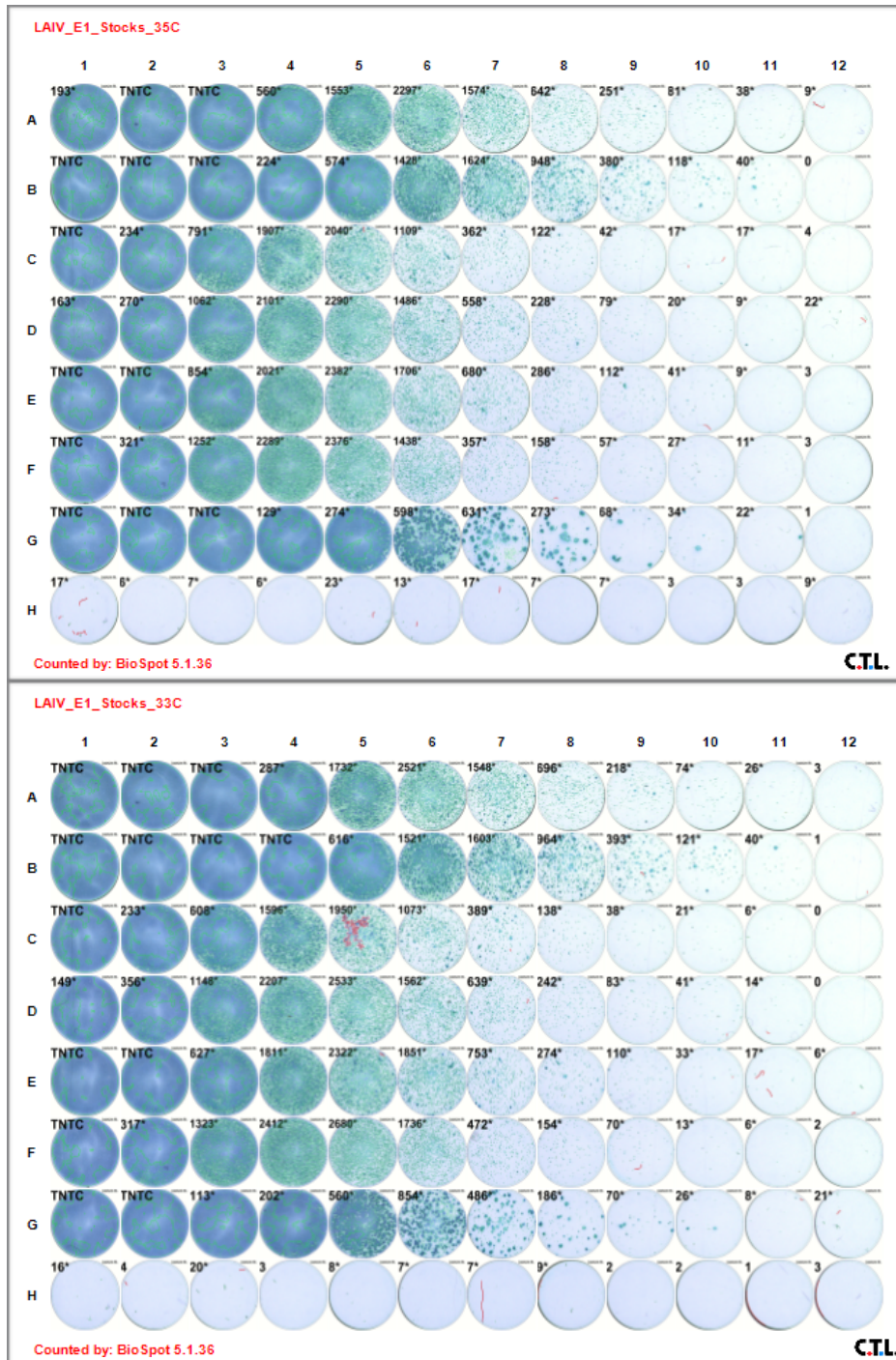


Sup.Table 1. Ferrets excluded from the immune response analysis in FER-16-09 trial

Ferret #	LAIV virus	Post-LAIV				Challenge virus	Post-Challenge			
		vRNA NFW	Virus Spot NFW	Clinics	HAI serum titre to the vaccine stain		vRNA NFW	VirusSpot NFW	Clinics	HAI serum titre to the challenge virus
F3856	SW 6:2	neg	neg	-	5	HK w/t	neg	neg	-	5
F3859	TX 5:3	neg	neg	-	5	HK w/t	neg	neg	-	5
F3865	Mock	na	na	na	5	HK w/t	ct>30	-	-	5

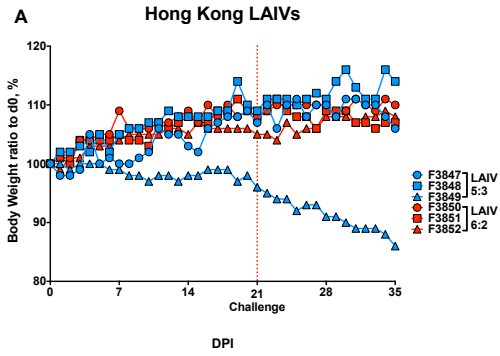
Sup.Table 2. Ferrets with clinical signs of illness after LAIV inoculation in study FER-16-09

Ferret #	Sex	Chorulon Treatment	LAIV virus	Post-LAIV					Challenge virus	Post-Challenge				
				vRNA NFW	VirusSpot NFW	weight loss, %	temp rises (>2 °C)	HAI serum titre to the vaccine stain		vRNA NFW	VirusSpot NFW	weight loss, %	temp rises (>2 °C)	HAI serum titre to the challenge virus
F3849	Female	No	HK 6:2	Pos	Pos	3 %	-	640	HK w/t	Neg	Neg	14 %	-	640
F3857	Female	No	SW 6:2	Pos	Pos	18 %	On day 5	80	HK w/t	Neg	Neg	8 %	-	80
F3859	Female	No	TX 5:3	Neg	Neg	4 %	-	5	HK w/t	Neg	Neg	8 %	-	5

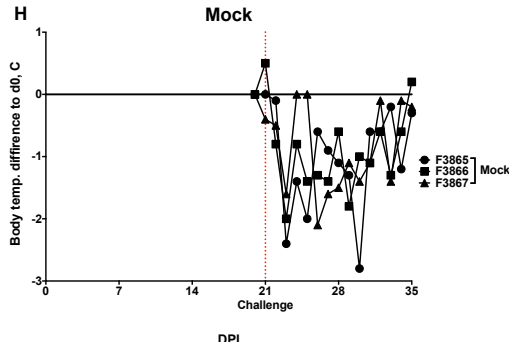
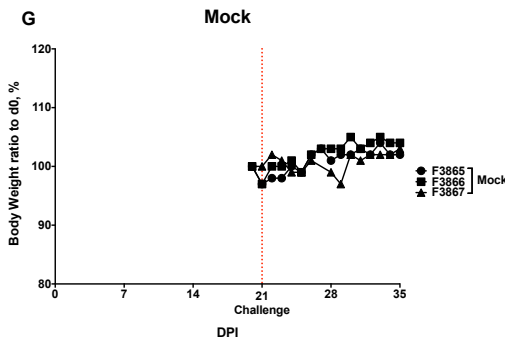
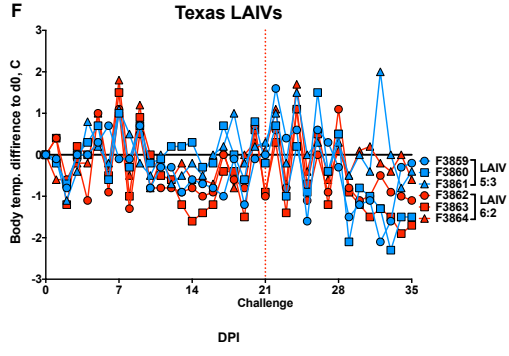
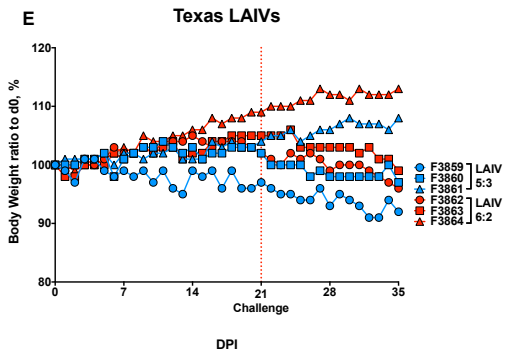
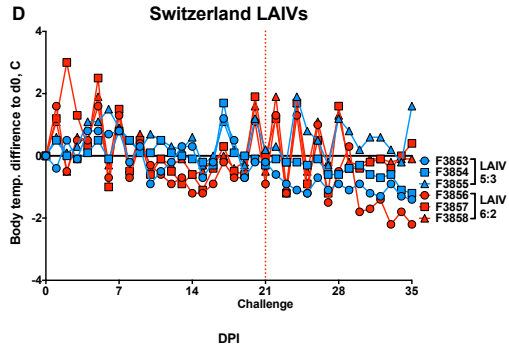
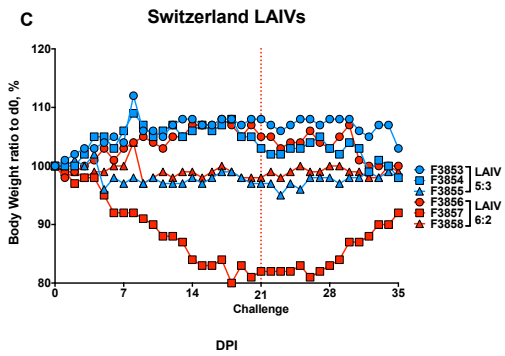
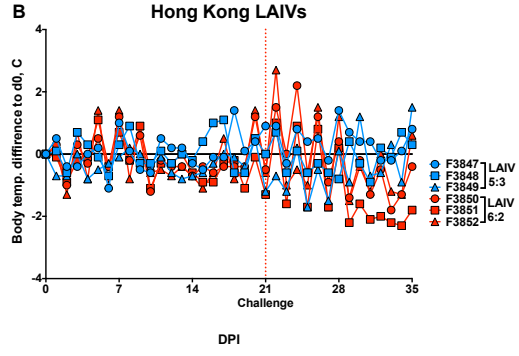


Supplementary Figure 1. Virospot analysis of viral stocks growing activity at 35°C (upper panel) and 33°C (lower panel). Each row represent virus stock half-log dilutions from -1 to -6 Log₁₀ (columns 1-11): A - TX LAIV 5:3, B - TX LAIV 6:2, C - SW LAIV 5:3, D - SW LAIV 6:2, E - HK LAIV 5:3, F - HK LAIV 6:2 and G - HK/14 (wild type virus).

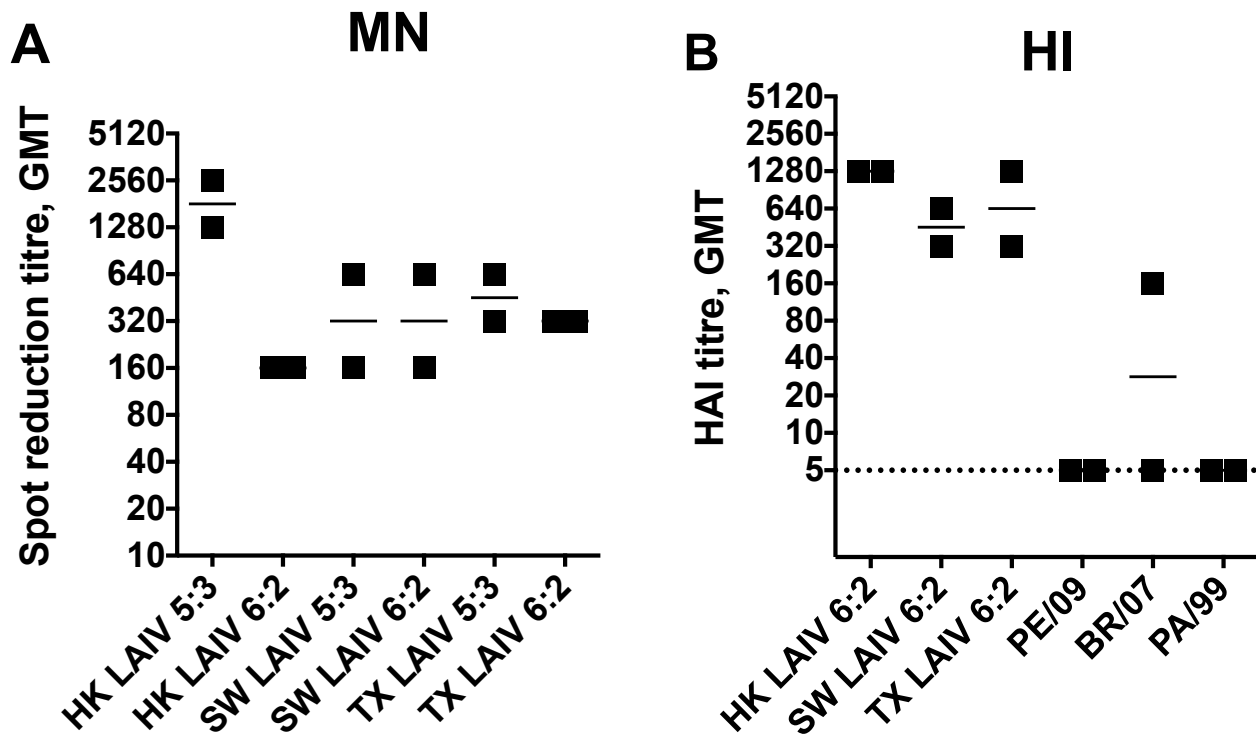
Ferret body weight changes



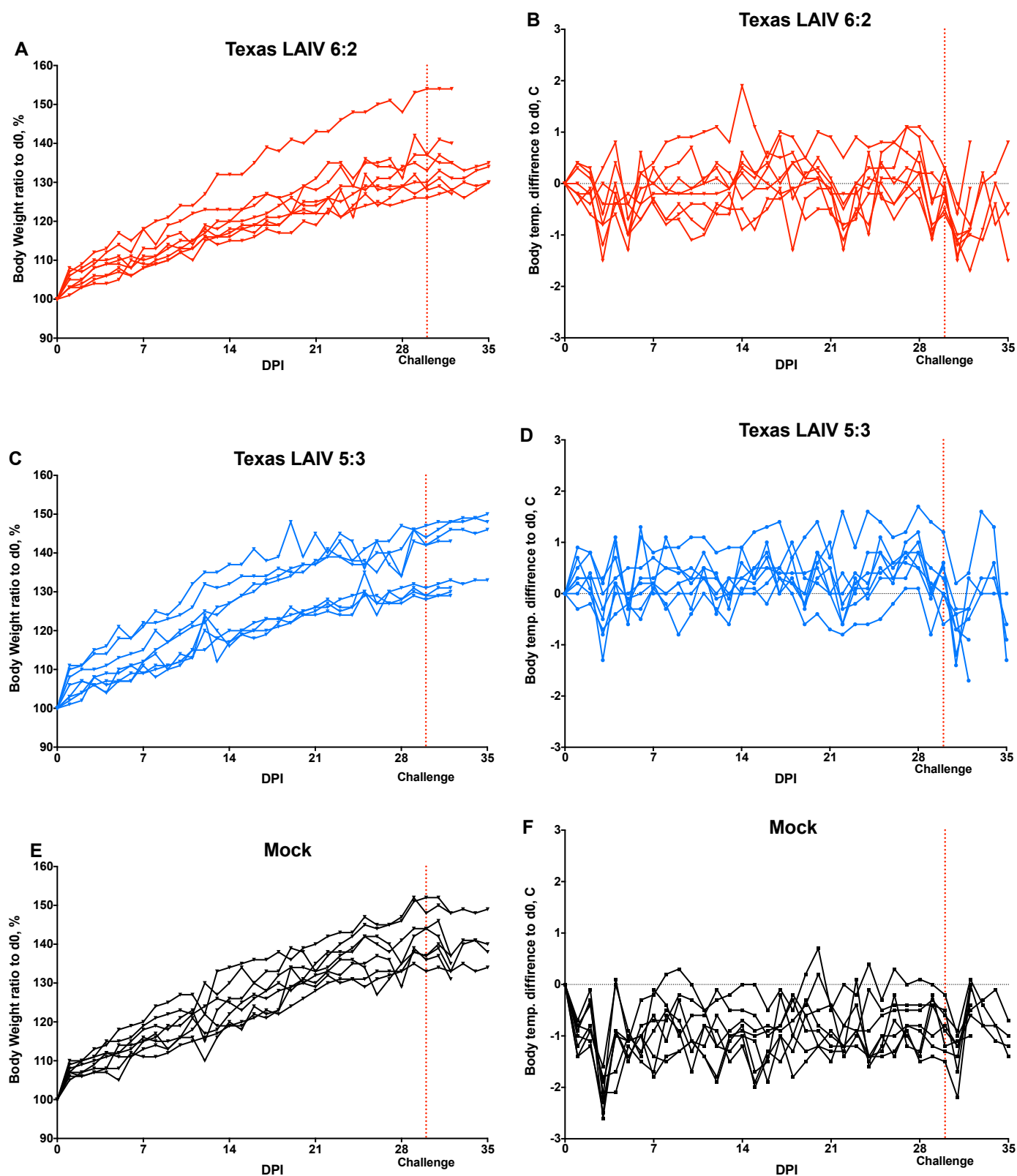
Ferret body temperature changes



Supplementary figure 2. Ferret body weight and temperature dynamics in experiment FER-16-09. Animals received intranasally 10^5 EID₅₀/500 uL of either LAIVs. 21 days after LAIV administration, animal were challenged with 10^3 TCID₅₀ in 500uL of A/Hong Kong/4801/2014 (H3N2) virus (vertical red dotted line). Body weight ratio and body temperature difference to 0 DPI were monitored daily for groups inoculated with HK LAIVs (A and B), SW LAIVs (C and D), TX LAIVs (E and F) and Mock-inoculated groups (G and H). LAIVs 5:3, LAIVs 6:2 and Mock data are visualized in blue, red and black colors respectively.



Supplementary figure 3. Virus-neutralizing (A) and HI antibody (B) titers in post-challenge serum samples from the Mock-immunized group in study FER-16-09. Mock-immunized ferrets were intranasally challenged with 10^3 TCID₅₀ in 500uL A/Hong Kong/4801/2014 (H3N2) virus. After 14 days of the challenge serum samples were collected. Serum samples from ferret F3865 (Mock) were excluded from analysis. All Pre-LAIVs serum samples (14 days before vaccination) were negative. Dotted line denotes assay limit of detection.



Supplementary figure 4. Ferret body weight and temperature dynamics in study FER-17-01. Four groups of 8 ferrets each were inoculated intranasally on day 0 with 10^7 EID₅₀ in 500 uL of TX LAIVs or Mock (PBS). After 30 days, A/Brisbane/10/2007 (H3N2) challenge virus was inoculated intranasally at dose 10^7 TCID₅₀ in 1000uL (vertical red dotted line). Body weight ratio and body temperature difference to 0 DPI were monitored daily for groups inoculated with TX LAIV 6:2 (A and B), TX LAIV 5:3 (C and D) and Mock inoculated groups (E and F).