

# The trail of HBV-C subgenotypes along the beachcomber route followed by the first wave of humans out of Africa

Lilly Yuen  
Victorian Infectious Diseases Reference Laboratory  
Melbourne, Victoria 3000  
AUSTRALIA



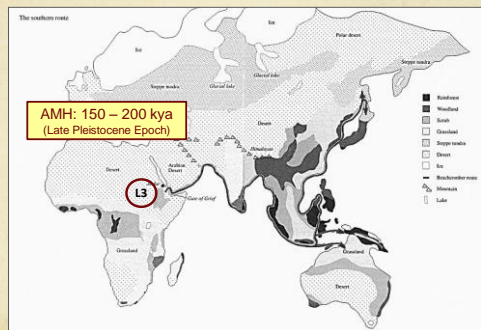
## Putting HBV-C4 in Context

“Indigenous Australians are infected with a unique HBV subgenotype C4 which may very well represent the oldest strain of HBV infecting anatomically modern humans”

Davies, J et al 2013. *J Gastro Hepatol*;28:1234  
Littlejohn, M et al 2014. *J Med Virol*;86:695

## Origins of Modern HBV Reconsidered

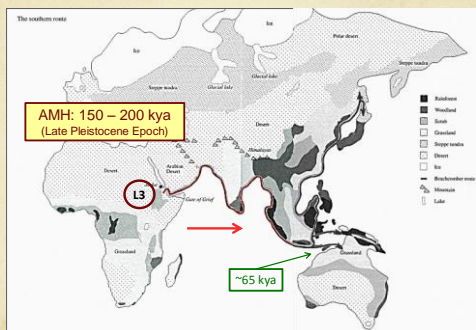
## Great Human Journey: The Coastal Express



Around 85,000 to 90,000 years ago, a group of Africans (mtDNA L3) left East Africa

Oppenheimer, S. *Out of Eden* 2004.

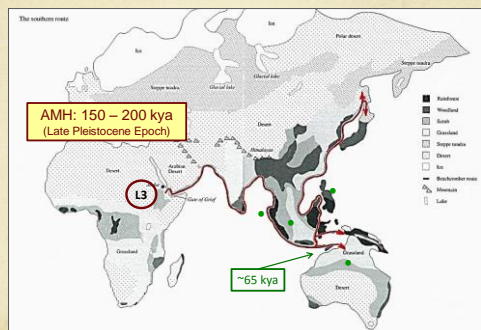
## Great Journey: The Coastal Express



Around 85,000 to 90,000 years ago, a group of Africans (mtDNA L3) left East Africa

Oppenheimer, S. *Out of Eden* 2004.

## Great Journey: The Coastal Express



Around 85,000 to 90,000 years ago, a group of Africans (mtDNA L3) left East Africa

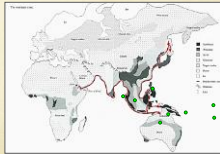
Oppenheimer, S. *Out of Eden* 2004.

## Hypothesis

- Characterisation of HBVs amongst (isolated) non-African Indigenous and Relict Populations along the Southern coastal route, could provide unique insights into HBV origin and evolution

### Great Journey

- Jarawas Tribe (Andaman Is)
- Orang Asli (Malaysia)
- Torres Strait Islanders (TSI/PNG)
- Australian Aboriginals (Arnhem Land)
- Philippine Mangyan Peoples
- Solomon Is/Vanuatu (Melanesians)
- Kiribati (Micronesia)
- Tonga (Polynesia)



*Journal of General Virology* (2001), 82, 883-892. Printed in Great Britain

## A novel variant genotype C of hepatitis B virus identified in isolates from Australian Aboriginals: complete genome sequence and phylogenetic relatedness

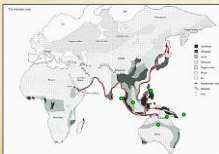
Fuminaka Sugauchi,<sup>1</sup> Masashi Mizokami,<sup>2</sup> Etsuro Orito,<sup>1</sup> Tomoyoshi Ohno,<sup>1</sup> Hideaki Kato,<sup>1</sup> Seiji Suzuki,<sup>1</sup> Yoshihide Kimura,<sup>1</sup> Ryuzo Ueda,<sup>1</sup> L. A. Butterworth<sup>3</sup> and W. G. E. Cooksley<sup>3</sup>

<sup>1,2</sup> Second Department of Internal Medicine and Laboratory Medicine<sup>1</sup>, Nagoya City University Medical School, Kawasumi, Mizuho, 467-8601 Nagoya, Japan  
<sup>3</sup> Royal Brisbane Hospital Research Foundation, Brisbane, Australia

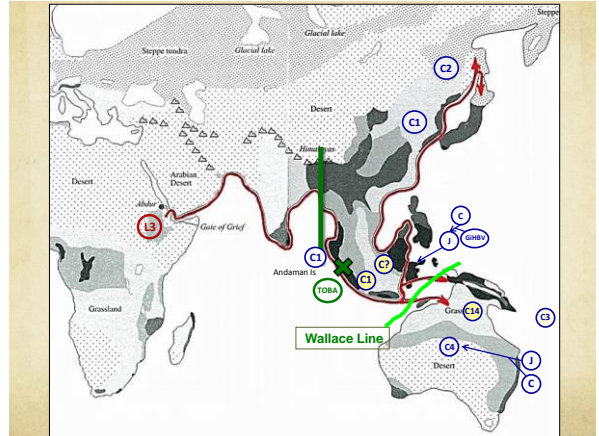
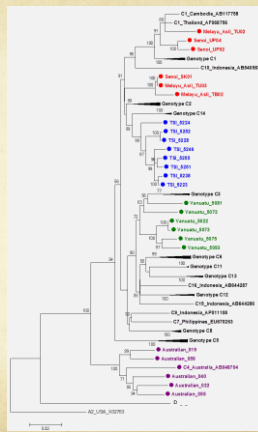
3 Strains: D-4  
 2 Strains: Novel Variant C (ayw3)

## Phylogenetic Tree of Indigenous HBV Samples (full-length genomes)

- Jarawas Tribe (Andaman Is)
- Orang Asli (Malaysia)
- Torres Strait Islanders (TSI/PNG)
- Australian Aboriginals
- Philippine Mangyan Peoples
- Solomon Is/Vanuatu (Melanesians)
- Kiribati (Micronesia)
- Tonga (Polynesia)



Littjejohn, M et al 2014. Hepatitis B and Delta Viruses. Pub: Cold Spring Harbour Book. In press



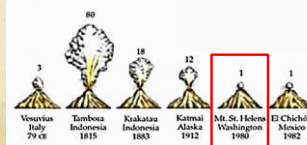
## Mount St. Helens, Washington (1980)



- Debris swept across landscape @ 1,095km/h
- Within minutes, ash plume rose 24 km into sky

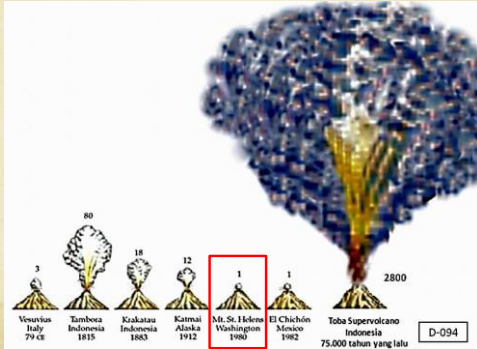
<http://www.scienceclarified.com/landforms/Ocean-Basins-to-Volcanoes/Volcano.html>

## Total Amount of ejected material (cubic kilometres)

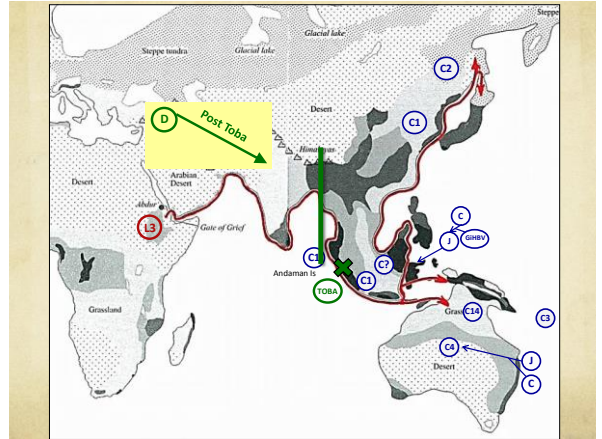


<http://historum.com/natural-environment/73415-toba-super-eruption.html>

### Total Amount of ejected material (cubic kilometres)



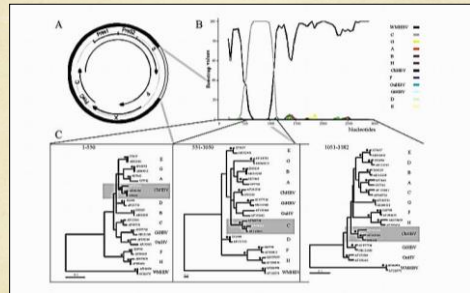
<http://historum.com/natural-environment/73415-toba-super-eruption.html>



### Recombination Between Human and Primate HBVs

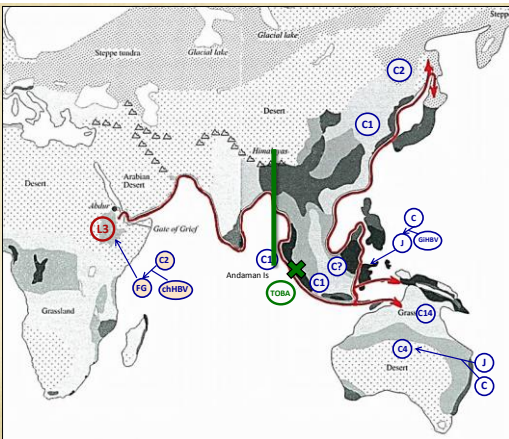
- Chimpanzee HBV-FG isolated from **wild caught**
  - Pan troglodytes schweinfurthii* in East Africa (Vartanian, J.P. et al 2002. J. Virol;76:11155)
- Chimpanzee/genotype C
  - Magiorkinis, E et al 2005. Gene;349:165

### Molecular Analysis of Chimpanzee FG HBV



**ChHBV and Genotype C2**

Magiorkinis, EN et al 2005. Gene;349:165-171



### Summary

**Genotype C is the oldest of the Modern non-African Human HBVs, arrived in Australia over 60,000 years ago, and can be traced back to Africa, along the coastal route, traversed by the original exodus of *H. sapiens***

- Current HBV evolved by a series of recombination events with other HBVs, both primate and human
- Public health implications of these cross-species transmissions and recombination are quite significant
- Endemic infection in nonhuman primates has potential for cross-species transmission which will hamper control of HBV in geographical regions where humans and primates (and bats) share habitats





## Acknowledgement

(No relevant conflicts to declare)



- **VIDRL, Australia**
  - Kathy Jackson
  - Margaret Littlejohn
  - Rosalind Edwards
  - Stephen Locarnini
- **Menzies School of Health Research (Royal Darwin Hospital)**
  - Josh Davis
  - Steven Tong
  - Jane Davies
  - Paula Binks
  - Krispin Hajkowicz
  - Sarah Whiting
  - Cathy Corbett
  - Sara Mgaieih
  - Cam Jeremiah
  - Bridget Barber
  - Claire Gordon
  - Suresh Sharma
- **TSI study - Cairns**
  - Kaurareg people (participants and traditional land owners of region where data collected)
  - Elayne Anderson
  - Dr Vincent Ho
  - Prof John McBride
  - Yoko Nakata, Sexual Health nurse
  - Cheryl Sendall, Hepatitis nurse
  - Dr Alexander Kippin (Rural Generalist Registrar)
  - Gilead – project sponsorship
- **University of Santo Tomas, Philippines**
  - Jose Soliano
- **Jalan Hospital, Malaysia**
  - Nazri Aziz

