Novel Horse Hepaciviruses: Epidemiological, Clinical and Zoonotic Features

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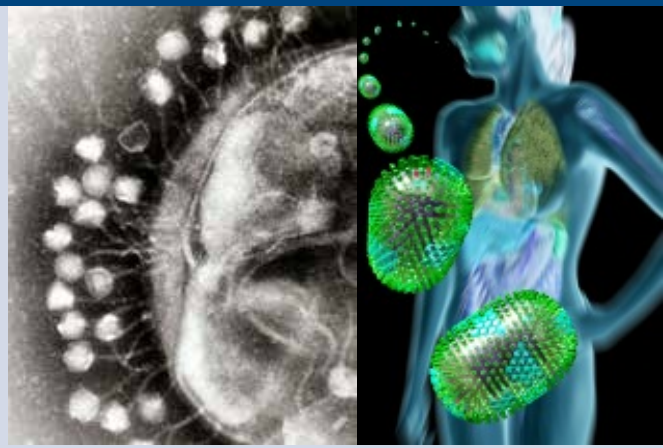
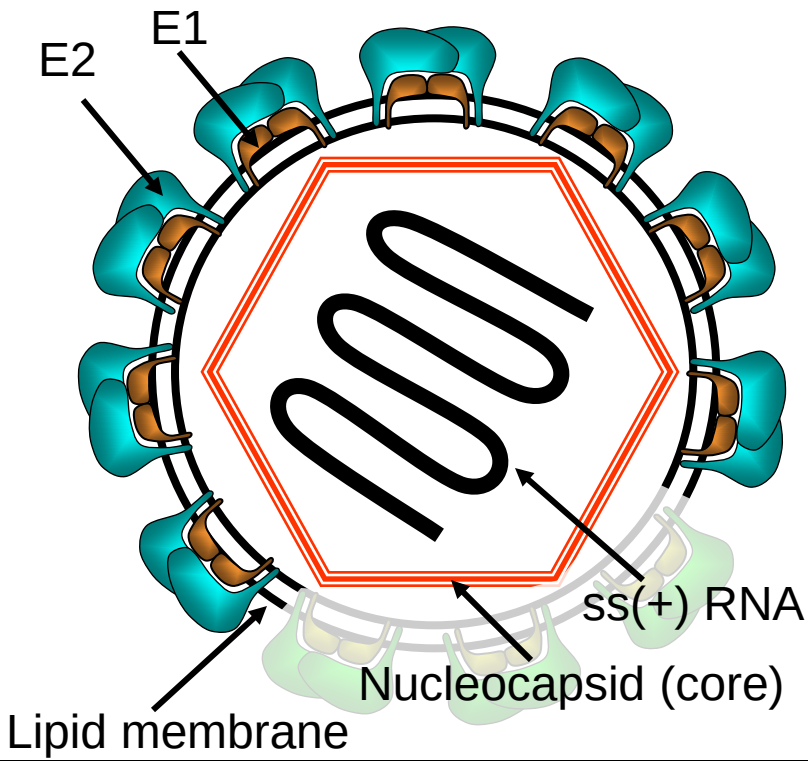
Institute of Experimental Virology, Twincore*

***joint venture between Medical School Hannover and Helmholtz Centre for Infection Research**



Hepatitis C Virus (HCV) Profile

Family:	*Flaviviridae*
Genus:	*Hepacivirus*
Species:	*Hepatitis C virus* (7 genotypes)
Size:	50-60 nm
Genome:	(+) ssRNA, ~9.6 kb
Prevalence:	160 million patients
Therapy:	IFN-a + Ribavirin+PI



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nature OUTLOOK

HEPATITIS C

PERSPECTIVE

Miles to go before we sleep

New drugs are generating much excitement, but a cure for all will take generations of therapies, argues **Charles Rice**.

Nature 2012

New homologs of HCV

BBC

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Hepatitis C: Closing in on its viral origins

The virus behind Hepatitis C has been the target of virologists, epidemiologists and geneticists for years, in a bid to find out the animal host from which it likely came. But Prof Jonathan Ball, a virologist at the University of Nottingham, UK, says early indications that bats are the culprit may yet be proven wrong.

Related Stories

Spread of hepatitis C

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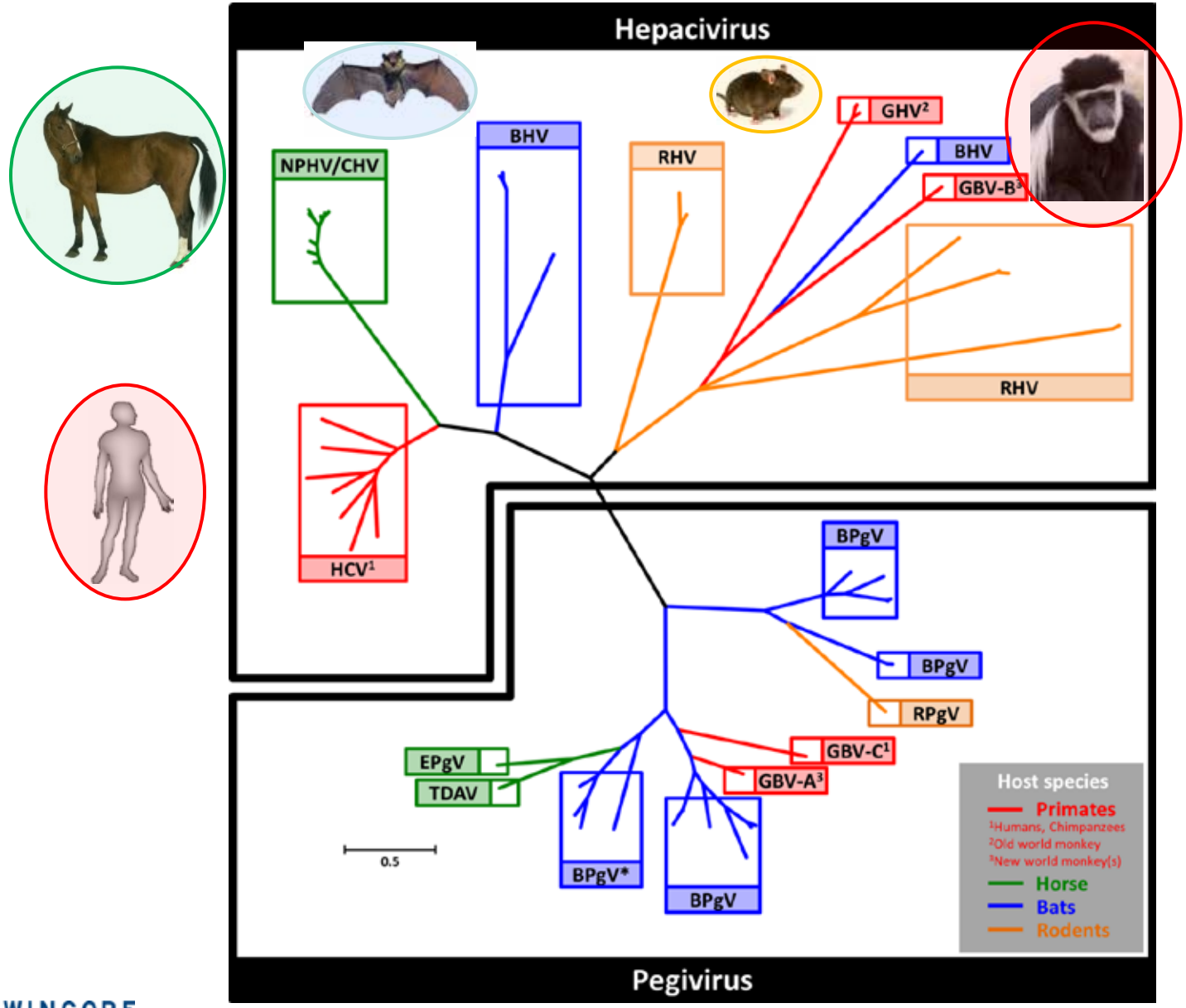
Identification of mammalian homologs of HCV

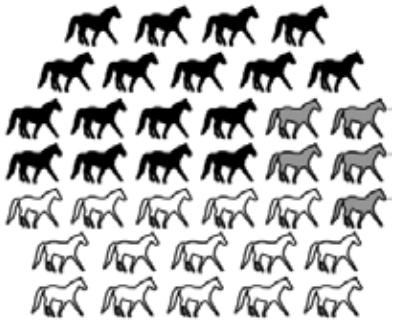


Pfaender et al. Emerging Microbes and Infection 2014

Characterization of non-primate hepaciviruses

Jessika Cavalleri
Karsten Feige

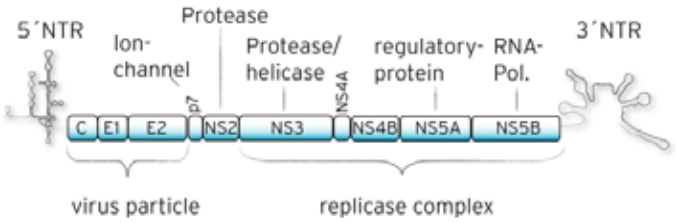
Emergence/
Epidemiology



adapted from 2013; Chandriani *et al.* PNAS

Course of infection
Tropism
Transmission

Molecular analysis



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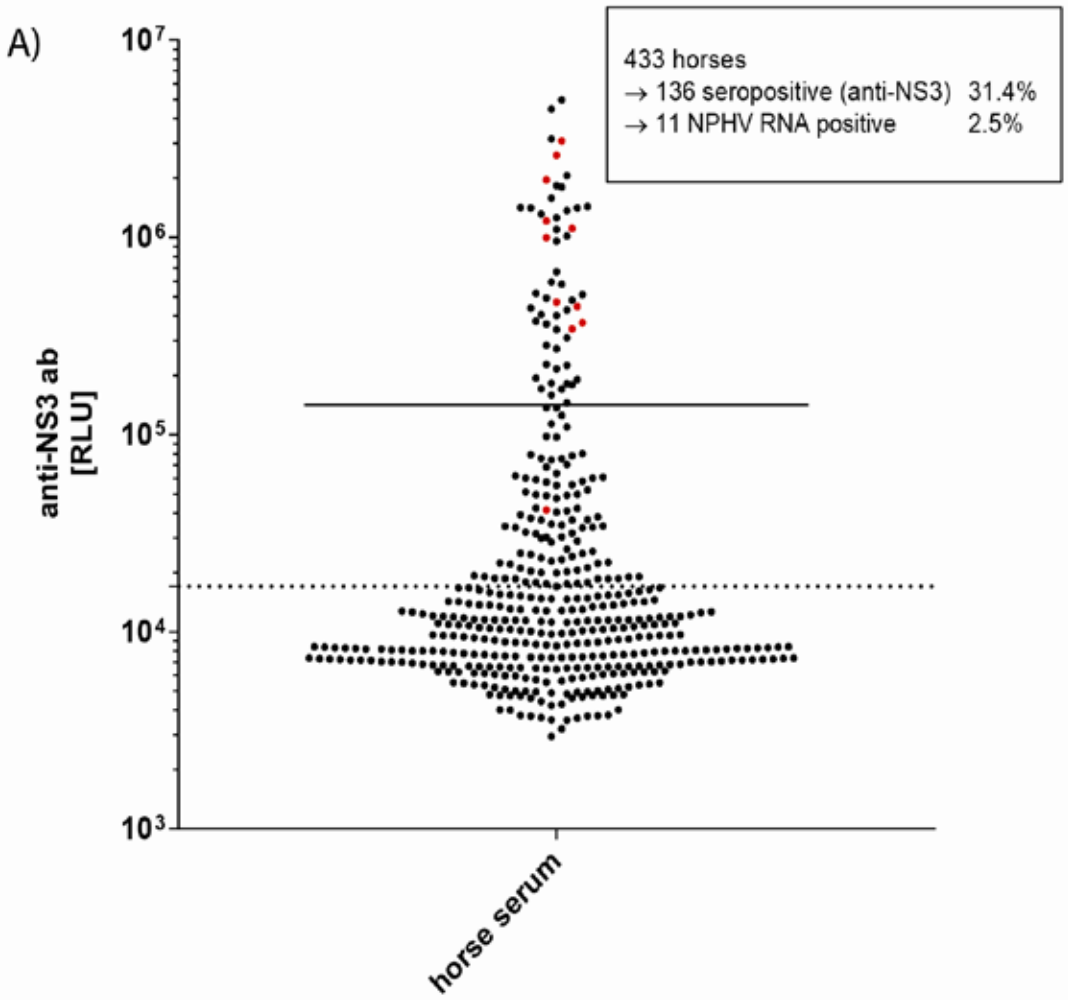
Characterization of non-primate hepaciviruses: Emergence/Epidemiology



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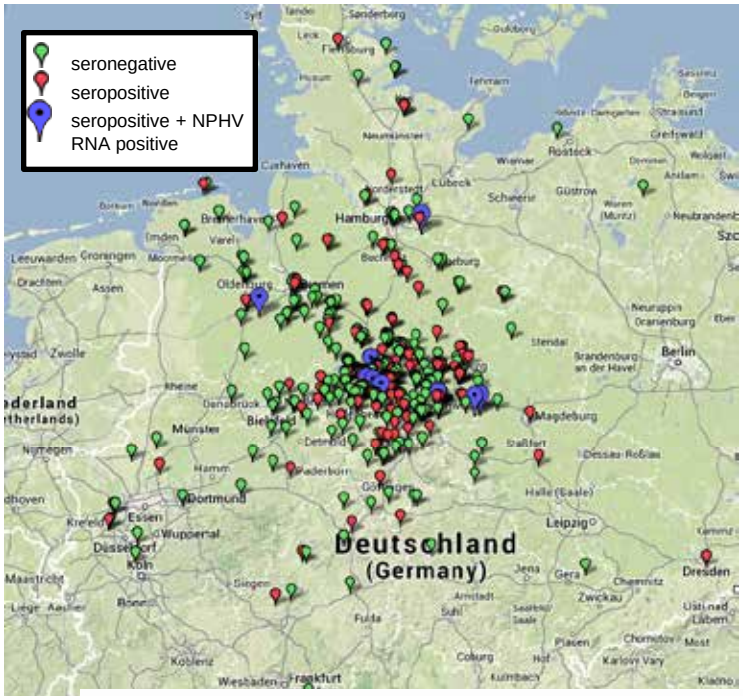
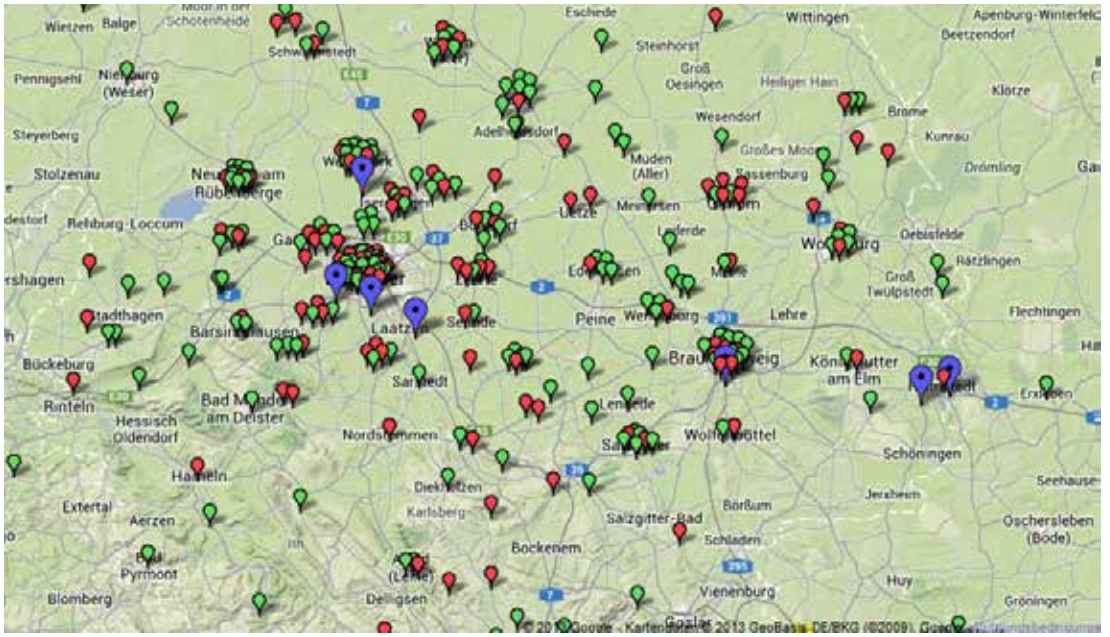
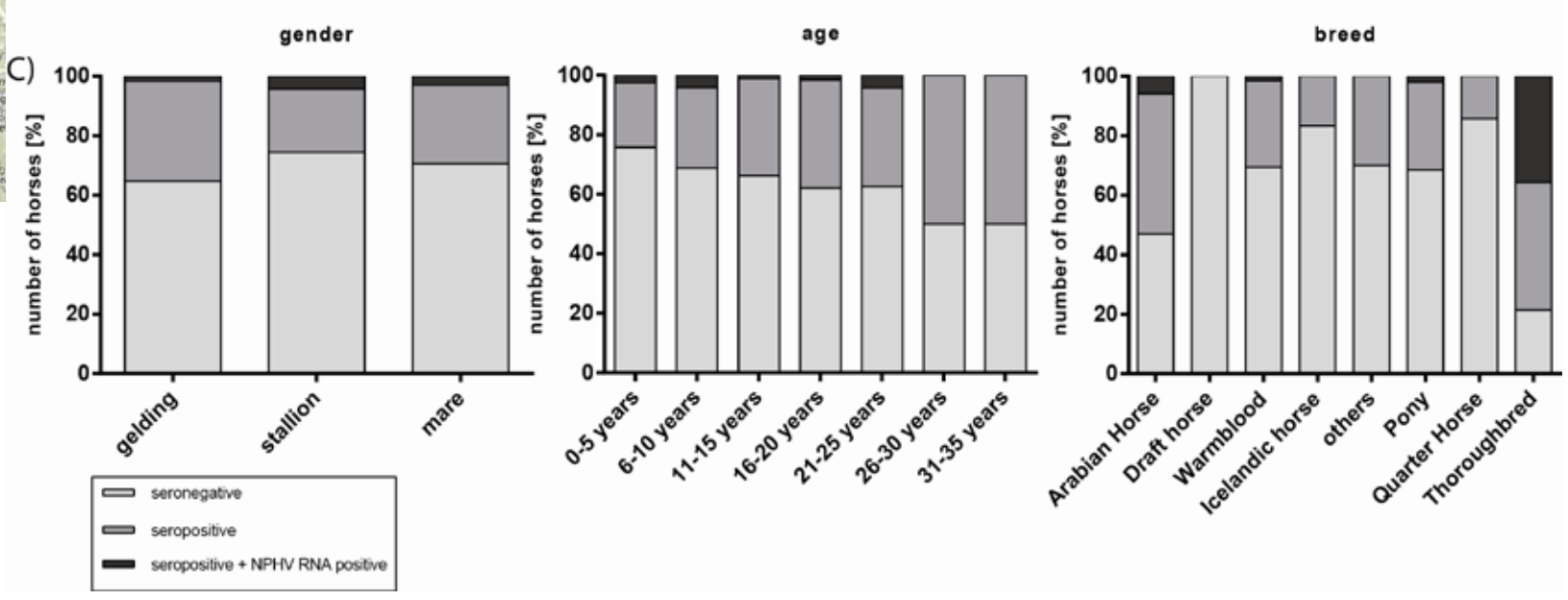
Characterization of non-primate hepaciviruses: Emergence/Epidemiology

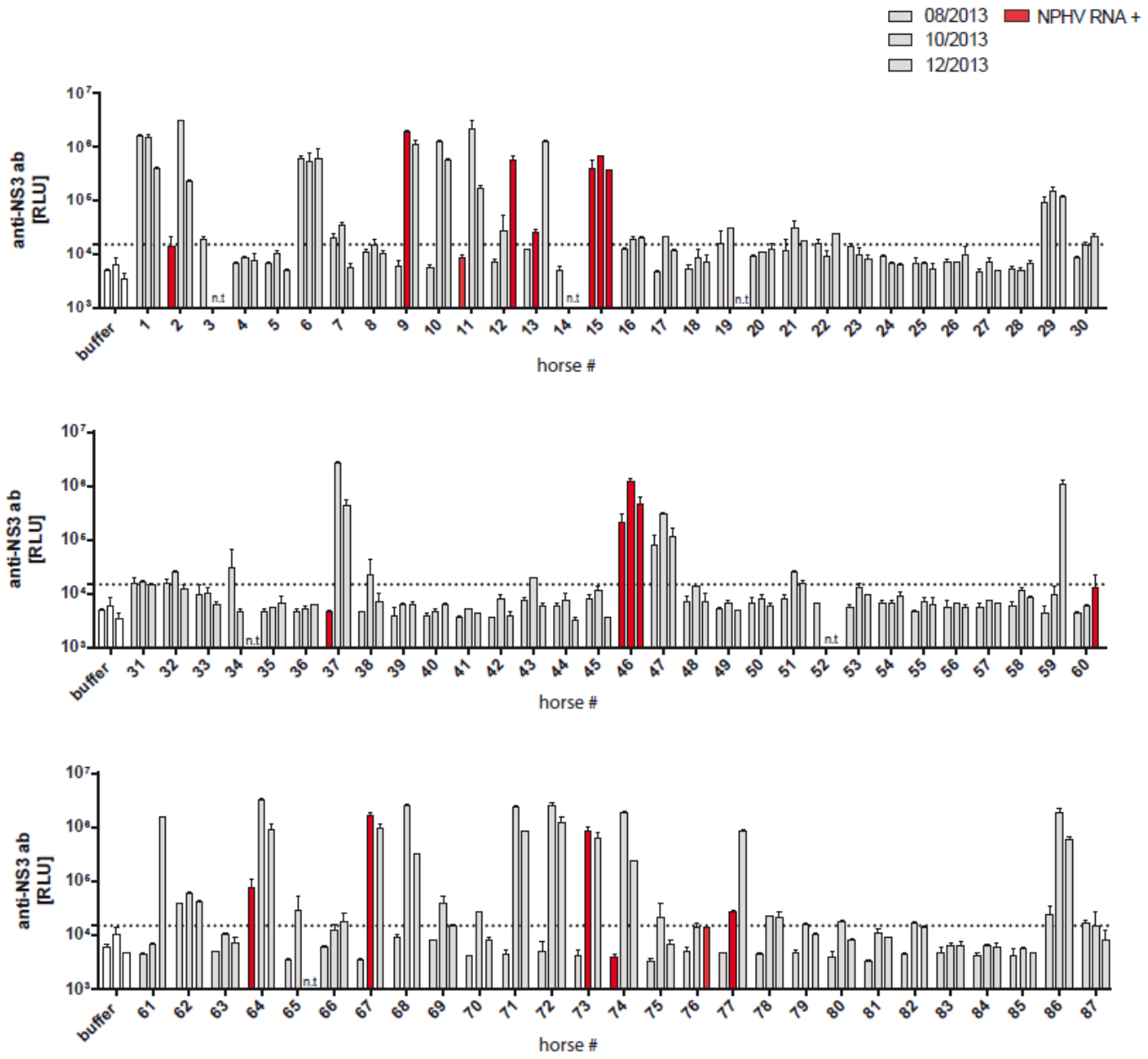




C)



Characterization of non-primate hepaciviruses: Emergence/Epidemiology



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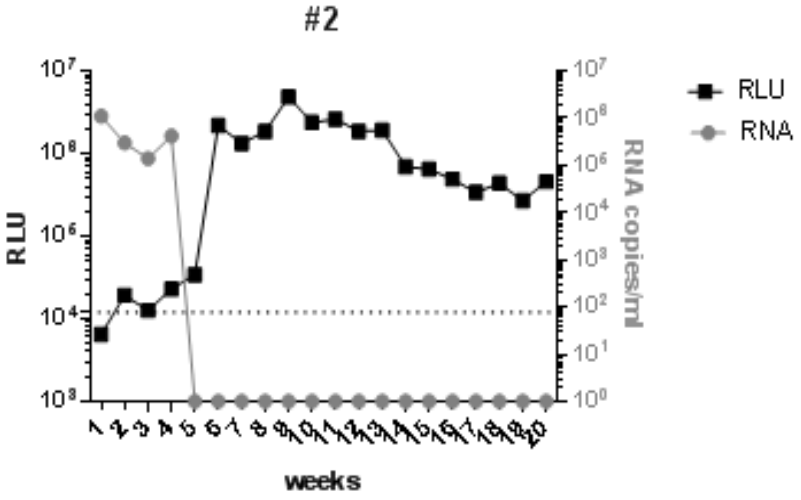
Acute and chronic infection with NPHV

a)



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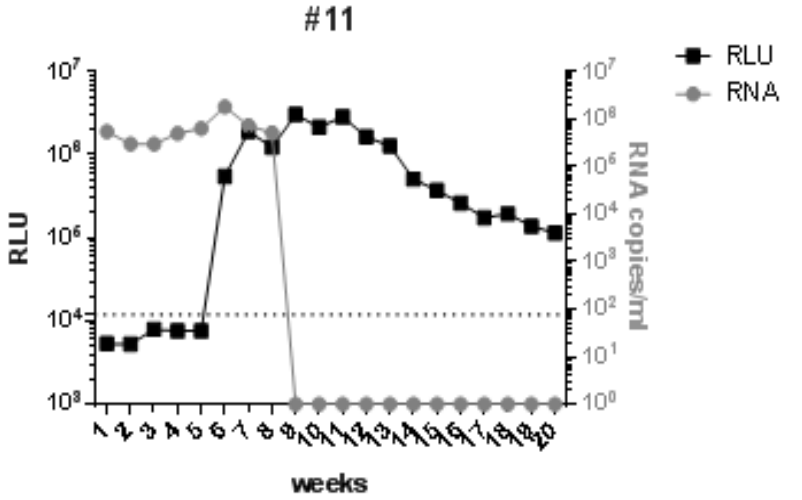

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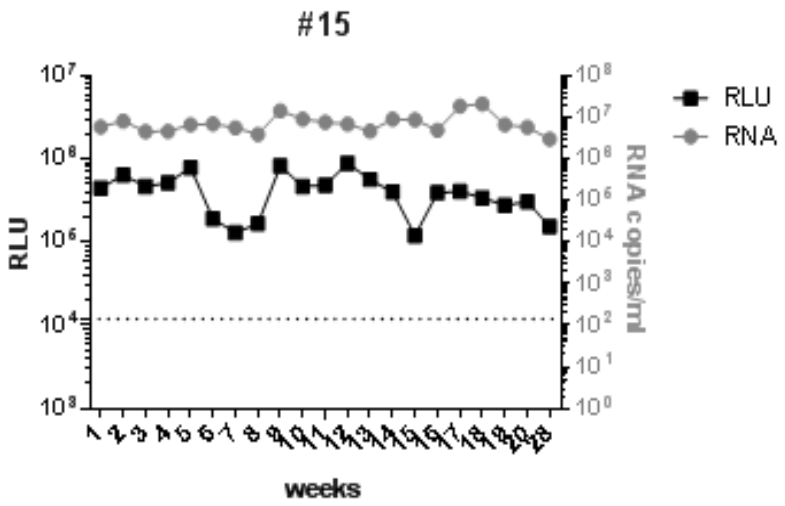
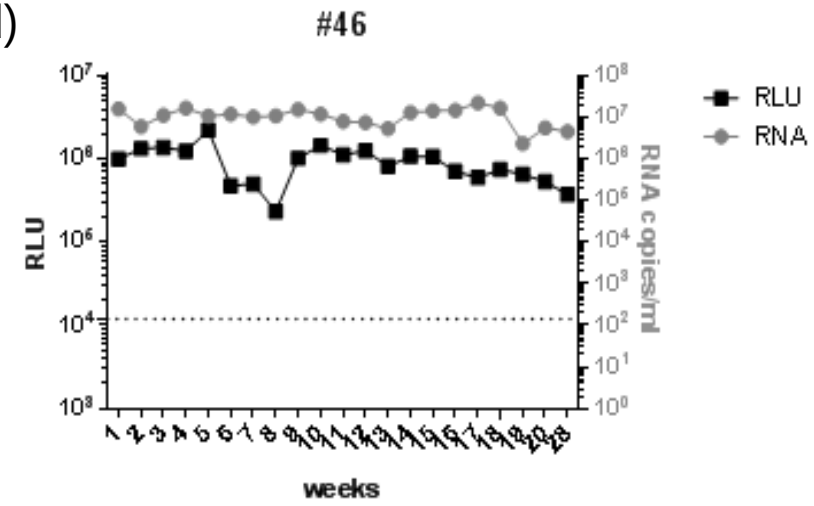


d)



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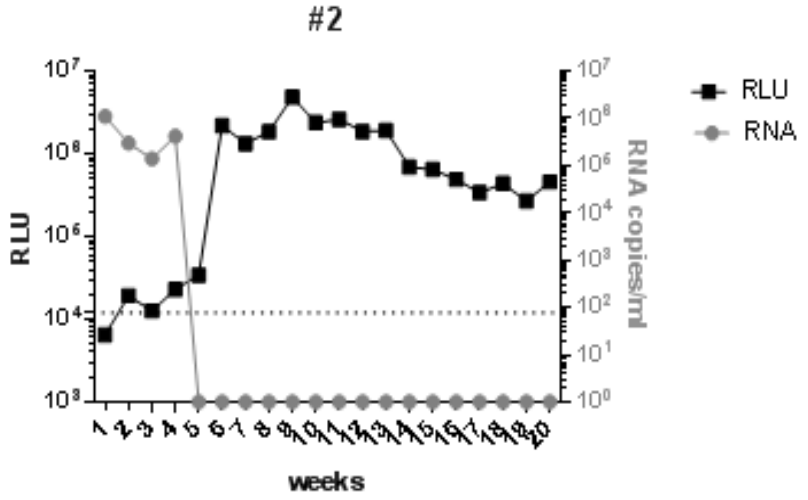
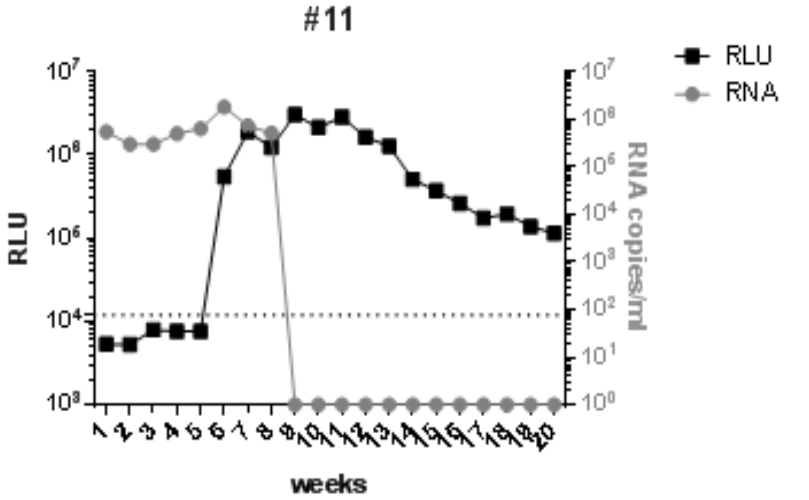
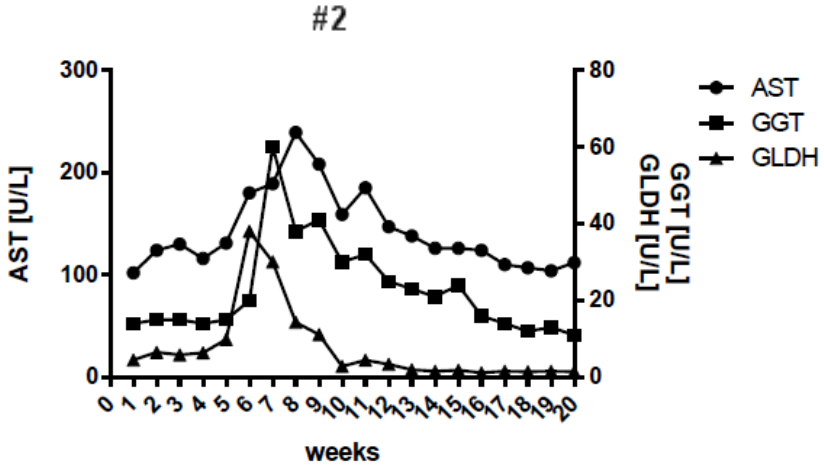
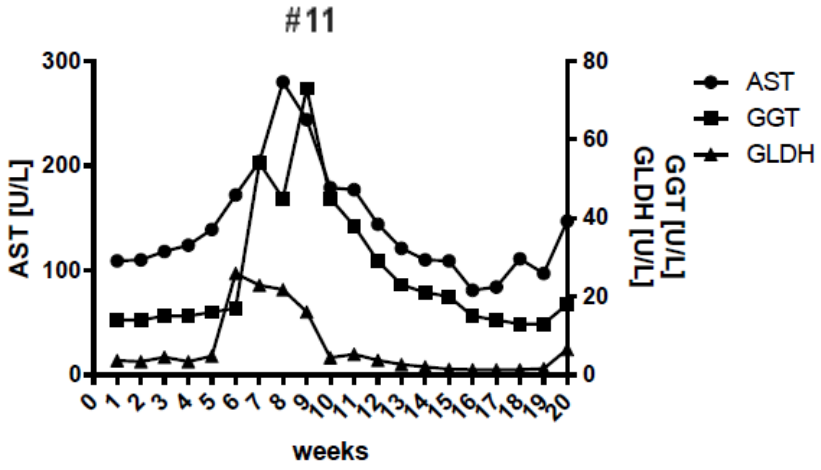
Liver parameters during infection



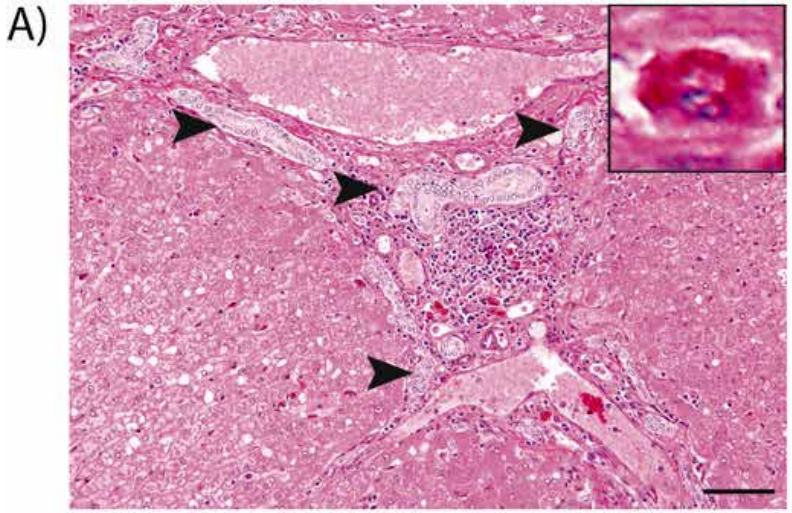


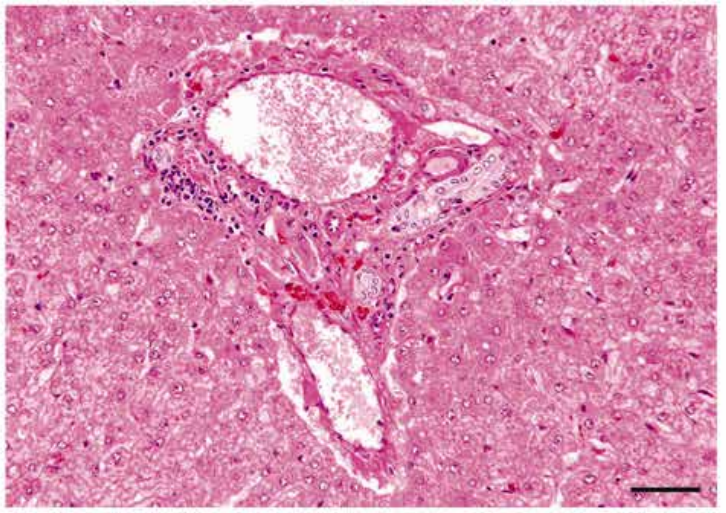


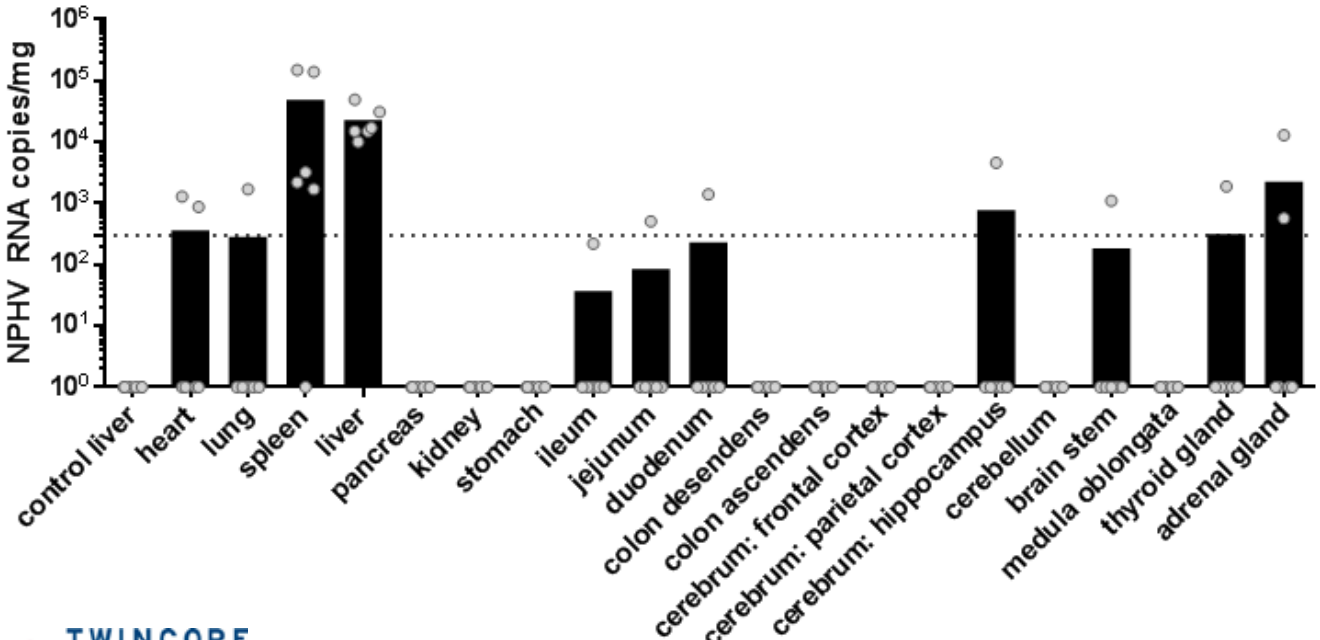


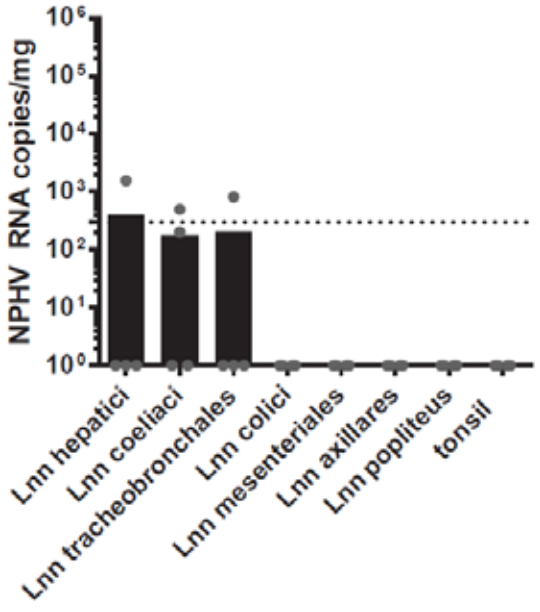
AST (aspartate amino transferase) (<250 U/L)
GGT (γ-glutamyl transferase) (<20 U/L)
GLDH (glutamate dehydrogenase) (<8 U/L)

Tissue tropism and pathology of NPHV









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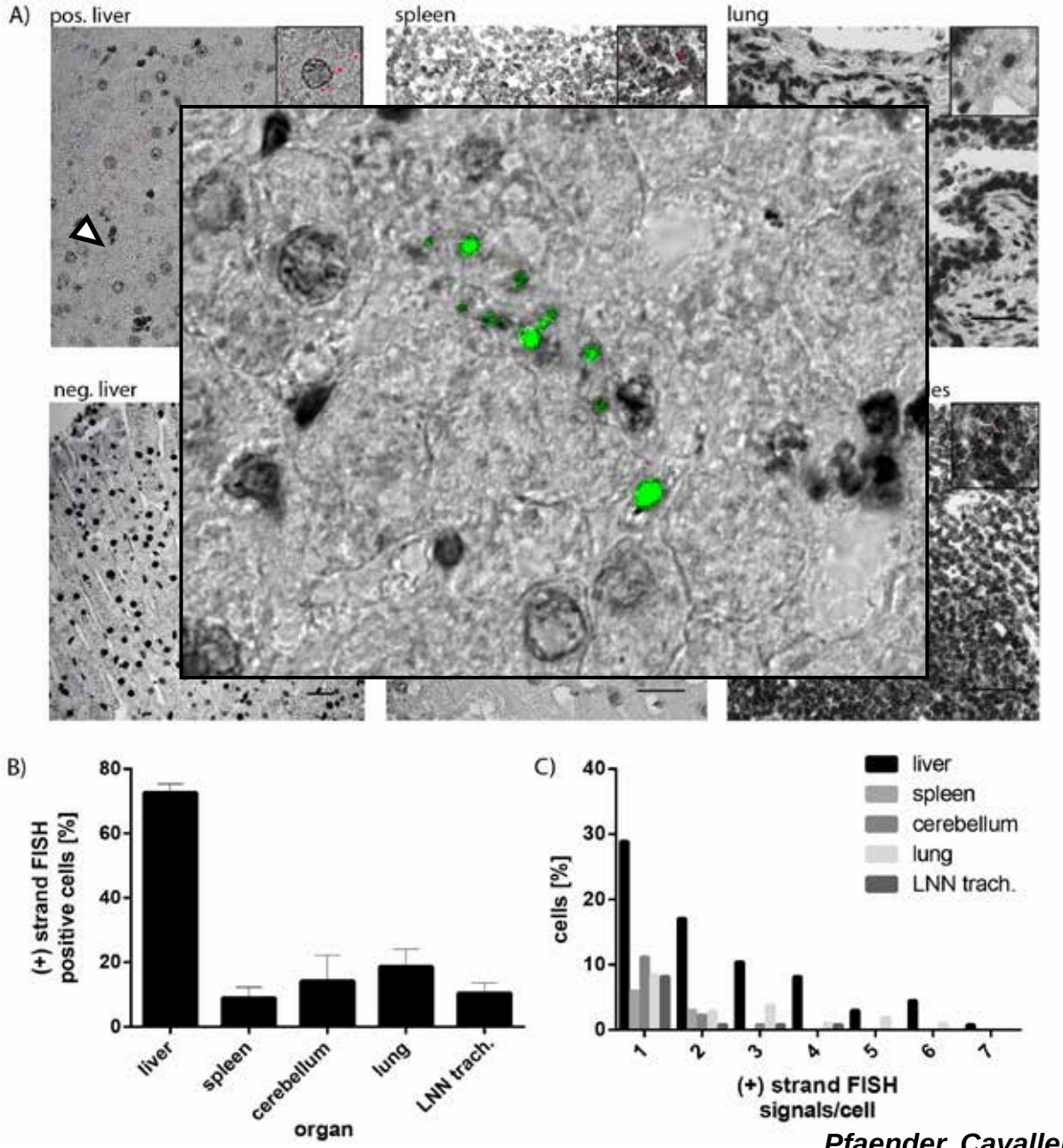
Fluorescent in situ hybridization (FISH) +/- strand RNA



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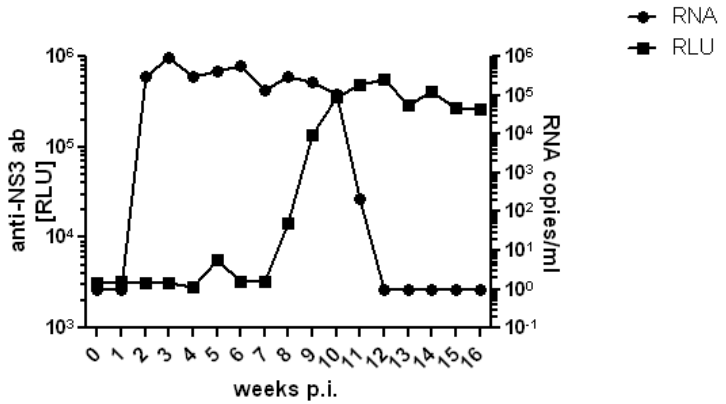
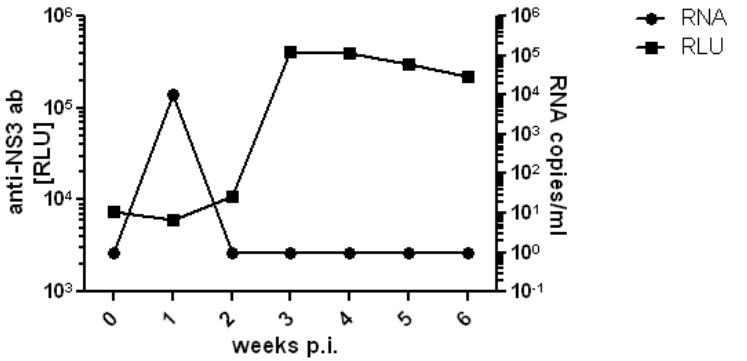
Pfaender, Cavalleri et al. Hepatology 2015

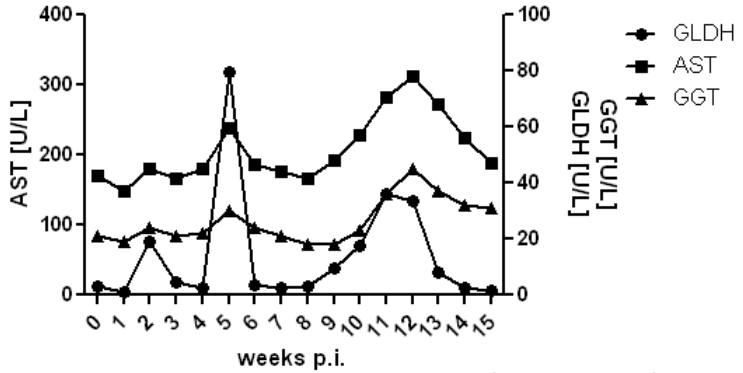
In vivo NPHV experiments

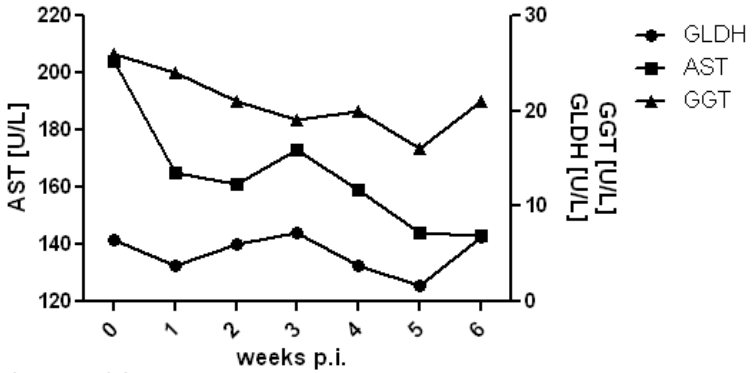
horse 1

horse 2









AST (aspartate amino transferase) (<250 U/L)
GGT (γ-glutamyl transferase) (<20 U/L)
GLDH (glutamate dehydrogenase) (<8 U/L)

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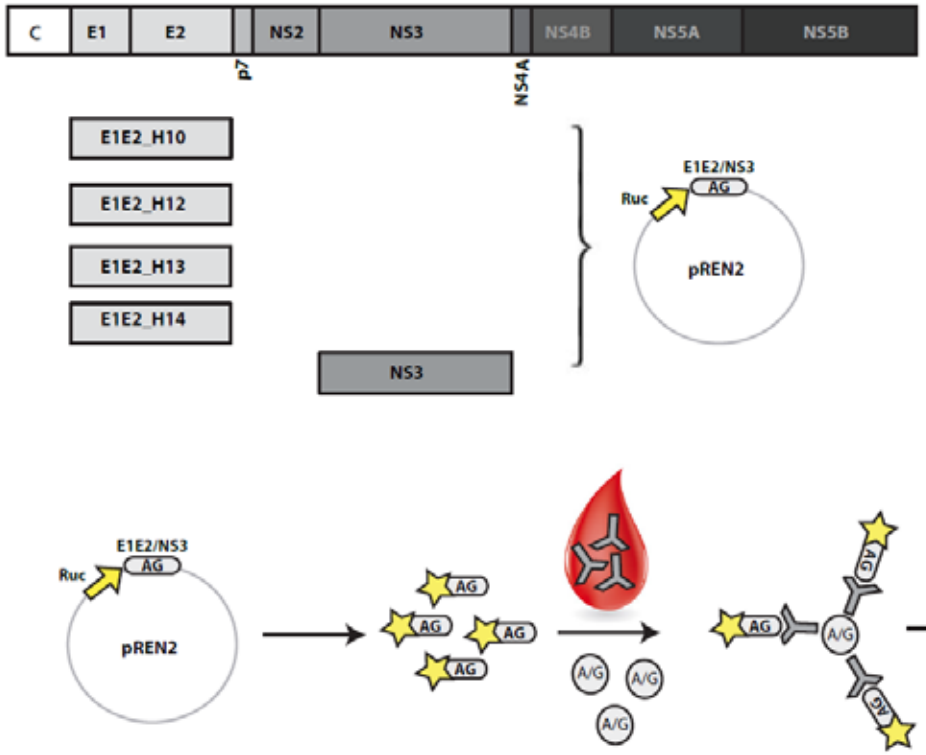
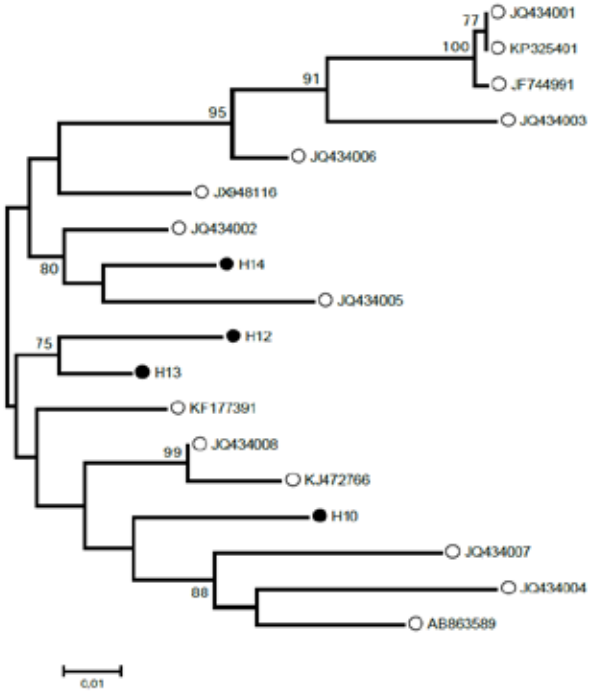
Analysis of cross-species transmission of NPHV

Screening of human sera for the presence of
- NPHV RNA by quantitative real time PCR
- anti-NPHV antibodies by luciferase immunoprecipitation system (LIPS)





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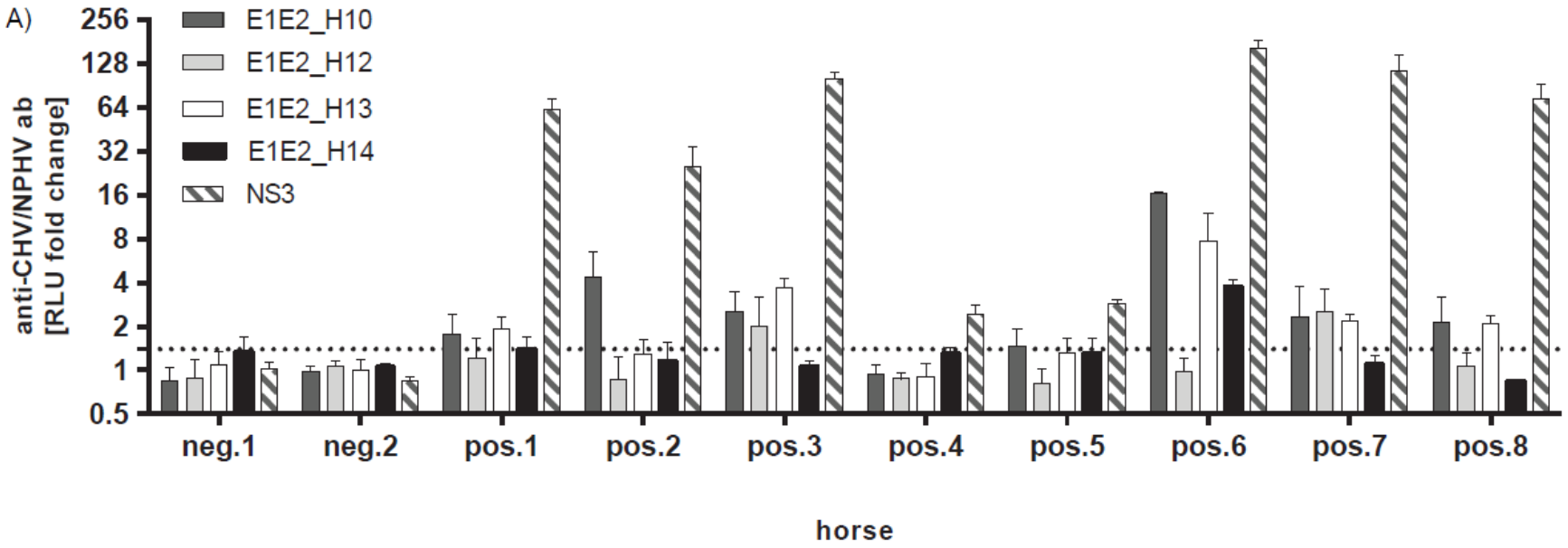
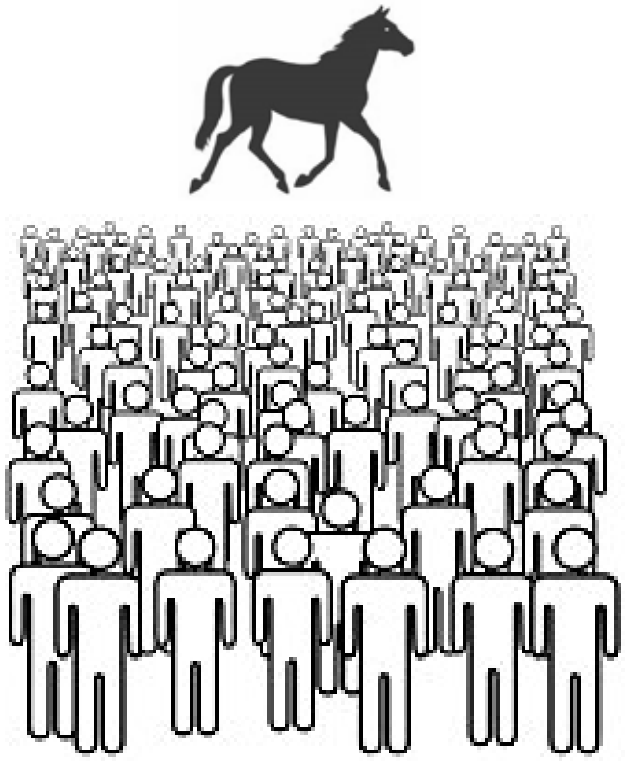
Validation of the LIPS assay



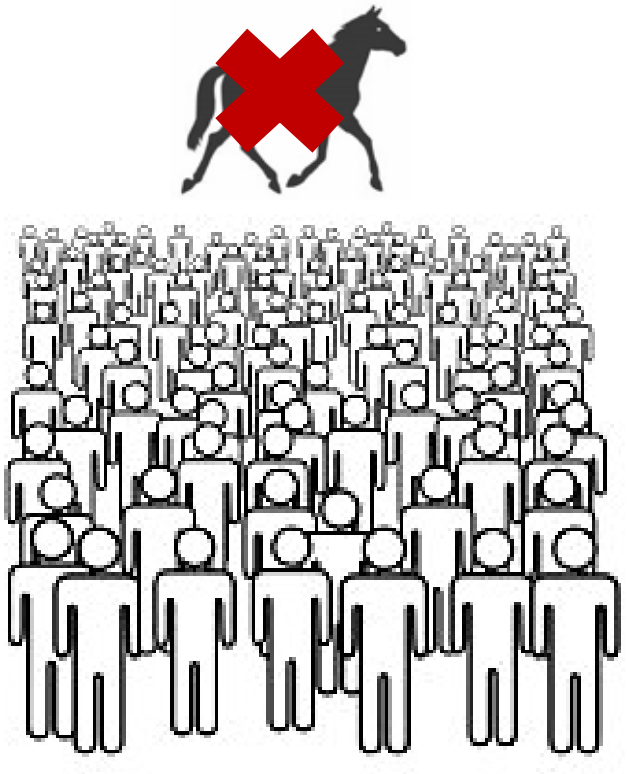
Analysis of two study groups

People with occupational horse contact



n=172

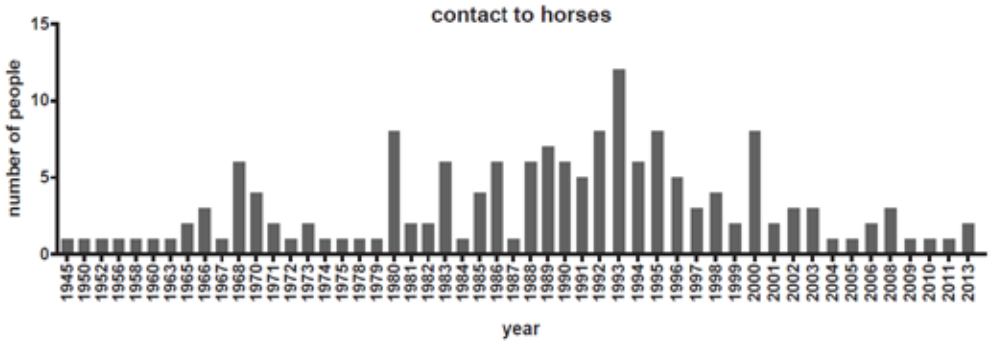
People with no horse contact



n=159

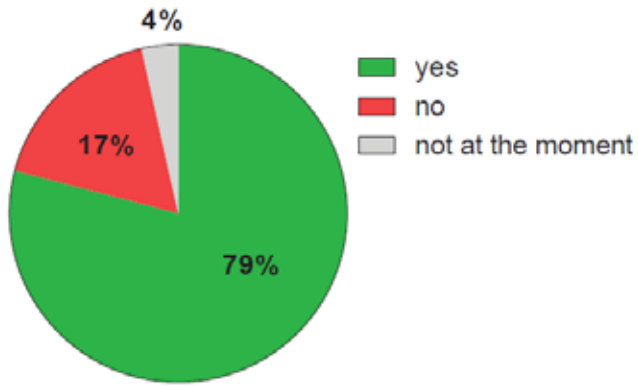
Questionnaire of people with occupational horse contact

Average: 8 years

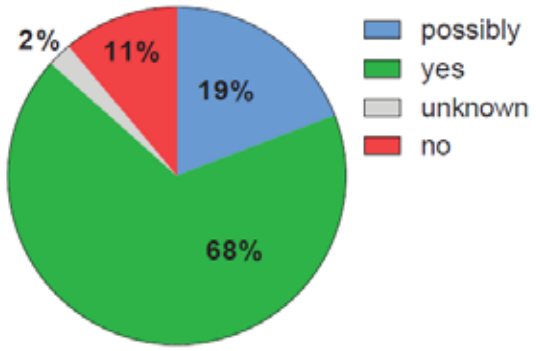


Average: 25 years

private contact to horses



blood-blood contact to horses



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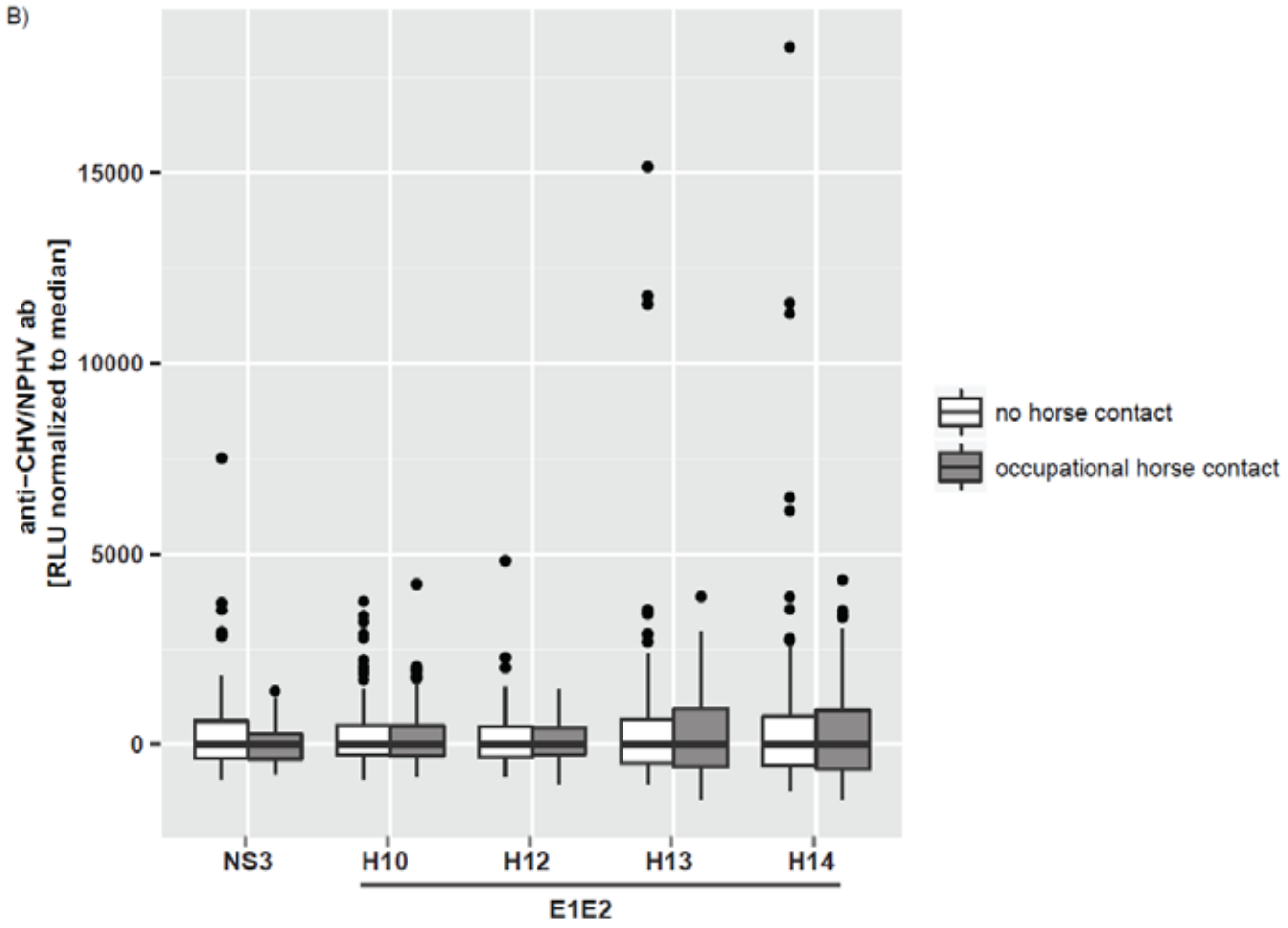
Low risk of cross-species transmission of NPHV



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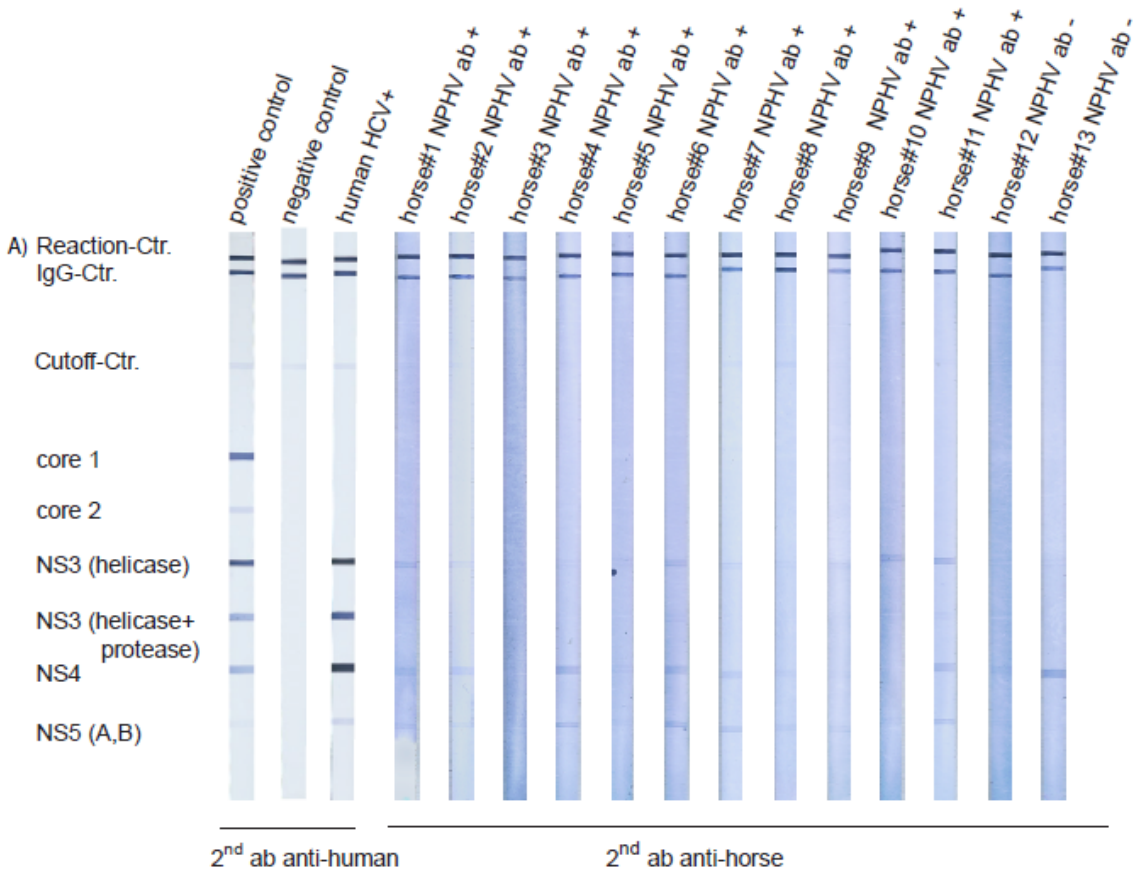
Cross-reactivity of NPHV antibodies with HCV antigens



B)

	positive control	negative control	human HCV+	horse#1 NPHV ab +	horse#2 NPHV ab +	horse#3 NPHV ab +	horse#4 NPHV ab +	horse#5 NPHV ab +	horse#6 NPHV ab +	horse#7 NPHV ab +	horse#8 NPHV ab +	horse#9 NPHV ab +	horse#10 NPHV ab +	horse#11 NPHV ab +	horse#12 NPHV ab -	horse#13 NPHV ab -
core 1	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
core 2	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
NS3 (helicase)	+	-	+	+	+	-	+/-	+/-	+	+	+/-	+/-	+	+	-	-
NS3 (helicase+ protease)	+	-	+	-	-	-	-	-	+/-	-	-	-	-	+/-	-	-
NS4	+	-	+	+	+	-	+	-	+	+	+/-	+/-	-	+	+/-	+
NS5 (A,B)	-	-	+	+	+	-	+	+/-	+	+	+/-	+/-	+/-	+	-	-

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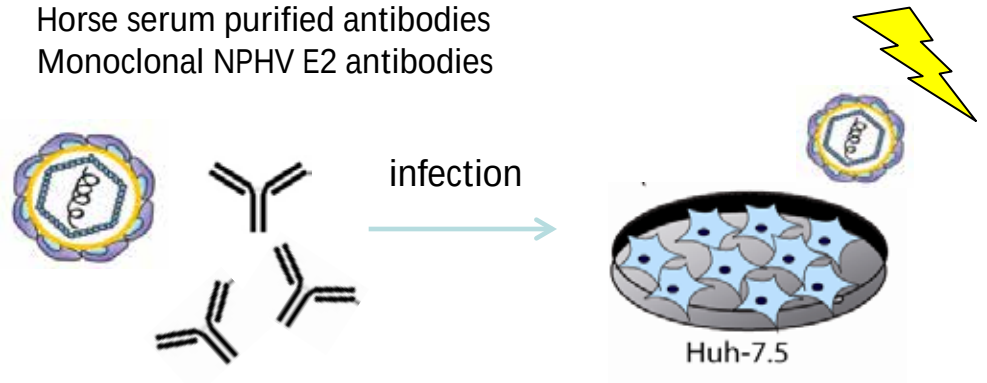
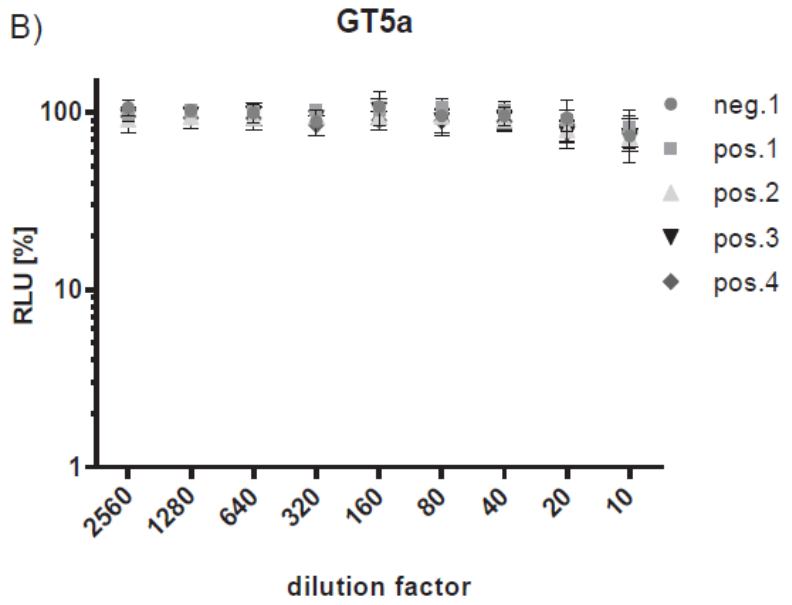
Analysis of cross-neutralization of NPHV antibodies to HCV cell culture derived particles

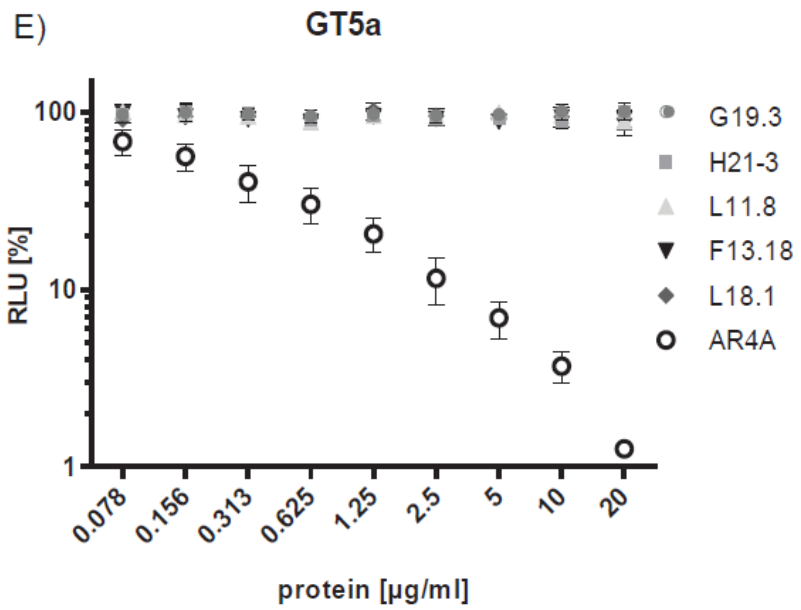
Virus neutralization:

HCV Genotype 2a
HCV Genotype 5a
HCV Genotype 7a

Horse serum purified antibodies
Monoclonal NPHV E2 antibodies







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Summary

- High prevalence of NPHV in horses in Germany
- Acute and chronic NPHV infection in an isolated horse cohort
- Tissue tropism reveals NPHV RNA mainly within the liver
- Low risk of cross-species transmission from horses to humans
- Novel surrogate system for HCV...

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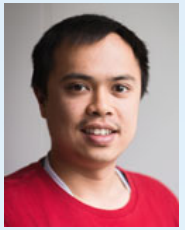
AG Goffinet

Stephanie Pfänder

Stephanie Walter

Juliane Dörrbecker


Anggakusuma

Aci Siddharta

Cooperations

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