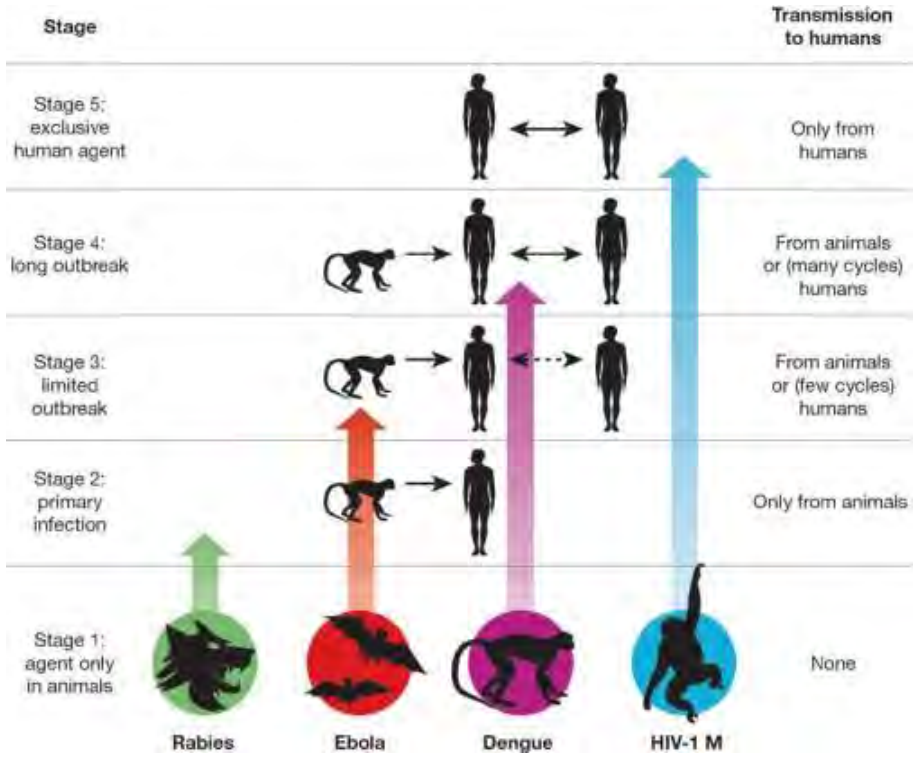
Evolutionary biology of hepatitis viruses

Jan Felix Drexler
Charité - Universitätsmedizin Berlin

Origin of new viruses?



1.400 human pathogens:

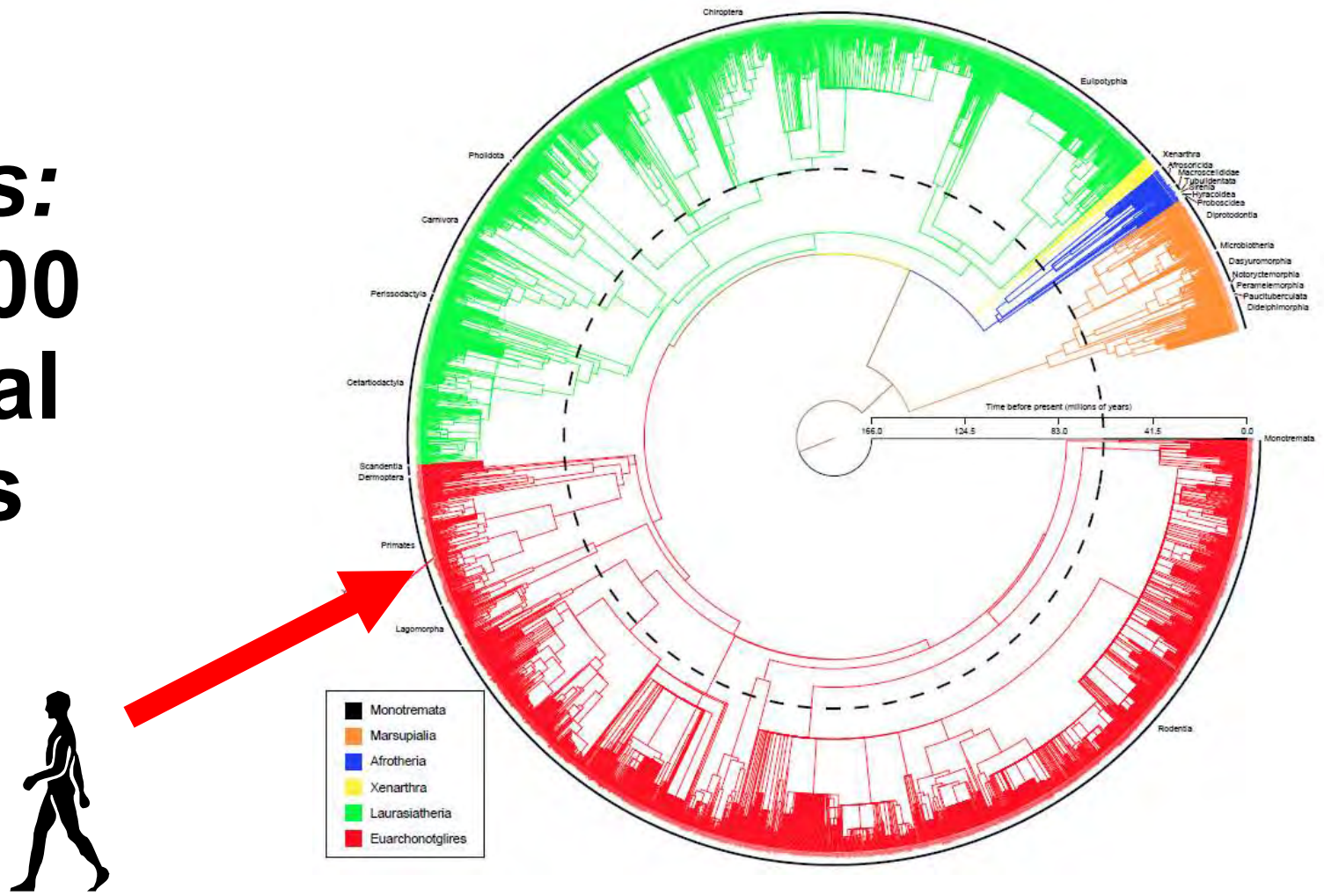
ca. 60% zoonotic

Wolfe 2007, Nature

Woolhouse, 2005, EID

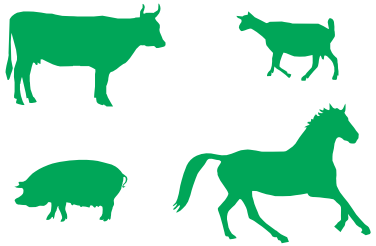
Relevant reservoirs?

Homo sapiens:
1 of 5500 mammal species

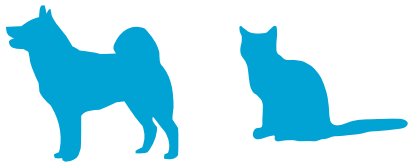


Bininda-Emonds, Nature 2007

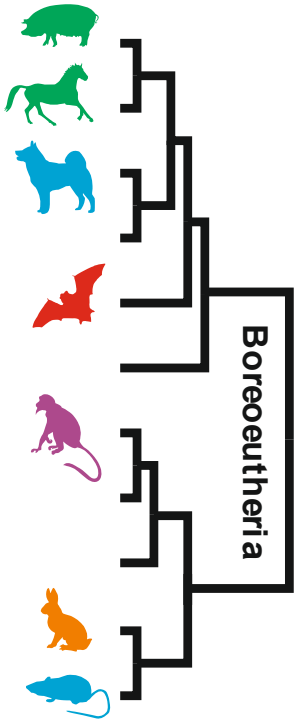
Reservoirs:
relevant for different reasons



Exposure

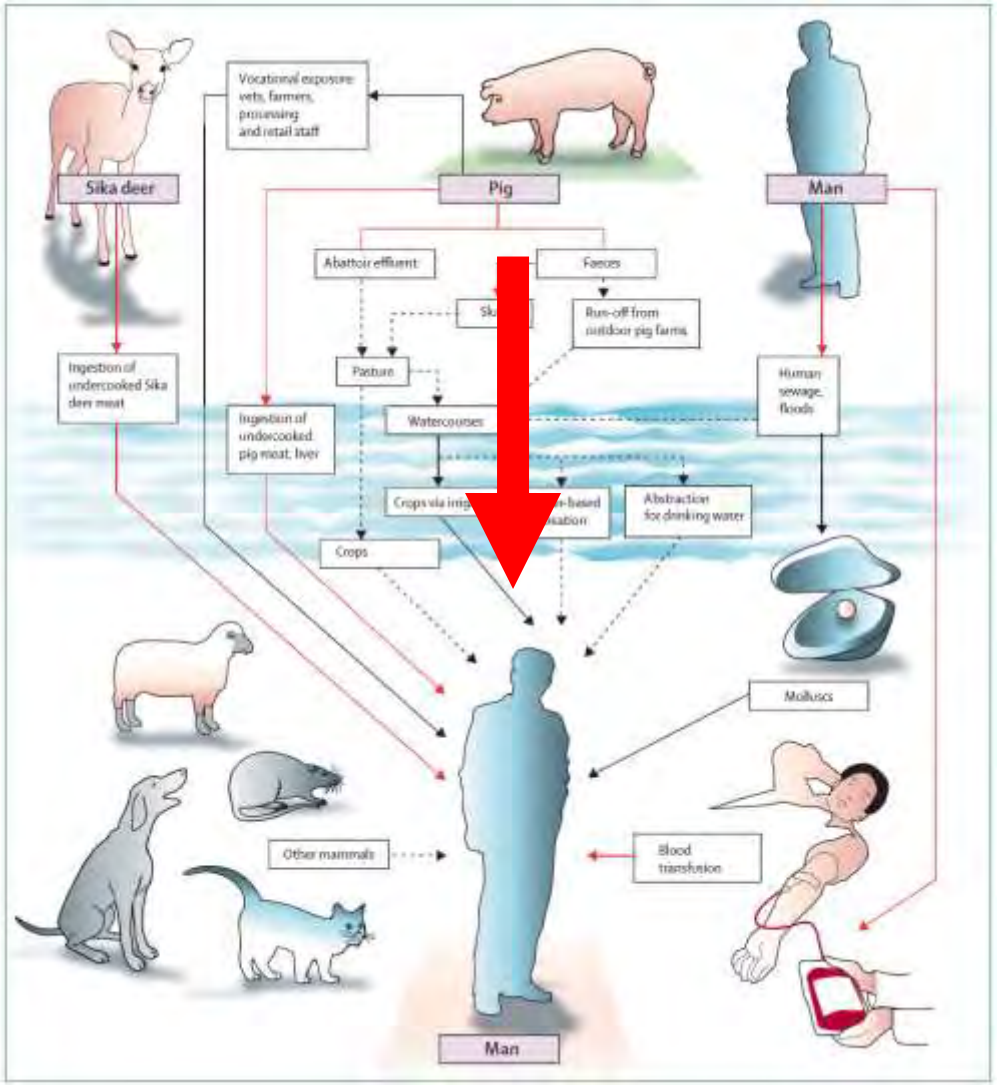


Evolution



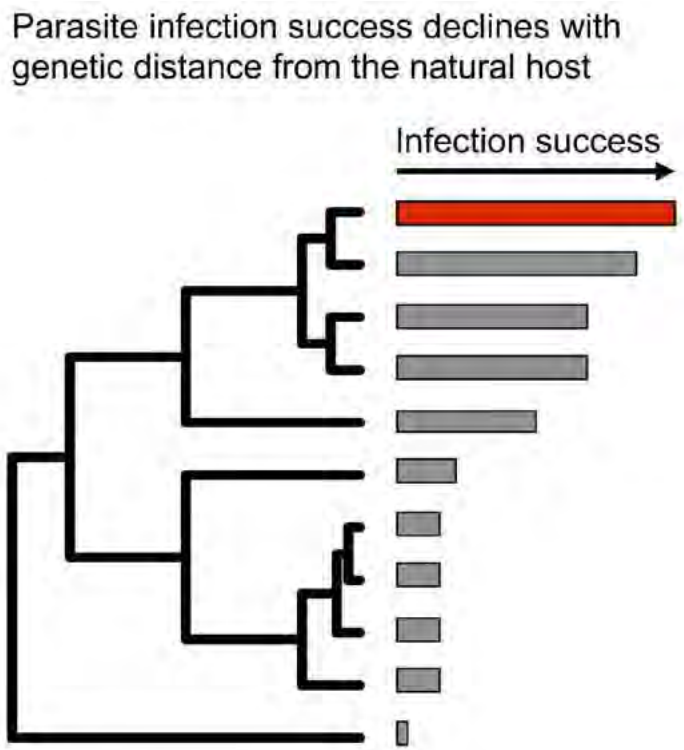
Ecology

Example exposure: hepatitis E virus

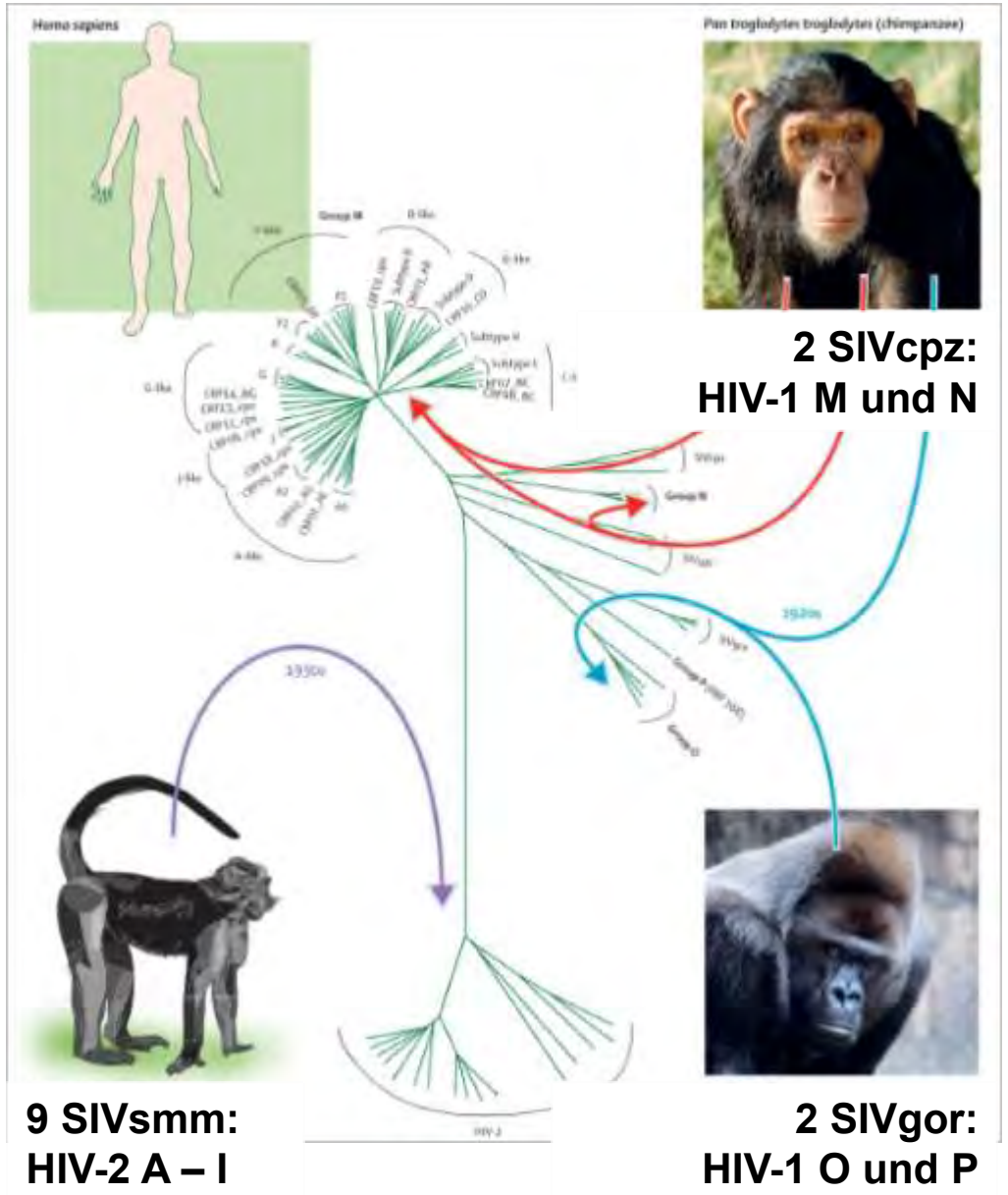


Dalton, Lancet ID, 2008

Example evolution: HIV



Longdon et al., PPAT, 2014



Tebit, Lancet ID 2011

Marburg virus

Example ecology: Dense bat populations

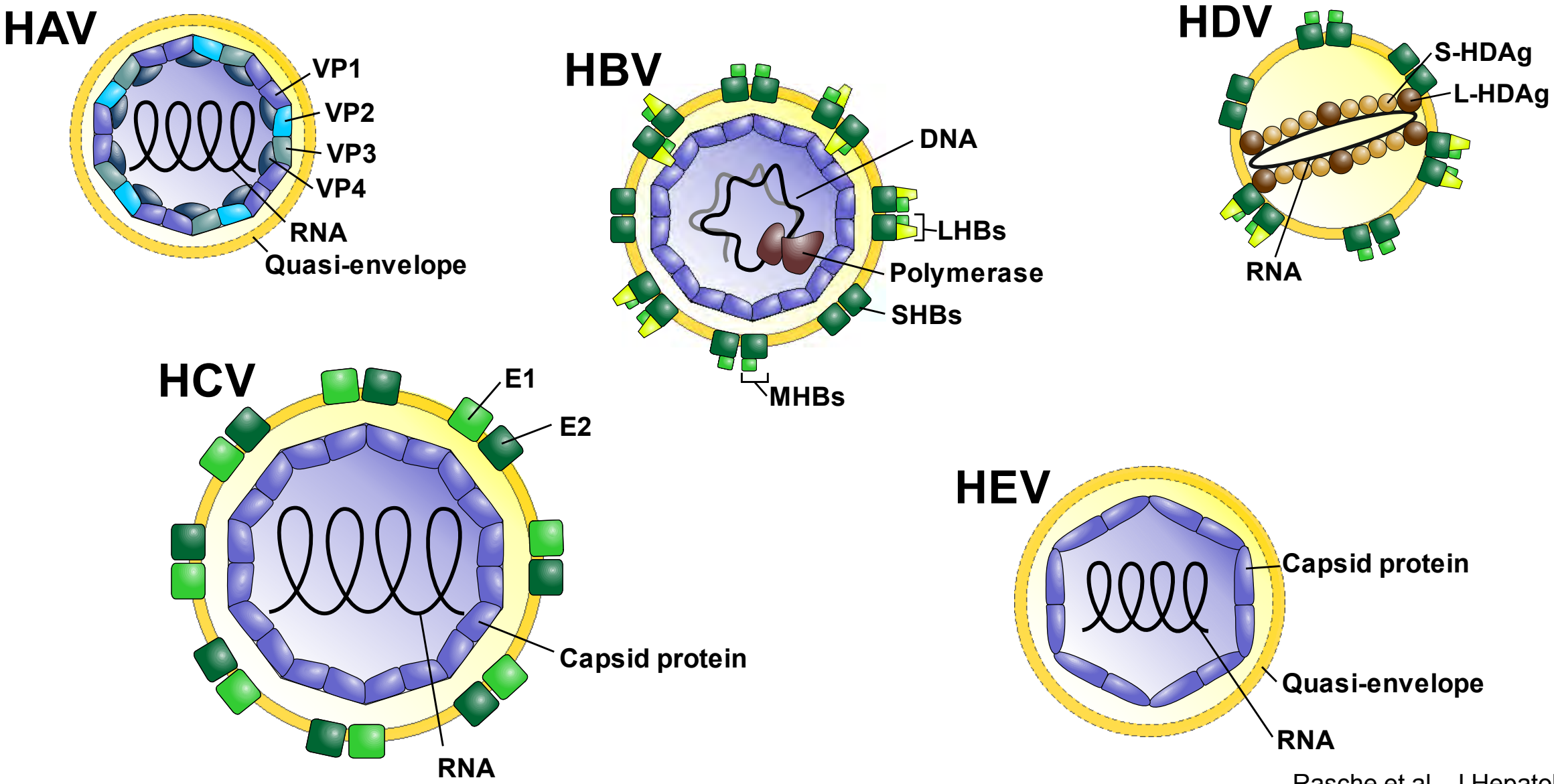
Example Ecology: Big rodent litters, Invasive behaviour

Hanta viruses

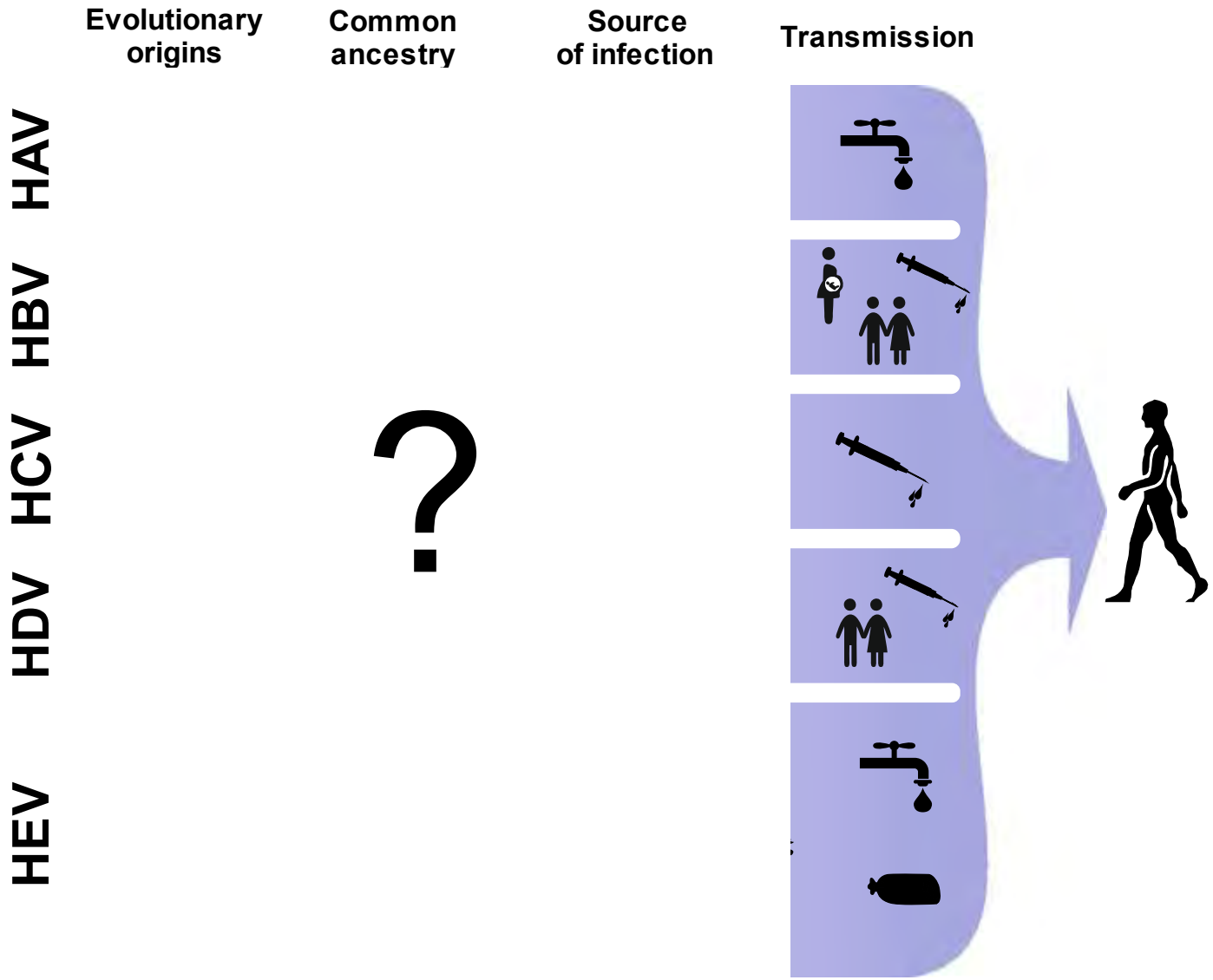
Olkowicz, Wikipedia

Rémi from Ratatouille, Copyright Pixar

5 different hepatitis viruses



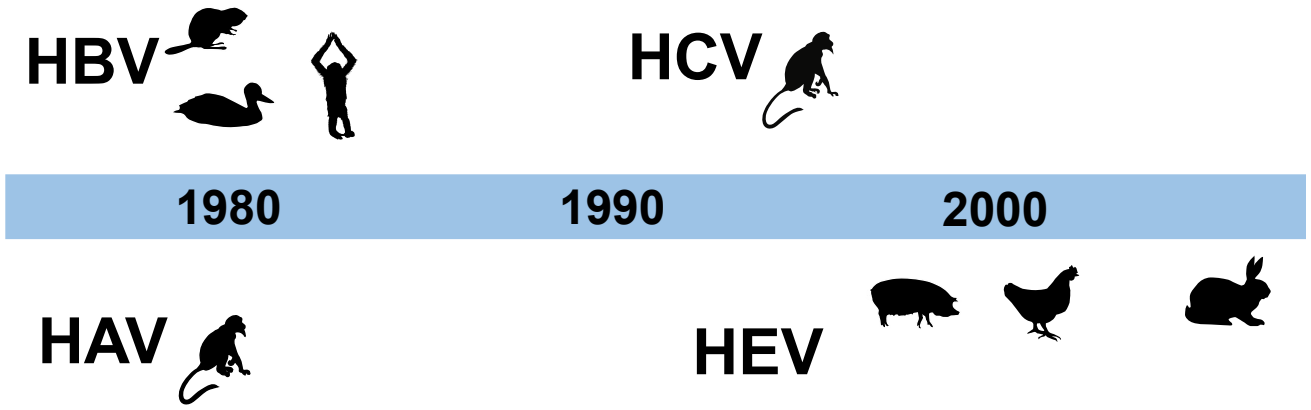
Rasche et al., J Hepatol., 2019



What can we learn from animal viruses?

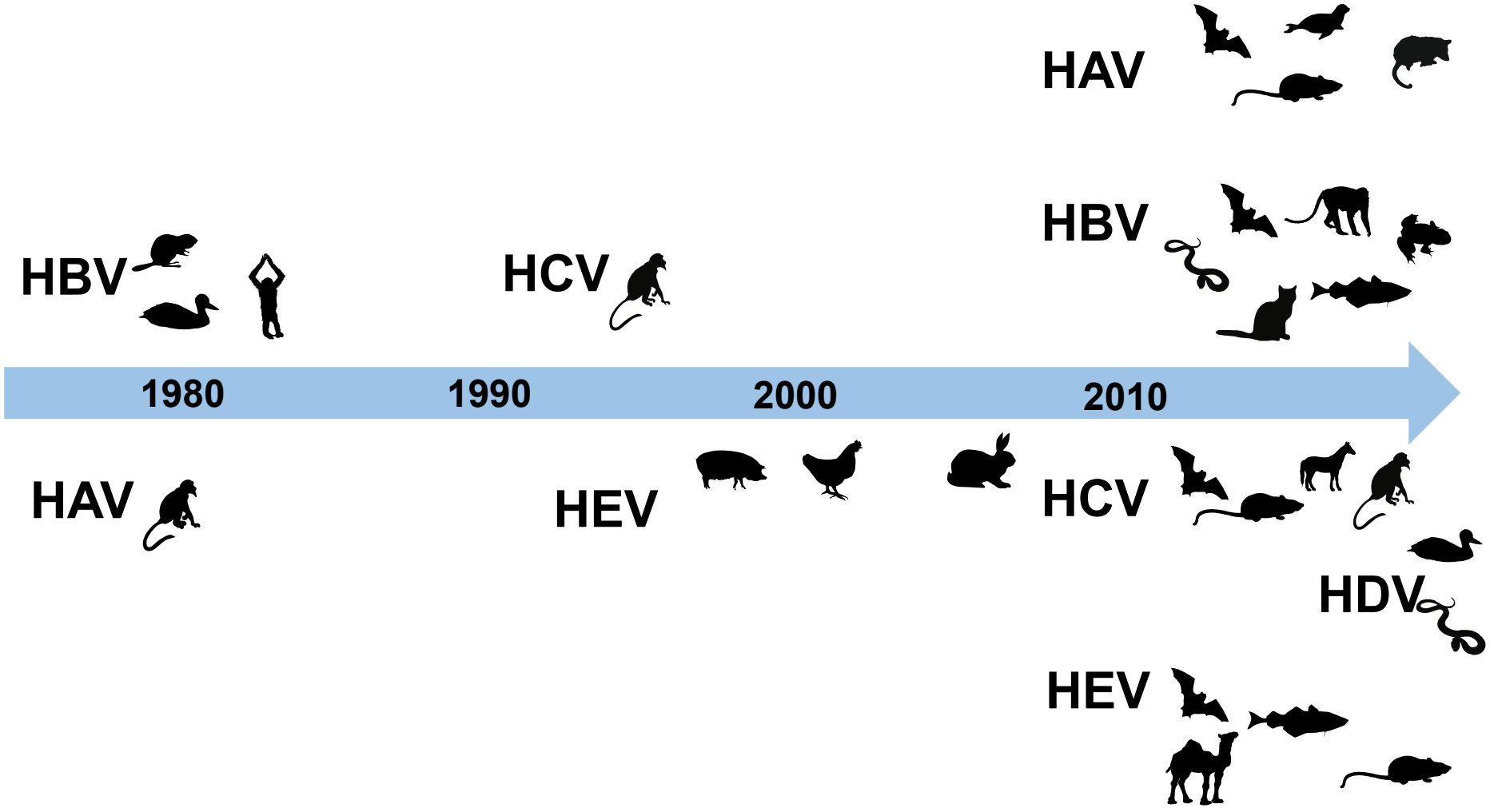
Rasche et al., J Hepatol., 2019

First detections of hepatitis viruses in animals were ground breaking – yet sporadic



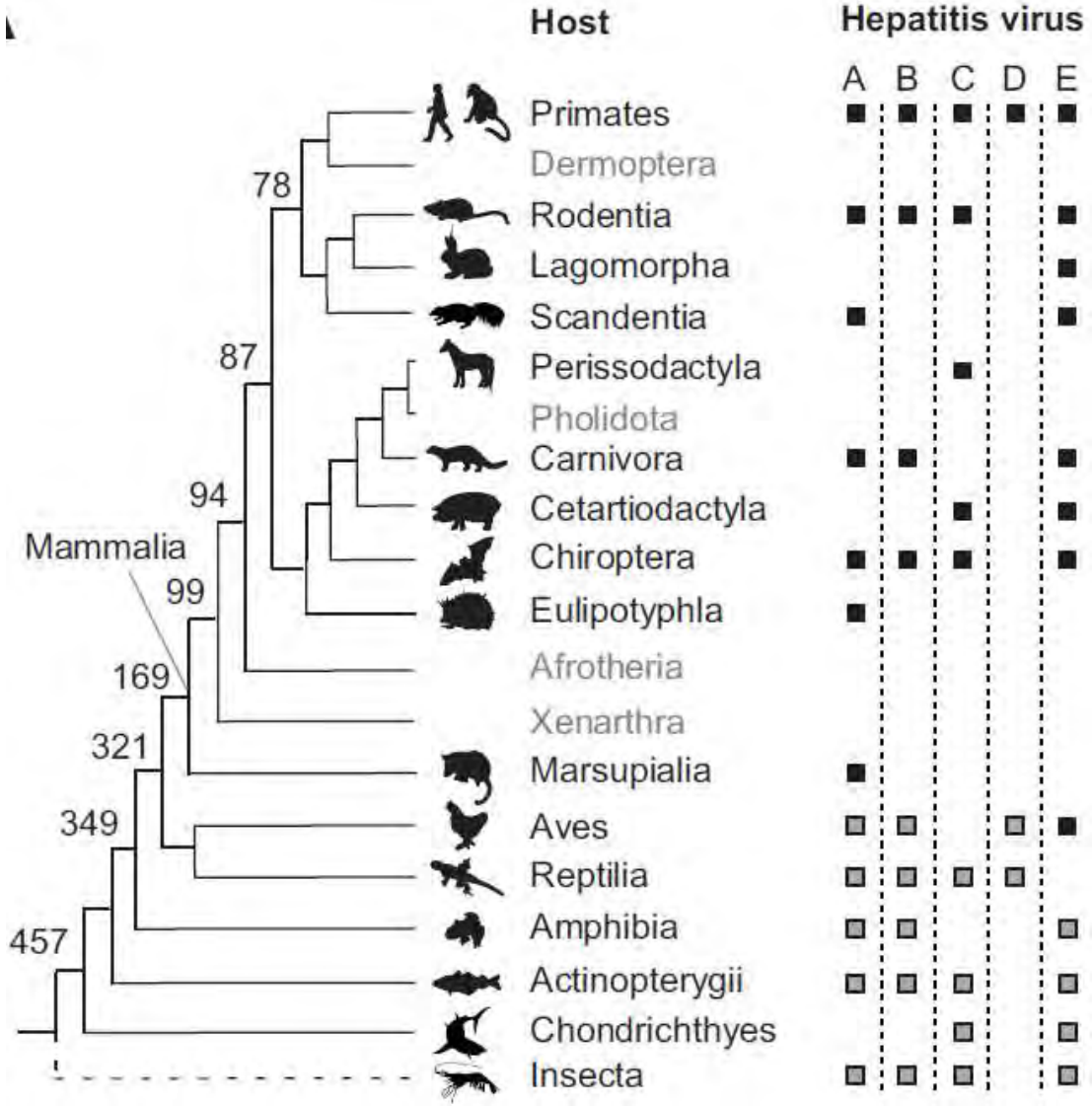
Rasche et al., J Hepatol., 2019

A new era of virus discovery



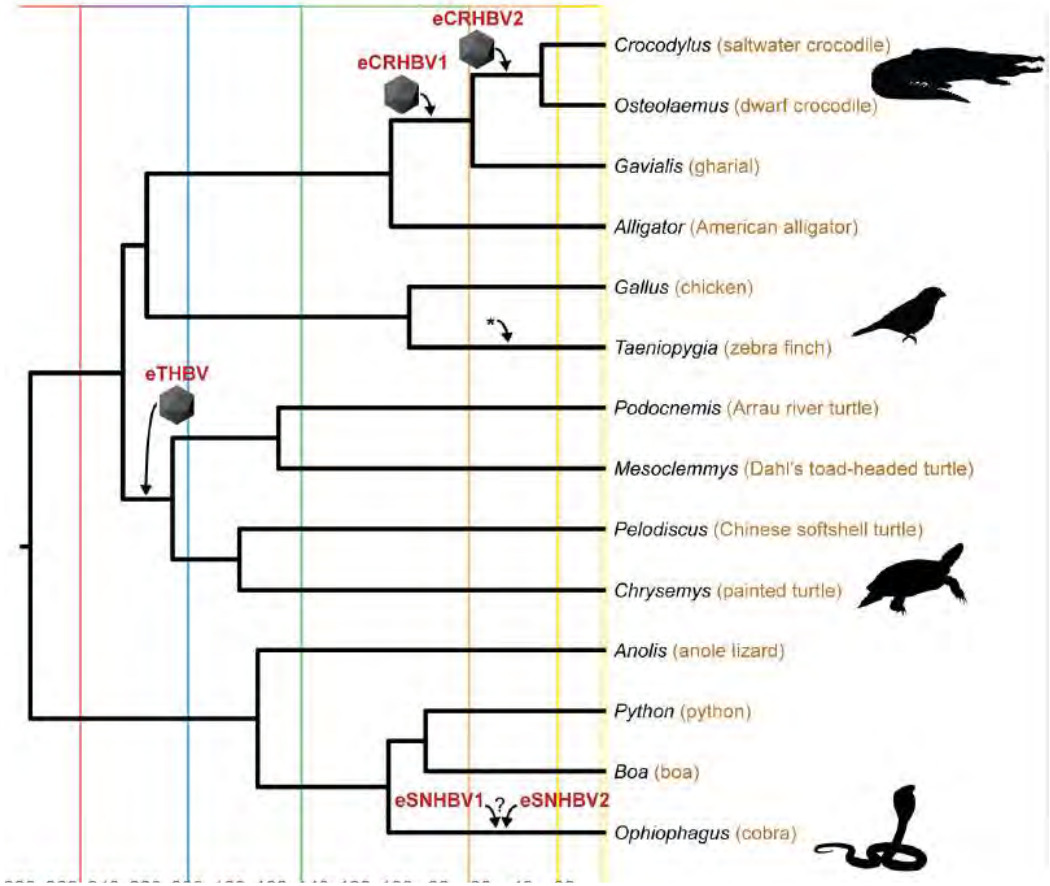
Rasche et al., J Hepatol., 2019

Long evolutionary association with vertebrates



Rasche et al., J Hepatol., 2019

Endogenous bird & reptile HBV
> 200 million years

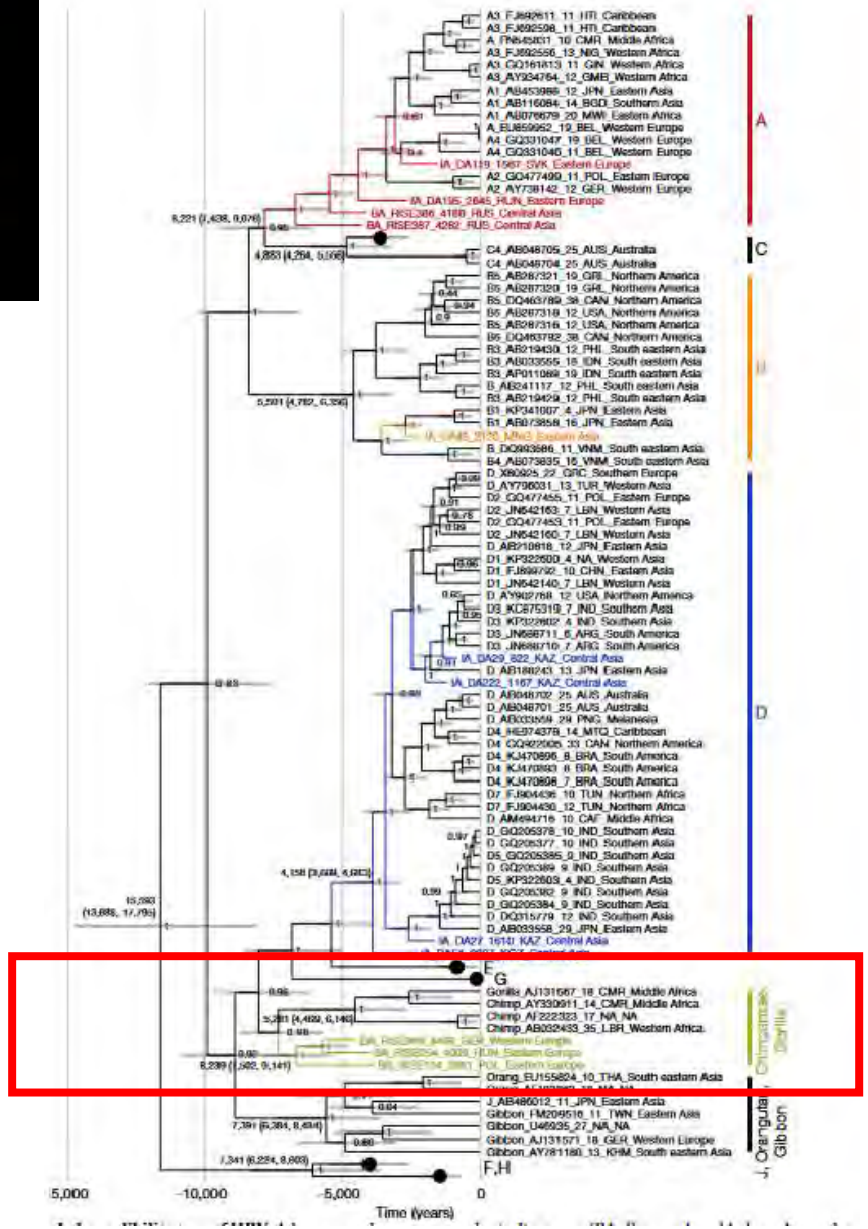


Suh, PLoS Gen, 2015

Suh, Nat comm, 2013

Ancient HBV >7000 years similar to contemporary strains

Extinct genotype



LETTER

https://doi.org/10.1038/s41586-018-0097-z

Ancient hepatitis B viruses from the Bronze Age to the Medieval period

Barbara Mühlemann[1], Terry C. Jones[1,2], Peter de Barros Damgaard[3], Morten E. Allentoft[3], Irina Shevnina[4], Andrey Logvin[4], Emma Usmanova[5], Irina P. Panyushkina[6], Bazartseren Boldgiv[7], Tsevel Bazartseren[8], Kadicha Tashbaeva[9], Victor Merz[10], Nina Lau[11], Václav Smrčka[12], Dmitry Vasyakin[13], Egor Kitov[14], Andrey Epimakhov[15], Dalia Pokutta[16], Magdolna Vicze[17], T. Douglas Price[18], Vyacheslav Moiseyev[19], Anders J. Hansen[3], Ludovic Orlando[3,20], Simon Rasmussen[21], Martin Sikora[3], Lasse Vinner[3], Albert D. M. E. Osterhaus[22], Derek F. Smith[1], Dieter Glebe[23,24], Ron A. M. Fouchier[25], Christian Drosten[26,27], Karl-Göran Sjögren[28], Kristian Kristiansen[29] & Eske Willerslev[3,27,30]*

Kahila Bar-Gal et al., Hepatology, 2012
Mühlemann et al., Nature, 2018
Krause-Kyoran et al., eLife, 2018

Eradication potentially possible – if no reservoirs

Editorial

EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

To have B or not to have B: Vaccine and the potential eradication of hepatitis B

Harvey J. Alter*

Department of Transfusion Medicine, Warren G. Magnuson Clinical Center, National Institutes of Health (NIH), Bethesda, MD, USA

JGH Journal of Gastroenterology and Hepatology JGHF

doi:10.1111/j.1440-1746.2009.06165.x

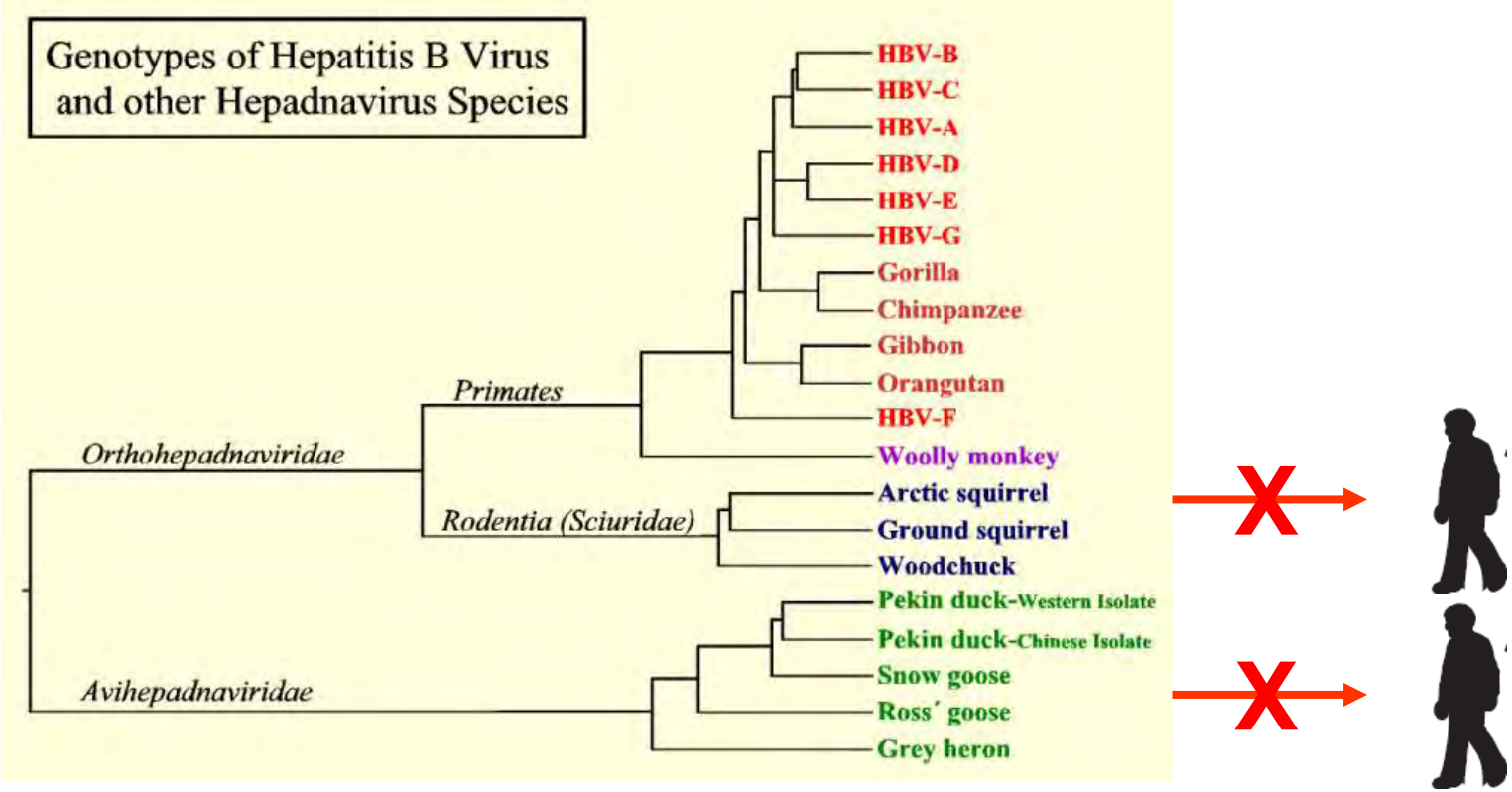
REVIEW

Toward elimination and eradication of hepatitis B

Ding-Shinn Chen

Department of Internal Medicine, National Taiwan University College of Medicine, Hepatitis Research Center, National Taiwan University Hospital, Taipei, Taiwan

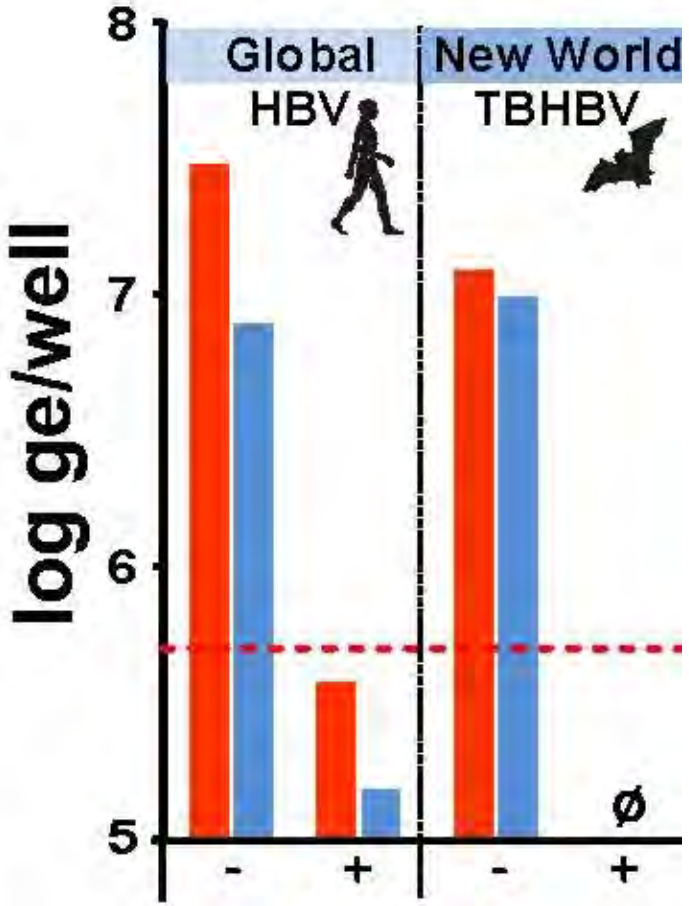
Textbook: animal HBVs cannot infect humans



Schäfer/Glebe

Potentially zoonotic? A New World bat HBV can efficiently infect human hepatocytes

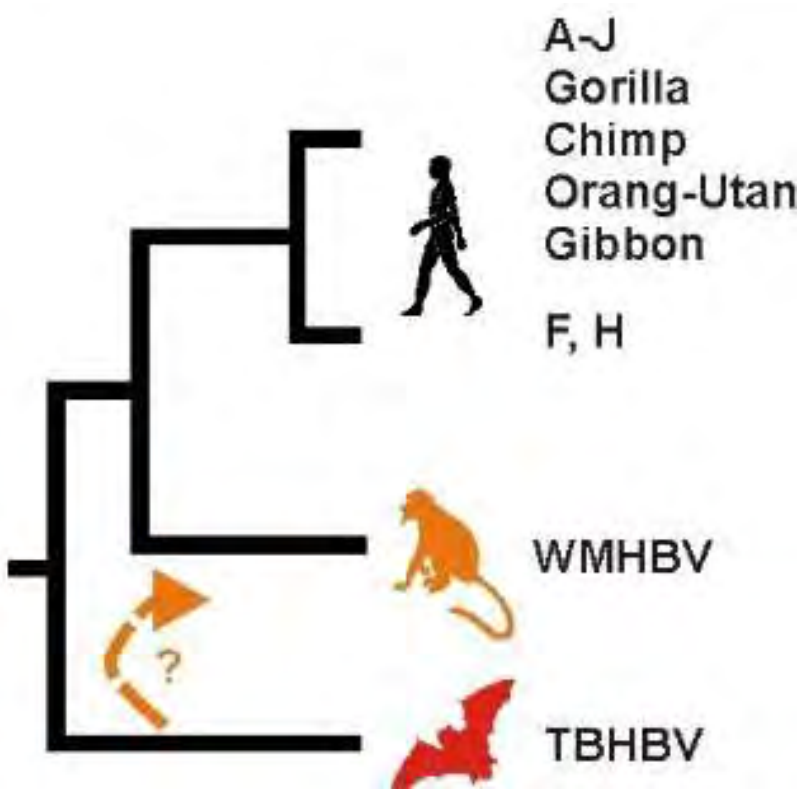
Tent-making bat
U. Bilobatum –
host of TBHBV



Immage: natalie's Life List, inaturalist.org

Drexler/Geipel et al., 2013, PNAS

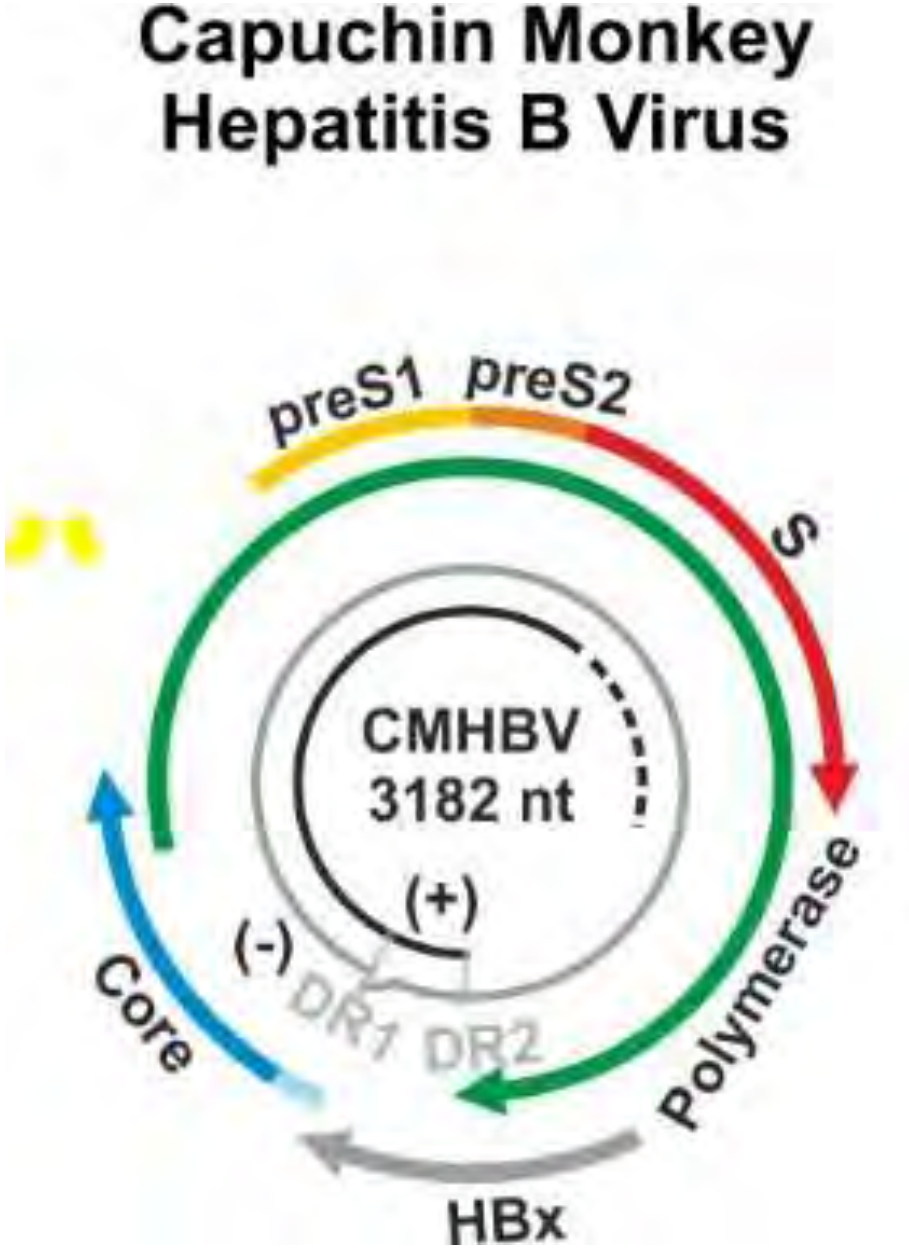
From bats into primates?



Rasche et al. CoV, 2016

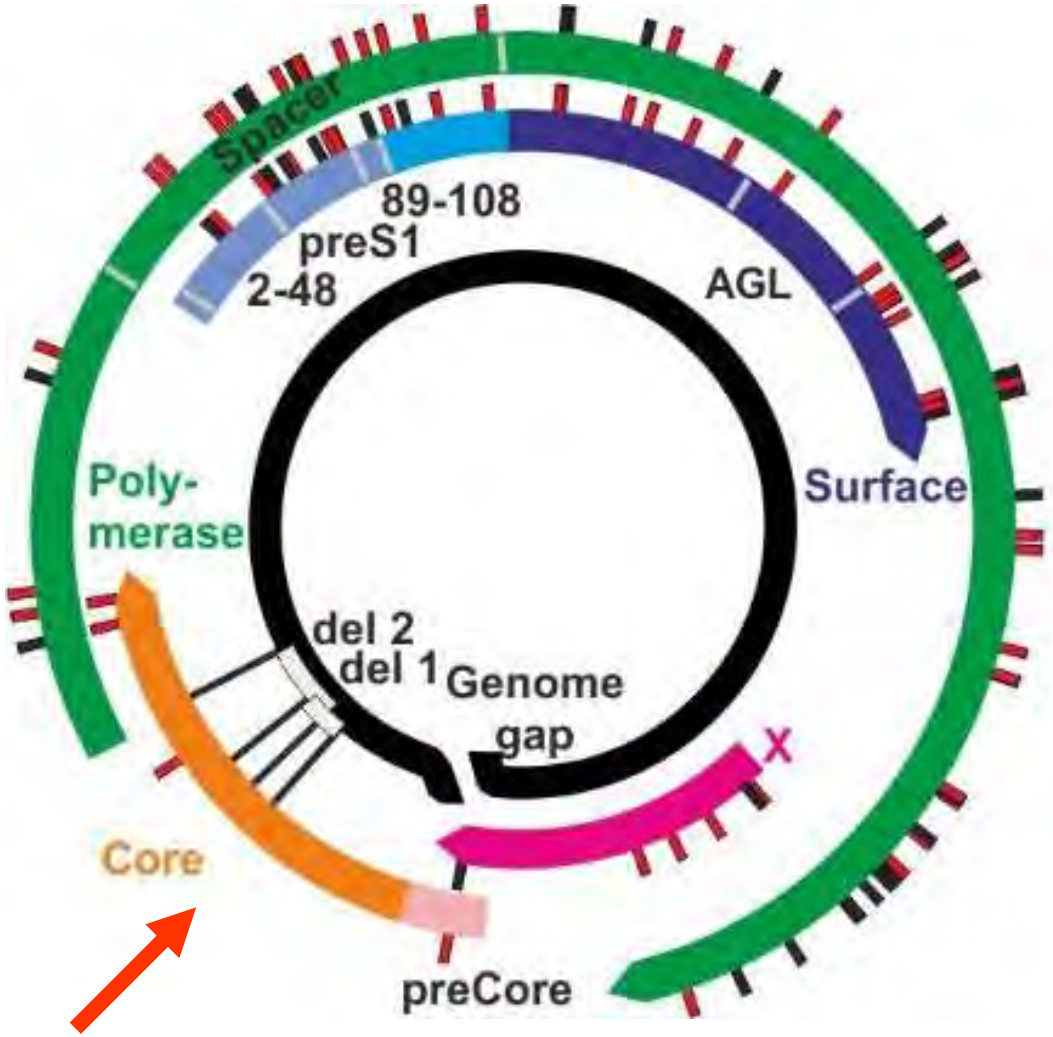
Brazil:
Highest primate diversity worldwide

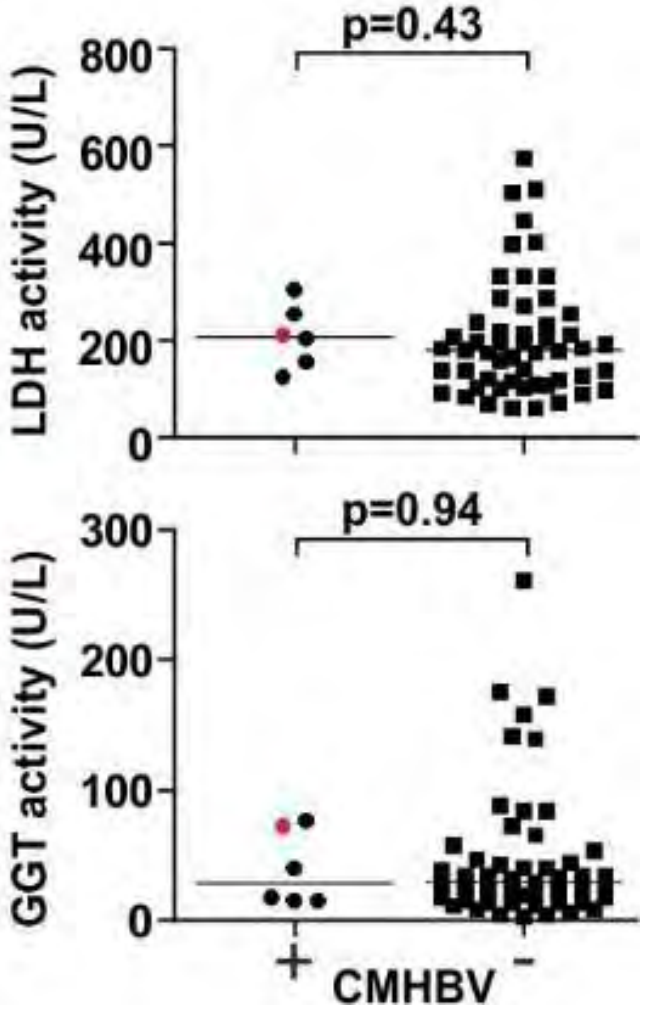
New CMHBV



Dominguez/König/Rasche et al., J Hepatol 2018

Chronic infection? Core deletions and no signs of inflammation





Dominguez/König/Rasche et al., J Hepatol 2018

Zoonosis? New World monkey HBVs can enter human hepatocytes

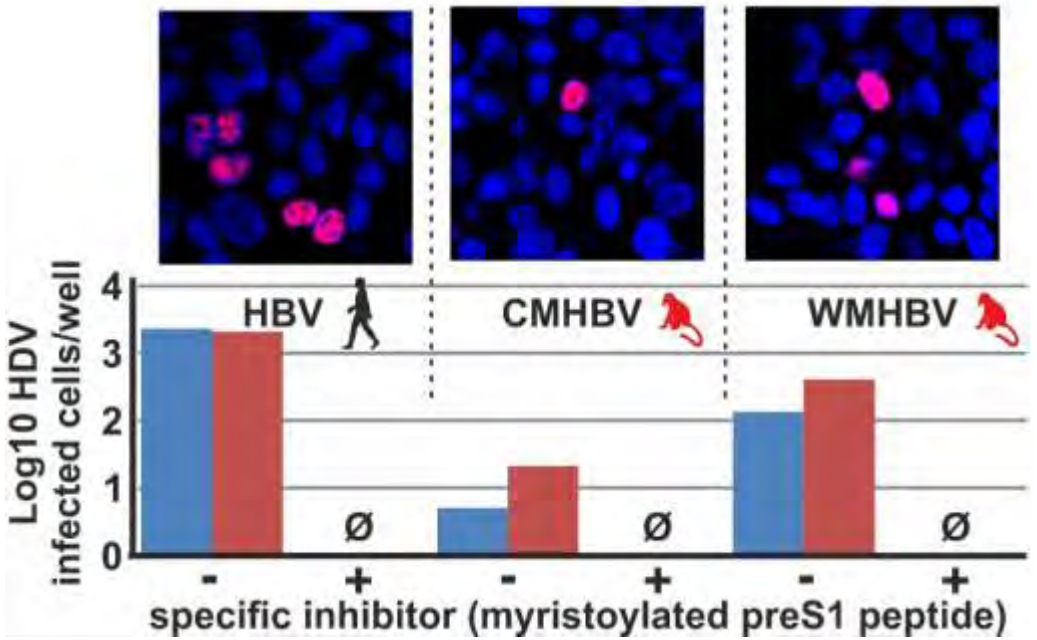


Image: National Geographic

Dominguez/König/Rasche et al., J Hepatol., 2018

Fresh data on animal HDV:
no HBV – conservation of infection patterns?

Cold Spring Harbor Laboratory

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New Results

A divergent hepatitis D-like agent in birds

Michelle Wille, Hans J Netter, Margaret Littlejohn, Lilly Yuen PhD, Mang Shi, John-Sebastian Eden, Marcel Klaassen, Edward C. Holmes, Aeron Christopher Hurt

doi: https://doi.org/10.1101/423707

Cold Spring Harbor Laboratory

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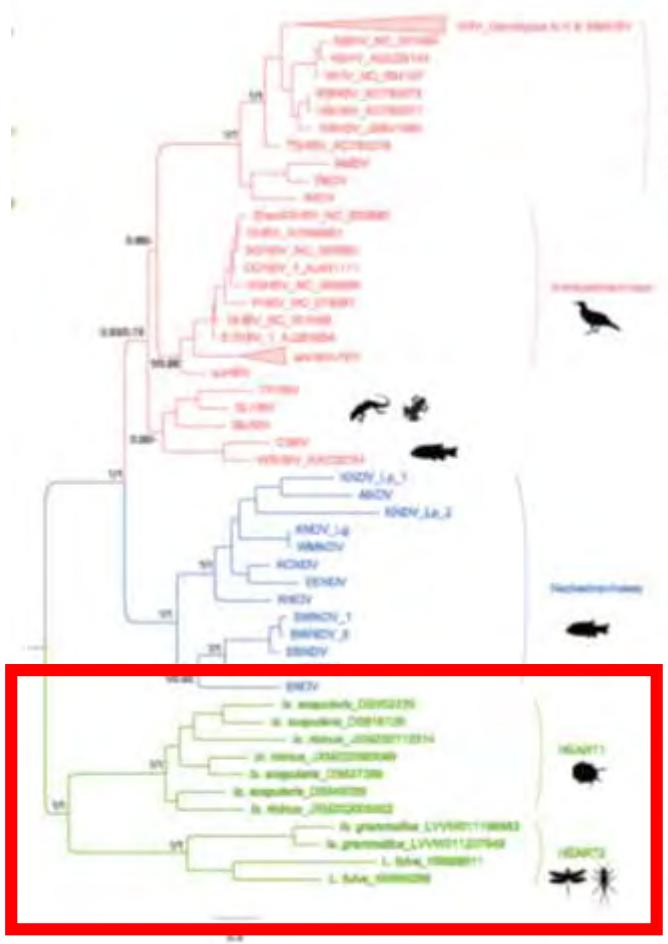
New Results

Identification of a novel deltavirus in Boa constrictor

Udo Hetzel, Leonora Szirovicza, Teemu Smura, Barbara Prahauser, Olli Vapalahti, Anja Kipar, Jussi Hepojoki

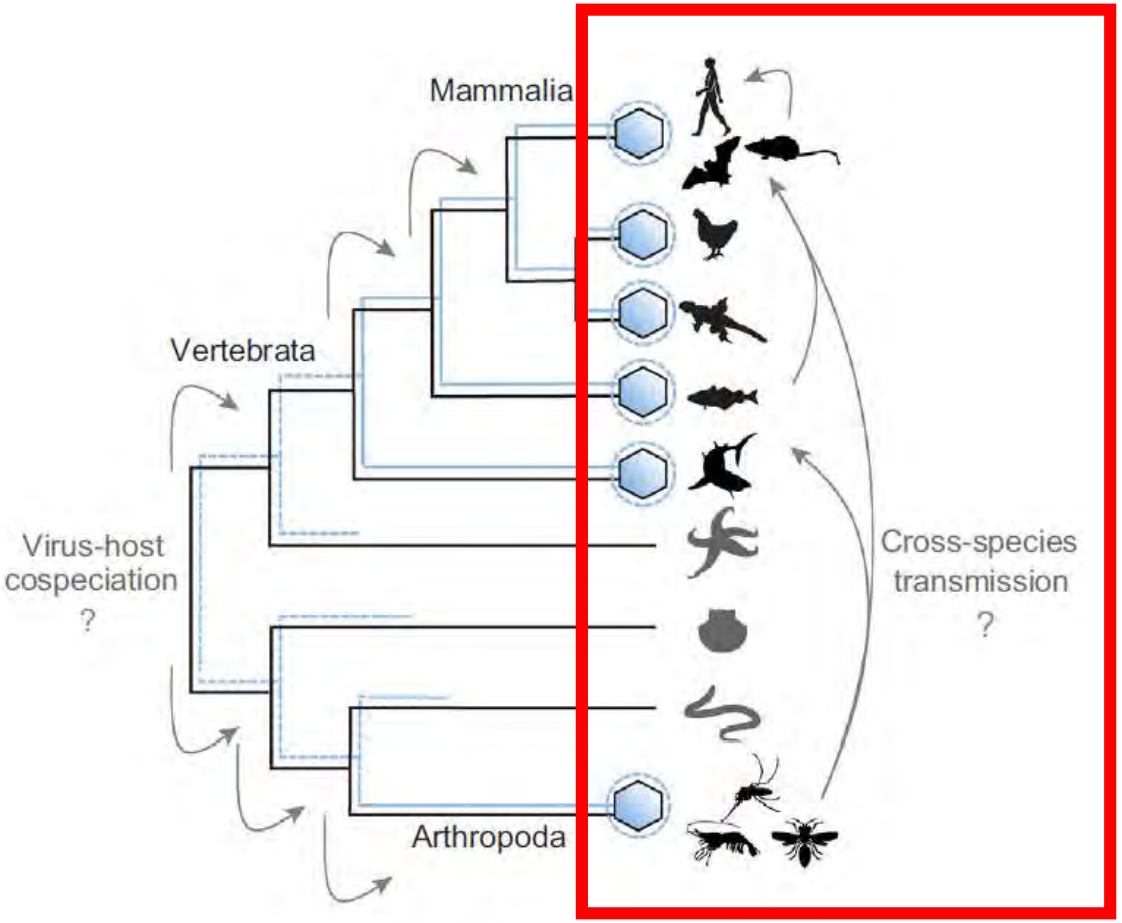
doi: https://doi.org/10.1101/429753

Acquisition of insect precursors by ancient insectivorous mammals?



HBV

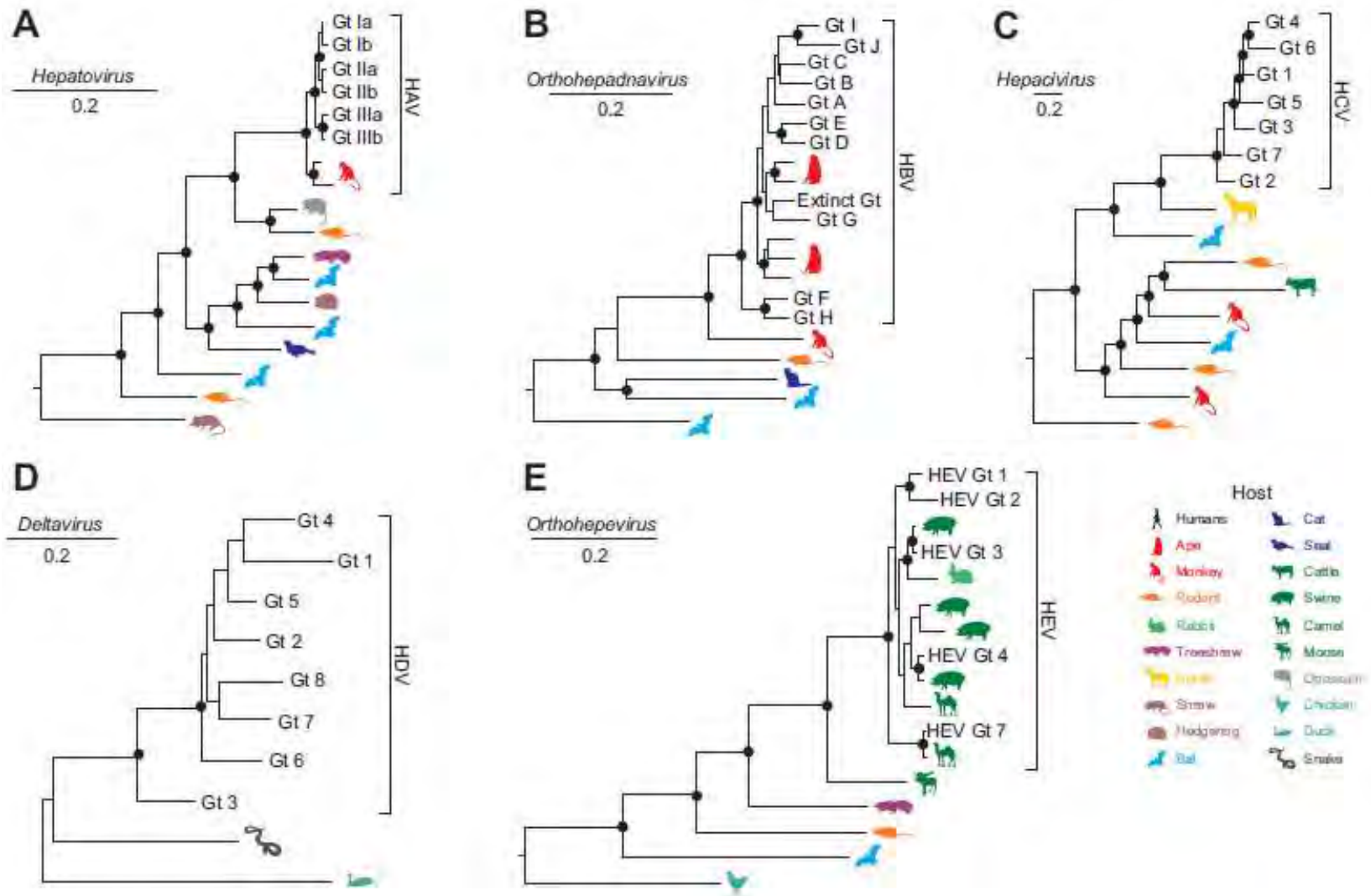
Nackedna



Gong/Han, Mol Biol Evol. 2018

Rasche et al., J Hepatol 2019

Hepatitis viruses origins beyond primates

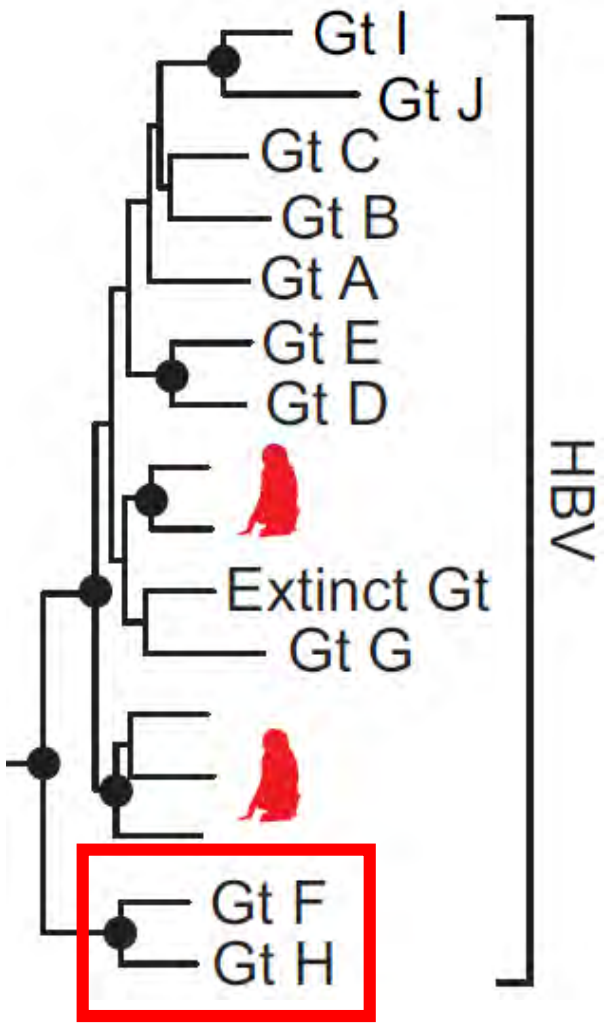


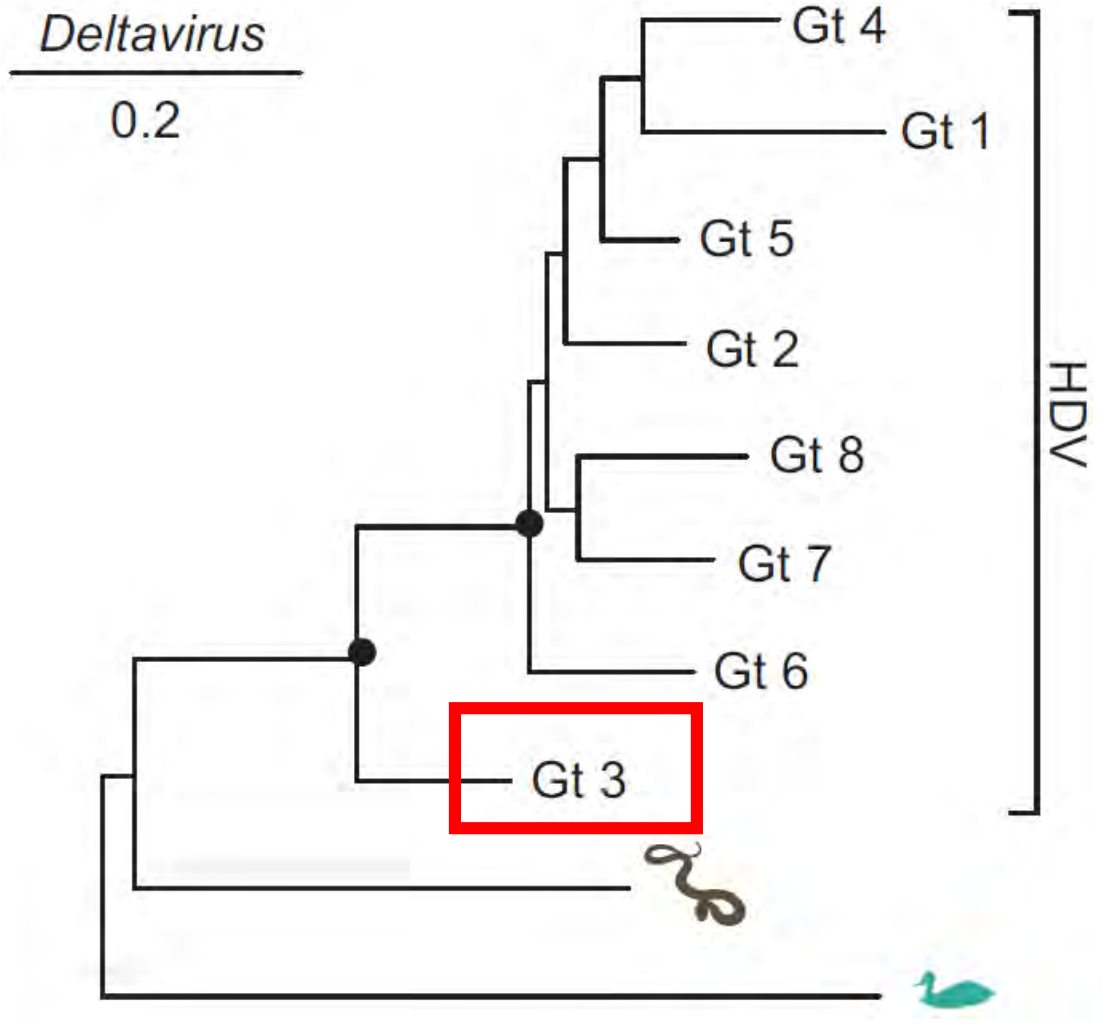
Rasche et al., J Hepatol., 2019

Unclear origin of New World HBV/HDV genotypes

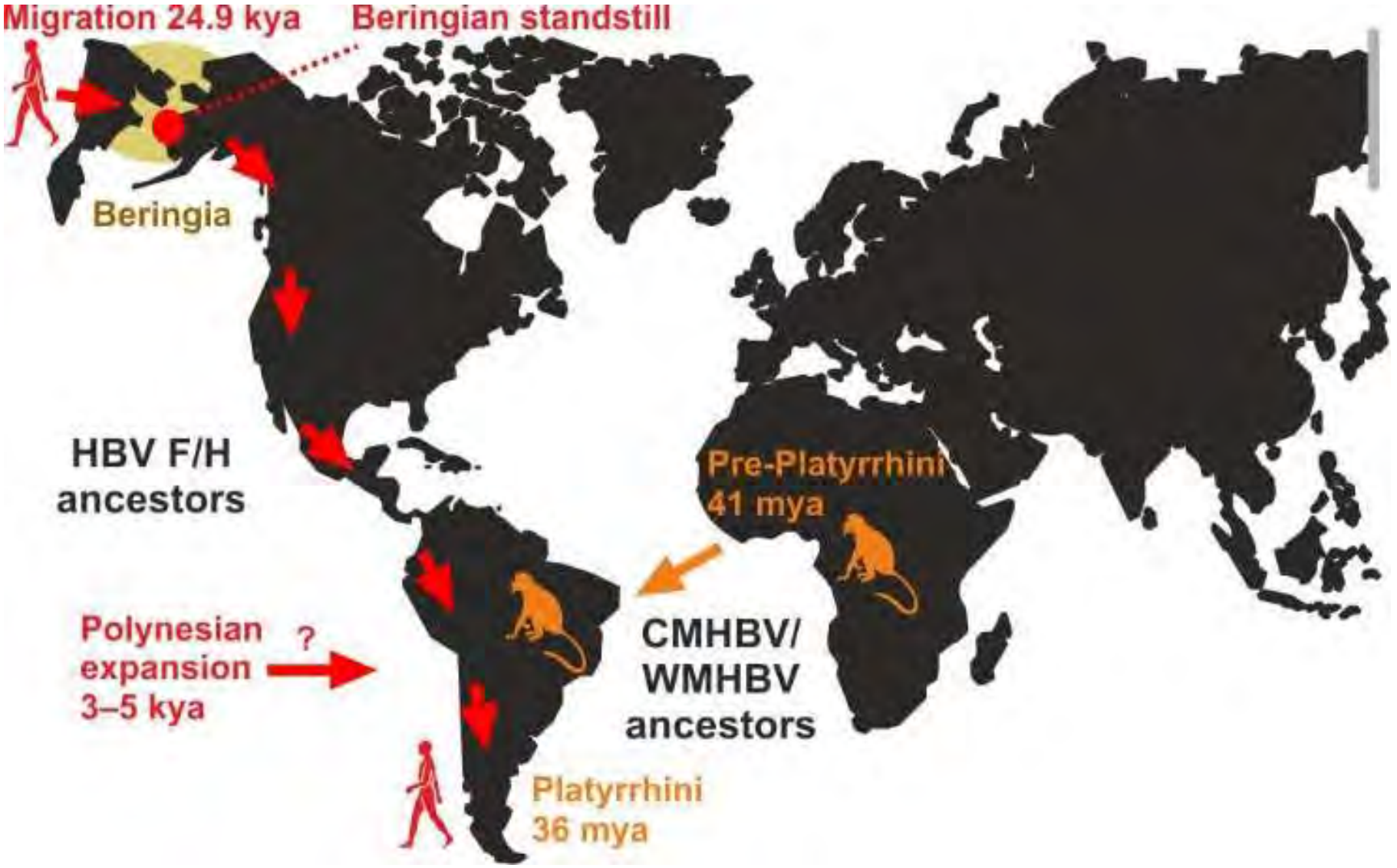
Rasche et al., J Hepatol., 2019

Rooting the trees by new animal viruses – surprising similarities



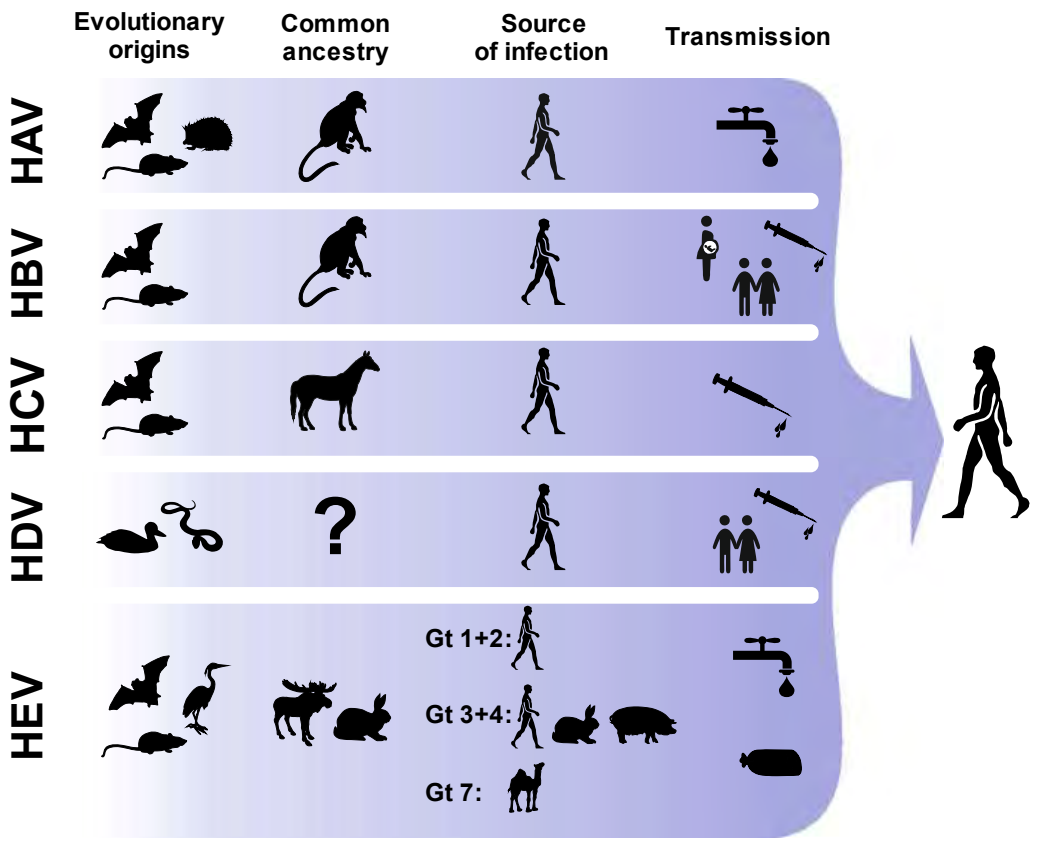


Rasche et al., J Hepatol., 2019



Introduction along human migration?

Dominguez/König/Rasche et al., J Hepatol, 2018



- **All human hepatitis viruses were once zoonotic**
- **The direct ancestors of human hepatitis viruses remain unknown**
- **Biological properties we took for certain are called into question**
- **Unique opportunities to understand pathogenesis**

Rasche et al., J Hepatol., 2019

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Roberto Franke
Eduardo Netto
Ana Bispo
Fernando Bozza

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