



Global Foot-and-Mouth Disease Research Alliance

Scientific Meeting

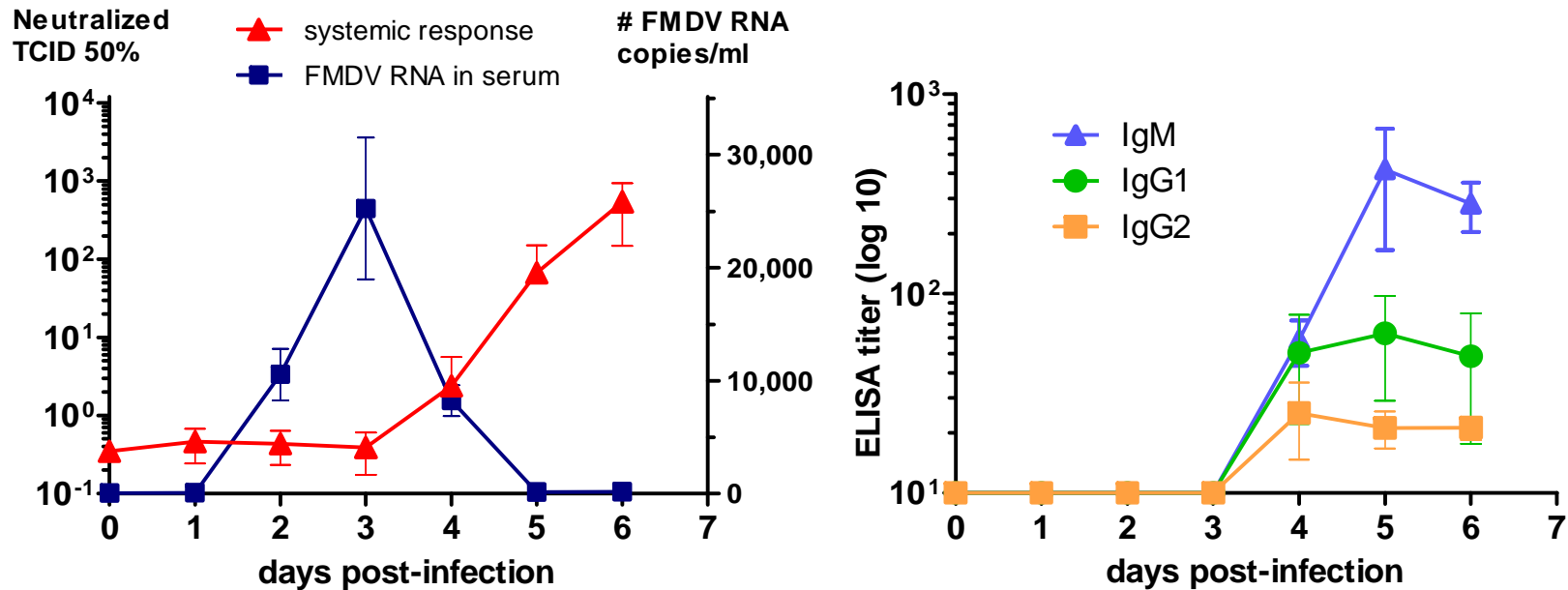
In Incheon, Korea 25-27 October 2017

Systemic Antibodies Administered by Passive Immunization Prevent Generalization of The Infection by Foot-and-Mouth Disease Virus in Cattle After Oronasal Challenge

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Adaptive responses in naive cattle after oronasal challenge

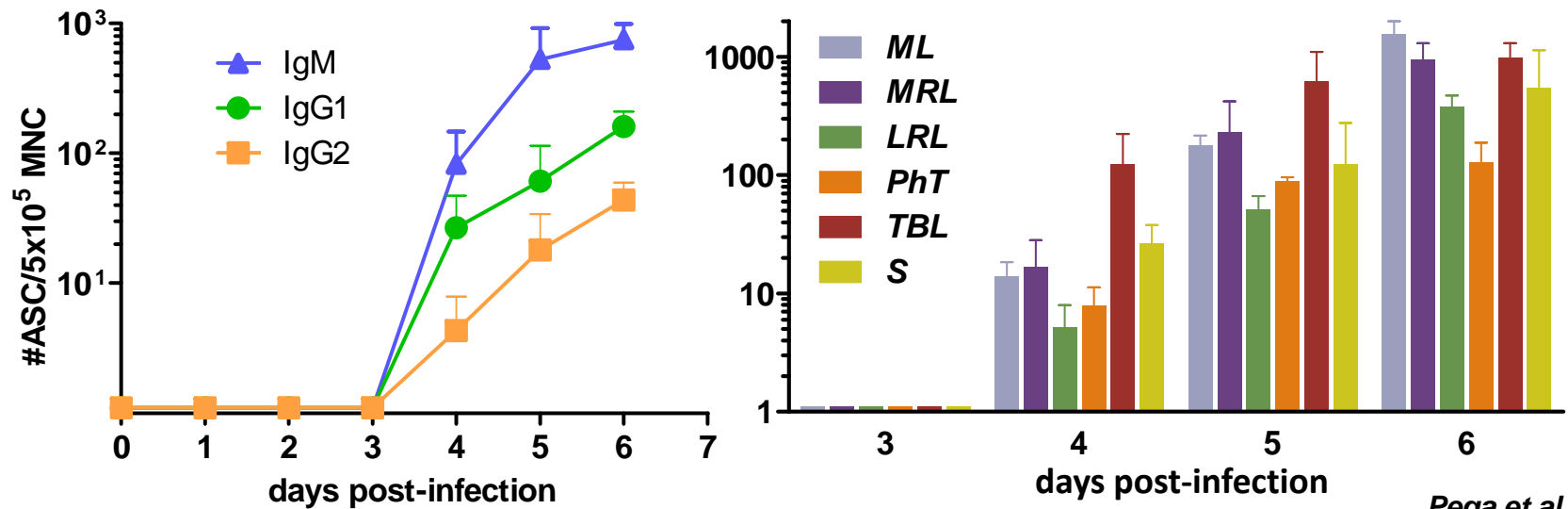


Pega et al. J Virol (2013)
87: 2489–2495

- Systemic antibody responses start at 4 dpi and clear viremia by 5 dpi
- Clearance of viremia is carried out by anti-FMDV IgM antibodies

Adaptive responses in naive cattle after oronasal challenge

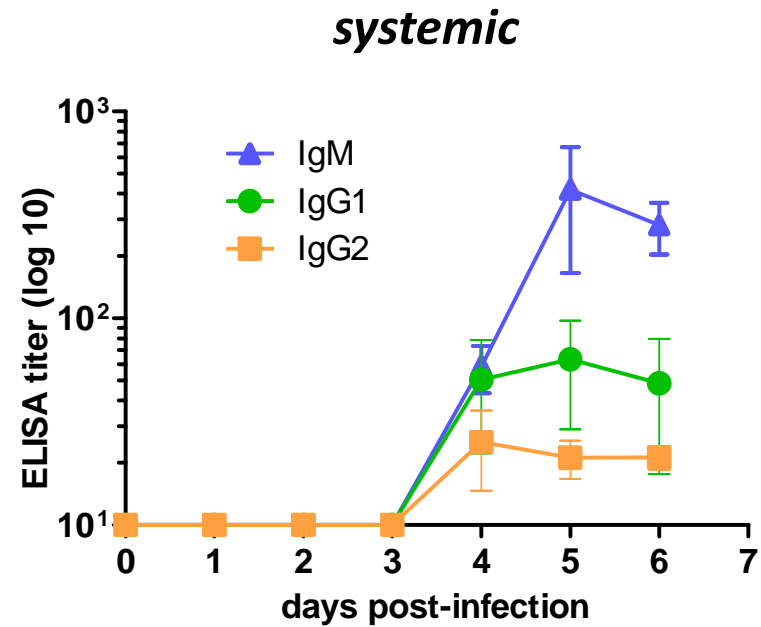
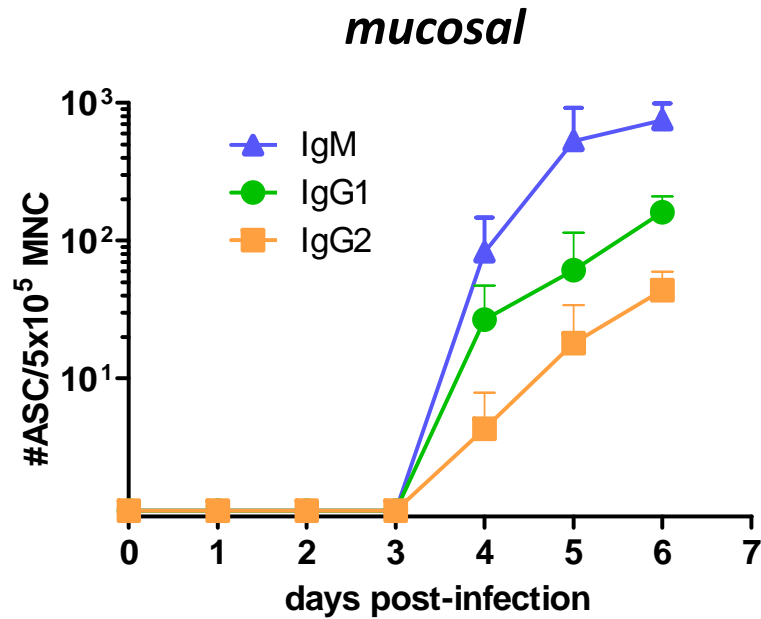
Mucosal responses



Pega et al. J Virol (2013)
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- Oronasal infection induces a genuine local antibody response starting at 4 dpi
- LN stimulation along the respiratory tract corresponds with virus replication

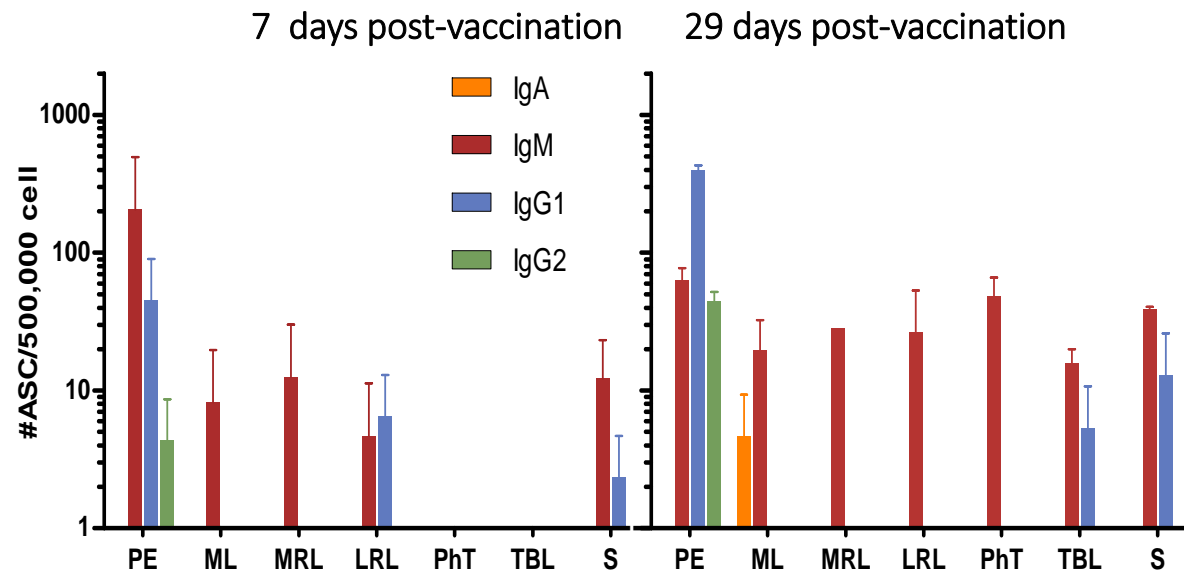
Adaptive responses in naive cattle after oronasal challenge



*Pega et al. J Virol (2013)
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- Local antibody responses show similar isotype and kinetics patterns as systemic responses

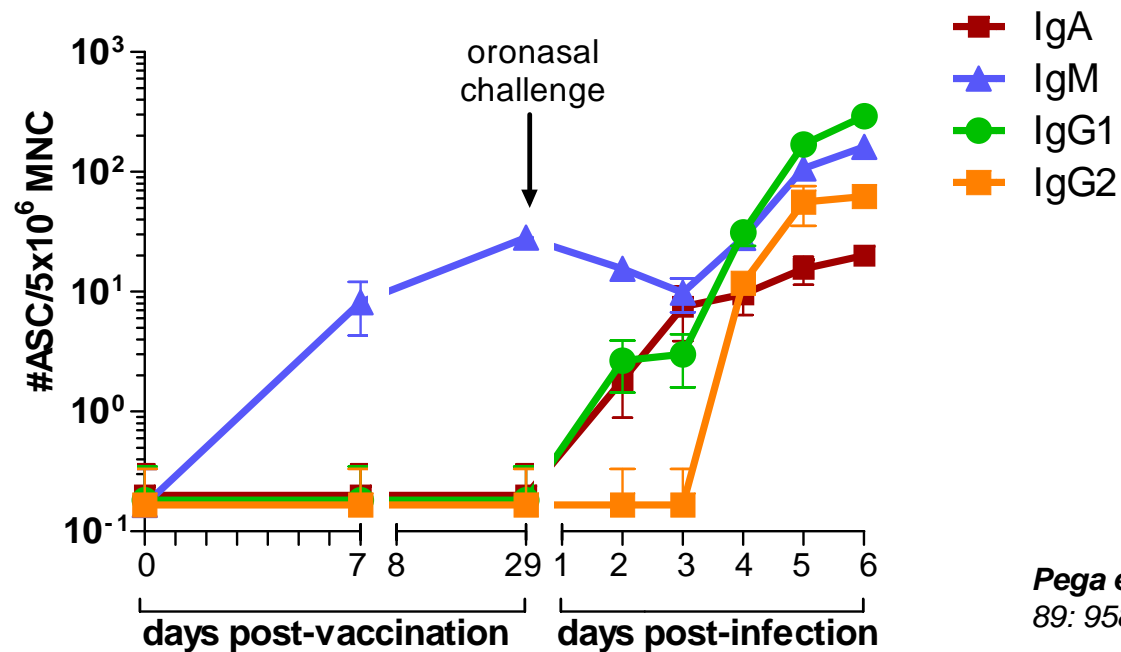
Adaptive responses in vaccinated cattle



*Pega et al. J Virol (2015)
89: 9581–9590*

- Systemic vaccination promotes the presence of FMDV-specific ASC (mostly IgM isotype) in lymphoid tissues along the respiratory tract

Adaptive responses in vaccinated cattle after oronasal challenge

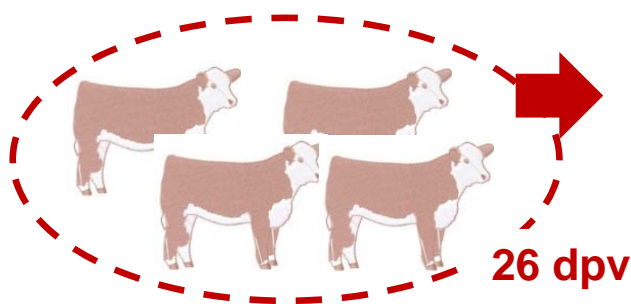
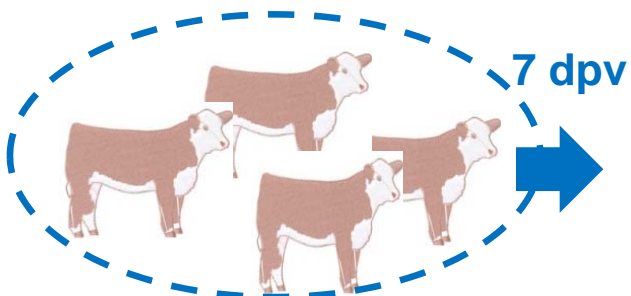


*Pega et al. J Virol (2015)
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- Oronasal challenge in vaccinated cattle (29 dpv) induces local secondary responses from 2 dpi (rapid isotype switch & increase in magnitude)

Oronasal challenge in cattle carrying only systemic antibodies

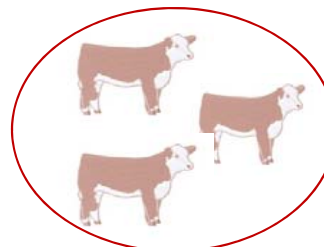
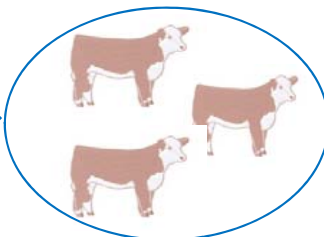
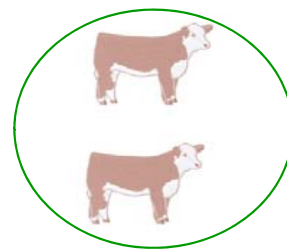
Adult naïve cattle (n=8) vaccinated with a high potency monovalent FMD vaccine (22 µg/dose O1Campos)



Vaccination (IM)

passive transference of immune serum pools to naïve steers

naïve

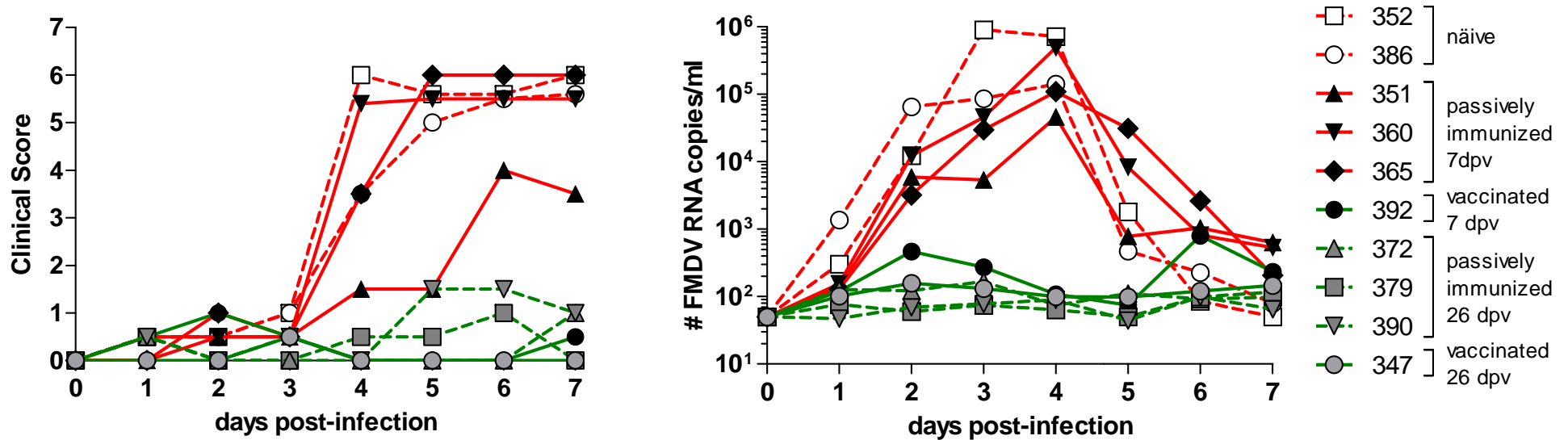


Oronasal Infection

VFA O1C 10^7 SMLD_{50%}

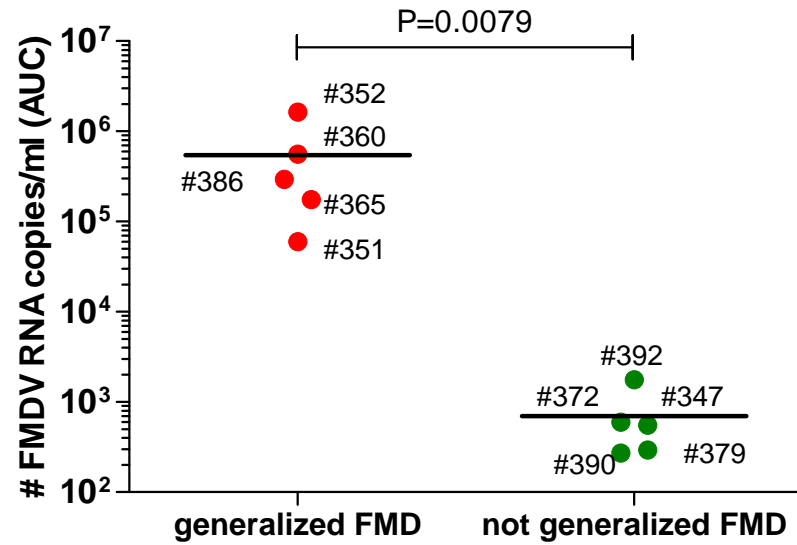
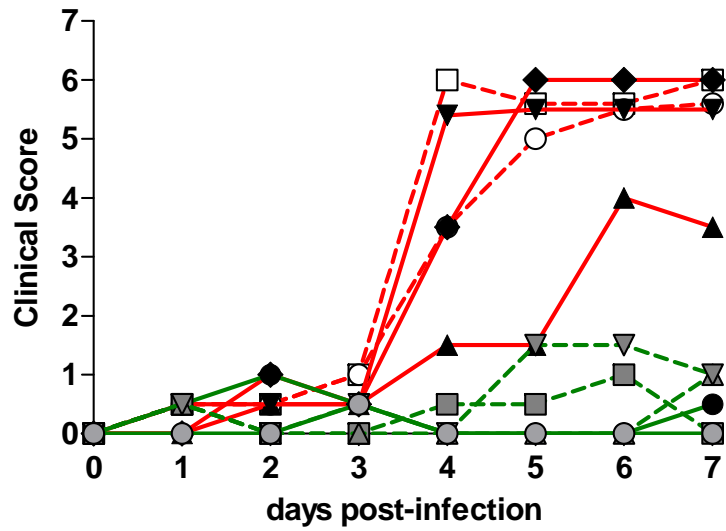
- ✓ Daily monitoring for FMD symptoms
- ✓ Daily blood and serum sampling
- ✓ Tracheobronchial (TBL) and medial retropharyngeal lymph nodes (MRL) taken at 7 dpi for ASC detection by ELISpot

Clinical scores and viremia



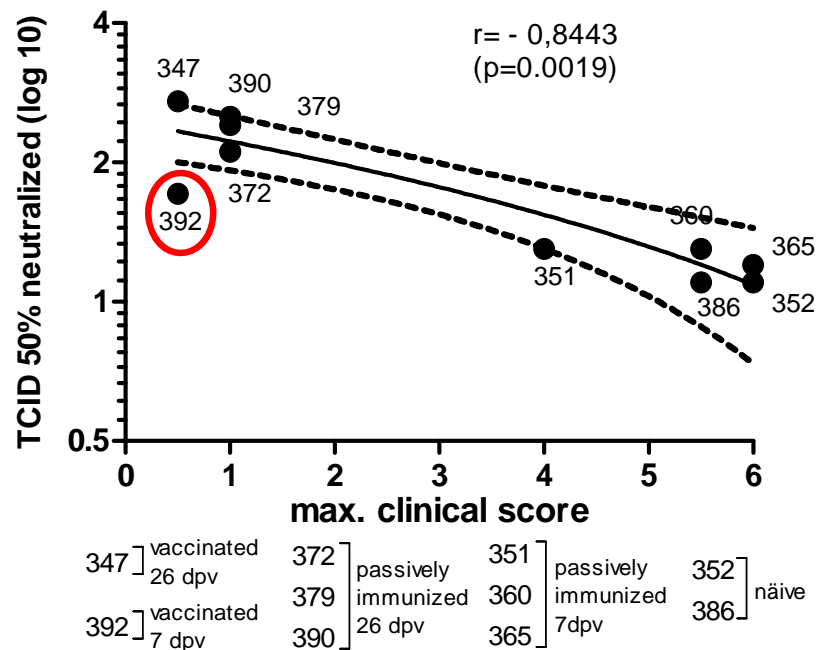
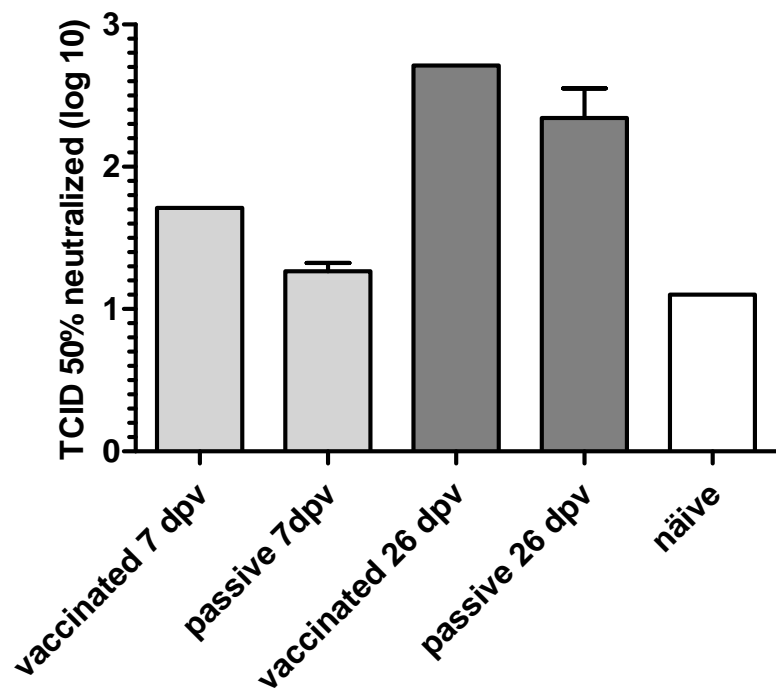
- Naïve steers and those passively immunized with the 7-dpv serum pool showed generalized FMD symptoms
- Vaccinated steers and those passively immunized with the 26-dpv serum pool did not developed FMD

Clinical scores and viremia



- Severity of the clinical signs correlates with the magnitude of the viremia

Clinical scores and pre-existing Nab

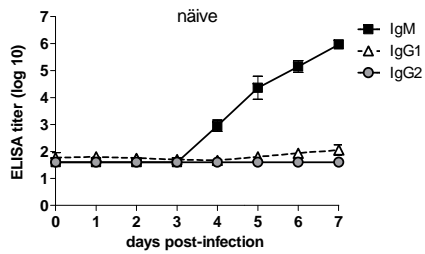


- We also found a significant inverse association between the clinical score and the level of systemic NAb prior oronasal challenge

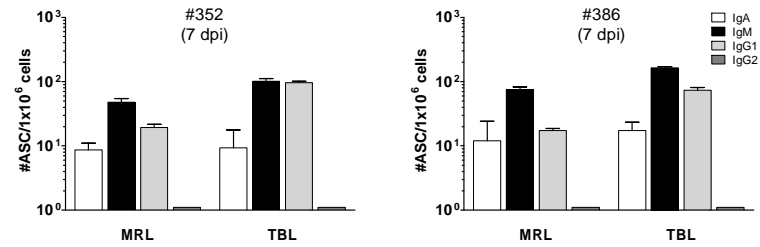
FMDV-specific antibody responses after oronasal infection

näive

systemic immunity

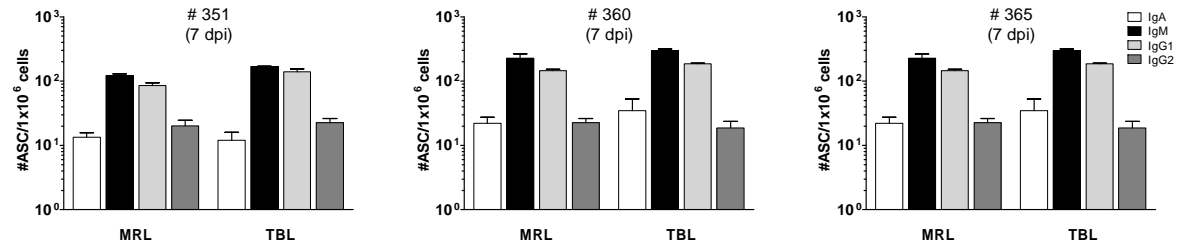
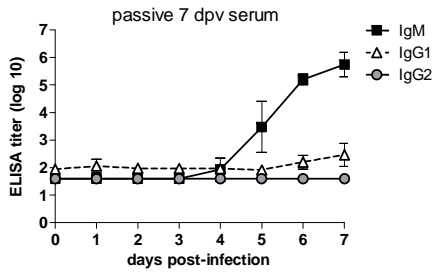


mucosal immunity (at 7 dpi)

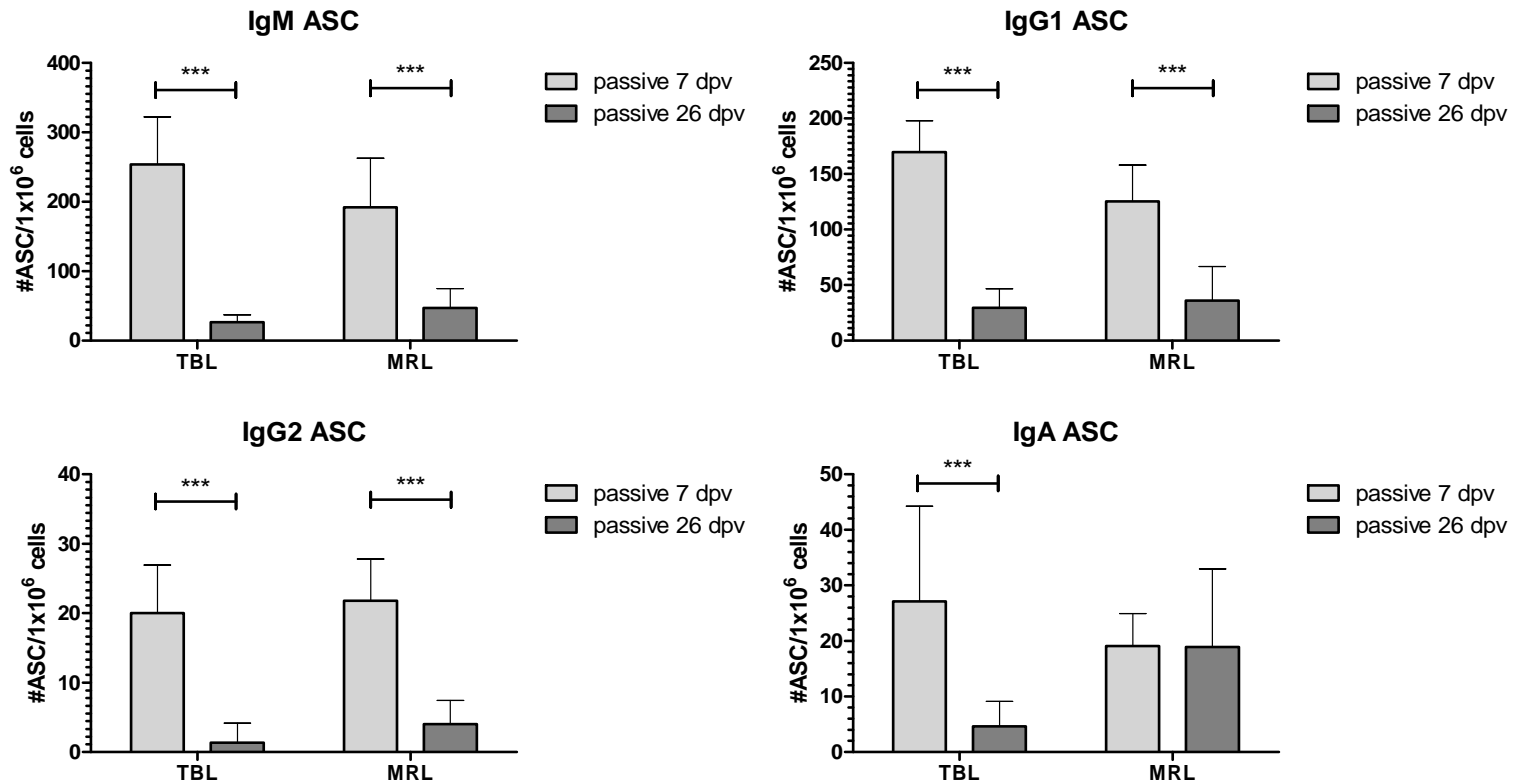


passively immunized

passive 7 dpv serum

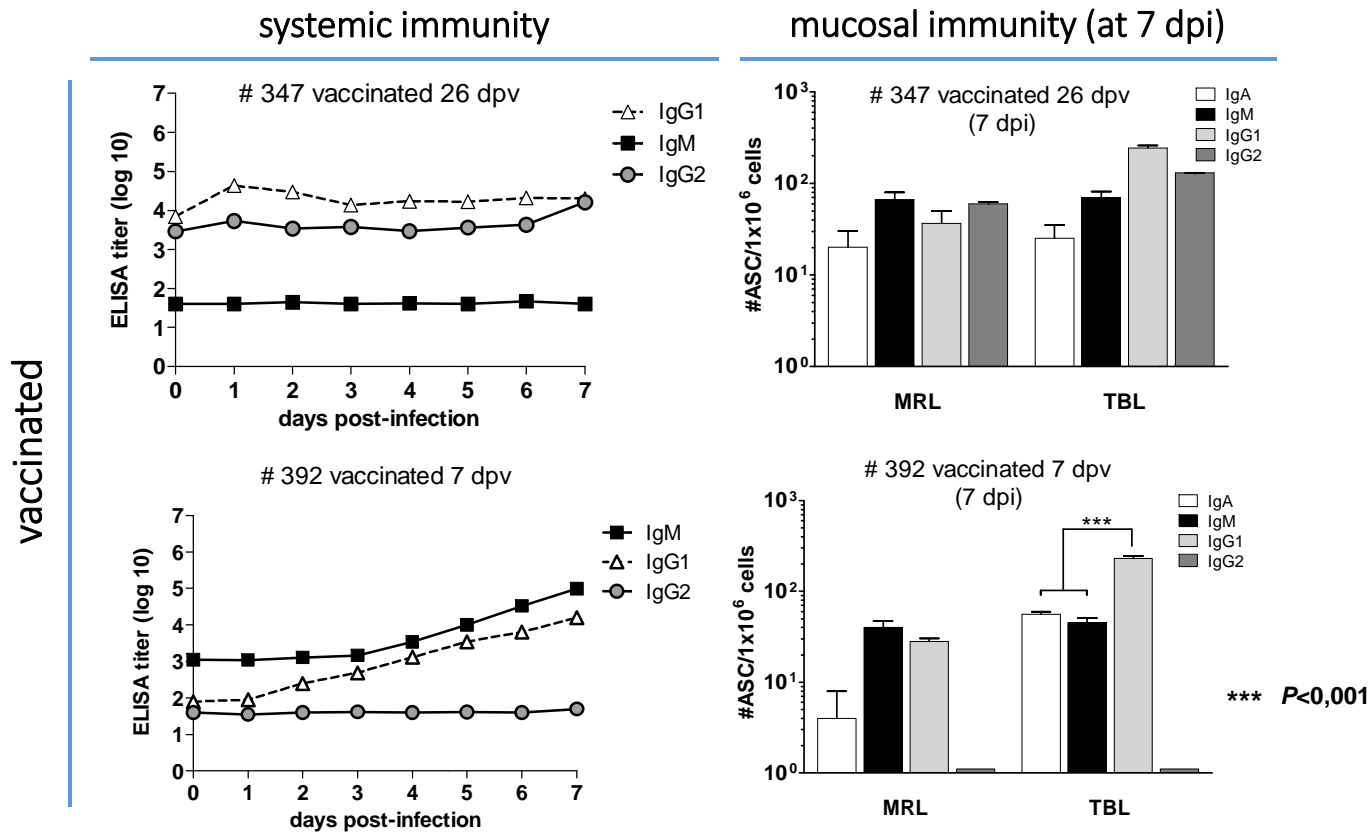


Pre-existing Ab in passively immunized cattle reduce the development of local adaptive responses against FMDV



*** $P < 0,001$

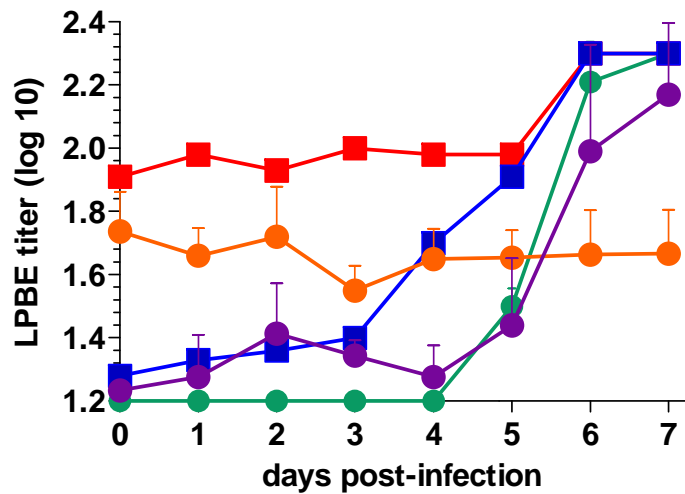
FMDV-specific antibody responses after oronasal infection



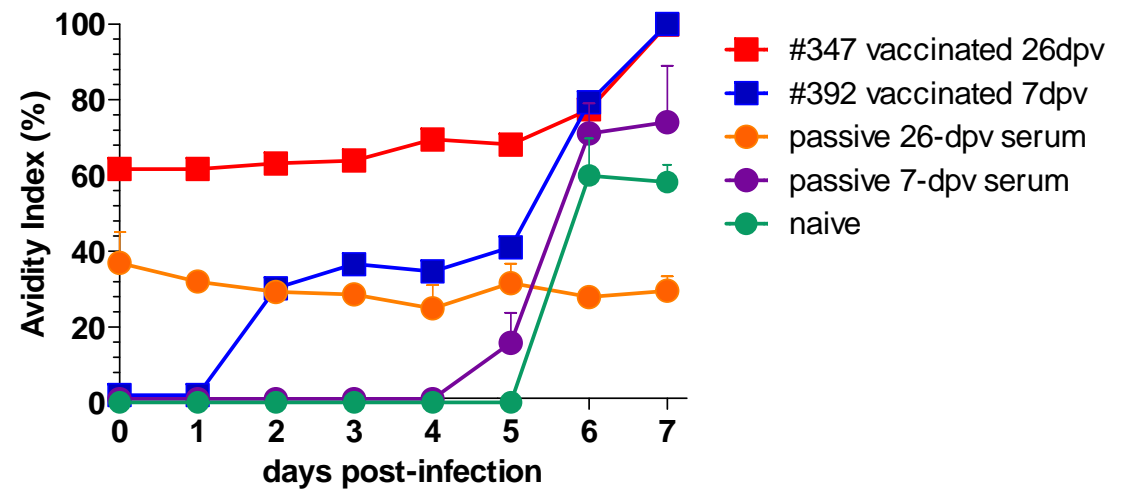
- aerogenous infection at 7 dpv prompted a rapid increment in IgG1 titers at systemic level (after 1 dpi) and predominant numbers of IgG1 ASC at the TBL (at 7 dpi)

FMDV-specific antibody responses after oronasal infection

Total anti-FMDV systemic antibodies



Avidity of systemic antibodies



- aerogenous infection at 7 dpv increased the avidity of systemic antibodies (after 1 dpi) and total Ab titers (after 3 dpi)

CONCLUSIONS

- The outcome of the experimental infection, at least in the passively immunized steers, is basically related to the level of circulating FMDV-neutralizing Ab prior aerosol challenge
- Circulating antibodies in sufficient titers will restrain the dissemination of the virus after primary replication, irrespectively of the infection portal
- Pre-existing systemic antibodies are able to rapidly associate with the FMDV entering through aerogenous route, interfering with its replication in the respiratory system and decreasing its availability to act as stimulating antigen for FMDV-adaptive responses
- Oronasal challenge triggered a booster reaction only in primary vaccinated steers even at 7 dpv. These responses were characterized by a rapid isotype switch to IgG1 at both systemic and local levels, increased titers of total Ab and a marked enhance of the avidity in circulating Ab

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