How to present molecular findings on HIV/HCV as evidence in court?

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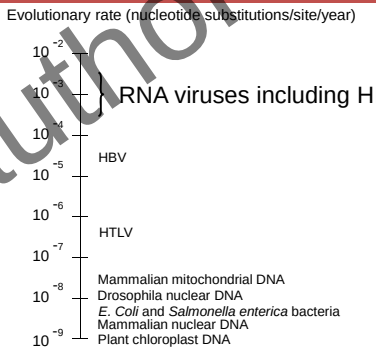
Prosecution of reckless transmission

- Reckless transmission of *[HIV or HCV]* is a criminal act in many countries.
- Phylogenetic analysis has been used as evidence for HIV and HCV transmissions in court cases.
- Such evidence has contributed to convictions in a number of cases in recent years.
- Using phylogenetic analysis, also called molecular epidemiology, for forensics has its powers and pitfalls.

Bernard *et al* HIV Medicine 2007, Abecasis *et al* Lancet Infect Dis 2011, Leitner *et al* Nature 2011, González-Candelas *et al* BMC Biol 2013, Vandamme *et al* BMC Biol 2013,

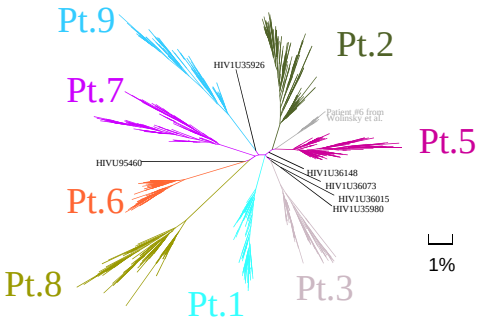
HIV molecular epidemiology in forensic investigations

Measurable evolving viruses



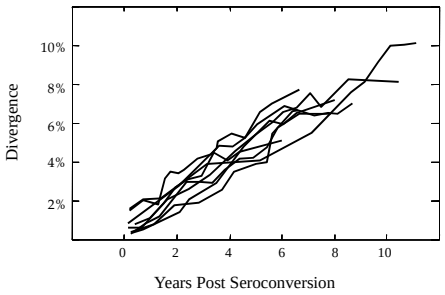
Adapted from Lemey, 2003

Within patient HIV-1 envelope evolution for eight infected patients



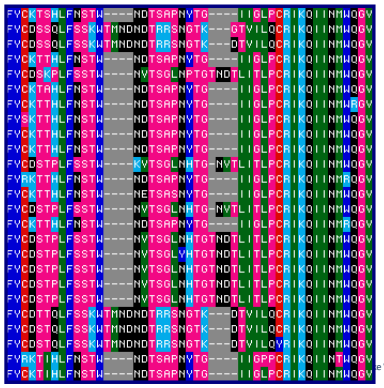
Shankarapa et al 1999, JVI 73:10489

Genetic divergence of HIV-1 sequences from founding population in eight infected patients



Shankarapa et al 1999, JVI 73:10489

HIV-1 within patient: quasispecies



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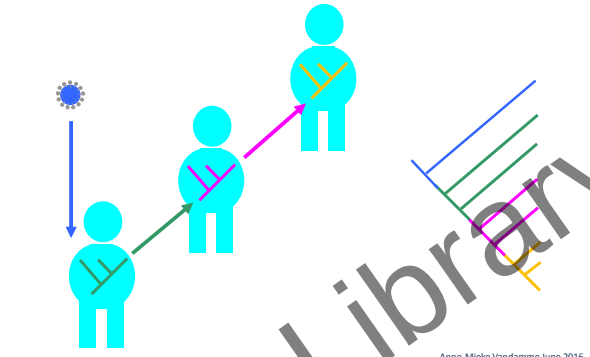
Transmission investigation



Adapted from Lemey, 2003

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Population sequencing vs. next generation sequencing

Population sequencing

1. Avoids the problem of PCR or NGS-induced mutations
2. Tree reconstruction with less sequences, thus more individuals can be included

NGS

1. If individual reads are too short: haplotype reconstruction is possible (however often problematic)
2. Allows assessment of within-sample variability

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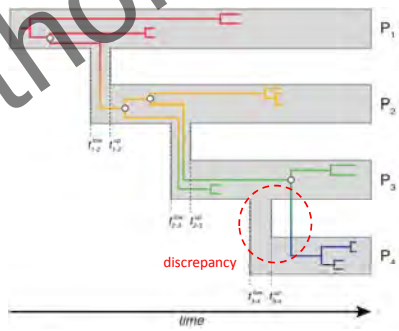
Coalescence node does not equal transmission event



Vrancken *et al* PLOS Comp Biol 2014

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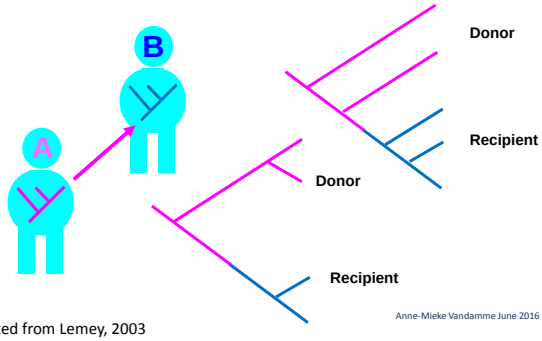
Direction of transmission: NGS



Adapted from Lemey, 2003

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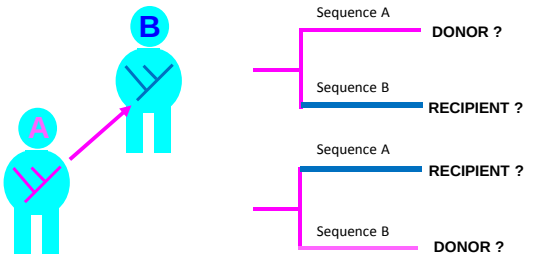
Direction of transmission: population sequencing



Adapted from Lemey, 2003

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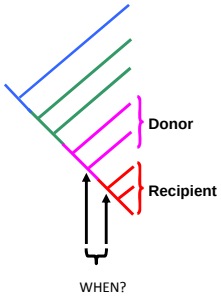
Dating coalescence nodes in phylogenies



Branch lengths / Rate of evolution → time

nucleotide/subst/site / nucleotide/subst/site/year → years

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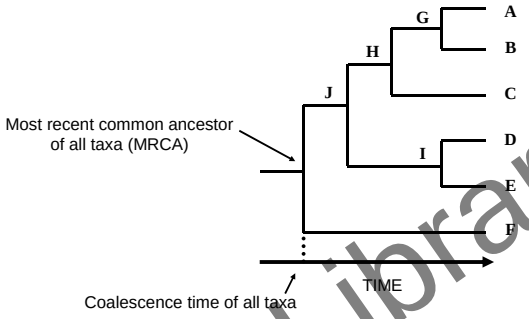
Coalescence time on a rooted tree



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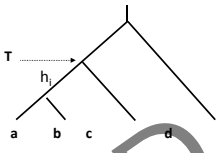
Using genetic divergence to date Coalescence time



- clock like branch length hi (nt subst /site)
- known rate of evolution r (nt subst /site/year)
- divergence time :

$$T = h_i / r$$

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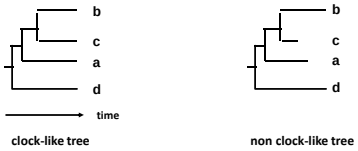
The molecular clock hypothesis

In general HIV or HCV do not evolve according to a molecular clock



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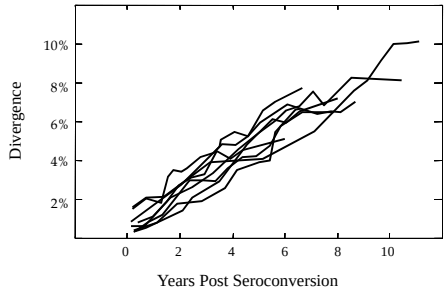
Evolutionary rate through serial samples

Molecular clock ?



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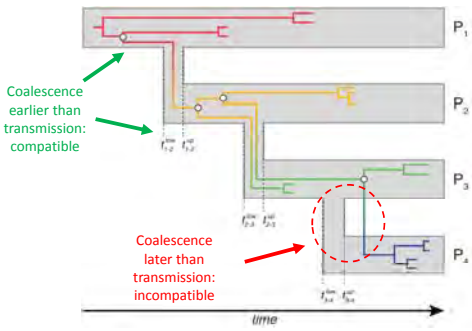
Coalescence node does not equal transmission event



Vrancken *et al* PLOS Comp Biol 2014

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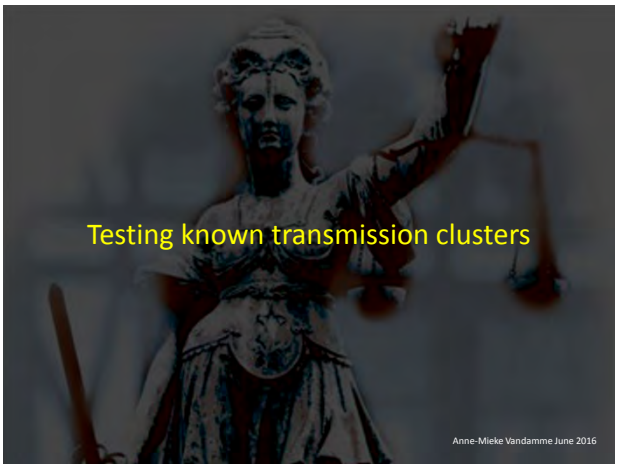
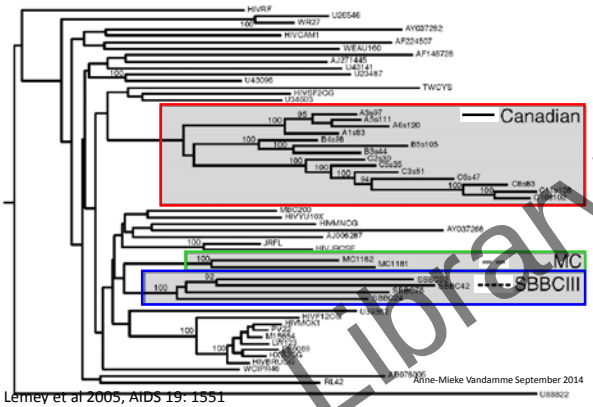
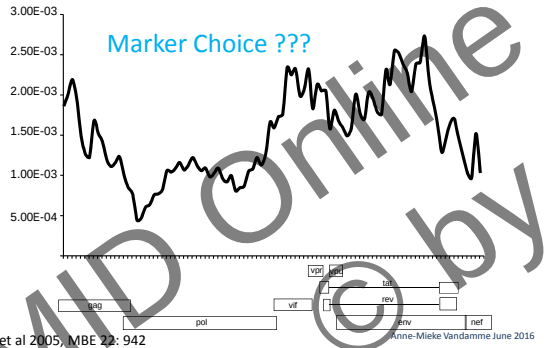


Testing known transmission clusters



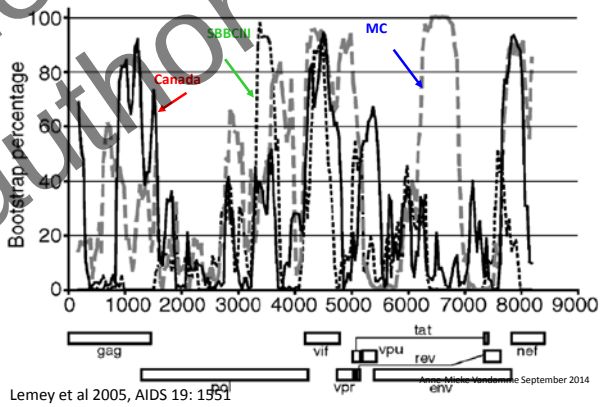
Lemey et al 2005, AIDS 19: 1551

Evolutionary rate across the HIV-1 genome



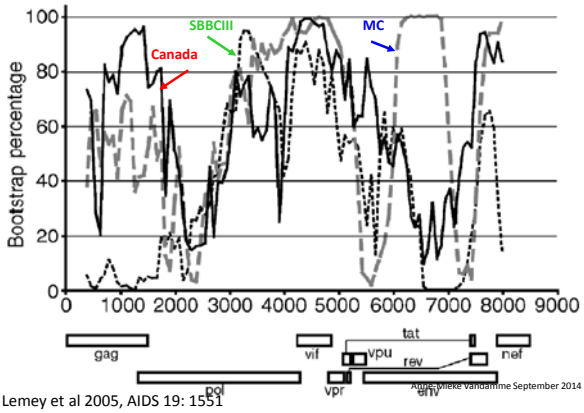
Lemey et al 2005, MBE 22: 942

Bootstrap window size of 400 nts



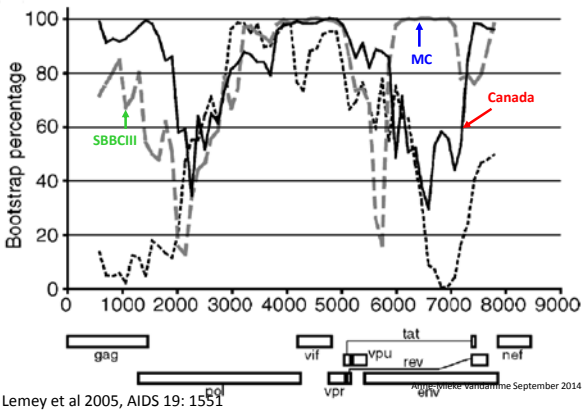
Lemey et al 2005, AIDS 19: 1551

Bootstrap window size of 800 nts



Lemey et al 2005, AIDS 19: 1551

Bootstrap window size of 1200 nts



Lemey et al 2005, AIDS 19: 1551

Region to use? Size of the fragment?

- In gag, there is only significant support for the Canadian transmission cluster and best at 1200 nts, moderate mother–child transmission support and virtually no support for the SBBCIII.

Lemey et al 2005, AIDS 19: 1551

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Region to use? Size of the fragment?

- Gag is not always optimal
- Only the mother–child cluster is significantly supported in the env gene, more particular in the V1–V5 gp120 region. The larger the region, the better.

Lemey et al 2005, AIDS 19: 1551

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Region to use? Size of the fragment?

- Gag is not always optimal.
- V3 is sometimes also problematic.
- The 3' part of the polymerase gene up to the envelope gene appears to provide relatively good support for all three transmission clusters. The larger the region, the better.

Lemey et al 2005, AIDS 19: 1551

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What to conclude from this?

- Not all transmission clusters are the same.
- The larger the region the better.
- More than one region should be tested.
- No specific region is the best, but convenience supports using as large a region as possible in pol, for which most information will be available when choosing controls.
- Poor bootstrap support can never be interpreted as evidence against transmission

Lemey et al 2005, AIDS 19: 1551

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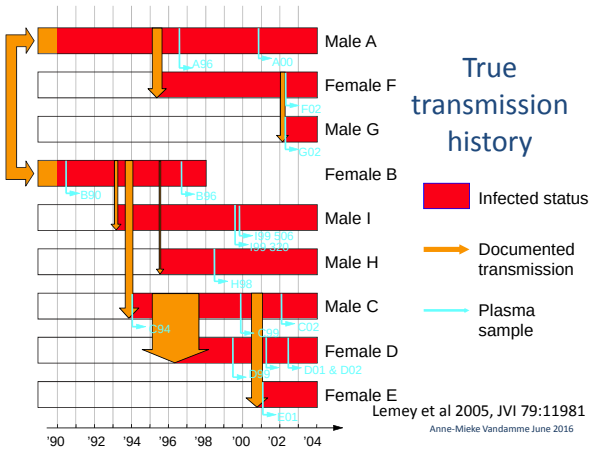

Lemey et al 2005, JVI 79:11981

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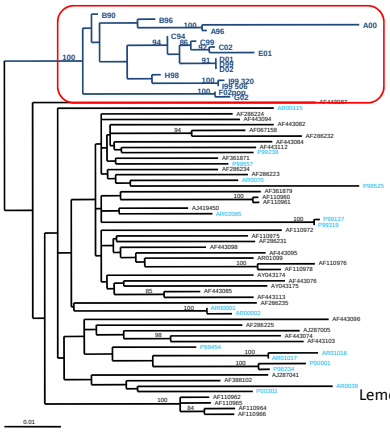

Subtype C unrooted ML tree including local controls

Lemey et al 2005, JVI 79:11981

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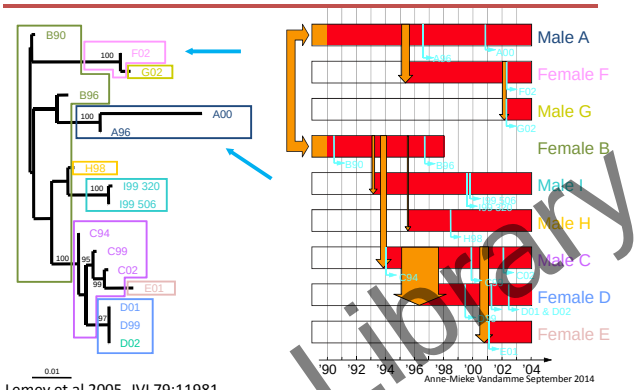
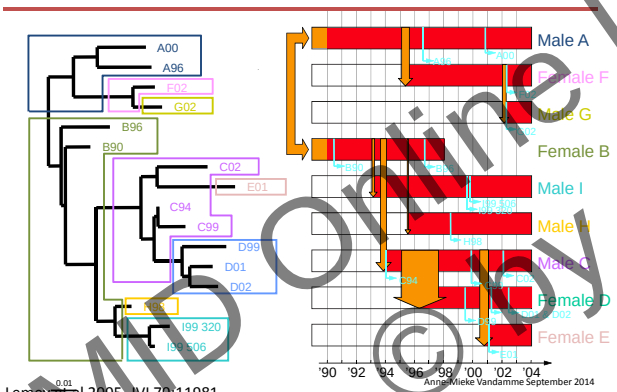
Pol ML tree is incompatible

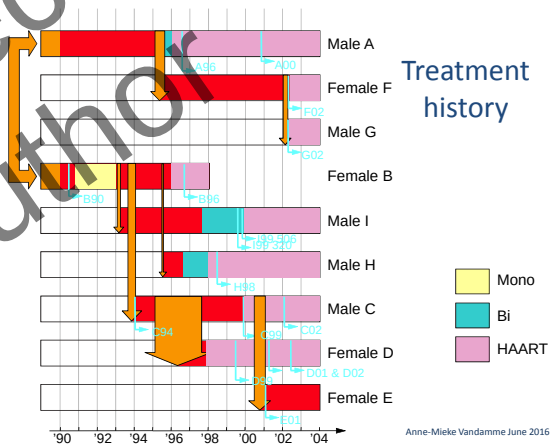


Lemey et al 2005, JVI 79:11981

Pol dS tree is compatible



Lemey et al 2005, JVI 79:11981



Selective pressure

- Selective pressure disturbs phylogenetic inferences, it makes sequences under similar pressure look more similar
- Selective pressure was the cause of the incompatibilities found
- *pol* gene is under strong drug positive selective pressure, causing convergent evolution
- Many drug resistance mutations were observed in most viruses of the cluster
- When removing resistance positions, the pol tree became compatible with known transmission history
- Drug resistance selection was the cause of the incompatibilities found

Lemey et al 2005, JVI 79:11981

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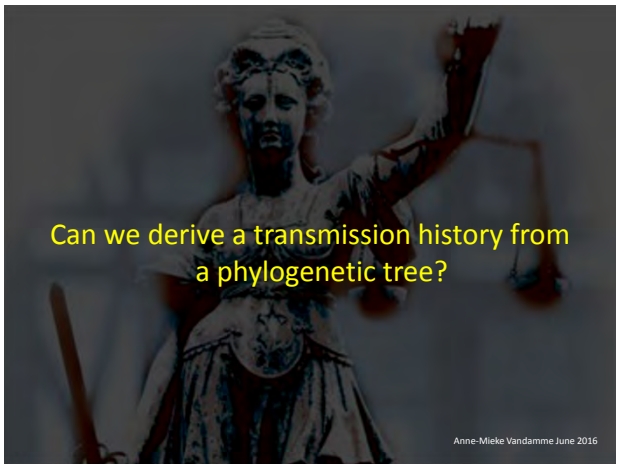
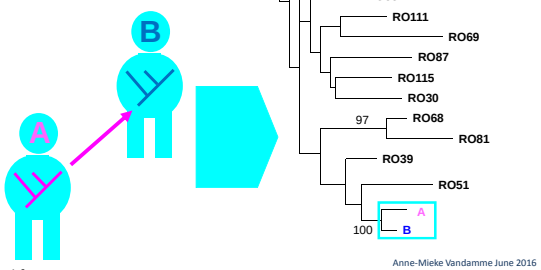


From documented direct transmission to phylogenetic analysis



Adapted from Lemey, 2003

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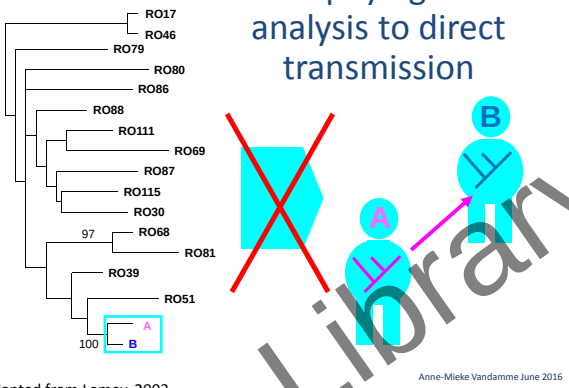
From phylogenetic analysis to direct transmission



Adapted from Lemey, 2003

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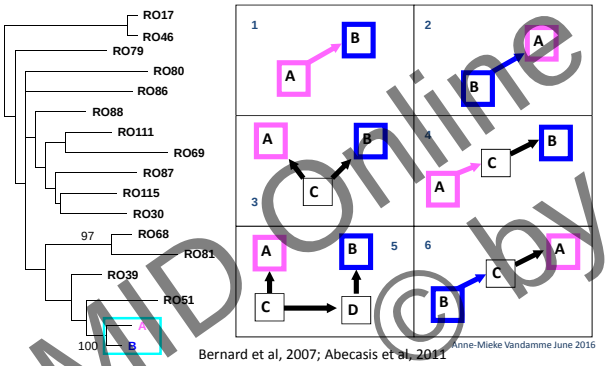
Compatible scenarios



Bernard et al, 2007; Abecasis et al, 2011

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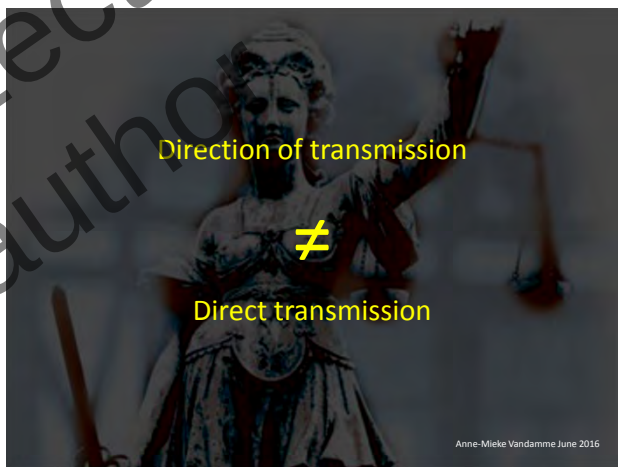
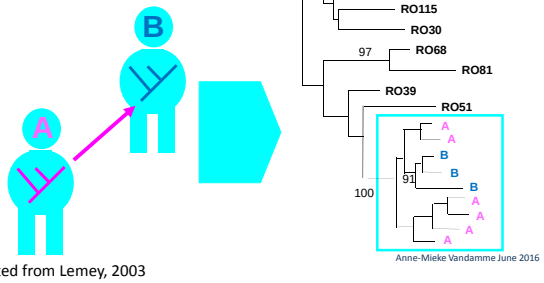


From documented direct transmission to phylogenetic analysis



Adapted from Lemey, 2003

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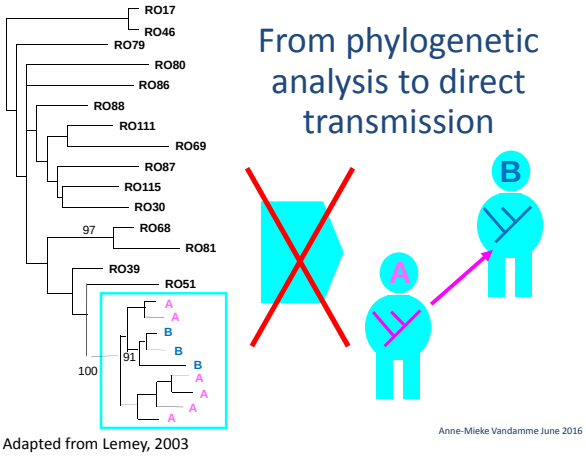
From phylogenetic analysis to direct transmission



Adapted from Lemey, 2003

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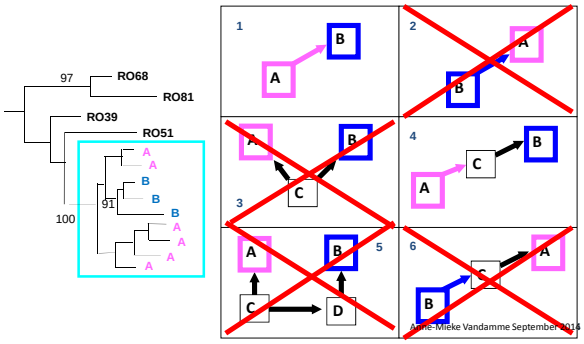
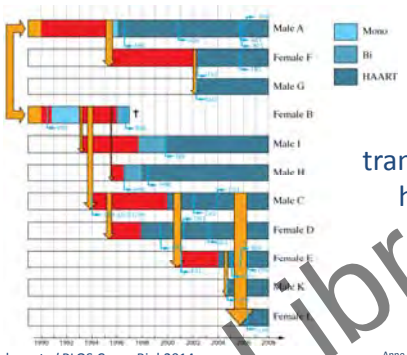
Compatible scenarios



Anne-Mieke Vandamme September 2014

Onwards transmission



True transmission history

Vrancken *et al* PLOS Comp Biol 2014

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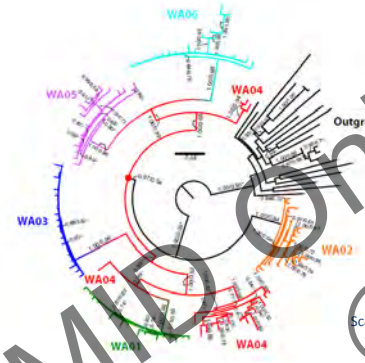
Direction of transmission



Direct transmission can not be derived from paraphyly alone

Scaduto, PNAS 2010

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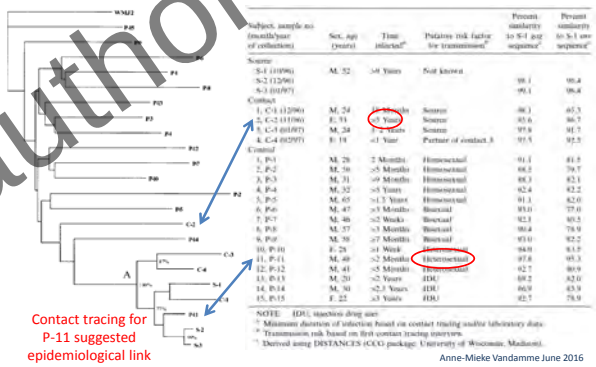
Problems may arise: clustering with latest contacts



Contact tracing for P-11 suggested epidemiological link

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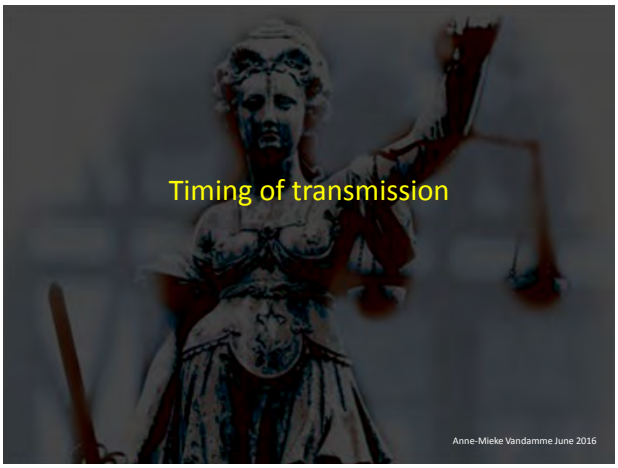

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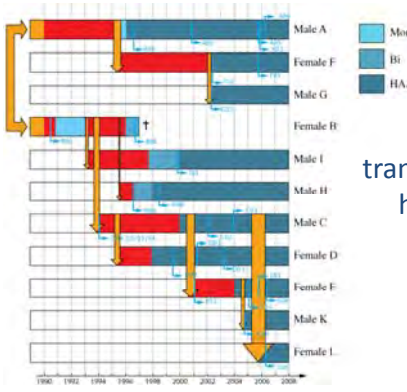

True transmission history

Vrancken *et al* PLOS Comp Biol 2014

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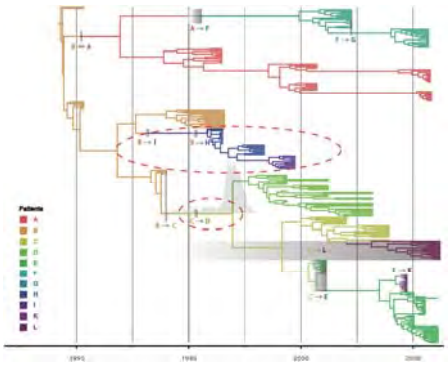
Reconstructed POL tree



Vrancken *et al* PLOS Comp Biol 2014

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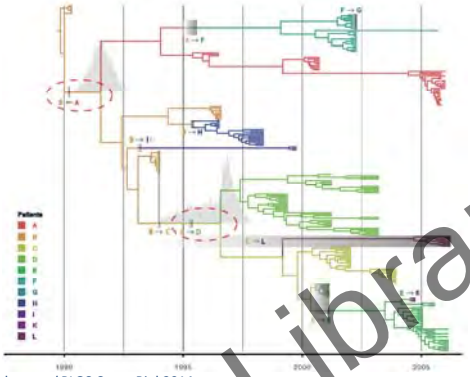
Reconstructed ENV tree



Vrancken *et al* PLOS Comp Biol 2014

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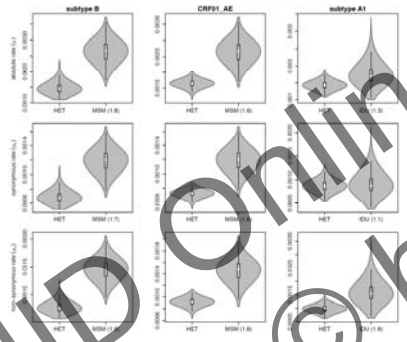
Evolutionary rate depends on shape of epidemic



Vrancken *et al* AIDS 2015

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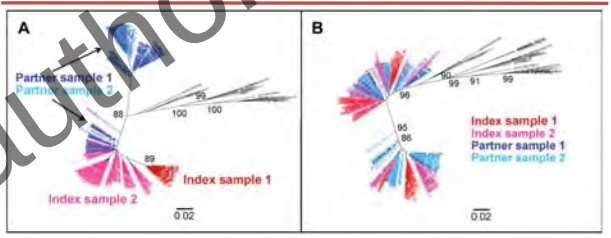
HIV-1 linkage studies in treatment as prevention: use of NGS



- Only consensus sequences with >10 primary NGS reads were used
- Samples were taken shortly after seroconversion
- NGS within-patient diversity useful mostly with samples early after transmission

HPTN 052 Eshleman JID 2011

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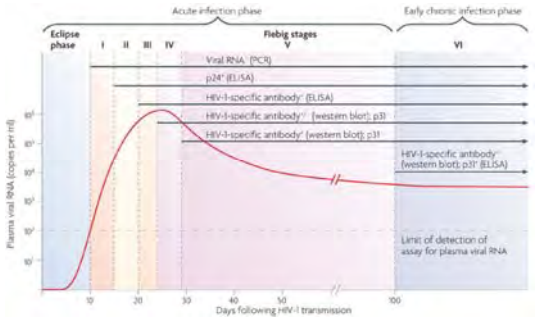
Window of detection for a typical patient



Fiebig et al 2003, AIDS; McMichael et al 2010, Nature Reviews Immunology

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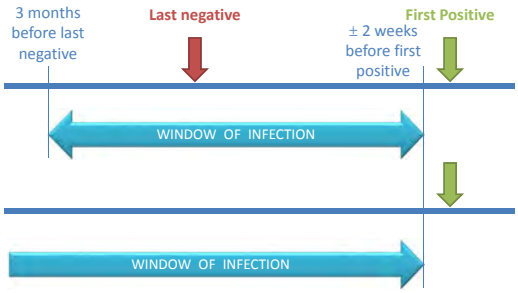
Is there a last HIV-negative test?



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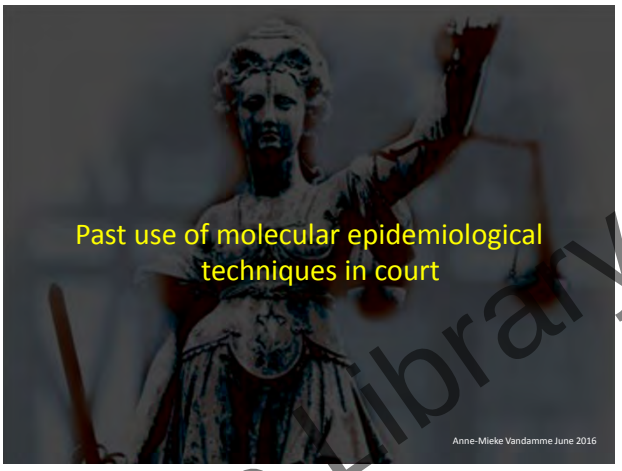
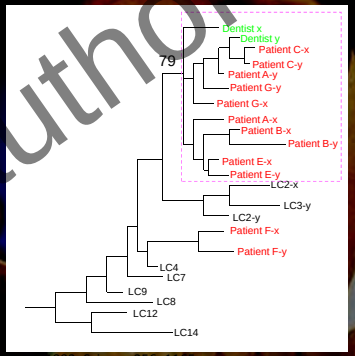


The Florida dentist case



Mode of transmission not established

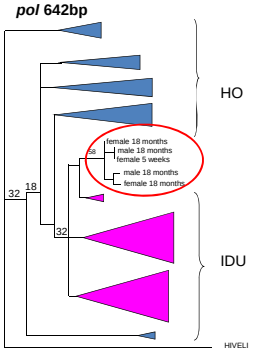
Settled out of court

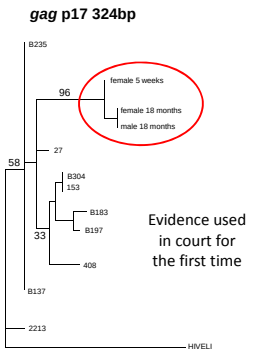
Heavily criticized

Patient	Other risk factor
Patient A	No
Patient B	No
Patient C	No
Patient D	Yes
Patient E	No
Patient F	Yes
Patient G	No
Patient A	No

Anne-Mieke Vandamme September 2014

The Stockholm rape case





Evidence used in court for the first time

Albert et al 1994, JVI 68: 5918.

Anne-Mieke Vandamme June 2016

The state of Louisiana vs. Richard J. Schmidt

In 1995, a nurse in Lafayette, L.A., accuses Richard J. Schmidt, a local gastroenterologist, of deliberately infecting her with HIV and HCV.

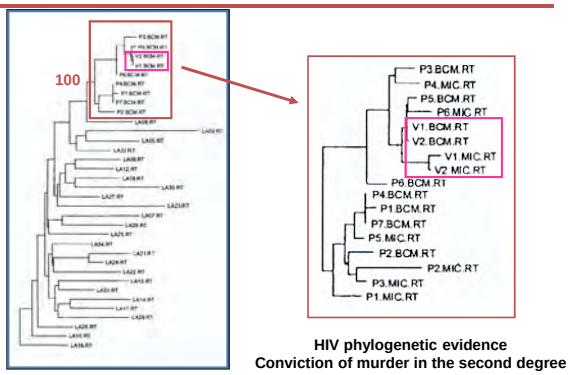
She claimed that after she had threatened to break of her decade-long affair with Schmidt, he infected her with tainted blood in place of one of her vitamin injections

The blood, the state argued in court, came from two of Schmidt's patients, one of whom had hepatitis C and the other of whom had HIV

26 local controls

Anne-Mieke Vandamme June 2016

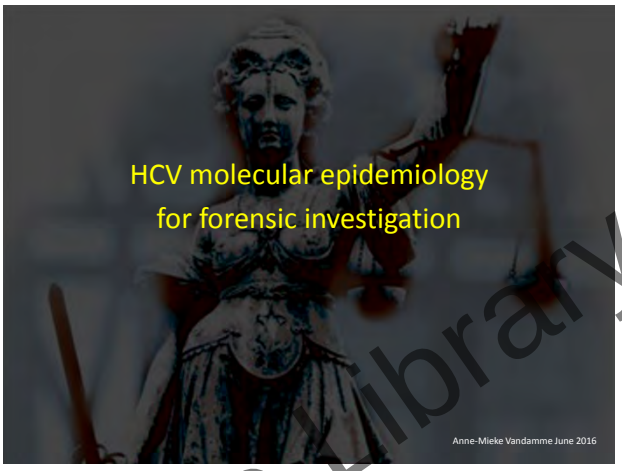
The state of Louisiana vs. Richard J. Schmidt



HIV phylogenetic evidence
Conviction of murder in the second degree

Metzker et al 2002, PNAS 99: 14292 .

Anne-Mieke Vandamme June 2016



Background

- HCV is spread mainly through nosocomial infection (e.g. hemodialysis patients).
- Although dialysis patients with HCV infection respond well to interferon-based therapy, relapse is frequent: re-infection or relapse?
- Phylogenetic tree analysis using partial HCV-NS5B sequences at pre-treatment (T0) and 6 months after end-of-treatment (T18) in non-sustained responders.
- Identical subtypes were detected in 10 patients at T18. Five patients changed genotypes at T18, suggesting nosocomial re-infection.

Arrais et al 2008, J Med Virol 80: 80-86.

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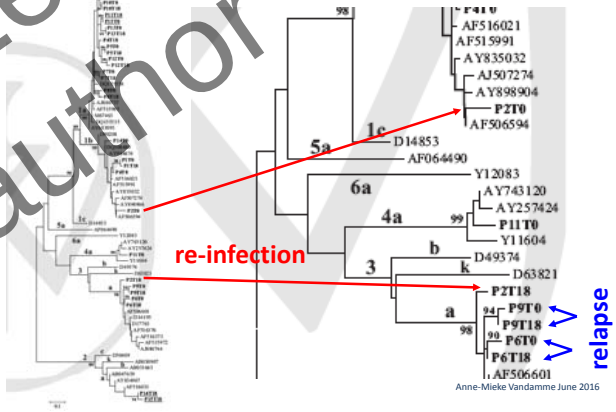
Nosocomial re-infection with HCV



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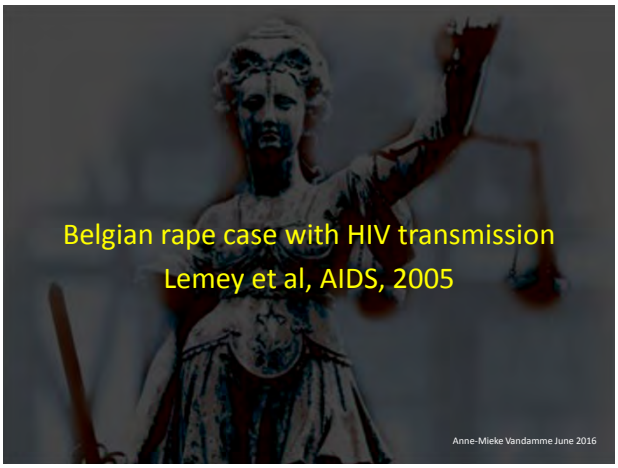
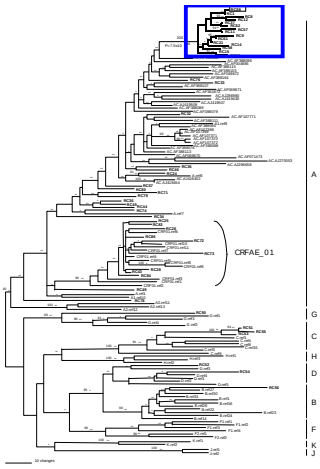


Background

- 7 female victims and 1 male suspect, 1 victim died of AIDS before the case came to court
- 6 of 7 victims had a documented seronegative test before the events and were HIV positive in their first test after the event
- All victims had positively identified the suspect
- The suspect was independently identified in the vicinity of the victims at the time of the events
- The suspect originates from a high prevalence country (Ruanda)
- The victims report no other risk factor apart from the rape

Lemey et al 2005, AIDS 19:1649

Anne-Mieke Vandamme June 2016



All local and database controls cluster significantly outside of the case cluster in *pol*

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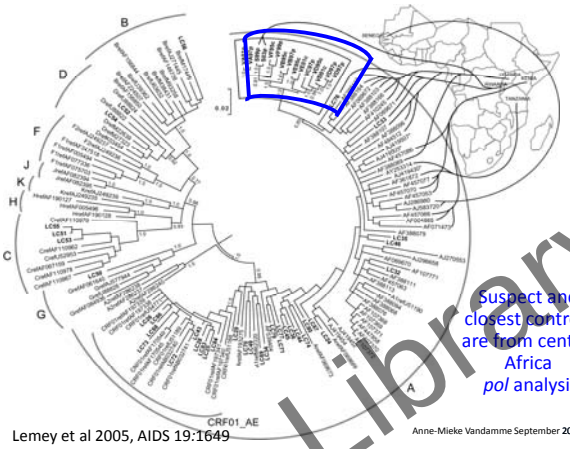

Suspect and closest controls are from central Africa *pol* analysis

Lemey et al 2005, AIDS 19:1649

Anne-Mieke Vandamme September **2016**

Facts

- The case strains are clustering together and none of the local or database controls fall into the transmission cluster in 3 gene regions for 2 samples of each (*gag*, *pol*, *env*)
- The distinct clustering of the case strains is statistically highly significant in *pol* and in *env*
- The closest related strains found are from Central and East Africa, the area of origin of the suspect. Neither of these strains fulfilled all epidemiological criteria, meaning that this type of strain most probably is not circulating among possible contacts of the victims.
- Considering the subtype (A) and its distribution at that time, and the age of the victims at seroconversion, the most likely route of infection is heterosexual.

Lemey et al 2005, AIDS 19:1649

Anne-Mieke Vandamme June 2016

Interpretation

- There is a close epidemiological link between the strains of the suspect and of all the victims analyzed, all strains belong to a single transmission cluster.
- We can say that we could not find any HIV strain in Belgium and world wide that is closer related to the strain of one of the victims than the strain of the suspect or the strains of the other victims.
- Our phylogenetic analysis does not allow to discriminate between direct transmission or indirect transmission. The methodology does also not allow to make claims on the direction of transmission. We can not exclude a hypothetical 3rd contact.

Lemey et al 2005, AIDS 19:1649

Anne-Mieke Vandamme June 2016

Conviction

- The suspect was convicted for multiple rape
- The phylogenetic analysis was just one of the many pieces of evidence


VRIJDAG 3 JUNI 2005

Man die zeven gehandicapte vrouwen verkrachtte voorlopig vrij door leugen

NIJVEL — Nachtwaker Paul Rulinda (42) loopt weer vrij rond in Tienen. Hij overtuigde de rechter in Nijvel gisteren met een leugentje over een vaste job om hem niet onmiddellijk voor acht jaar op te sluiten. Rulinda is wel veroordeeld voor de verkrachting van zeven geestelijk gehandicapte vrouwen in een opvanghuis in het Waals-Brabantse Chastre, tussen 1993 en 1995. Hij besmette hen daarbij met het aids-virus. Eén slachtoffer is intussen overleden. De andere vrouwen, tussen 30 en 64 jaar, worden behandeld met aids-remmers.

Advocate Nathalie Colette-Basecqz was oppositie na de zware veroordeling: «Het gerecht heeft de getuigenissen van de mentaal gehandicapte vrouwen nooit geloofd. Gelukkig is er het schitterende werk van de Leuvense professor Anne-mieke Vandam. Zij toonde in een gerechtelijk verslag aan dat het aids-virus bij de vrouwen van dezelfde oorsprong is als dat van de nachtwaker. De oorsprong ligt in Centraal-Afrika. De nachtwaker woonde tot aan de volkerenmoord in Rwanda.»

Rulinda houdt al tien jaar zijn onschuld staande. Na de veroordeling van het opvanghuis in Chastre in '96 bleef hij aan de slag als nachtwaker en later als verpleger. Hij werd erkend als politiek vluchteling en kreeg de Belgische nationaliteit.

ONWETTIG AFWEZIG

De openbare aanklager vroeg gisteren de onmiddellijke opsluiting van Rulinda. Rechter Craysmans ging daar niet op in, onder meer omdat Rulina een vaste job heeft. «Ik werk deeltijds als verpleger in het opvanghuis voor drugverslaafden MASS in Brussels, zei de veroordeelde tot de rechter. Directeur Emmanuel Gailly van MASS spreekt dat echter tegen: «Meneer Rulinda heeft twee maanden geleden zelf ontslag genomen, omdat hij onwettig afwezig was. Wij wisten niets van zijn gerechtelijk verleden. Bij zijn sollicitatie legde hij een bewijs van goed zedelijk gedrag voor. In ons opvanghuis heeft hij altijd in team gewerkt en nooit 's nachts.»

De advocaat van Rulinda wil enkel kwijt dat zijn cliënt beroep heeft aangetekend tegen de veroordeling. (BLA)

Paul Rulinda, glimlachend bij het verlaten van de rechtszaal

Lemey et al 2005, AIDS 19:1649

Anne-Mieke Vandamme June 2016

Background

- HCV outbreak among patients anesthetized by a single anesthetist suspected of sharing needles with the patients due to a morphine addiction
- Hundreds of patients were infected over 25 years, many of which had no other risk factor than the surgery
- Other epidemiological information pointed towards the anesthetist as most likely source: the problem occurred in all hospitals where he served and only in patients when he was serving
- There was no confession

González-Candelas et al, BMC Biology, 2013

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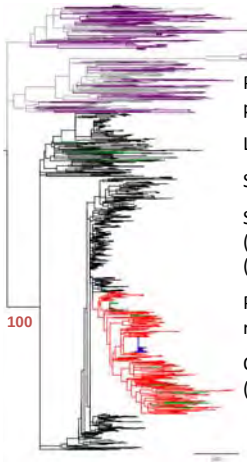

E1-E2 region including HVR1 and HVR2

Patients excluded from the outbreak (dark purple)

Local controls (grey)

Suspected source (dark blue)

Smallest monophyletic clade including all (but not only) suspected source variants (red)

Patients with strains inside + outside the red clade (green)

Other patients belonging to the outbreak (black)

González-Candelas et al, BMC Biology, 2013

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Molecular clock analysis

González-Candelas et al, BMC Biology, 2013

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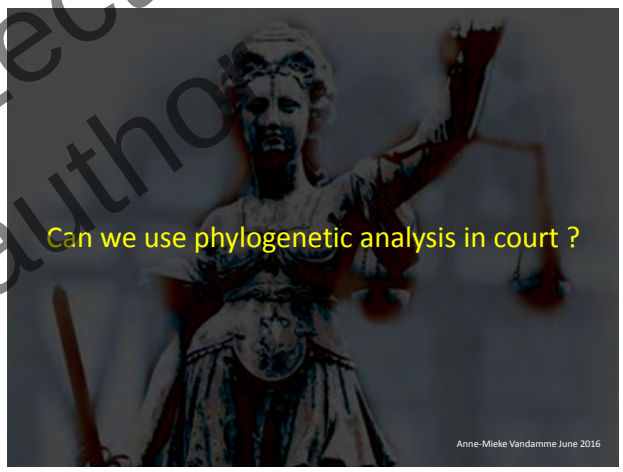

The Daubert criteria

Used by US judges to determine reliable scientific evidence:

1. The theory or technique is testable
2. It has been subjected to peer review or published
3. Scientists generally accept it works
4. There is a known error rate
5. There are maintainable standards controlling the use of the technique

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Phylogenetic analysis in court for HIV transmission investigation

1. Empirical testing has been done
2. The technique has been peer reviewed and published
3. Precedent of their proper use in court has been established
4. Error can be assessed
5. URGENT NEED FOR GUIDELINES FOR FORENSIC TESTING

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Phylogenetic analysis can not be used in court to

- prove a criminal act, it can only be used to support other proof
- indicate the direction of transmission. Who infected who? (this is still a research area, but progressing fast)
- document the timing of the transmission (this is still a research area)
- quantify how close the link is, did the individuals infect each other or were both part of a wider transmission cluster

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Phylogenetic analysis can be used in court to

- exonerate individuals by rejecting the hypothesis of transmission when the viruses are found not to be related
- indicate whether HIV from two individuals are closer related to each other than to viruses from other individuals with the same epidemiological profile, thus proving that they belong to the same transmission network

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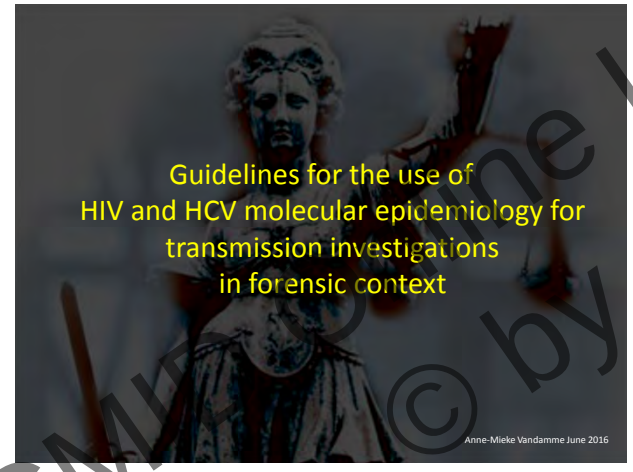

Expertise of the lab and the expert needs to be documented

- Performing phylogenetic analysis for research purposes is not sufficient as expertise

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Expertise of the lab and the expert needs to be documented

- Phylogenetic expertise ≠ forensic expertise
- The lab needs to document that it has experience, or collaborates with labs that have experience, in transmission investigations for forensic purposes

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Expertise of the lab and the expert needs to be documented

- Phylogenetic expertise ≠ forensic expertise
- Document experience in transmission investigations
- The lab needs to take part in regular genotyping proficiency panel testing which unravel the chances of a lab error (assessing sample mix-up, PCR contamination, sequencing performance)

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Expertise of the lab and the expert needs to be documented

- Phylogenetic expertise ≠ forensic expertise
- Document experience in transmission investigations
- Sequencing QC
- The lab needs to show that it has access to the appropriate control population: without access to the proper controls, don't do the court case! (or at least indicate you don´t have the proper controls)

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Expertise of the lab and the expert needs to be documented

- Phylogenetic expertise ≠ forensic expertise
- Document experience in transmission investigations
- Sequencing QC
- Access to appropriate control population
- The expert needs to show that he/she is aware of the powers and pitfalls of molecular epidemiology for forensic transmission investigation

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Sample handling

- At least 2 samples from all involved individuals need to be tested taken at different time points, one of which is as close as possible (< 2 years) to the presumed transmission time, and taken preferentially in different clinical settings
  - To minimize errors from sample mix up (e.g. different technicians, different labs)
  - To increase reliability of interpretation

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Sample handling

- 2 samples from each: to minimize sample mix up and to increase reliability of interpretation
- Samples from involved individuals need to be drawn or retrospectively taken under court order and tracking needs to be documented. If stored sequences are requested under court order, avoid breaching anonymity of other patients.

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Sample handling

- 2 samples from each: to minimize sample mix up and to increase reliability of interpretation
- Case samples (sequences?) to be drawn or taken under court order.
- Control samples or sequences need NOT to be taken under court order, but ethical approval is needed, except for sequences obtained from publicly available anonymous databases. Testing needs to be done anonymously to protect the control individuals, thus the code linking control individuals to their sequence should be made unavailable to those involved in the analysis and to court.

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Sample handling

- 2 samples from each: to minimize sample mix up and to increase reliability of interpretation
- Case samples (sequences?) to be drawn or taken under court order.
- Control samples need to remain anonymous
- Samples need to be offered blindly to technicians performing the genetic tests and the technicians performing the phylogenetic analysis. Unblinding happens AFTER the analysis is done upon writing the report or in court.

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Analysis needs to be done in the context of a priori hypothesis testing

- A priori hypothesis testing based on other evidence: no fishing expedition (prosecutors fallacy)
- Control samples to find evidence to REJECT the a priori hypothesis
- ~ 30 epidemiologically matching local controls (what strains are circulating in epidemiologically similar individuals?)
  - Compared to the victim
  - Compared to the suspect
- As many similar database controls as feasible (e.g. through a BLAST scan for all involved individuals).

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Possible criteria for epidemiologically matching controls

At least one and preferentially several of the following:

- The same transmission risk group
- The same geographic area of residence or of alleged transmission event or attending the same hospital as donor or recipient
- Taken in the same period as recipient
- Same gender, nationality, age …
- Being infected with the same subtype

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Try to document the transmission network

- If available, include strains with a documented epidemiological link to donor or recipient
- These can not be considered as controls since
  - this would artificially increase the number of control strains, without increasing the possible variability encountered in the matched population
  - it is expected that these strains will fall within the transmission cluster
- They give an indication how documented links are clustering in this specific phylogenetic analysis

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Phylogenetic methods

- Test at least 2 appropriate genetic regions
  - the env region (V1-V5) and the gag region have been used in many cases
  - preferentially > 500 nts, depending on the genetic region
  - the pol region can be conveniently used
    - excluding resistance related positions
    - gives possibility to check transmission of resistance
- Choose appropriate evolutionary model (e.g. Modeltest)
- Use preferentially a maximum likelihood and/or Bayesian approach, especially if neighbor joining proves not to be robust enough, (e.g. problems with different dates)
- Assess robustness of the tree (e.g. bootstrapping)

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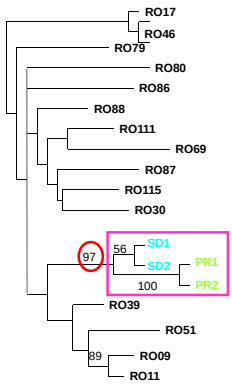

The cluster of suspected donor (SD) and the presumed recipient (PR) is significantly supported and does not include other control strains

Anne-Mieke Vandamme June 2016

Significant clustering of the case strains

- You can testify that you could not find any HIV strain in a similar population and world wide that is closer related to the strain of the presumed recipient than the strain of the suspected donor

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Significant clustering of the case strains

- Case strains are closer related to each other than to controls
- If your controls were appropriate, you can claim that they belong to the same transmission cluster (unless another region contradicts this conclusion). If you do not have access to appropriate controls, don't make claims with regard to transmission chain, only with regard to local epidemic.

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Significant clustering of the case strains

- Case strains are closer related to each other than to controls
- Same transmission cluster
- You can NOT testify that there was a direct transmission between suspected donor and presumed recipient. In fact you should testify that phylogenetic analysis can NEVER claim direct transmission

Anne-Mieke Vandamme June 2016

Significant clustering of the case strains

- Case strains are closer related to each other than to controls
- Same transmission cluster
- No evidence for direct transmission
- You can NOT discriminate who is donor or who is recipient. In fact you should testify that the presumed recipient could equally well have been the actual donor (unless contradicted by other medical evidence through documented seronegative result)

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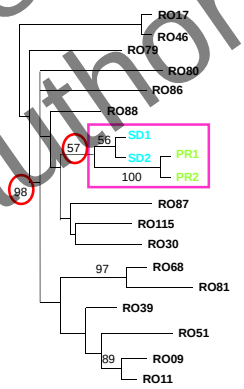

The cluster of suspected donor and the presumed recipient does not include other control strains but is not significantly supported There is significant support for an epidemic clade

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No significant support for the cluster

- You can not make conclusions about transmission clusters
- You could suggest they belong to the same epidemic

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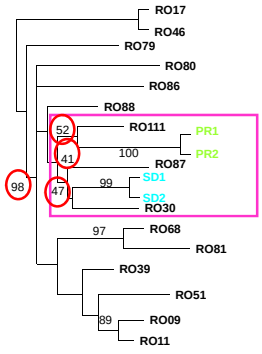

The cluster of suspected donor and the presumed recipient does include other control strains but no significant support separates suspected donor and presumed recipient There is significant support for an epidemic clade

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The case strains cluster separately but this is not significantly supported

- You can not make conclusions about transmission clusters
- You could suggest they belong to the same epidemic

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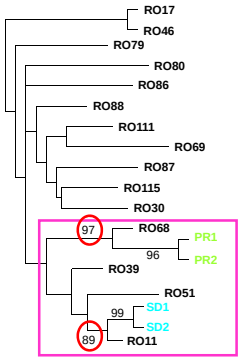

The cluster of suspected donor and the presumed recipient does include other control strains and significant support separates both

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There is separate clustering and this is significantly supported

- You can testify that the suspected donor did not infect the presumed recipient (at least with this strain, and provided controls are not epidemiologically linked)

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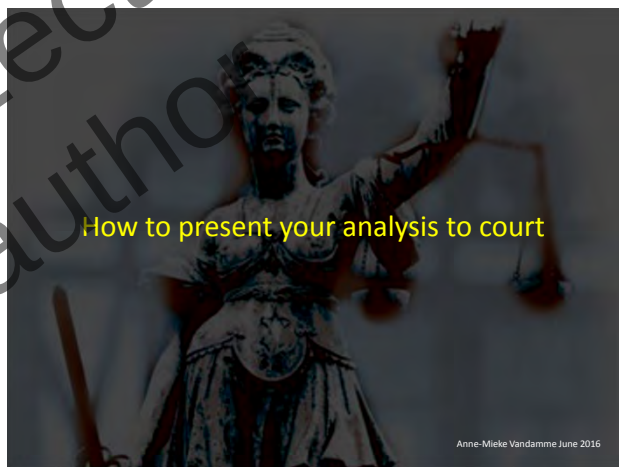

Getting involved in court cases

- Invited by prosecution or defense, but you stay an independent scientific expert
- Get your quotation approved up front
- Do not talk to the other party unless invited by court, otherwise you risk a mistrial
- Take your time to do a proper job
- Present your written report only to the party that invited you, but try to convince your party to share it with the other party, and to get permission to come to an agreement with the expert of the other party
- Be prepared to be examined and cross examined: your expertise will be questioned. Any document you use to help you in this needs to be disclosed.

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Phylogenetic evidence in court

- The documented expertise of the lab and expert
- An HIV primer and brief history of the use of phylogenetic analysis in court
- A brief explanation on the concept of phylogenetic analysis and of how to interpret the results
- Specific statements on what phylogenetic analysis can and can not prove
- The documented choice of the epidemiological controls
- The published context of the database controls
- The phylogenetic clustering of the case including the statistical support
- **The conclusion with the necessary notes of caution**

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Contact tracing in court

- The phylogenetic evidence can never prove transmission
- Information on window of infection is crucial to perform contact tracing
- Contact tracing is needed to investigate HIV status of all potential risk contacts during window period of infection
- **The phylogenetic evidence should be considered along with evidence from window of infection and contact tracing**

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Conditions to establish transmission

The conditions to establish beyond reasonable doubt that the defendant infected the complainant are as follows:

1. Reliable full contact tracing shows that no other possible source of the infection of the complainant can be found.
2. The window period of infection of both establishes that the complainant was infected later than the defendant.
3. The genetic analysis shows closer clustering of HIV variants infecting complainant and defendant than with other local controls.

On the other hand, observation of quite different strains or subtypes of HIV infecting two individuals provides strong evidence against transmission of HIV between them.

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Agreement between Prof Peter Simmonds and Prof Anne-Mieke Vandamme

Groningen case

- HIV outbreak among MSM linked to a particular series of parties
- One of the party organizers confesses to have injected several of the men with HIV contaminated blood
- **Can the following phylogenetic tree help to prove the case?**

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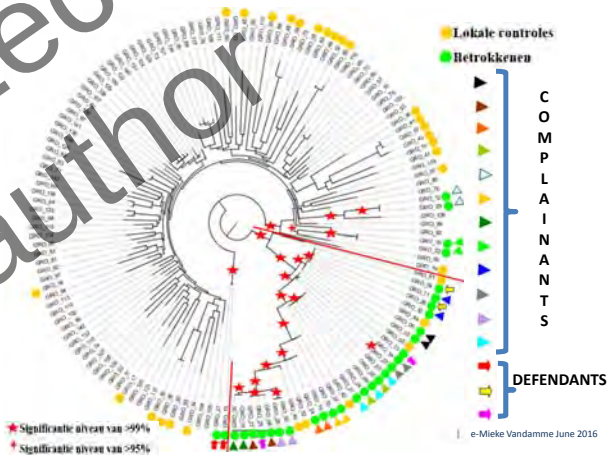

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Groningen case

AIDS Res Hum Retroviruses. 2011 Apr;27(4):429-33. doi: 10.1089/aid.2010.0175. Epub 2010 Nov 18.

Unusual cluster of HIV type 1 dual infections in Groningen, The Netherlands.

van der Kuyl AC(1), Jurriaans S, Back NK, Sprenger HG, van der Werf TS, Zorgdrager F, Berkhout B, Cornelissen M.

(1)Laboratory of Experimental Virology, Department of Medical Microbiology, Centre of Infection and Immunity Amsterdam (CINIMA), Academic Medical Centre of the University of Amsterdam, The Netherlands. a.c.vanderkuyl@amc.uva.nl

In 2007, 14 Dutch men having sex with men (MSM) filed a criminal case against three other men, accusing them of administering sedative drugs, sexual abuse, and deliberate subcutaneous injections with HIV-1-infected blood. Medical files showed that 9 of 17 men presented with an acute HIV-1 infection syndrome during 2006-2007. Two men were not infected with HIV. Analysis of viral strains in the 12 MSM and the three alleged donors showed that one donor and six recipients were double infected with two distinct HIV-1 subtype B strains, while another five recipients and one donor were single infected with either strain. Two men were infected with unrelated strains. The finding of multiple double infections with very similar HIV-1 strains is without precedent.

Bioinformatics Workshop 2016

"21st International Bioinformatics Workshop on Virus Evolution and Molecular Epidemiology (VEME)"

Korea University College of Medicine, Seoul, Republic of Korea

Sunday, August 14 - Friday, August 19, 2016

https://rega.kuleuven.be/cev/veme-workshop/2016

Phylogenetic Inference: DAMBE, IQ-Tree, MEGA, PAML, PAUP*, PHYLIP, PHYML, TREE-PUZZLE
Evolutionary Hypothesis Testing: BEAST1, Consel, IQ-Tree, MrBayes, TREE-PUZZLE, SpreaD3, Figtree, Tracer
Large Dataset Analasys: bowtie, bcftools, MEGAN, PLINK, QuRe, SPAdes, UGENE, Velvet
Large Phylogenies: Fasttree, IQ-Tree, PhyloPart, PhyloType, RAxML
Transmission clusters: BEAST2, Clusterpicker
Molecular Adaption: HYPHY
Recombination & Networks: RDP3, Simplot, SplitsTree, Neighbournet
Visualization: Figtree, Phylogeotool, R, SpreaD3, RStudio
Virus Analysis Tools: www.bioafrica.net/software.php

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