

Maternal antibodies do not inhibit swine influenza virus multiplication in piglets but reduce excreted virus infectivity and impair post-infectious immune responses

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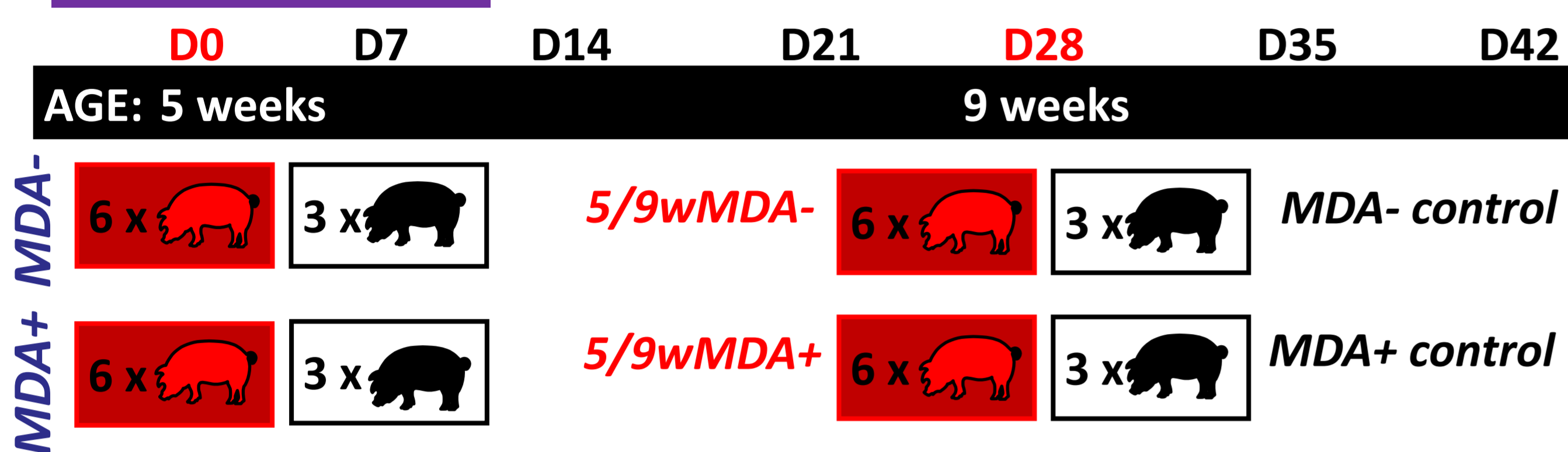
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Maternally-derived antibodies (MDA) reduce piglets' susceptibility to swine influenza A virus, but they favor the persistence of the virus in swine production units by extending the duration of spread within the population. Furthermore, a strong MDA interference with post-infectious immune responses was evidenced, raising questions about protection after passive immunity waning. To evaluate the dose-dependent effect of MDA during passive immunity decay, we studied the impact of residual MDA on virus excretion and immune responses in piglets infected at 5, 7 or 11 weeks of age. Subsequent protection towards a second homologous infection occurring 4 weeks after the primo-infection was also investigated.

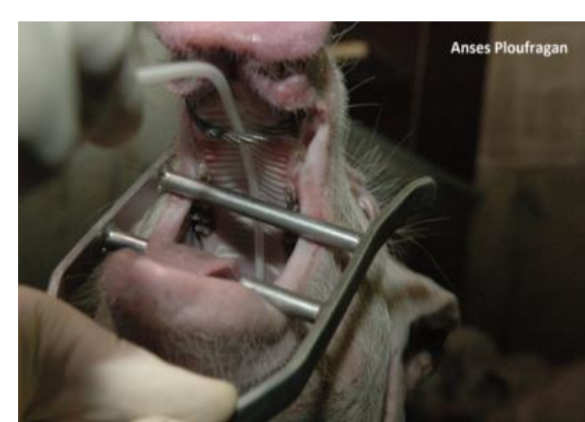
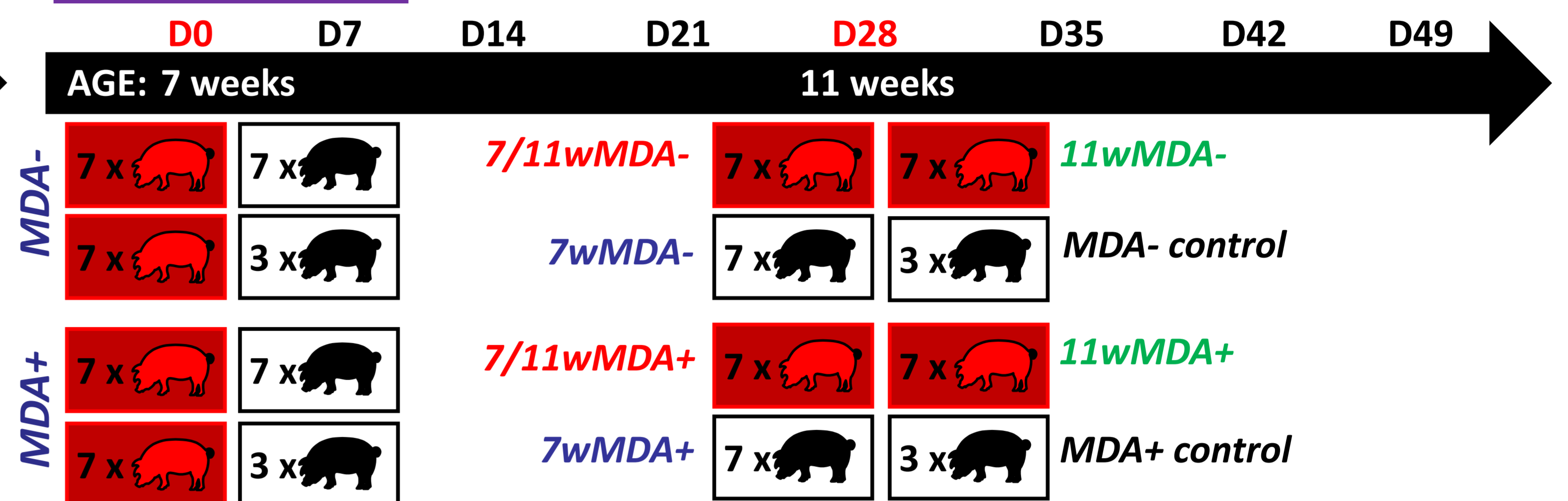
EXPERIMENTAL DESIGN

MDA- and MDA+ piglets born to unvaccinated or vaccinated sows. Primo-infections at 5, 7 or 11 weeks of age > MDA+ piglets with different MDA levels.

Experiment 1 (E1)



Experiment 2 (E2)



intra-tracheal inoculations:
 H1N1 virus (10^5 TCID₅₀ / 5 ml / pig)
 MEM (5ml / pig)

Daily evaluation of clinical signs - nasal swabs and blood samples regularly collected for evaluation of virus excretion and immunological responses, respectively

RESULTS

Clinical signs

	5 weeks	7 weeks	11 weeks
% of pigs showing clinical signs (hyperthermia ± weight loss) after a primo-infection	100 %	29 %	86 %
	MDA-		
	0 %	36 %	100 %
	MDA+		

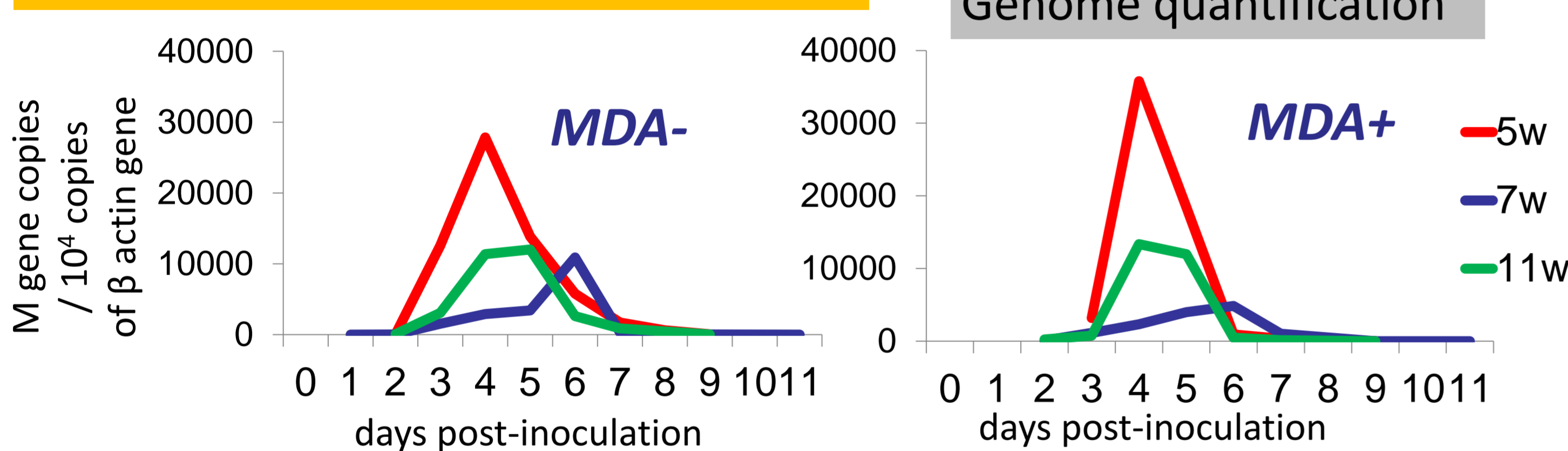
> Impact of age on flu severity

> Impact of MDA level on flu severity

No clinical signs in MDA- and MDA+ animals after the second homologous infection

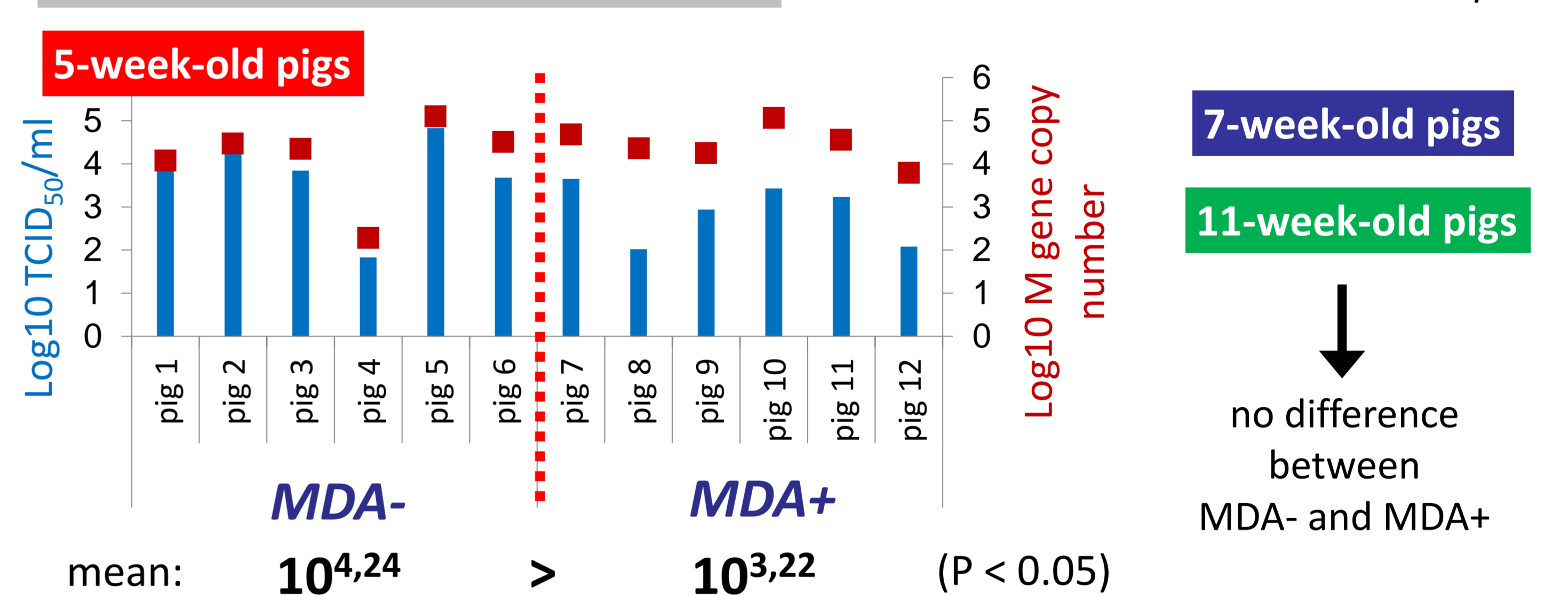
> Establishment of protection after the 1st infection

Virus excretion after primo-infection



- > Younger animals shed more virus than others
- > Excretion peak delayed for 7w animals – lower AUC
- > No impact of MDA on the shedding profiles whatever the age

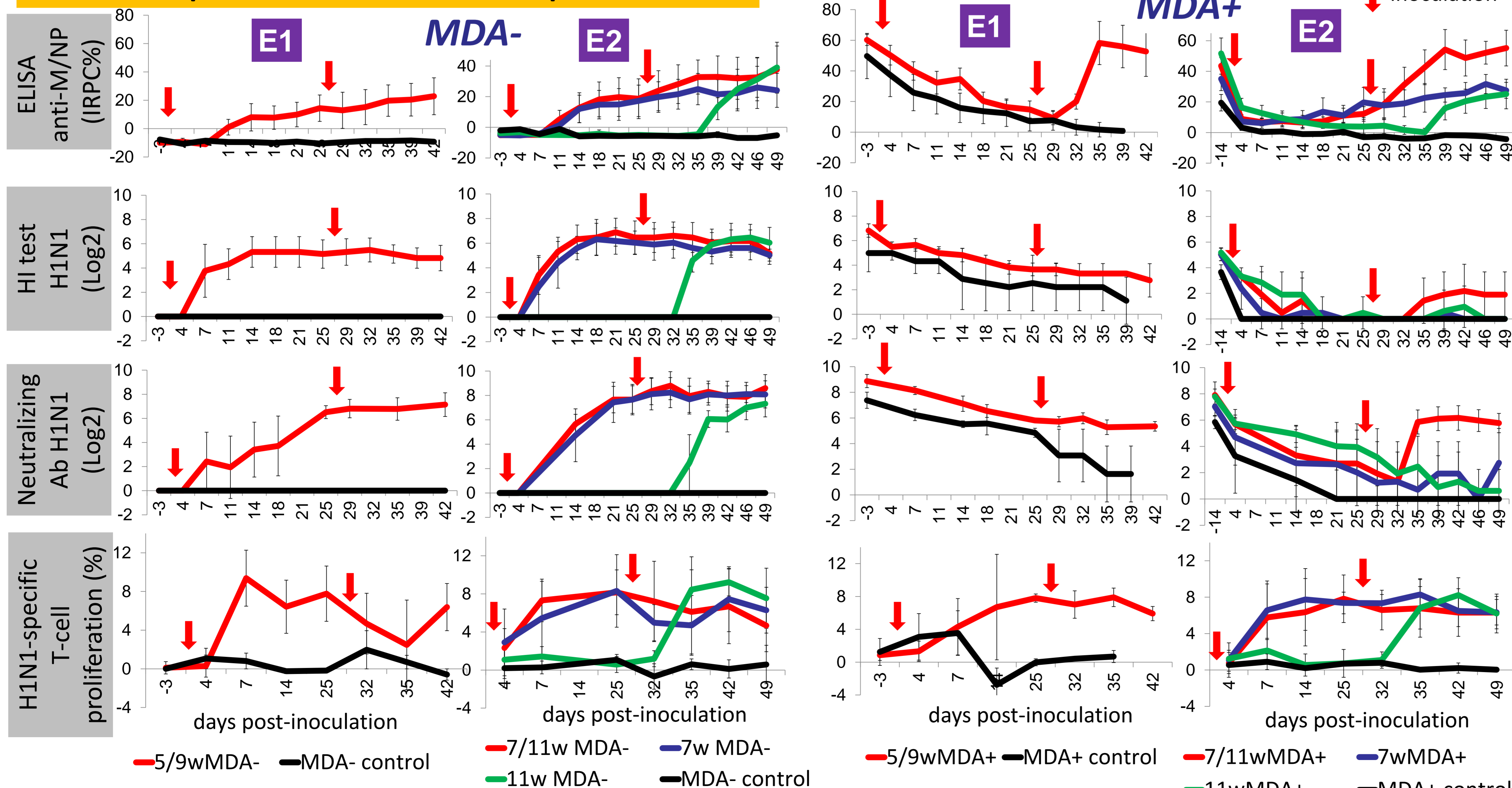
Infectious potential of excreted virus Individual virus titration at excretion peak



> MDA+ 5w piglets excreted less infectious particles than MDA-

No virus excretion after second infection

Humoral response in sera and T-cell response in PBMC



MDA- > Similar Ab profiles in all groups whatever the diagnostic tests / No impact of 2nd infection

> Maximum level of T-cell proliferation from 7 dpi whatever the age / No impact of 2nd infection

MDA+ > Anti-M/NP Ab production inhibited, delayed and normal in pigs infected at 5, 7 and 11w, respectively. No anti-HA or neutralizing Ab whatever the age / 2nd inf. : boost of anti-M/NP responses whatever the MDA level, boost of anti-HA and neutralizing responses in 7/11w but not 5/9w

> T-cell response slightly delayed in animals with high MDA levels (5/9wMDA+) / No impact of 2nd infection

Pigs' responses to H1N1 were impacted by the age at infection, i.e. the physiological development, whatever the immunological status.

MDA conferred clinical protection in a dose-dependent manner but did not prevent virus replication. Moreover, only high MDA levels slightly neutralized neo-formed virus particles. Post-infectious humoral responses were more or less inhibited depending on the accessibility of the target antigen and the MDA levels. However, adaptive immunity was efficient enough to induce immune memory and confer protection against a second homologous infection, at least during 4 weeks after primo-infection.