



Public Health
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publique du Canada

Canada

Hepatitis B virus in the circumpolar Arctic: Where did it come from?

Carla Osiowy

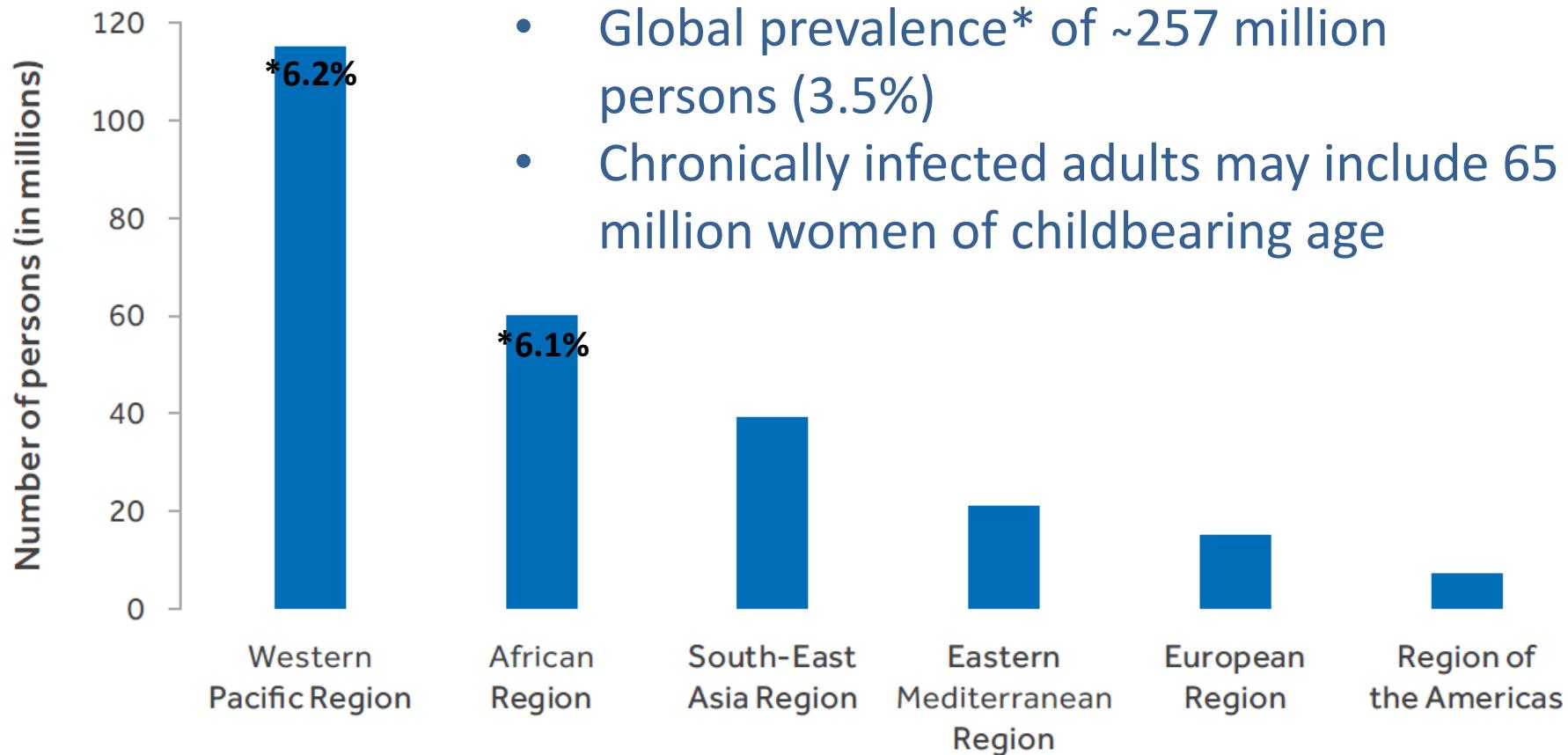
Viral Hepatitis and Bloodborne Pathogens section

National Microbiology Laboratory



PROTECTING AND EMPOWERING CANADIANS
TO IMPROVE THEIR HEALTH

Prevalence of HBV infection (HBsAg) in the general population by WHO region, 2015



Vertical transmission

Mucosal

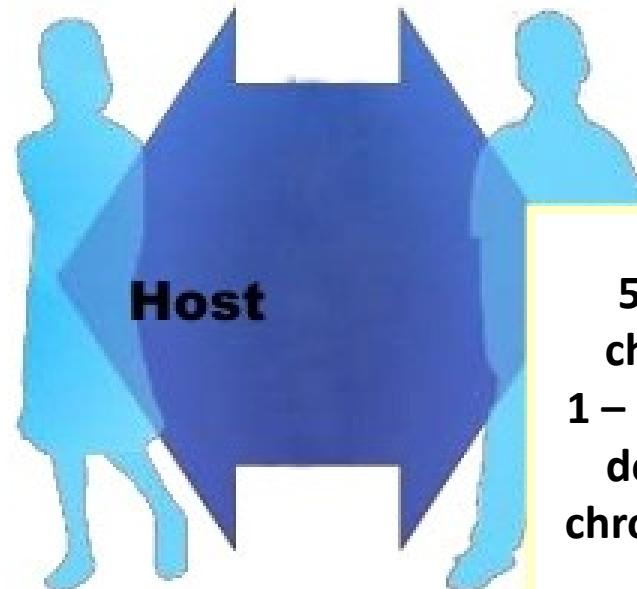
Perinatal

90% of infected infants develop chronic HBV



Horizontal transmission

Mucosal or percutaneous



50% of children 1 – 5 yrs old develop chronic HBV

Recipient

Child-to-child
Contaminated needles
Sexual contacts
Healthcare worker
Blood transfusion

Vaccinating children for hepatitis B is incredibly important



Risk of becoming chronically infected is as high as

90% for infants infected during their first year¹

Hepatitis B vaccine is three or four separate doses

**TAKE ACTION:
GET VACCINATED
GET PROTECTED**

PREVENT HEPATITIS: IT'S UP TO YOU

Hepatitis B is vaccine preventable
It can help protect against liver cancer

Some groups of people are more at risk than others, these include:



Prison populations



People who inject drugs



Close contacts of people with chronic hepatitis B infection



People with multiple sexual partners



Healthcare workers



Travellers to high risk countries

Hepatitis B, countries or areas at risk



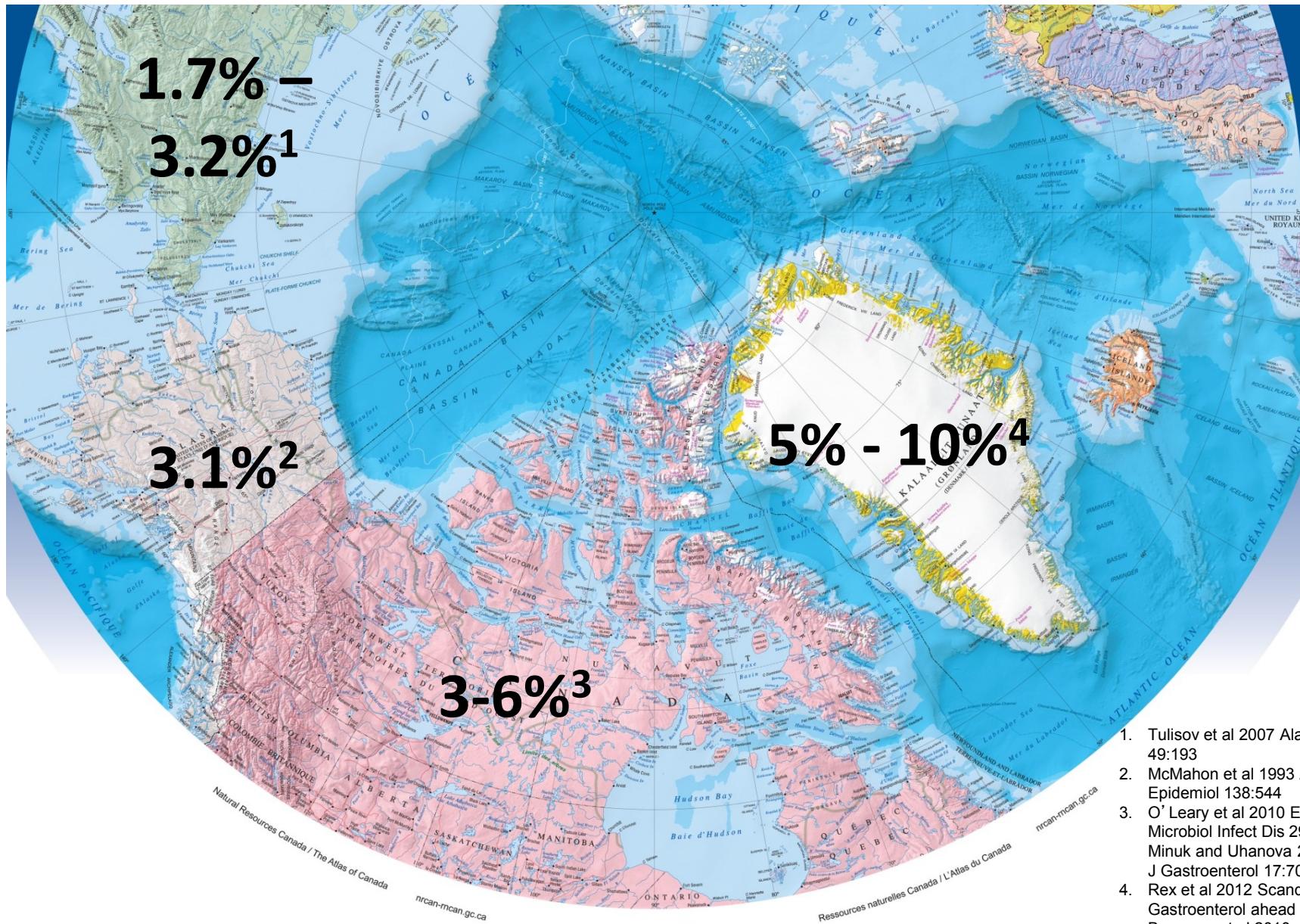
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization/CDC
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

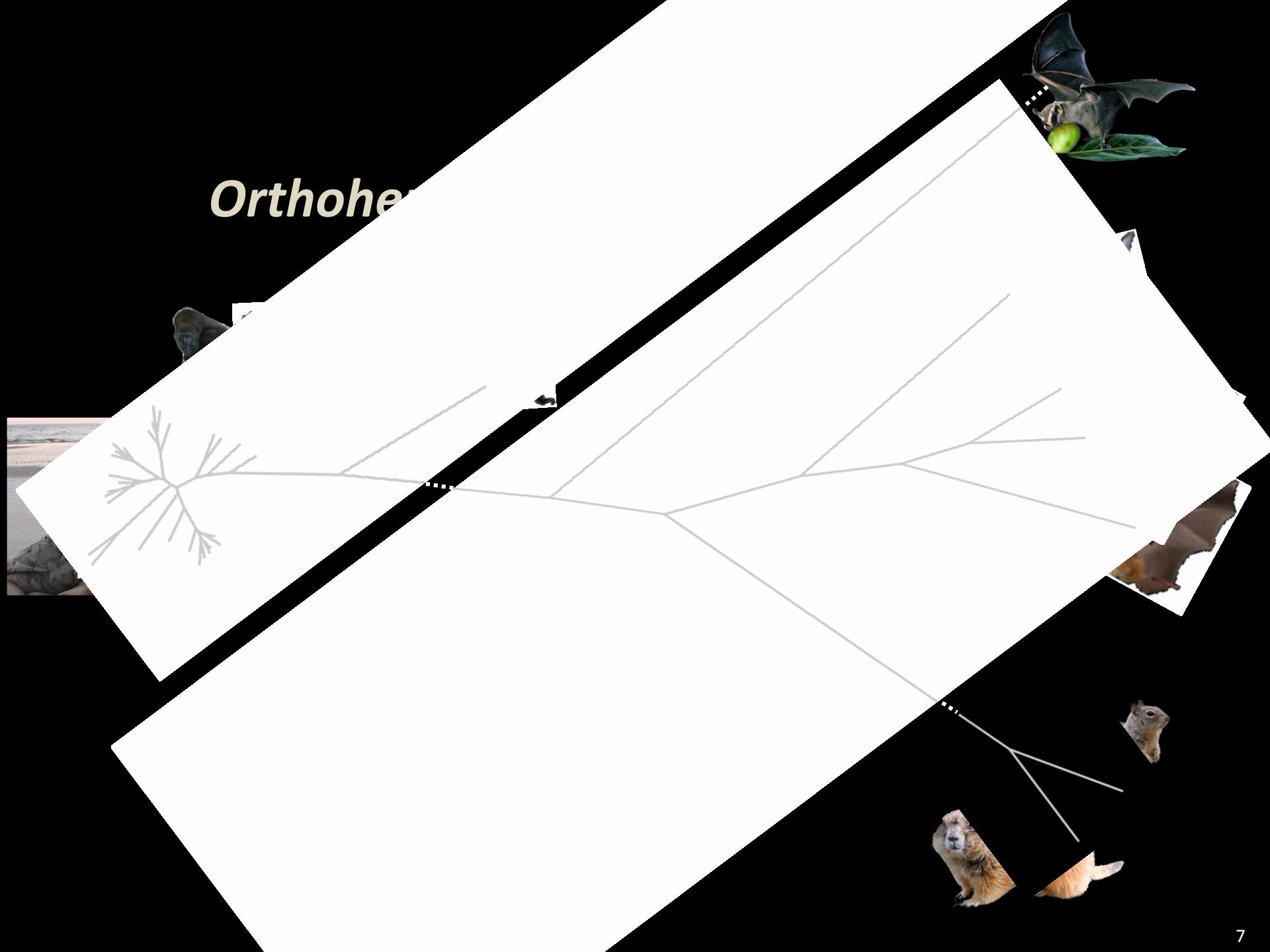


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Prevalence of CHB in Arctic Indigenous populations



Orthoherpetidae





LETTER

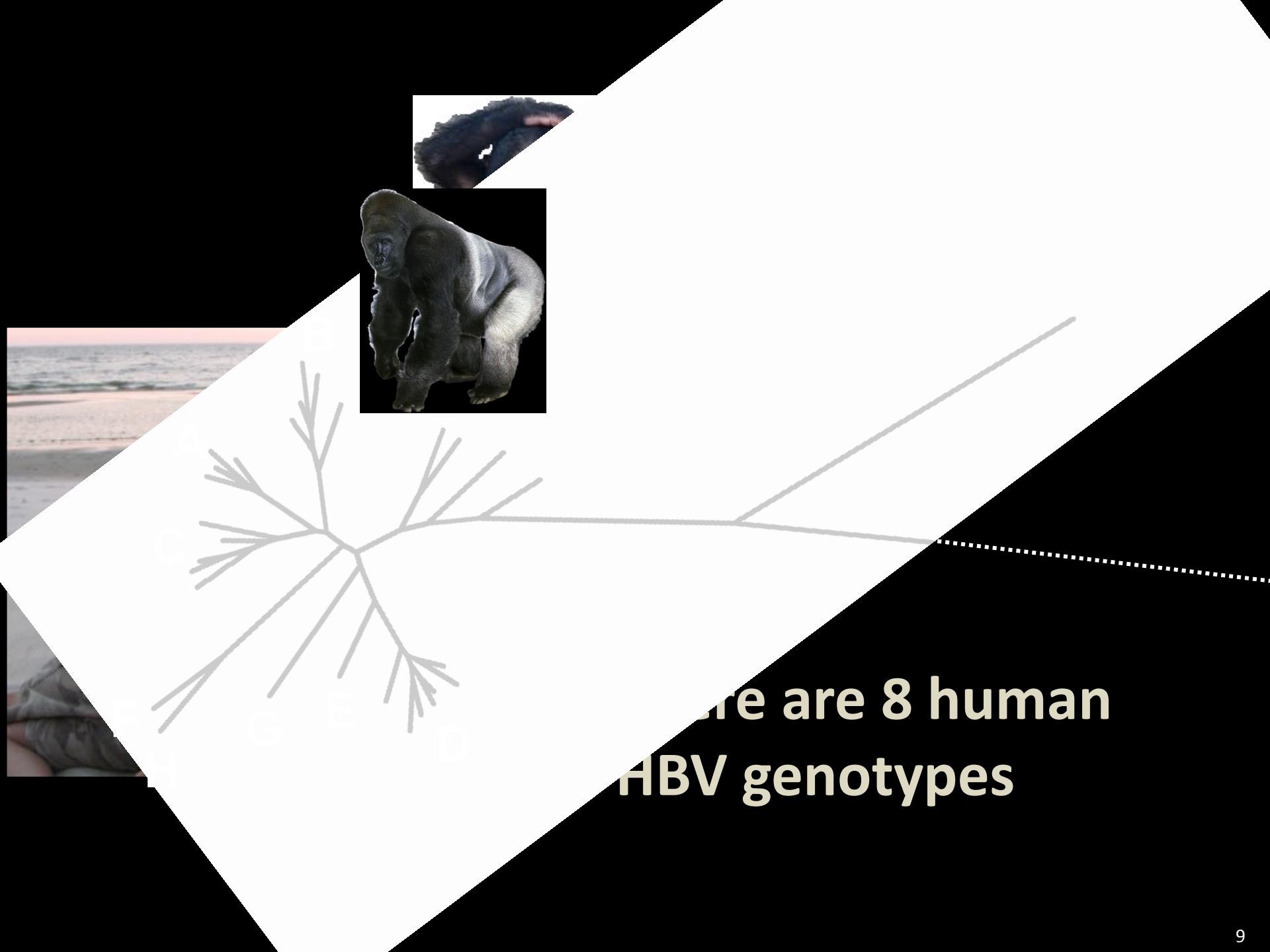
418 | NATURE | VOL 557 | 17 MAY 2018

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

Barbara Mühlemann^{1,29}, Terry C. Jones^{1,2,29}, Peter de Barros Damgaard^{3,29}, Morten E. Allentoft^{3,29}, Irina Shevina⁴, Andrey Logvin⁴, Emma Usmanova⁵, Irina P. Panyushkina⁶, Bazartsuren Boldgiv⁷, Tsevel Bazartsuren⁸, Kadicha Tashbaeva⁹, Victor Merz¹⁰, Nina Lau¹¹, Václav Smrčka¹², Dmitry Voyakin¹³, Egor Kitov¹⁴, Andrey Epimakhov¹⁵, Dalia Pokutta¹⁶, Magdalna Vicze¹⁷, T. Douglas Price¹⁸, Vyacheslav Moiseyev¹⁹, Anders J. Hansen³, Ludovic Orlando^{3,20}, Simon Rasmussen²¹, Martin Sikora³, Lasse Vinner³, Albert D. M. E. Osterhaus²², Derek J. Smith¹, Dieter Glebe^{23,24}, Ron A. M. Fouchier²⁵, Christian Drosten^{2,26}, Karl-Göran Sjögren¹⁸, Kristian Kristiansen¹⁸ & Eske Willerslev^{3,27,28*}



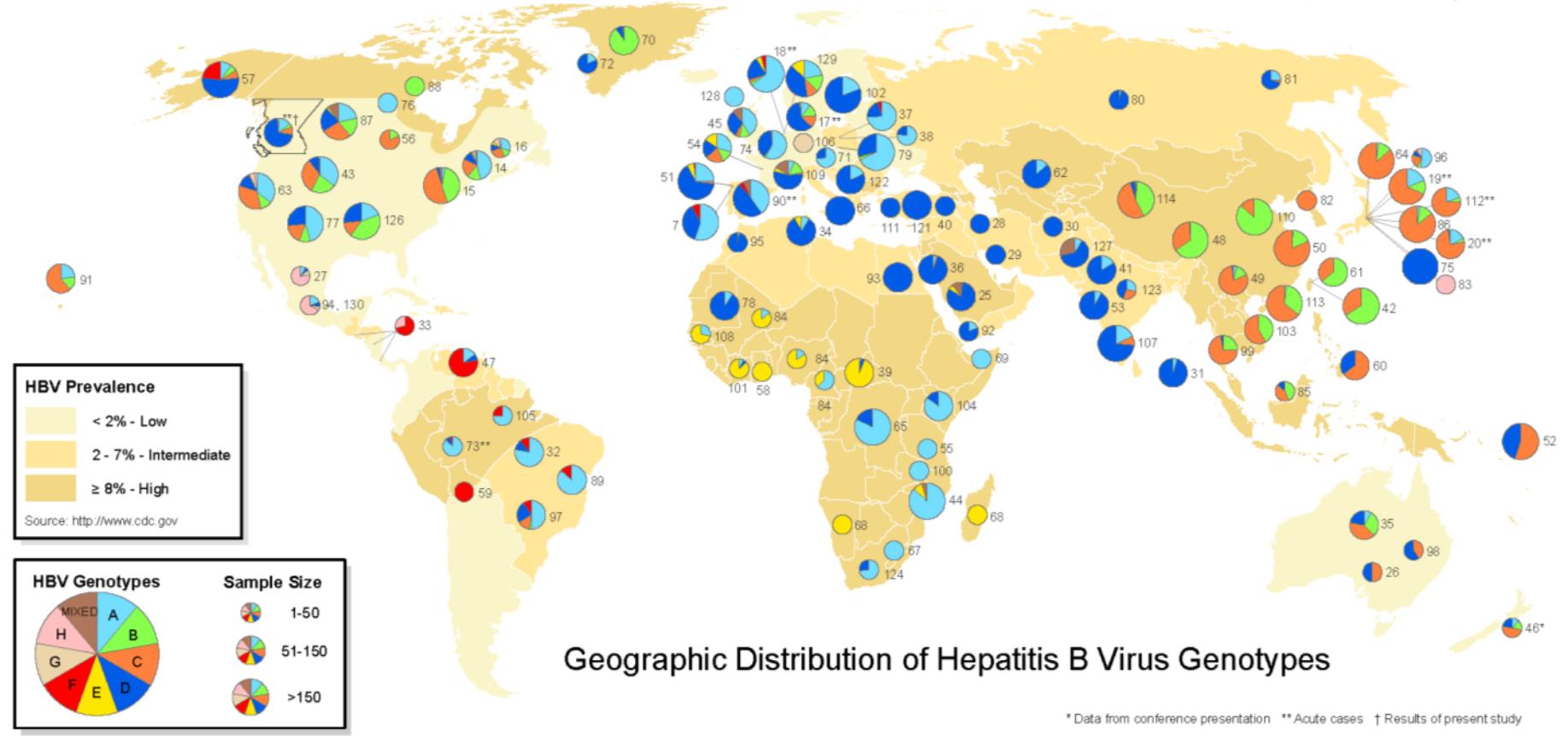
Ahh, the Bronze Age: fine jewellery, beautiful art ... and Hepatitis B.



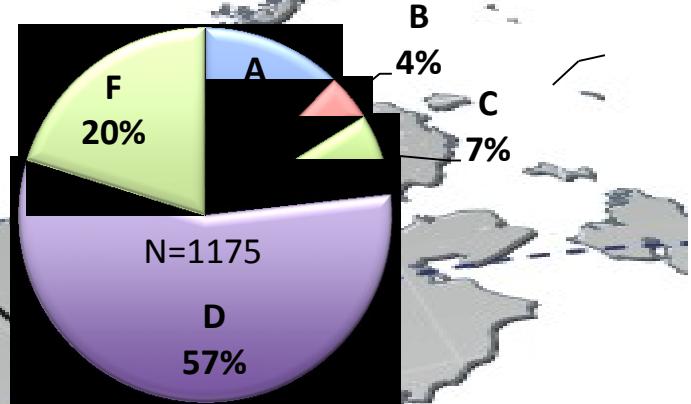
There are 8 human
HBV genotypes

Distribution of hepatitis B virus genotypes

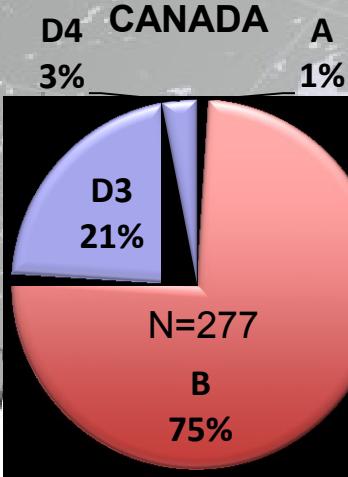
Panessa, C., et al. 2009 J Viral Hepatitis 16:64-73



HBV genotypes B and D are highly prevalent throughout the circumpolar Arctic

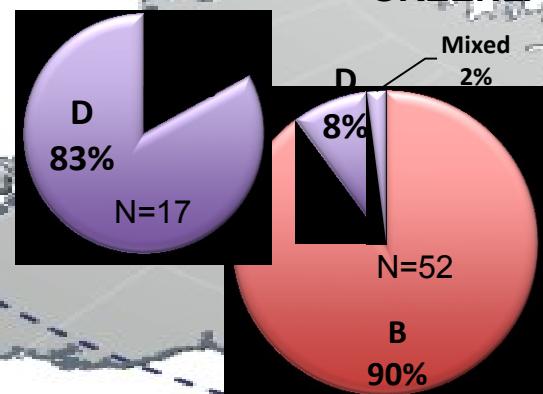


ALASKA (USA)

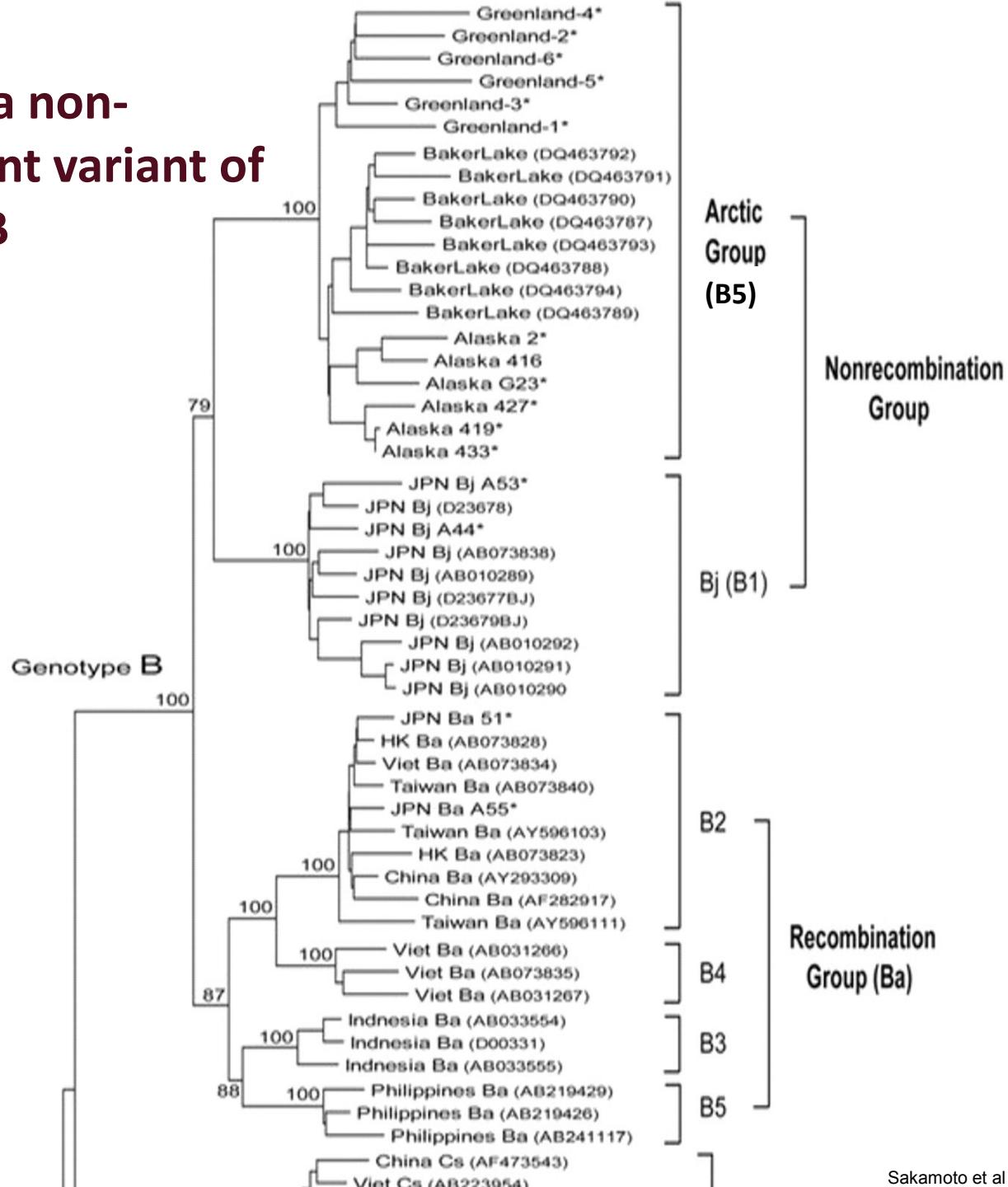


D4 CANADA A
3% 1%

GREENLAND



HBV/B5 is a non-recombinant variant of genotype B



Unique virological and clinical characteristics of HBV/B5

- HBV/B5 is a non-recombinant genomic variant unique to populations of the circumpolar Arctic region

Sakamoto, T., et al. 2007 J Infect Dis 196:1487

- HBV/B5 is highly associated with an inactive, benign infection

Minuk G., et al. 2013 J Viral Hepat 20:890

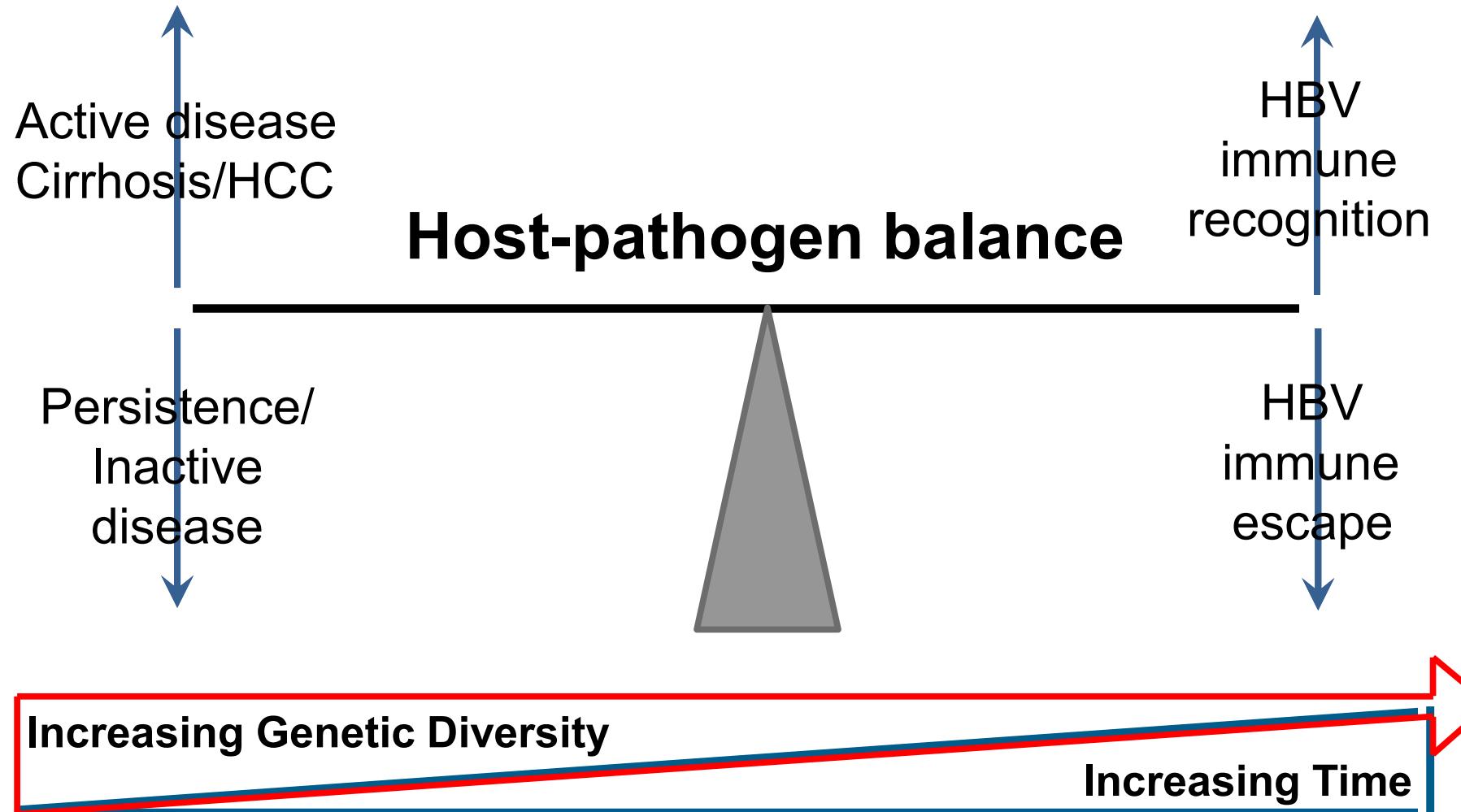
- B5 evolutionary rate is estimated to be slightly faster than previous estimates of HBV

Osiowy C., et al. 2006 J Virol 80:10307

- HBV/B5 demonstrates increased genetic diversity compared to other genotypes (D and F) that infect circumpolar Inuit

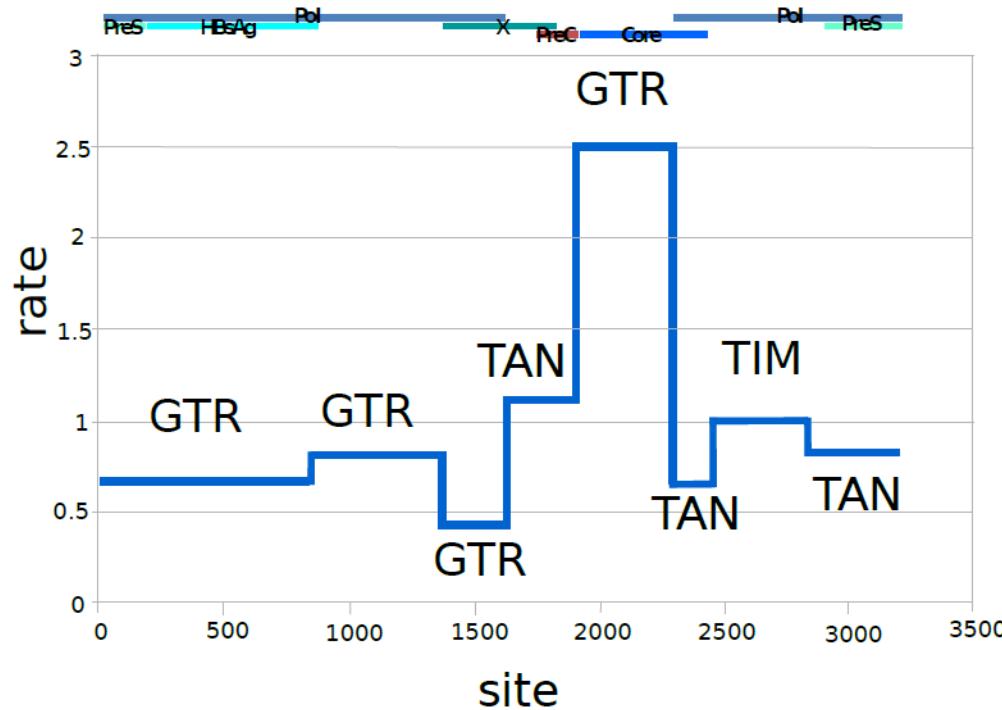
Kowalec K., et al. 2013 J Viral Hepat 20:122

HBV/B5: Co-adaptation

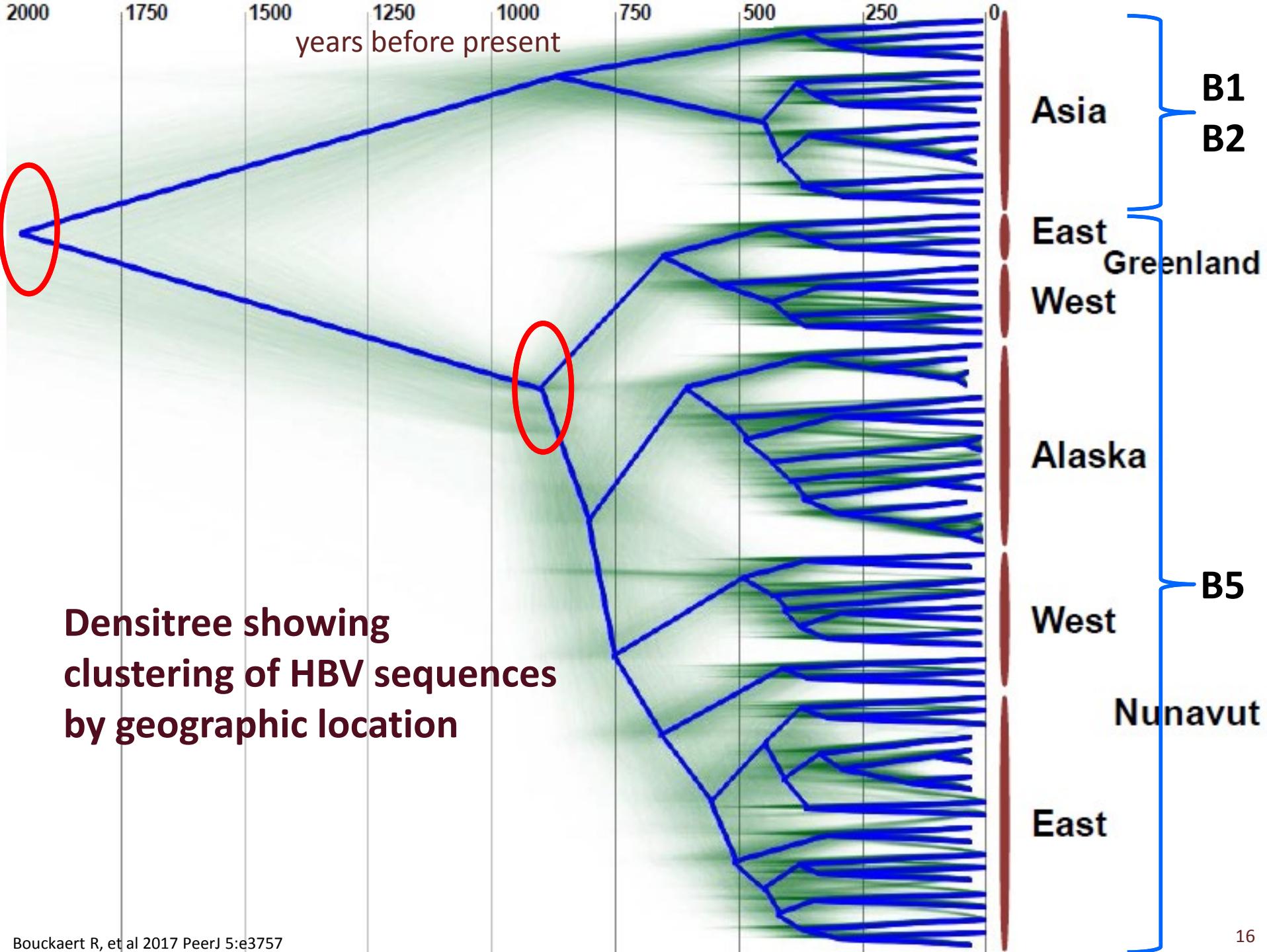


Study Methods:

- 57 HBV/B5 partial (17) and full (40) genome sequences plus 15 HBV/B reference full genome sequences (11 B1, 4 B2) having known geographic location and date of collection information
- BEAST analysis using a reversible jump-based substitution model: takes into account the overlapping ORF nature of the HBV genome



Bouckaert R, et al 2017 PeerJ 5:e3757

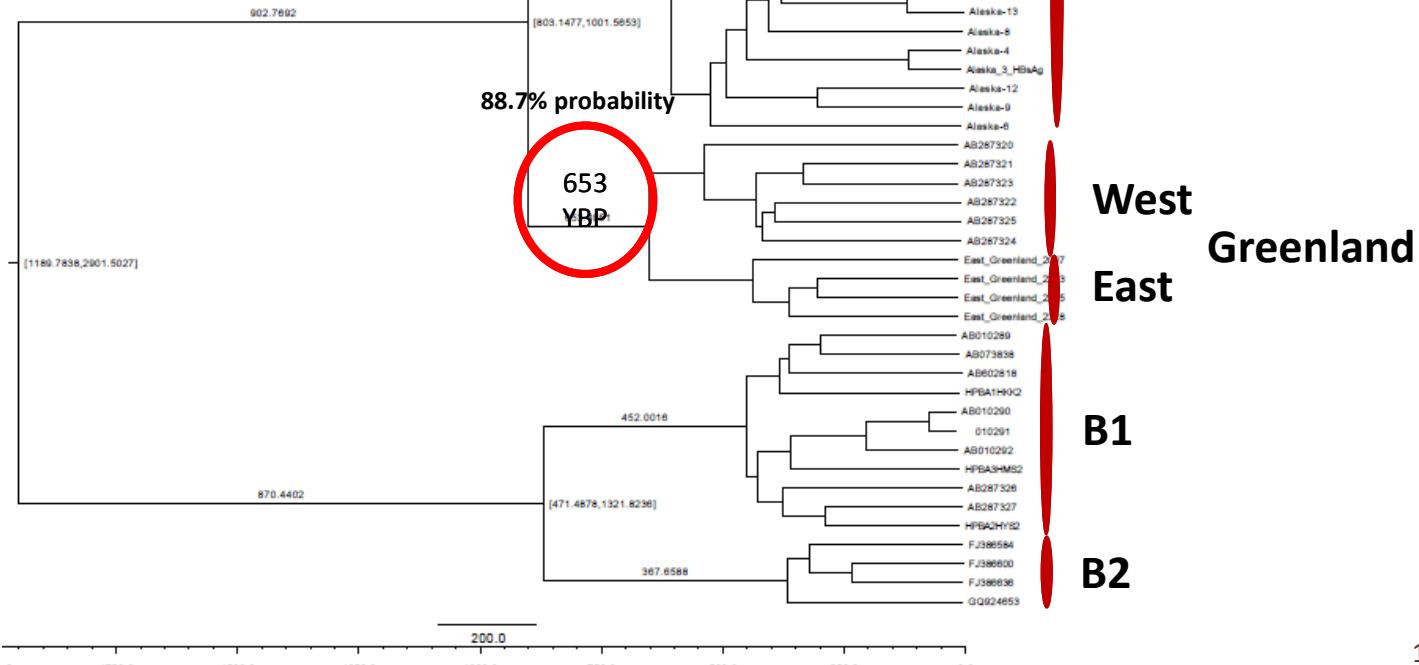


Summary tree showing older node heights for Greenland than for:

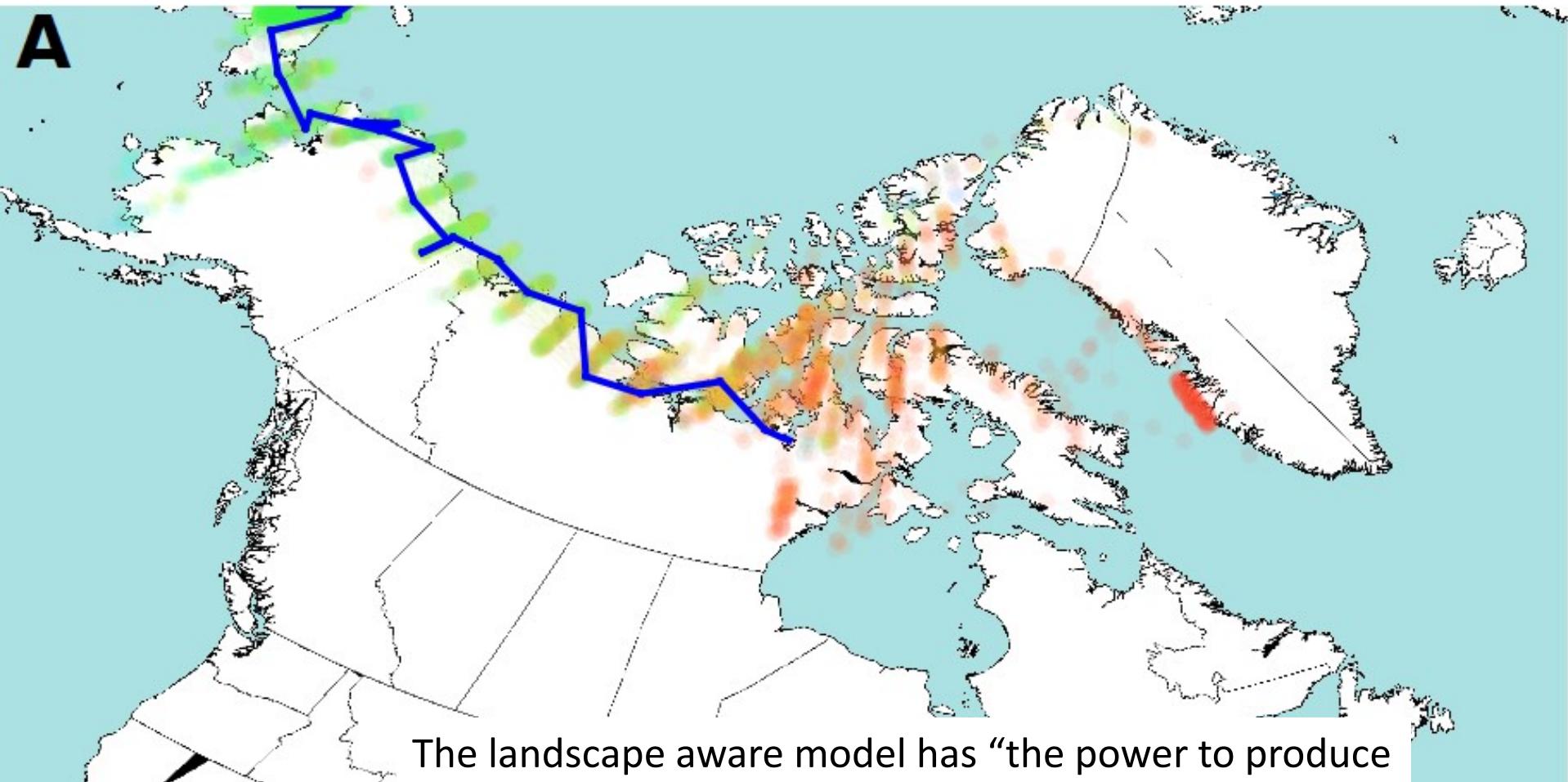
1) Alaska-West Nunavut/East NU
(27%)

or

2) Alaska/East and West Nunavut
(47%)

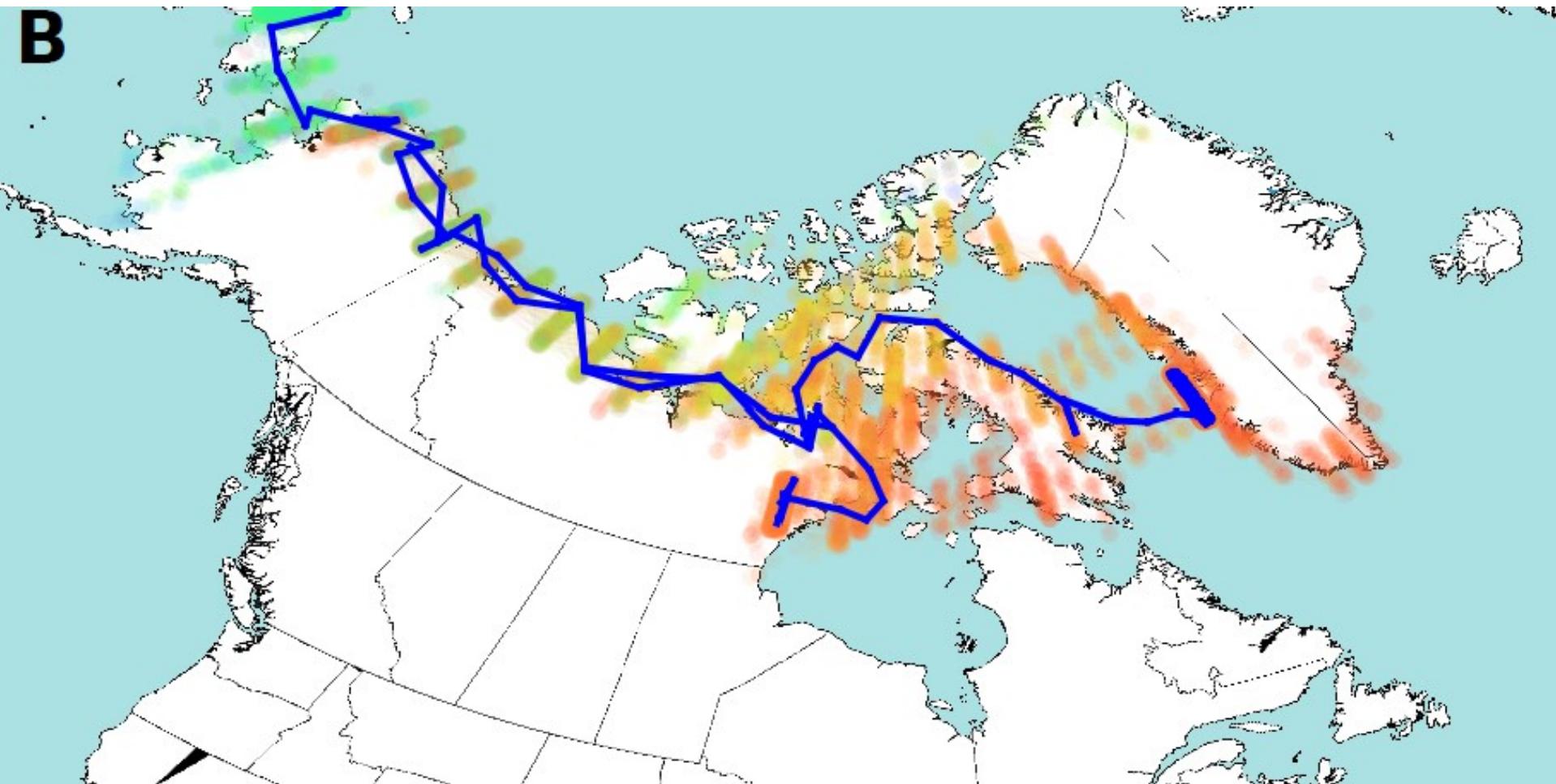


Estimated HBV dispersal routes into the high Eastern Arctic: 900 YBP

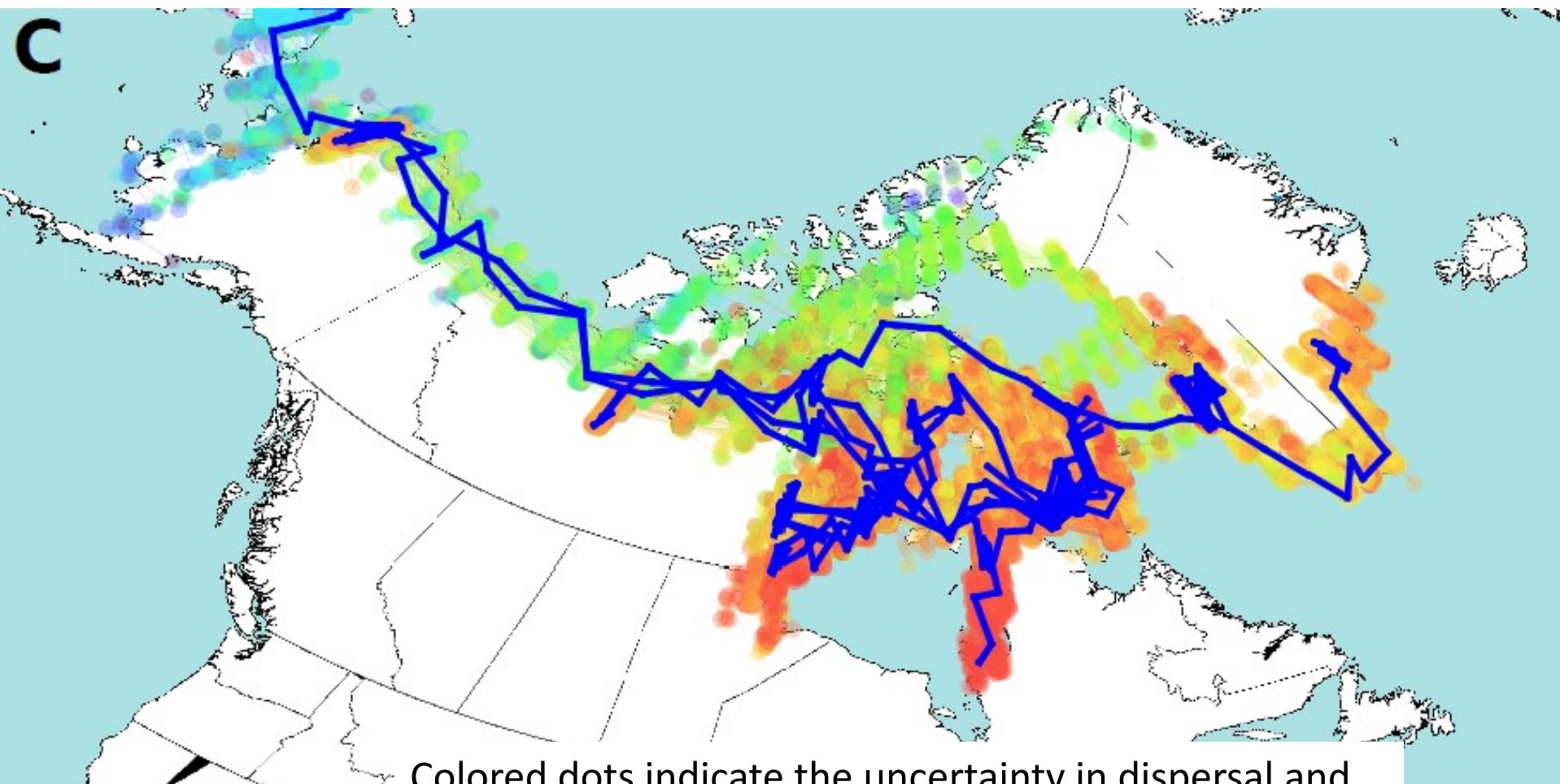


The landscape aware model has “the power to produce large differences in phylogeographical reconstruction based on non-uniform rates of migration over distinct landscapes, such as water, coastline and land”

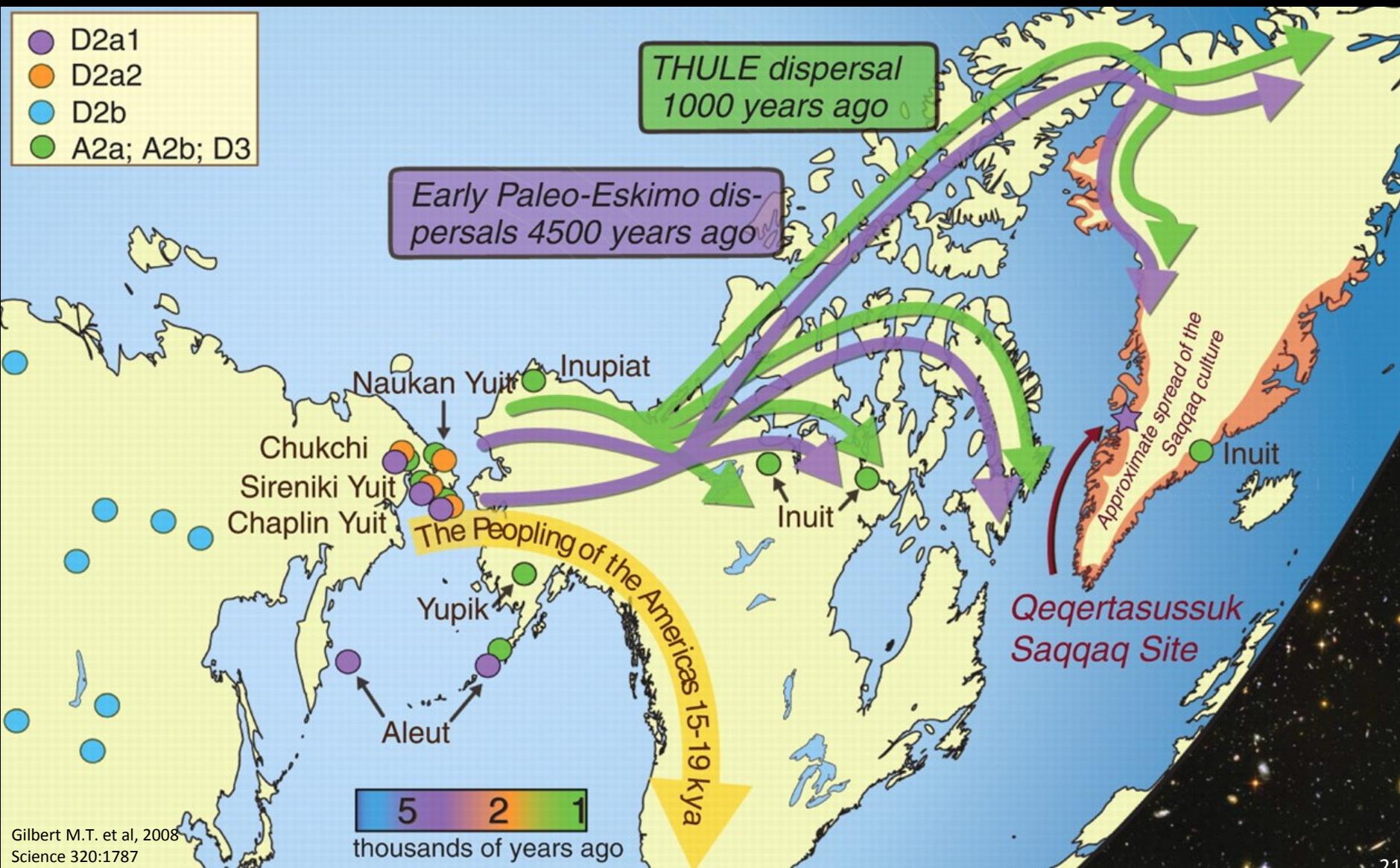
Estimated HBV dispersal routes into the high Eastern Arctic: 600 YBP

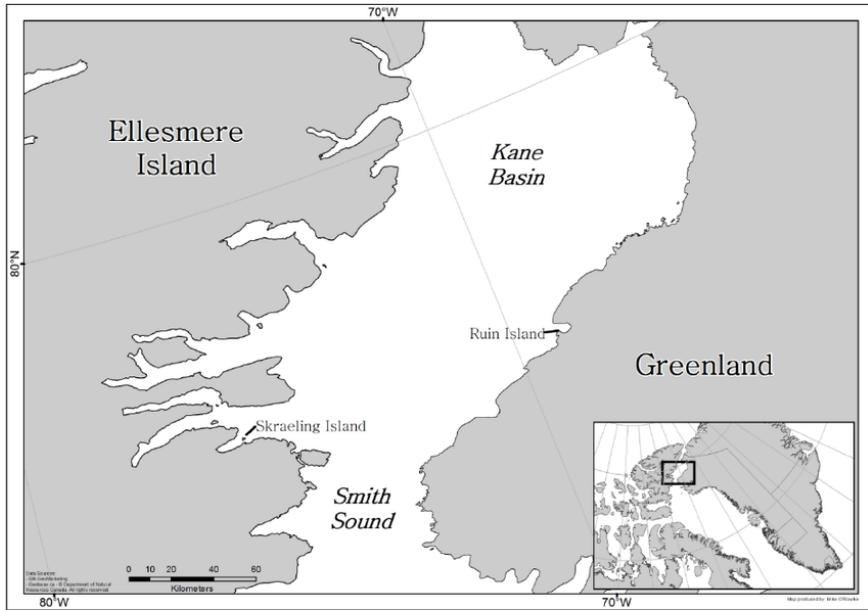


Estimated HBV dispersal routes into the high Eastern Arctic: Present



Thule dispersal: Complete displacement of previous Dorset culture and peoples...

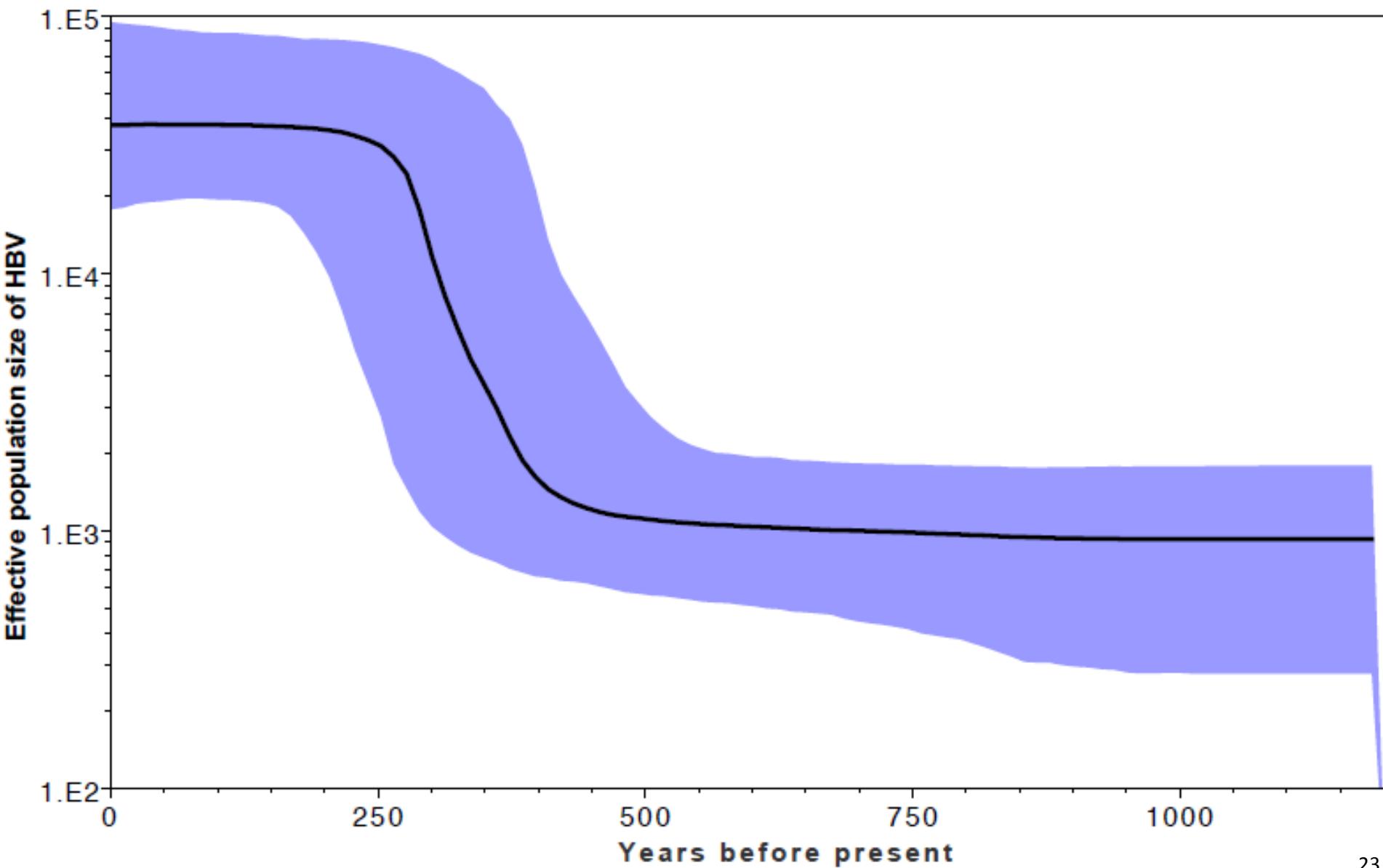


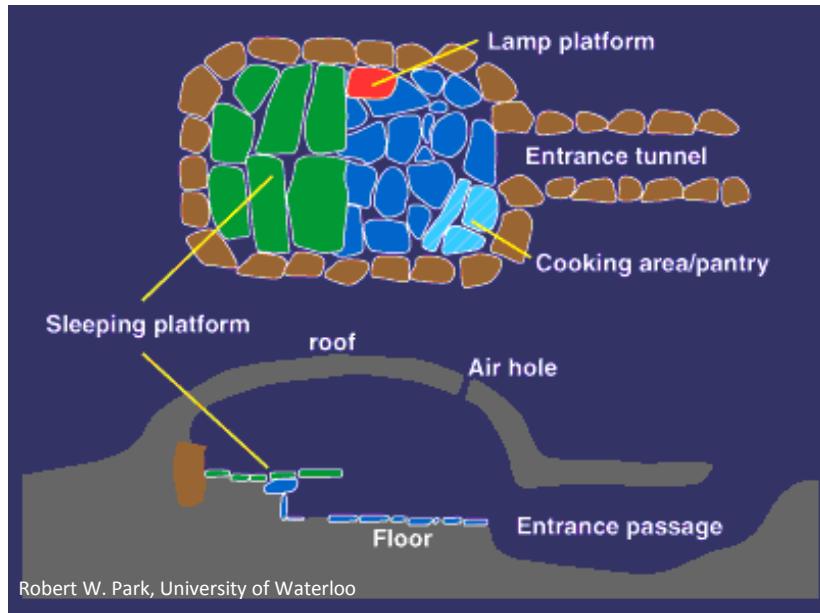


Ruin Island Thule



A rapid expansion in the HBV/B5 population is estimated to have occurred during CE 1600-1750

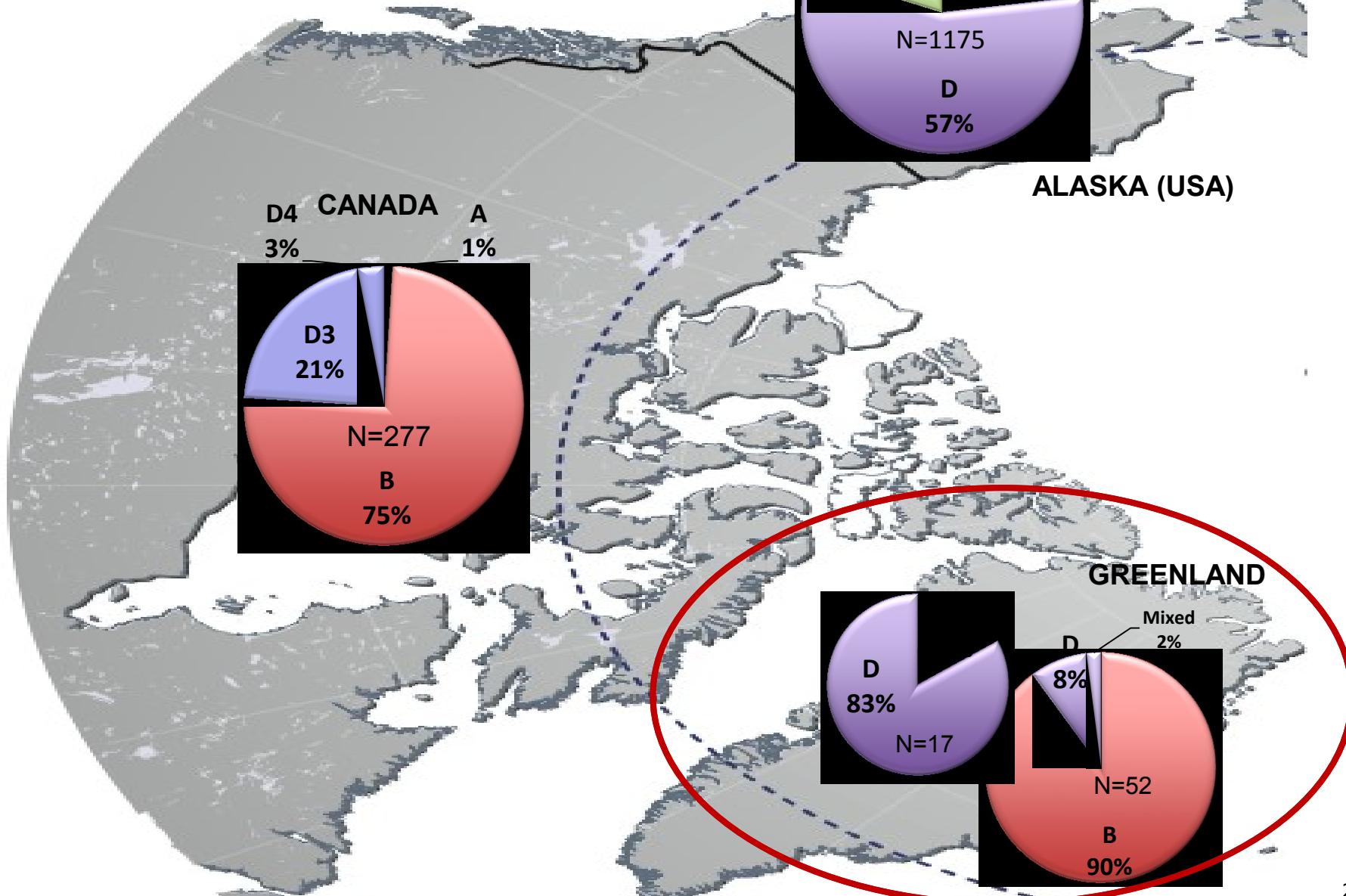




Transformation of the Thule culture starts ~500 YBP...

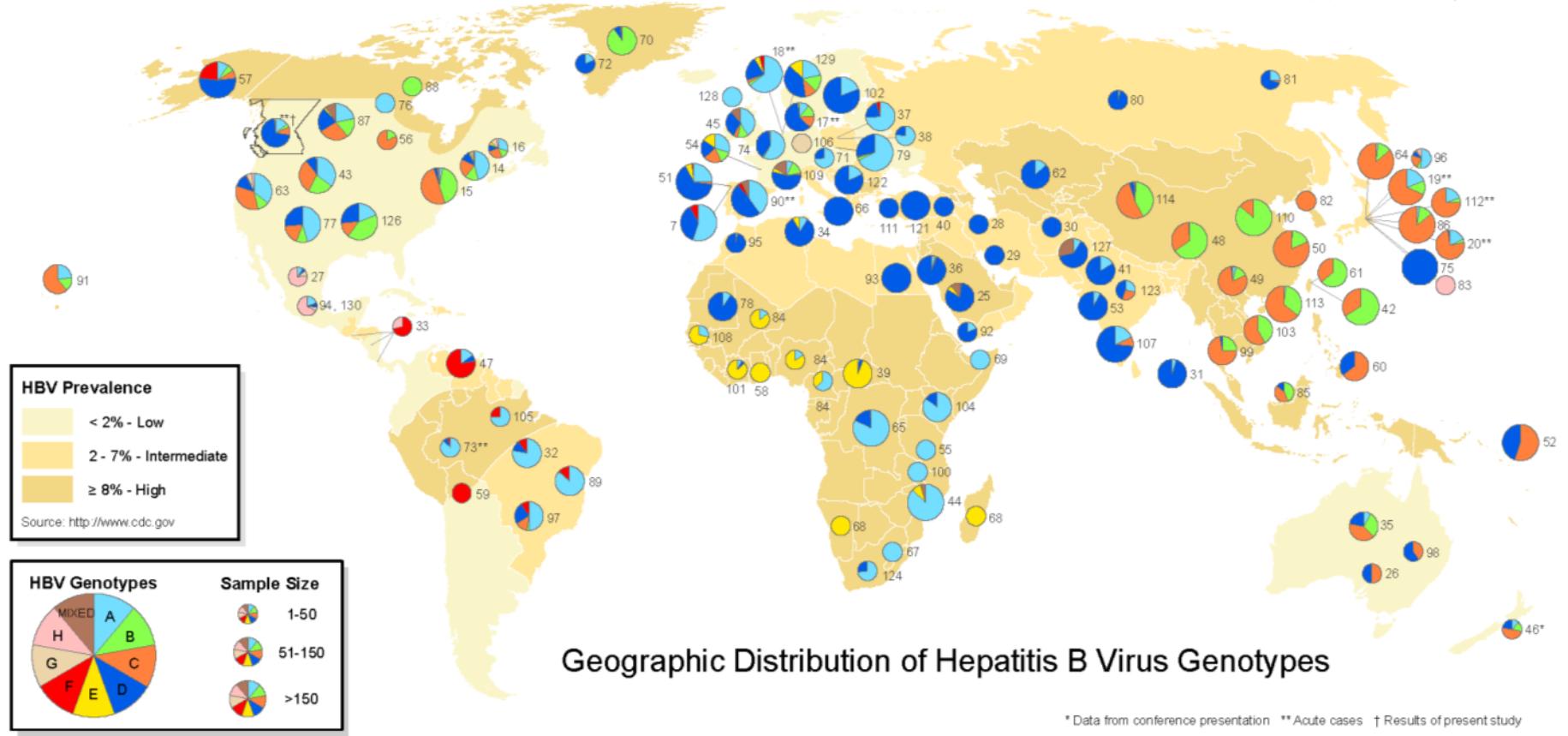


HBV/D in Greenland



Distribution of hepatitis B virus genotypes

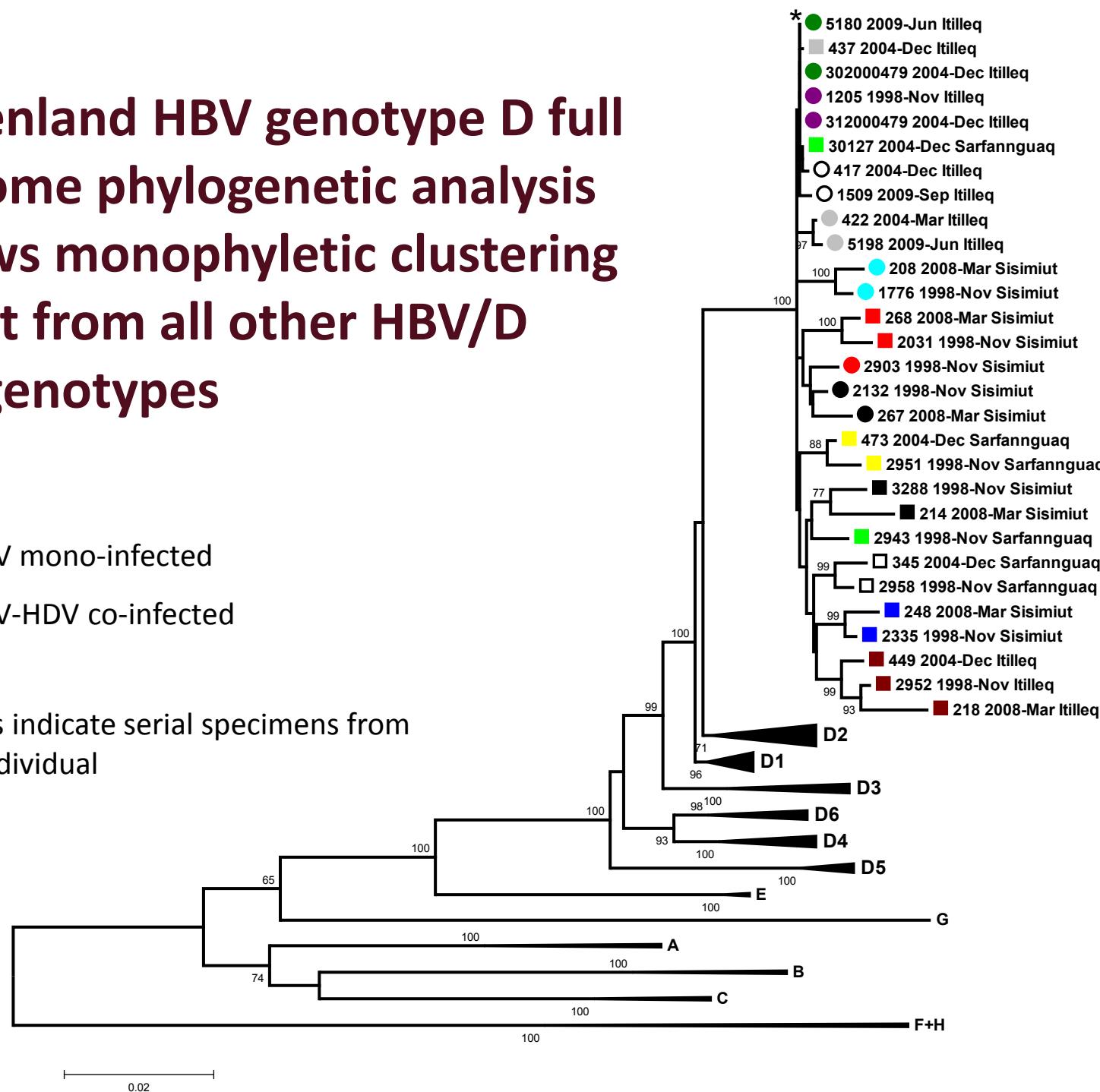
Panessa, C., et al. 2009 J Viral Hepatitis 16:64-73



Greenland HBV genotype D full genome phylogenetic analysis shows monophyletic clustering apart from all other HBV/D subgenotypes

- HBV mono-infected
- HBV-HDV co-infected

*colours indicate serial specimens from same individual



HBV/D in Greenland

Kalaallit Nunaat

Qaasuitsup

Sisimiut Itilleq
Sarfánguaq

Qeqqata

Sermersooq

Kujalleq

The Greenlandic HBV/D ancestor emerged ~225 YBP (95% HPD 330-130 YBP)

1500 YBP

1000 YBP

500 YBP

~225 YBP

Greenland

D1

D2

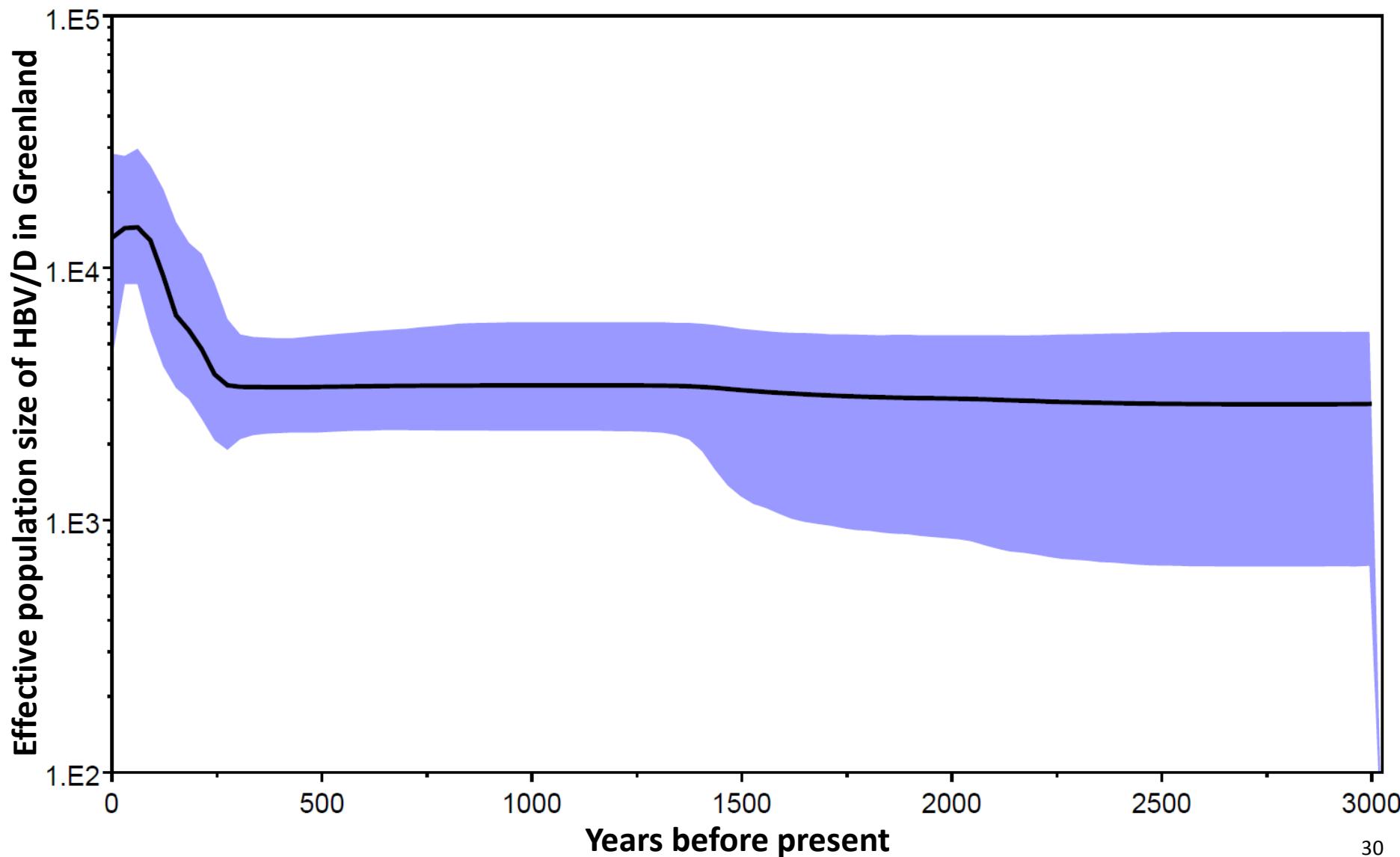
D3

D4

D5

A – C, E – H

The HBV/D population has expanded over the last 225-250 years



Hans Egede (1686-1758)



Greenlandic Whaling



Origin of genotype D in Greenland?

eLIFE Research article

Microbiology and Infectious Disease

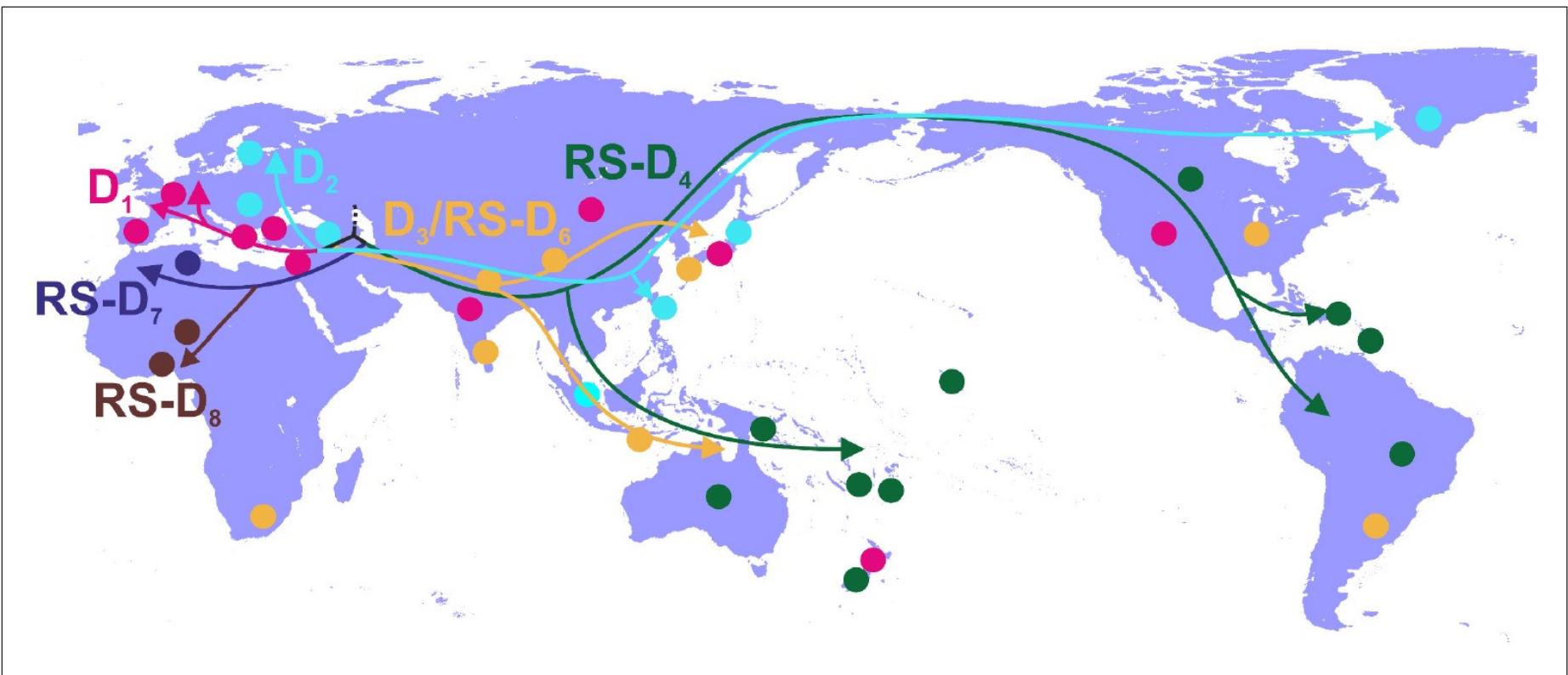
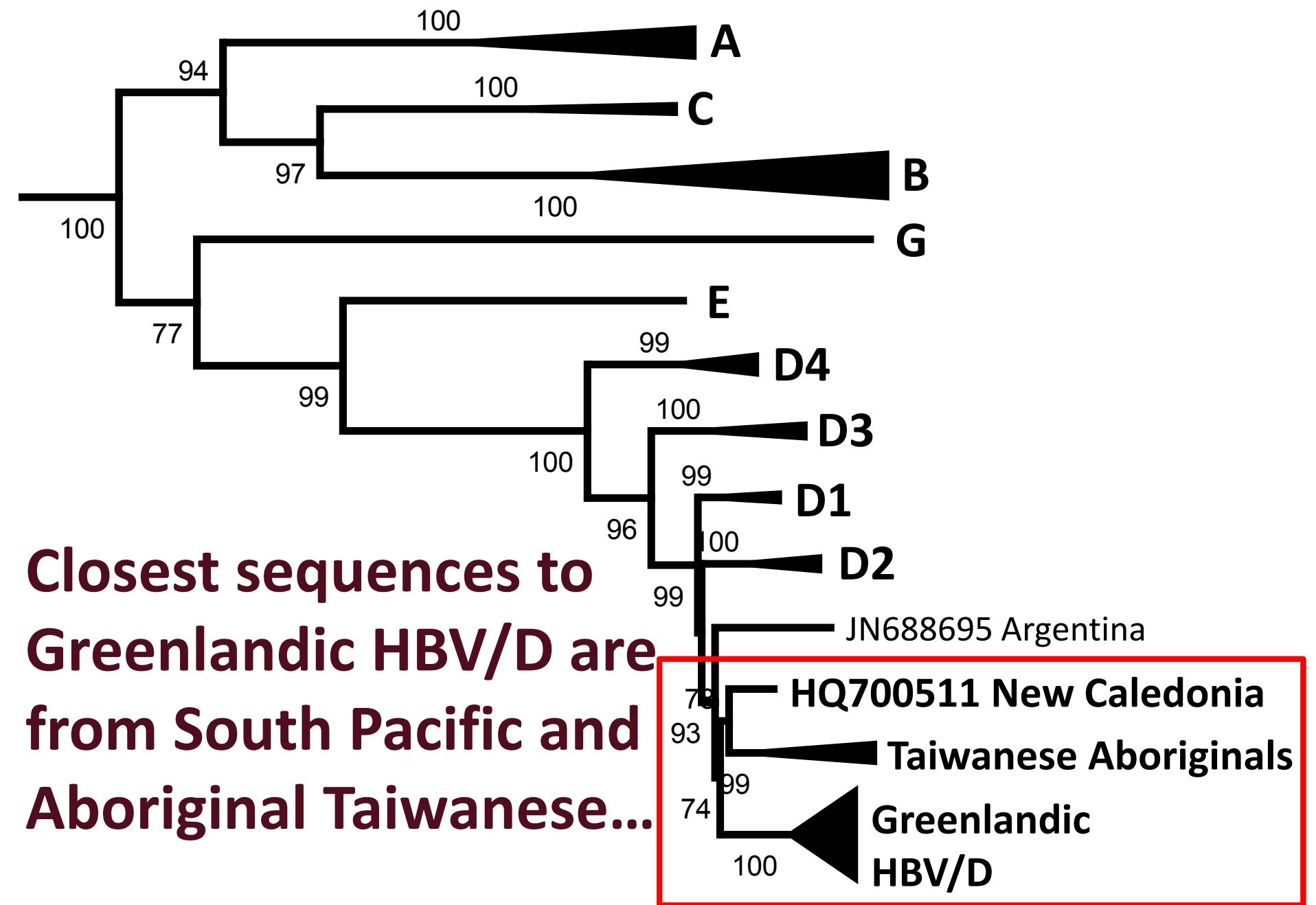


Figure 2. Putative major dispersal pathways of genotype D as estimated by phylogeographic analysis. The origin is depicted with dotted line. Subgenotypes and their corresponding dispersal routes are shown with different colors. Colored circles depict the geographic areas where subgenotypes are the most prevalent.

DOI: <https://doi.org/10.7554/eLife.36709.010>

Kostaki E, et al. eLife (2018) 7:e36709



Conclusions

- HBV/B5 was likely introduced into the circumpolar Arctic through migration of the first peoples almost 1000 years before present
- HBV/D may have been introduced to Greenland through colonization and contact with foreign expeditions during the 1700s

Acknowledgements

HBV/B5 (previously B6)

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- Henrik Krarup; Aalborg University Hospital

Greenland HBV/D

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