



Methamphetamine injecting is associated with phylogenetic clustering of hepatitis C virus infection among street-involved youth in Vancouver, Canada

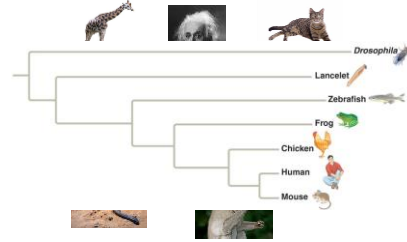
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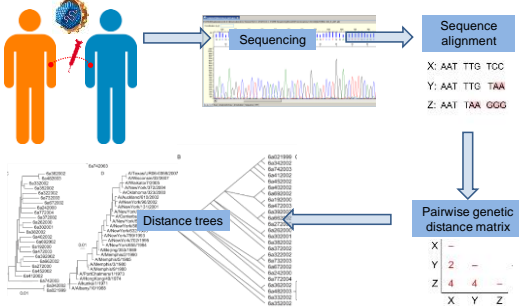


Phylogenetics

Groups sequences based on similarity / difference to other sequences



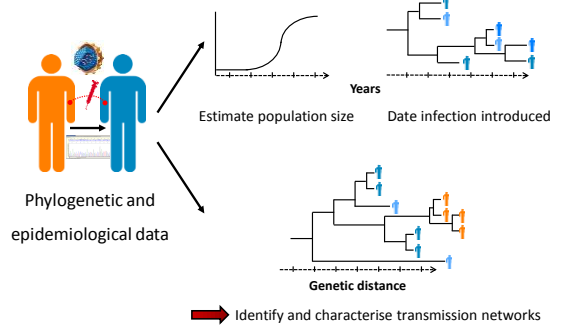
Viral phylogenetics



Lan, T. T. Y., Hsu, C. C., & Tang, J. W. (2013) Use of phylogenetics in the molecular, epidemiology and evolutionary studies of viral infections. *Crit. Rev. Clin. Lab. Sci.*, 47(1), 5-49.
Brenner, B. G., Wallberg, M. A. (2013) Fate of phylogeny in HIV prevention. *J. AIDS (65)*, 248-254

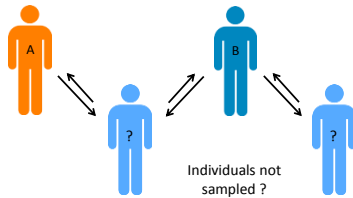


Molecular epidemiology



Limitations

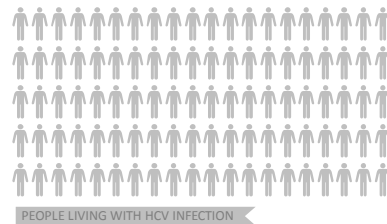
Two individuals sampled



Characteristics of highly connected populations



The majority of new HCV infections occur among PWID



1) Hajarizadeh B, et al. *Nature Rev Gastroenterol Hepatol* 2013. 2) Grebely J and Dore GJ *Antiviral Research* 2014.



The majority of new HCV infections occur among PWID

80% OF NEW INFECTIONS OCCUR AMONG CURRENT PWID

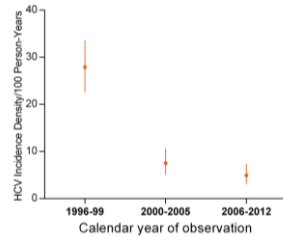


PEOPLE LIVING WITH HCV INFECTION

1) Hajarizadeh B, et al. *Nature Rev Gastroenterol Hepatol* 2013. 2) Grebely J and Dore GJ *Antiviral Research* 2014.



HCV transmission among PWID continues



- Factors associated with HCV acquisition
 - unstable housing, HIV infection, and injecting of cocaine, heroin
 - **Methamphetamine injecting**

Grebely J, et al *PLOS ONE* 2014



Limitations of previous work to date

- Traditional epidemiological analyses of HCV incidence measures acquisition, but not transmission of infection
- Identifying characteristics of people at high risk of HCV transmission may provide important information for the design and implementation of targeted strategies
- Phylogenetics provide an opportunity to model underlying transmission patterns that cannot be determined through epidemiological studies, as demonstrated in HIV^{1,2}

1) Lewis F *PLoS Med* 2008; 2) Brenner BG, *Journal of Infectious Diseases* 2007.



Specific Aims

- To investigate phylogenetic clustering of HCV in a prospective cohort of at-risk youth in Vancouver, Canada
- To examine factors associated with pair/cluster membership



Study participants

At-Risk Youth Study (ARYS, 2005-2012):

- Inclusion criteria: At-risk youth residing in the greater Vancouver area who were involved in illicit drug use other than or in addition to marijuana in the previous month

Recruitment:

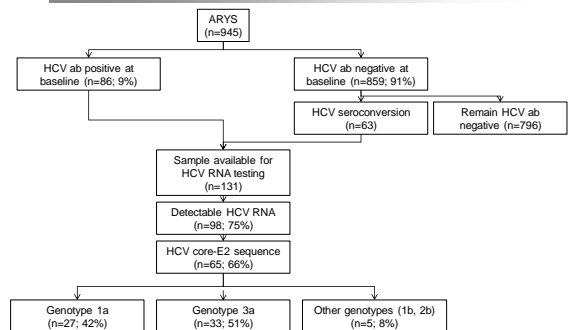
- Enrolment was done through targeted street-based outreach and through street youth recruiting their peers

Testing/questionnaires:

- Baseline and semiannual visits included serological screening for anti-HCV antibodies
- A questionnaire covered information on subjects' characteristics, injection and non-injection drug use, borrowing and lending of syringes



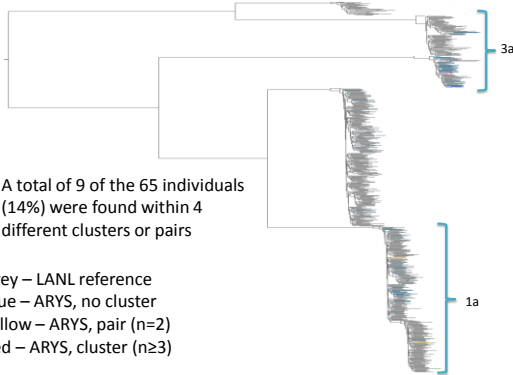
Participant disposition





Participant characteristics

Characteristics	Overall (n=65)
Female sex (vs. male sex)	20 (31%)
Age (median)	23 (15-30)
Unstable housing (vs. stable)	52 (80%)
Years injecting (median)	6 (1-14)
HCV acute/recent (vs. not)	40 (62%)
HIV infection (vs. none)	2 (3%)
Syringe borrowing (vs. none)	16 (24%)
Crack use (vs. none)	39 (60%)
Cocaine injecting (vs. none)	23 (35%)
Heroin injecting (vs. none)	39 (60%)
Methamphetamine injecting (vs. none)	39 (60%)



- A total of 9 of the 65 individuals (14%) were found within 4 different clusters or pairs

Grey – LANL reference
 Blue – ARYS, no cluster
 Yellow – ARYS, pair (n=2)
 Red – ARYS, cluster (n≥3)



Study methodology

Sequencing and phylogenetics

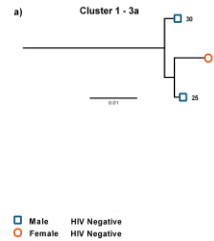
- First HCV antibody/RNA positive sample
- HCV Core-E2 region without HVR using a nested PCR
- Phylogenetic inference using RAxML maximum likelihood method with 1000 bootstrap replicates
- Clusters and pairs identified using ClusterPicker
 - 0.05 genetic distance threshold and 90% bootstrap

Statistical Analysis

- Factors associated with being in a cluster identified using fisher exact tests



All identified clusters



Methamphetamine injecting was found to be associated with membership in a cluster or pair using Fisher's exact test. (P=0.009)



Conclusions

- The prevalence of clustering among the ARYS cohort is 14%
- Membership in a cluster or pair is associated with methamphetamine injecting (P=0.009)
- This highlights who is playing a part in driving HCV transmission among a young cohort of current injectors



Acknowledgements

Australia

- Kirby institute
 - Brendan Jacka
 - Tanya Agglegate
 - Francis Lamouy
 - Sofia Bartlett
 - Greg Dore
 - Anthony Kelleher
 - Jason Gebely
- University of Western Australia
 - Silvana Gaudieri
- University of New South Wales
 - Fabio Luciani
 - Rowena Bull

United Kingdom

- Oxford University
 - Oliver Pybus
 - Gkikas Magiorkinis

Canada

- BC Centre for Disease Control
 - Mel Krajden
 - Andrea Olmstead
 - Vince Montoya
- BC Centre for Excellence in HIV/AIDS
 - Evan Wood
 - Richard Harrigan
 - Art Poon
 - Brandon Marshall
 - M-J Milloy
 - Kora DeBeck
 - Viviane Dias Lima
 - Thomas Kerr
 - Julio Montaner



National CIHR Research Training Program in Hepatitis C
 Subvention nationale de formation des IRSC sur l'hépatite C



- Simon Fraser University
 - Zabrina Brumme