Molecular Epidemiology of Full-Length Hepatitis C Virus Genomes in Recent Infection: The Inc3 Study

Chaturaka Rodrigo
Viral Immunology Systems Programme (VISP)
UNSW Australia

Disclosures

- No conflicts of interests
- Funding of InC3 cohorts
  - NHMRC, Australia
  - NIH

Introduction

- Limitations in phylogenetic studies in HCV
  - Acute vs. late infection
  - Within a limited geographical region
  - Using segments of the genome
- This study
  - Acute infections (within 180 days)
  - Cross-continental
  - Full genome

InC3

- The International Collaboration of Incident HIV and Hepatitis C in Injecting Cohorts (InC^3)
  - Four countries
  - Nine cohorts
  - Over 30,000 blood samples
  - Longitudinal behavioural data of approximately 4,900 recruited subjects

Objectives

- To establish a cross-continental repository of full length deep sequenced early infection HCV sequences
- To establish the behavioural and demographic associations with phylogenetic clustering
- To compare the phylogenetic signal of full length genome vs. segments of the genome

Methods

- Selection of early viraemic samples
  - Within 180 days since estimated date of infection

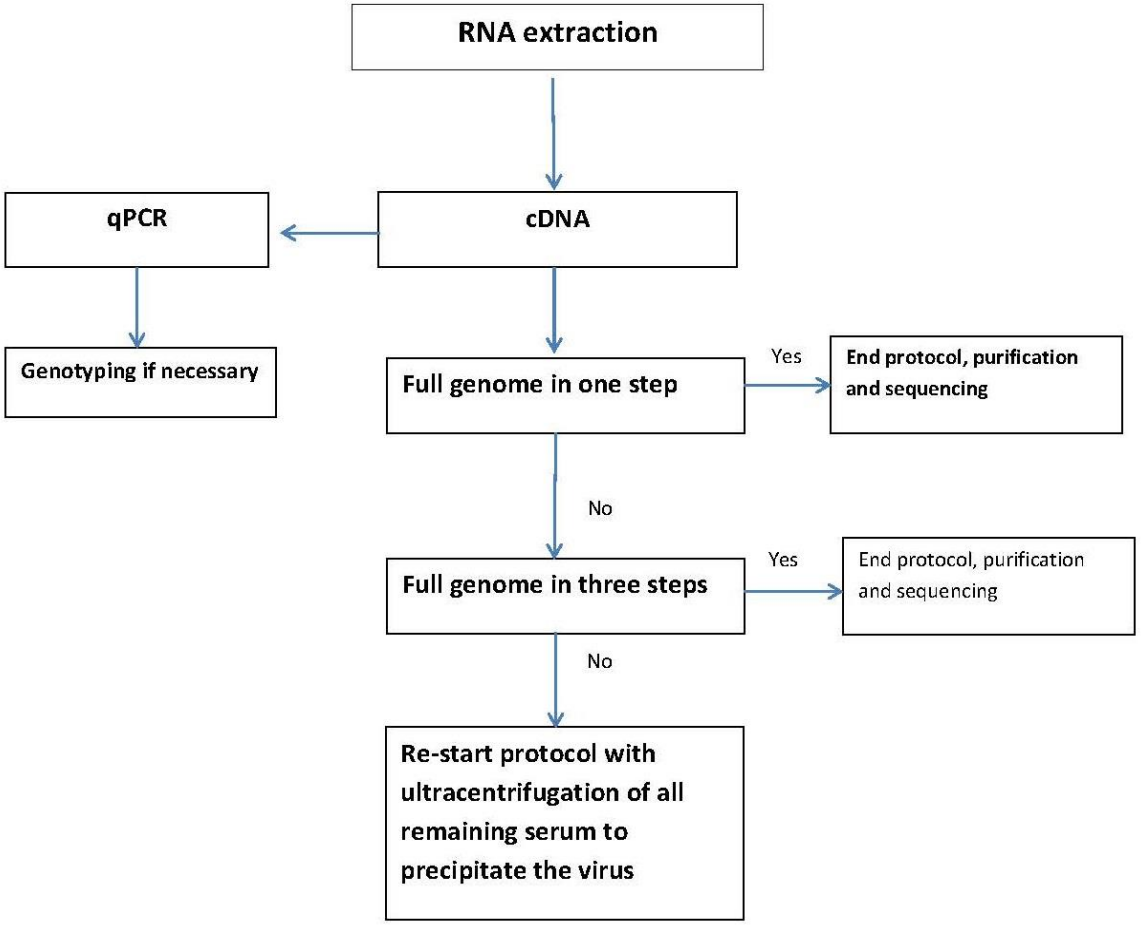
  AND

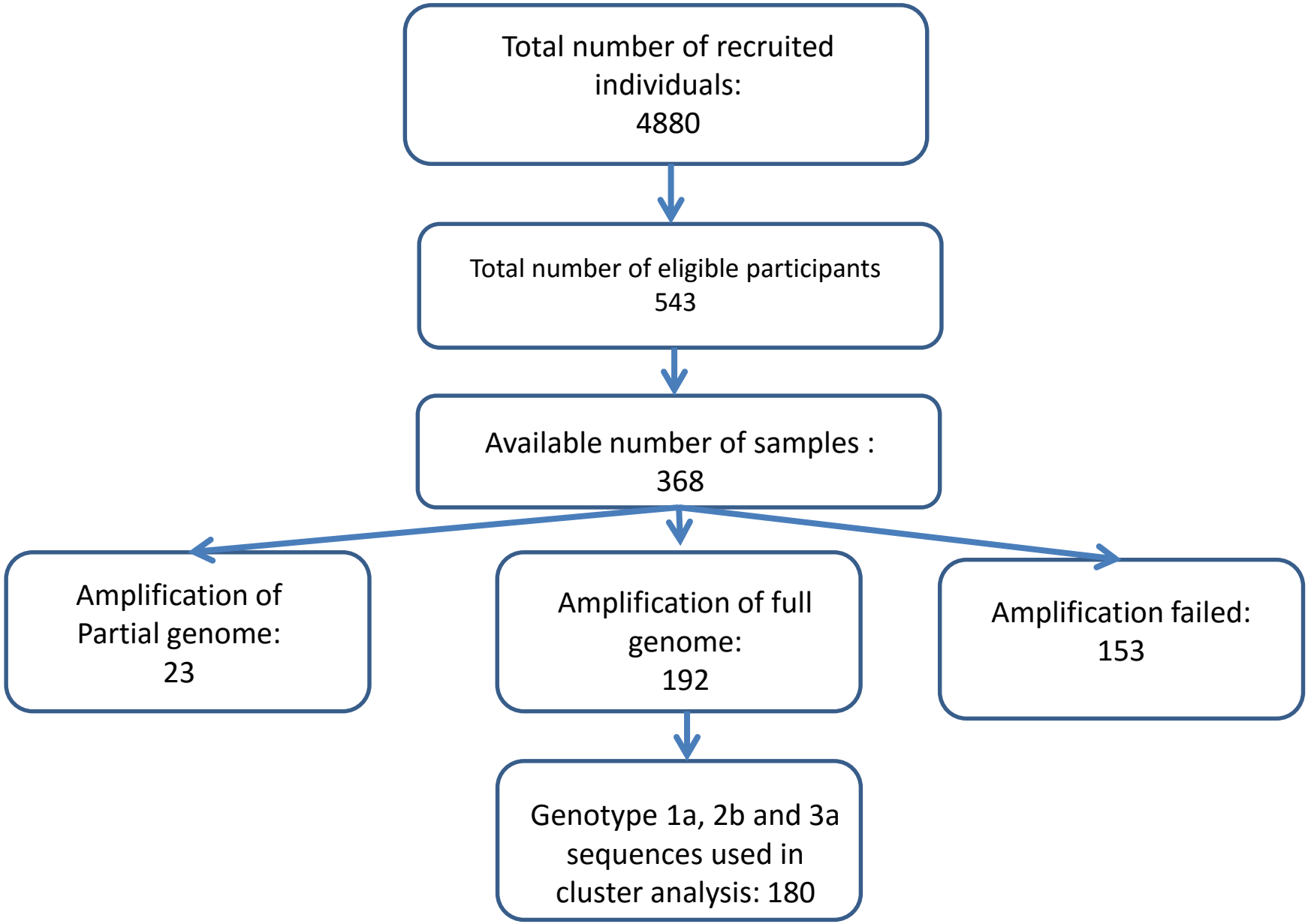
  - Quantitative viral load > 1000 IU/ml

  OR

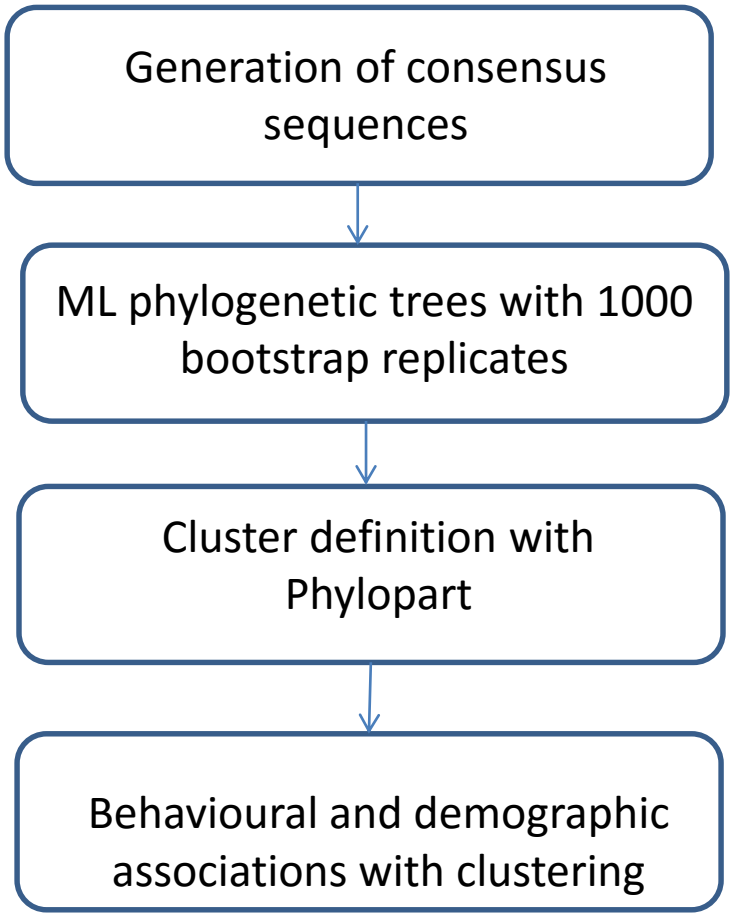
  - Qualitative RNA positivity

Experimental protocol – Wet Lab



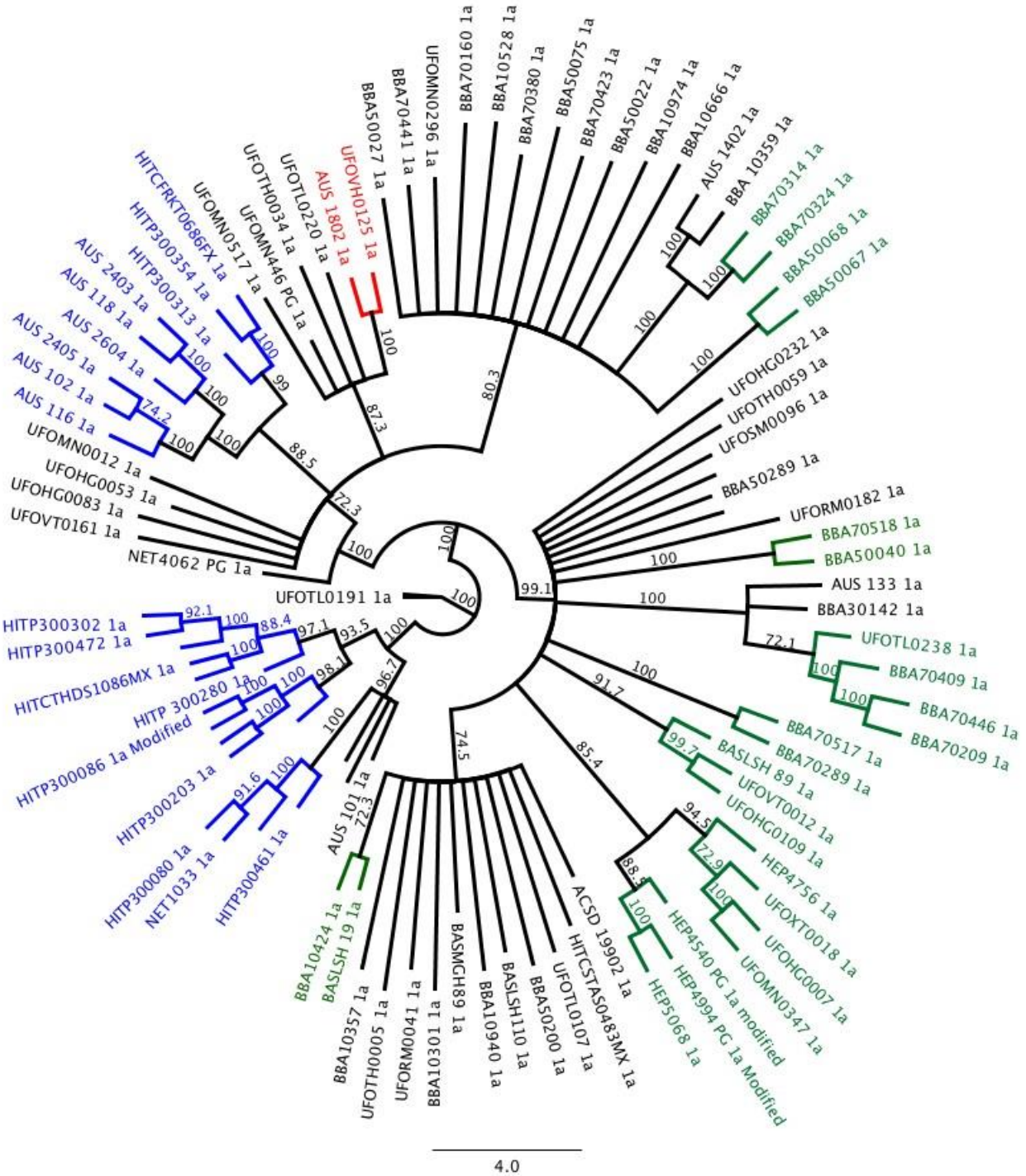

Total number of recruited individuals:
4880
Total number of eligible participants
543
Available number of samples :
368
Amplification of Partial genome:
23
Amplification of full genome:
192
Amplification failed:
153
Genotype 1a, 2b and 3a sequences used in cluster analysis: 180

Experimental protocol – Dry Lab



Results - Sequence repository

- Largest early HCV sequence repository in the world
- Largest genotype 3a full genome sequence repository in the world
- Largest genotype 1a and 3a full genome sequence repository for Australia



ML consensus tree for genotype 1a sequences with 1000 bootstrap replicates

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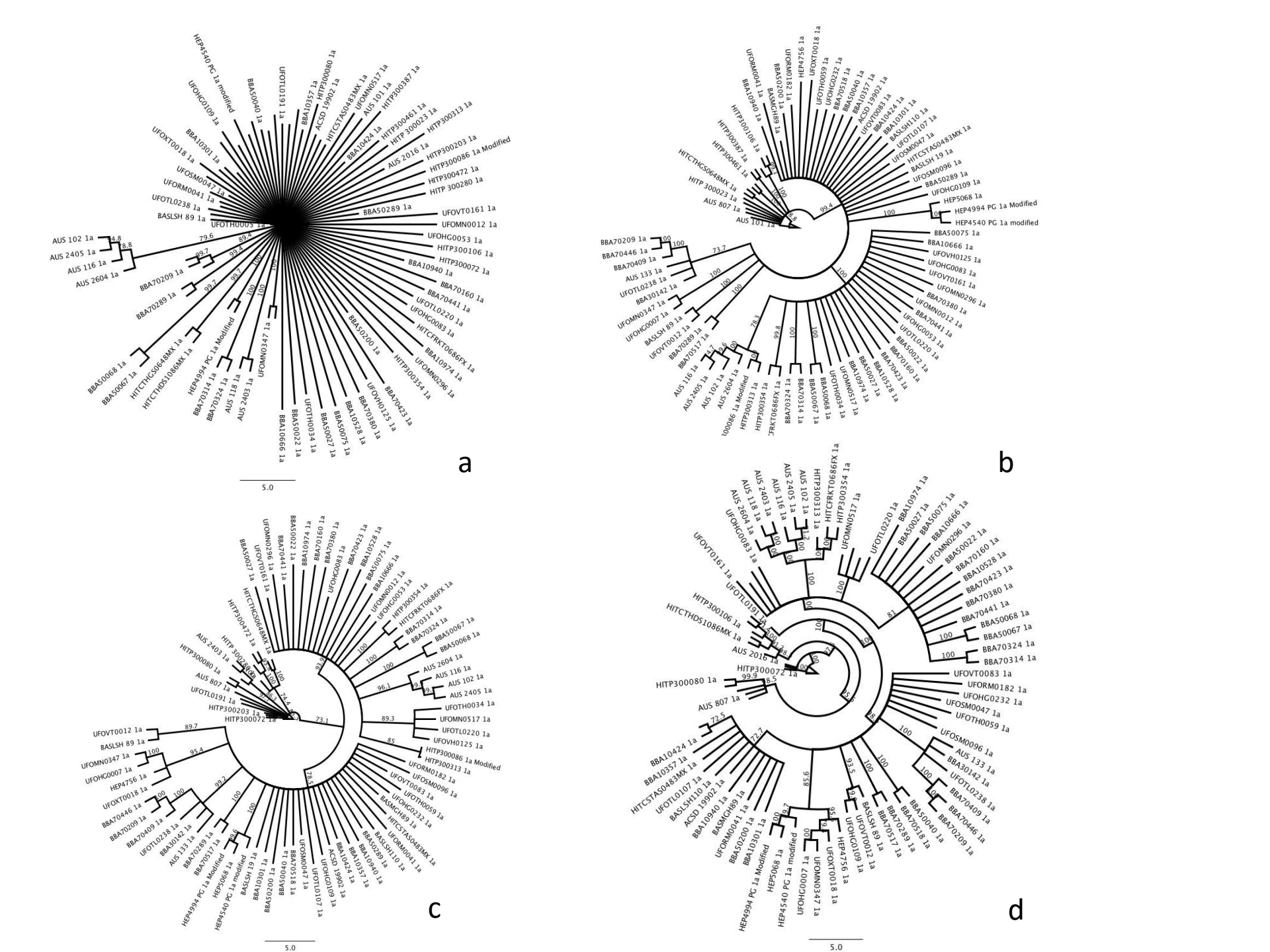
a
b
c
d
5.0
5.0
5.0

Associations with clustering

Did show a significant association	Did not show a significant association
Age*	Gender
Continent of origin	Sexual orientation
Being imprisoned at the time of enrolment	Level of education
Ethnicity*	Past history of imprisonment
	Type of drug injected
	Being on opioid replacement therapy
	HIV co-infection

*association persisted with binary logistic regression

Discussion

- Micro-epidemics in geographically isolated communities
  - Implications on a universal vaccine
- Phylogenetic diversity is added by few areas of the genome
  - Presence of immune epitopes in critical areas

Conclusions

- Established world's largest early infection deep sequenced HCV sequence repository
- HCV probably evolves independently within geographically isolated communities
- Full genome offers a better phylogenetic signal than any of the genomic segments

Acknowledgements

- InC3 collaborators
  - Andrew Lloyd
  - Kimberly Page
  - Naglaa Shoukry
  - Julie Brunaeu
  - Gregory Dore
  - Jason Grebely
  - Lisa Maher
  - Andrea Cox
  - Janke Schinkel
  - Maria Prins
  - Georg Lauer
  - Arthur Kim
  - Mageret Hellard
- Institutions
  - School of Medical Sciences, UNSW
  - Kirby Institute, UNSW
  - ASHM
- Supervisors
  - Andrew Lloyd
  - Rowena Bull
  - Fabio Luciani
  - Auda Etahla
- InC3 participants
- Staff and students of Viral Immunology Systems Programme, Kirby Institute, UNSW