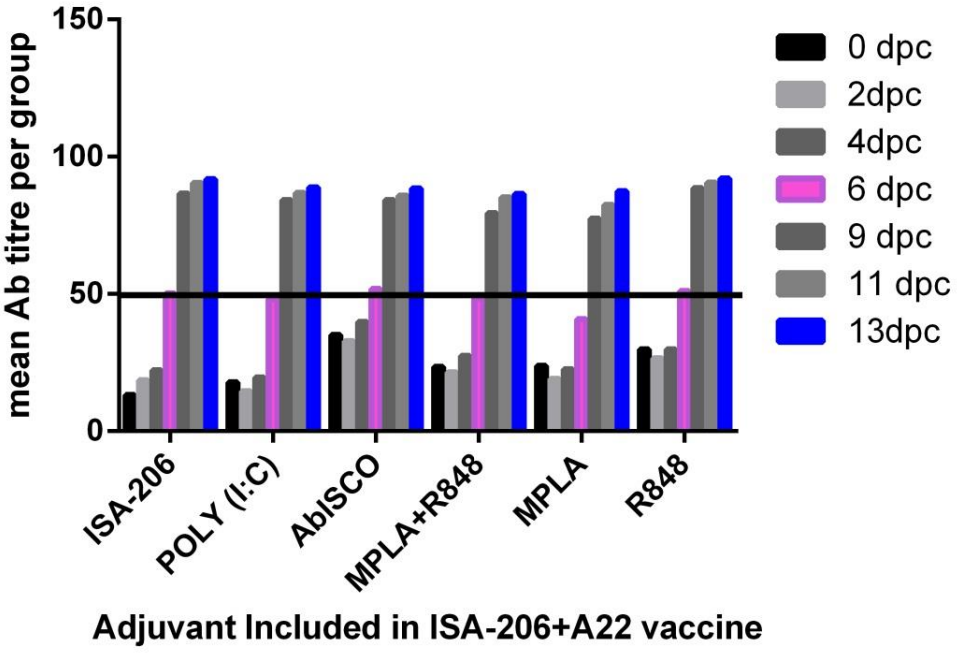
0 7 14 21 28 0 7 14 21 28 30

All calves had viraemia and sub-clinical infection

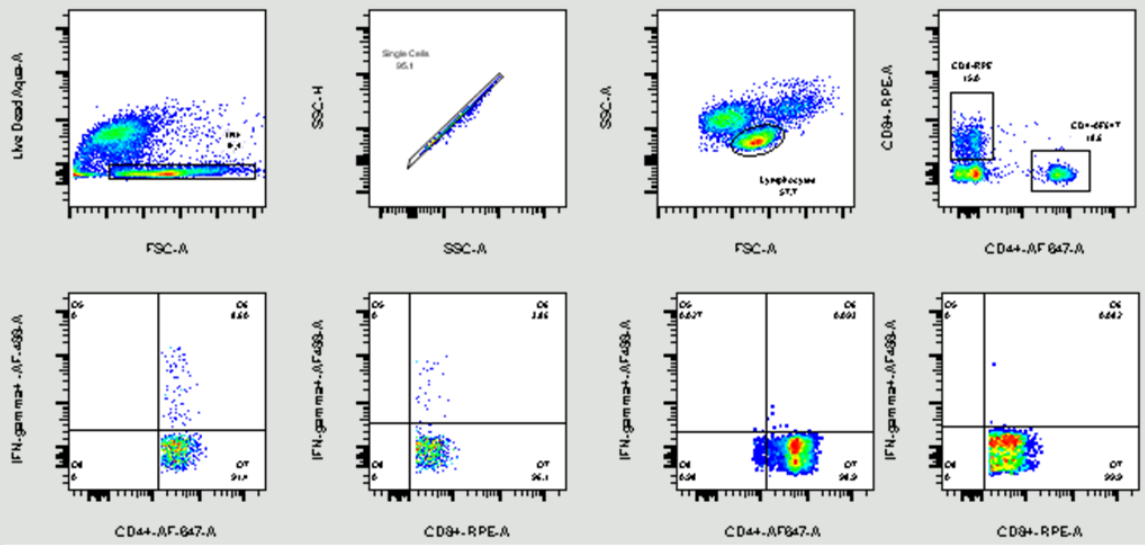
Genome copy in nasal secret

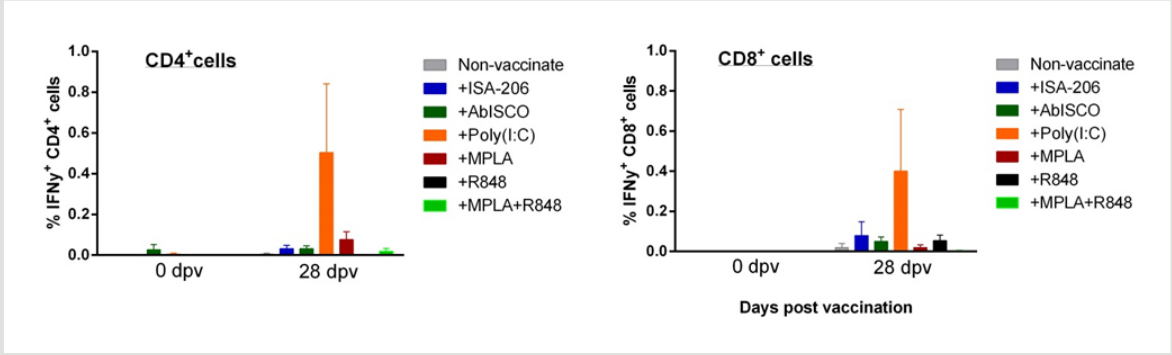


Abs in peripheral serum to NSP

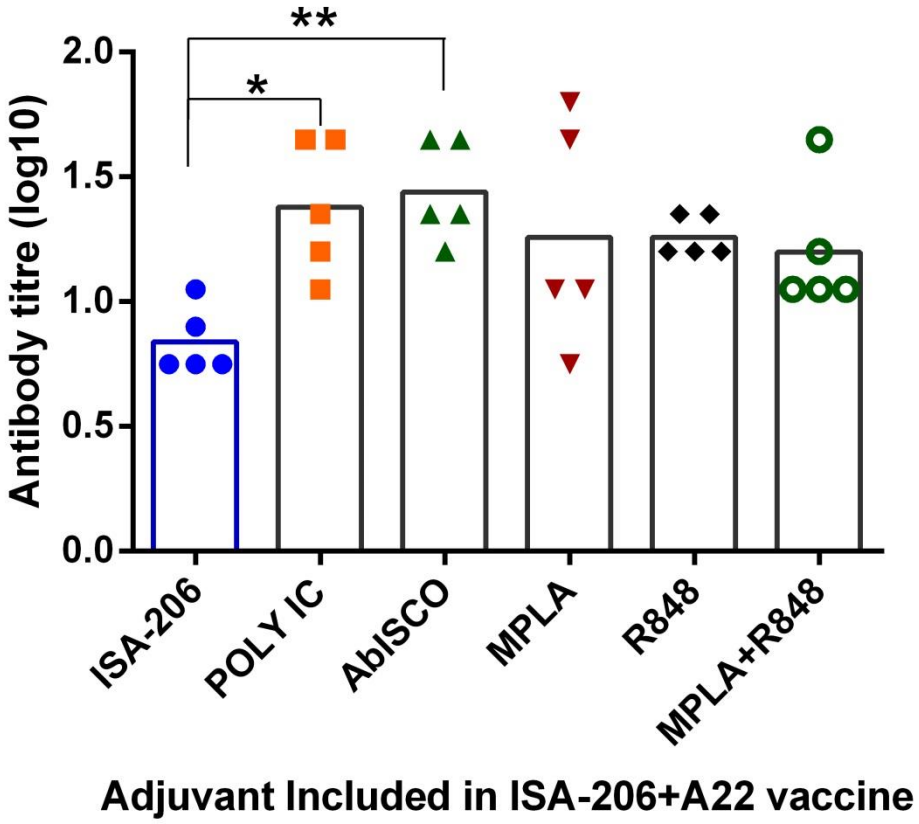


FACS analysis- IFN-γ from CD4+ and CD8+ cells





Poly (I:C) and AbISCO had significantly increased neutralizing antibodies on 28dpv compared to the ISA-206 control group



Summary-1

- Achieved an increased potency as indicated by

lack of clinical symptoms in Poly I:C and AbISCO groups (although not able to prevent sub-clinical infection)

- Significantly elevated neutralizing antibodies in Abisco and Poly I:C group cattle

- Some indication of IFN-g upregulation by $CD4^+$ and $CD8^+$ cells

Longer duration of immunity study

ISA 206 + Poly I:C 11 cattle

ISA 206 11 cattle

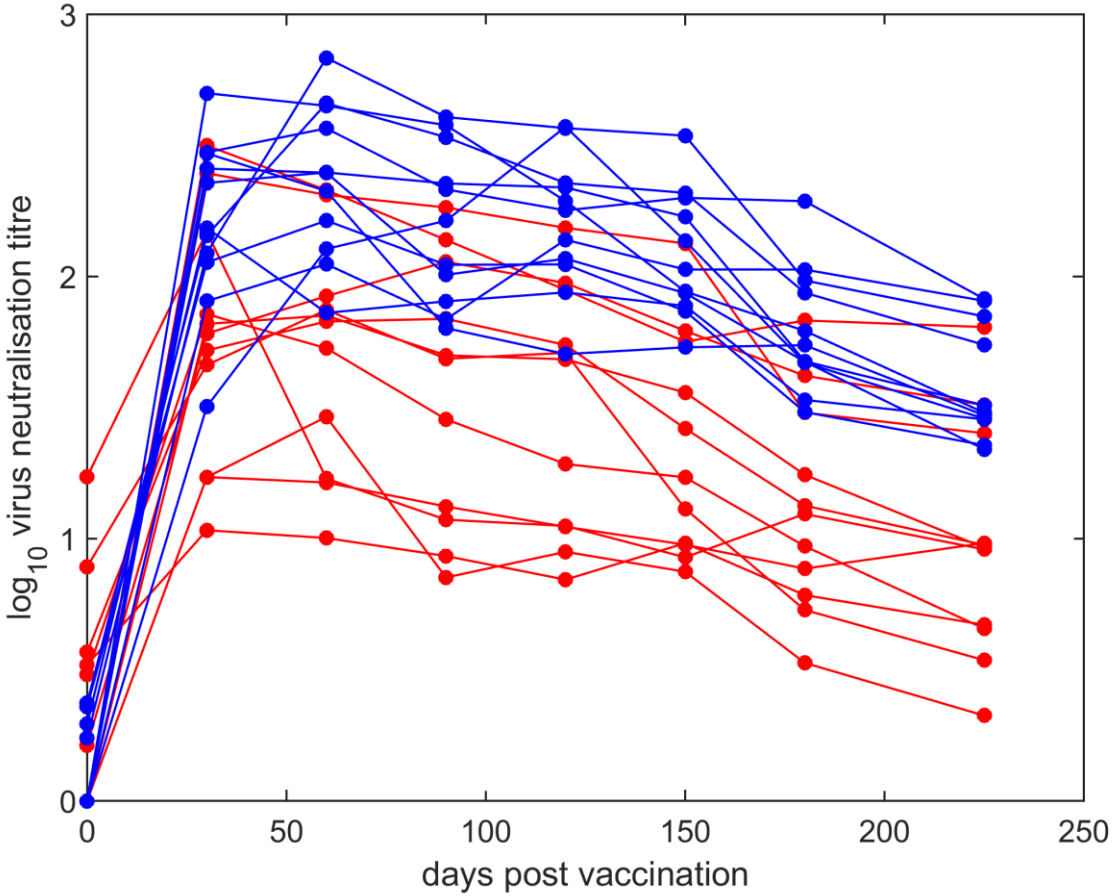
Type O antigen full dose- 10 microgram

Vaccinated cattle were monitored for 225 days (7.5 months) at Indian Immunologicals

Serum, PBMC and antigen specfic stimulated whole blood plasma were transported to Pirbright for analysis

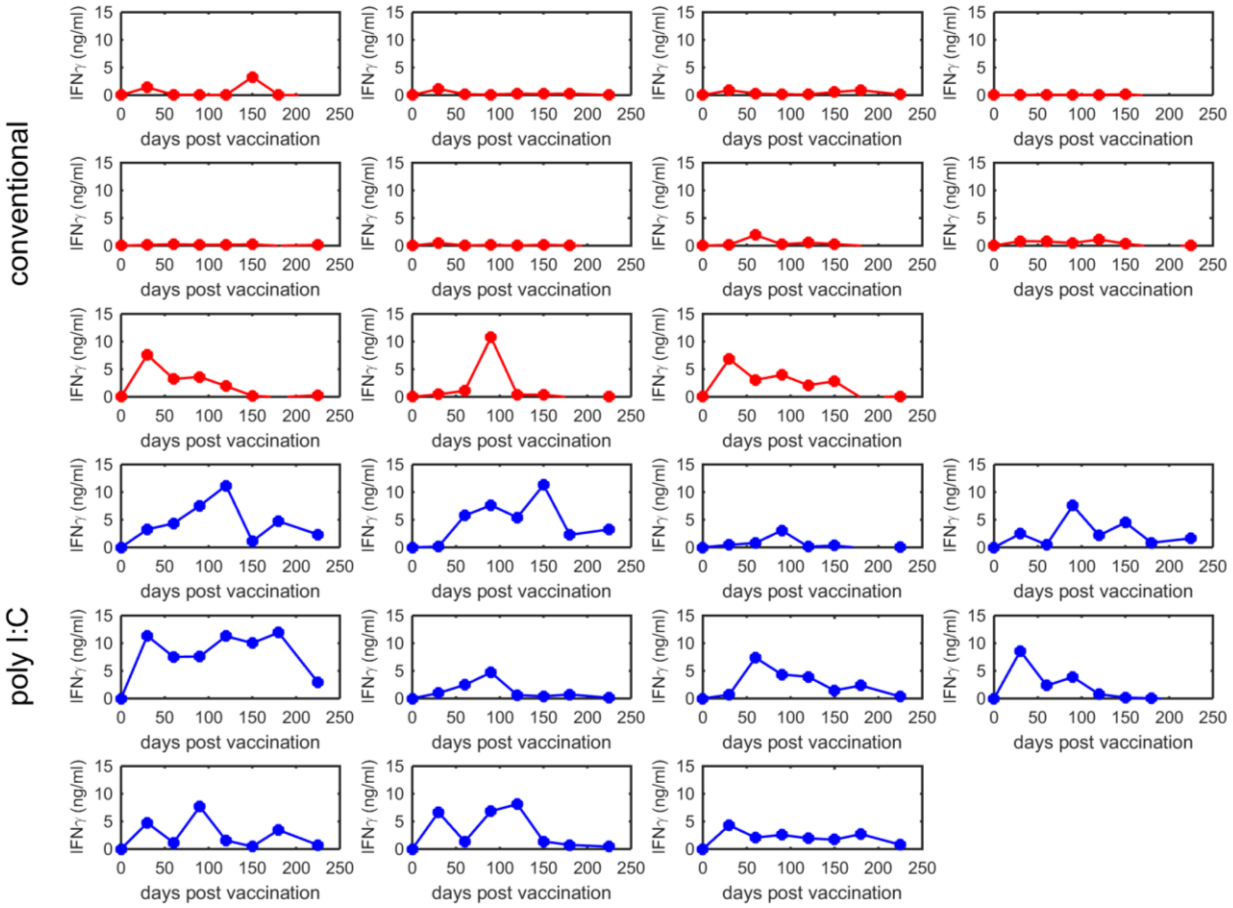
Virus neutralisation titres

- Titres significantly higher in cattle when vaccinated with poly I:C (blue) compared with conventional adjuvant (red)

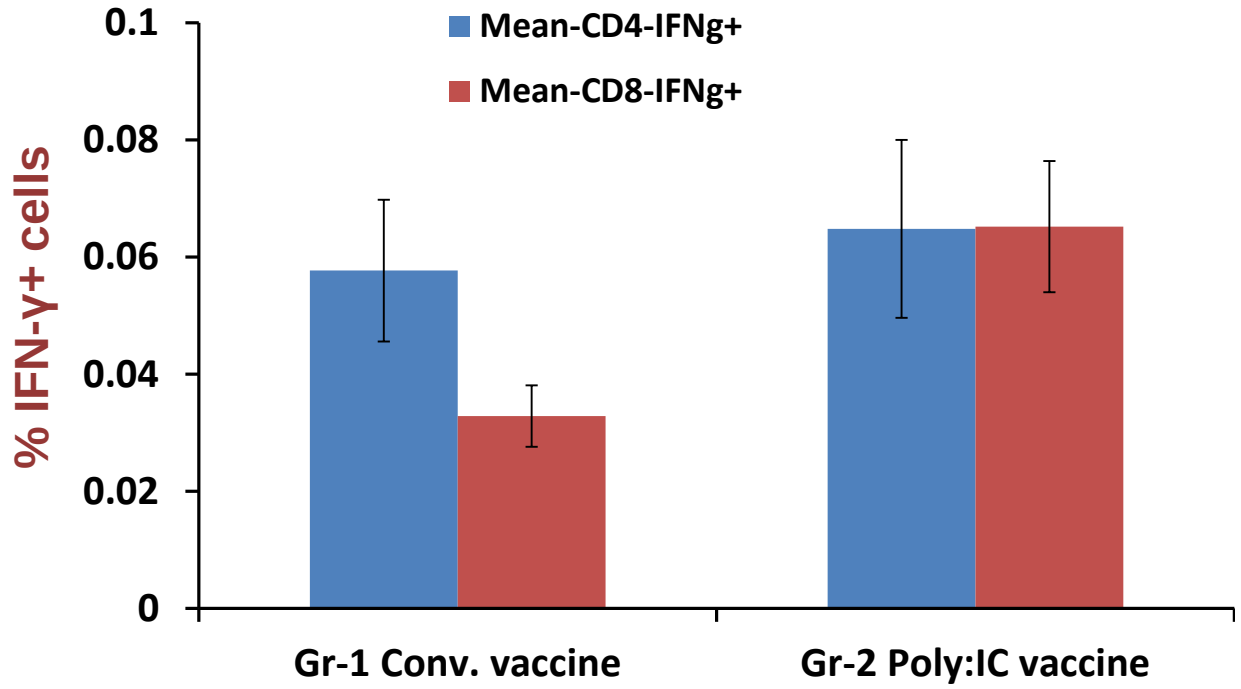


Whole blood Interferon-γ

- Significantly higher levels in cattle when vaccinated with poly I:C (blue) compared with conventional adjuvant (red)



IFN-γ production -flow cytometry on 120 dpv



% of CD4 or CD8 cells from the total live population showing antigen specific IFNγ expression

Summary-2

- Significantly higher VN titre in cattle vaccinated with poly I:C compared with conventional adjuvant
- By 4th month many of the conventional vaccinated animals lost the protective level of antibody titre

- IFNγ levels significantly higher in cattle when vaccinated with poly I:C when compared with conventional adjuvant

- Indication of IFN-gamma upregulation

  by $CD4^+$ and $CD8^+$ cells were observed in Poly I:C group in FACS analysis.

- Duration of immunity can be enhanced up to 6 months post-vaccination that covers the window of susceptibility before 2^{nd} vaccination

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