



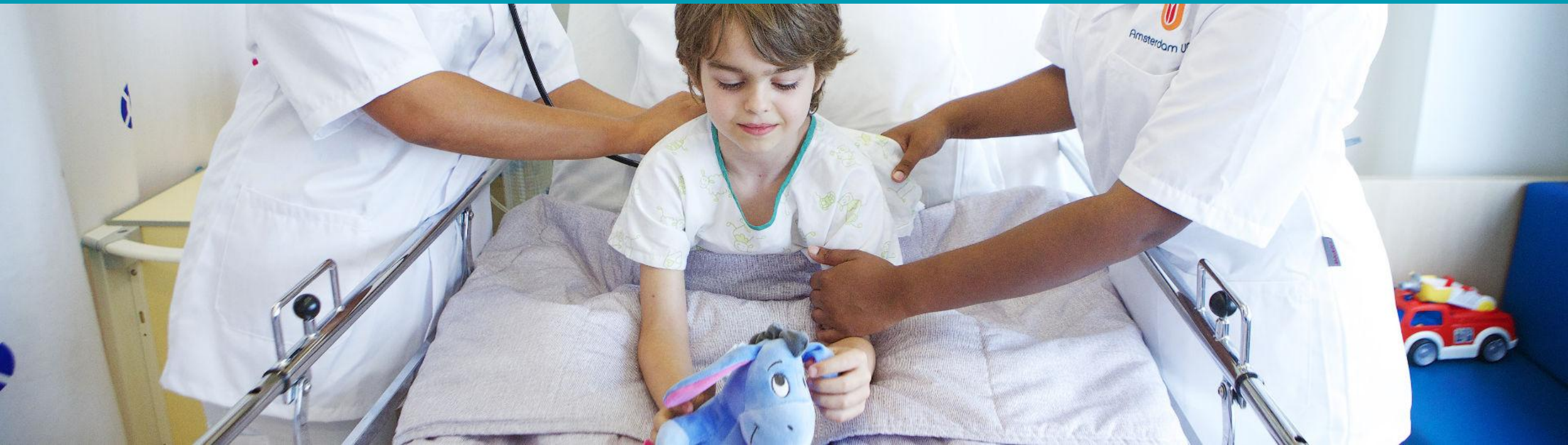
Emma Children's Hospital
Amsterdam UMC

Update on Anelloviruses: the most common viruses you rarely think of

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Almost every person in this room carries an anellovirus right now

- Lifelong persistence
- Abundant in blood, carried by most healthy donors
- Often unnoticed
- Poorly understood

Discovery

- 1997 → discovery of TTV
 - Transfusion transmitted virus
- Posttransfusion hepatitis
- Initially suspected pathogen
- Later found worldwide in healthy people



Regular Article

A Novel DNA Virus (TTV) Associated with Elevated Transaminase Levels in Posttransfusion Hepatitis of Unknown Etiology ☆

Tsutomu Nishizawa^a, Hiroaki Okamoto^a, Keiko Konishi^b, Hiroshi Yoshizawa^c, Yuzo Miyakawa^d, Makoto Mayumi^{a,1}

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How common in donors

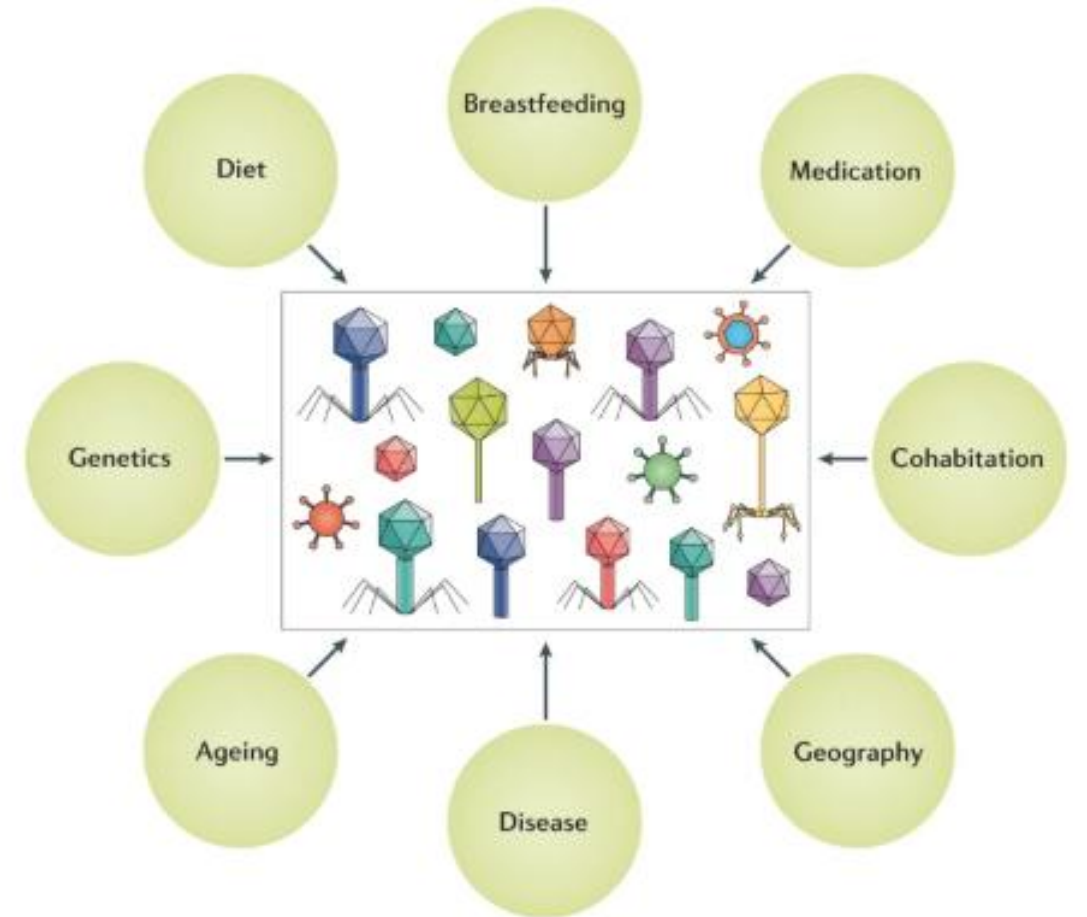
- Reported in 70-90% of healthy individuals
- Rates depend on assay sensitivity
 - Healthy persons: 2.3 log copies/mL
- No proven cause of disease
- Viral levels are stable in healthy individuals
- Likely linked to immune control





Anellome transmission

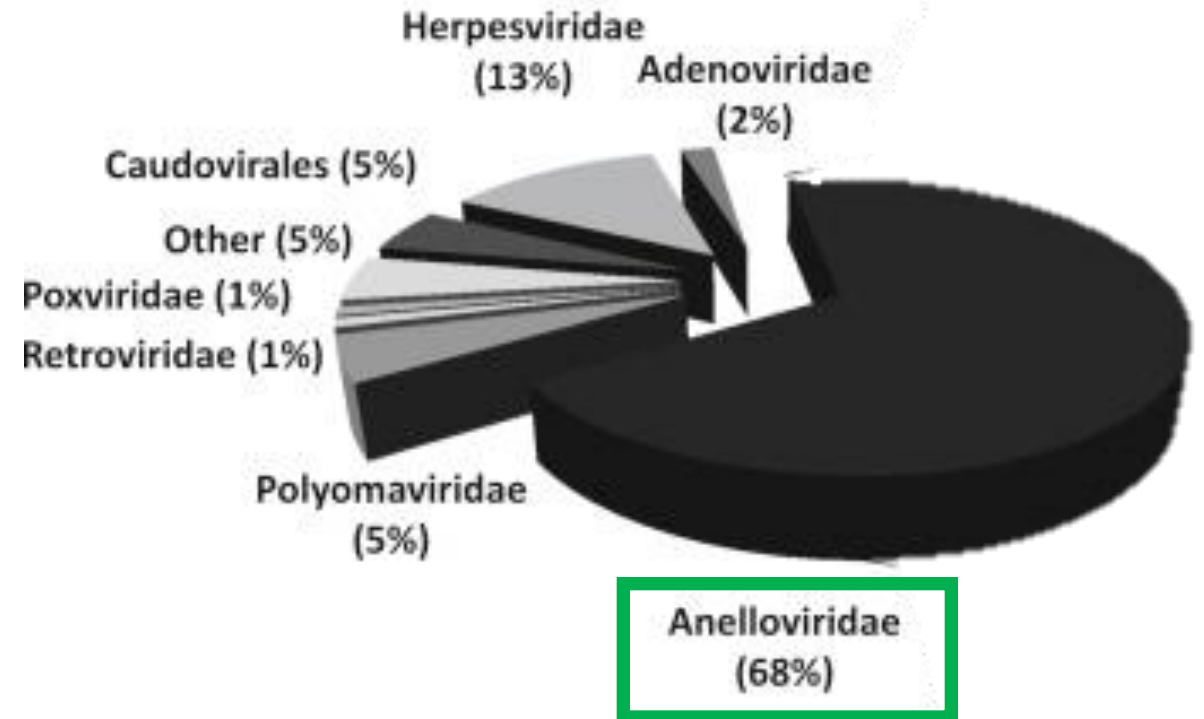
- Infection during early childhood
- Multiple anelloviruses can infect the same person
- Multiple transmission routes





Human anellome

- Anellome = anellovirus virome
- Anellome most abundant in human virome
 - TTV most abundant in anellome





> J Virol. 2022 Jun 8;96(11):e0010922. doi: 10.1128/jvi.00109-22. Epub 2022 May 16.

Diversity and Long-Term Dynamics of Human Blood Anelloviruses

Joanna Kaczorowska^{1 2}, Martin Deijs^{1 2}, Michelle Klein^{1 2}, Margreet Bakker^{1 2},
Maarten F Jebbink^{1 2}, Mila Sparreboom^{1 2}, Cormac M Kinsella^{1 2}, Anne L Timmerman^{1 2},
Lia van der Hoek^{1 2}

Affiliations + expand

PMID: 35575554 PMCID: PMC9175625 DOI: [10.1128/jvi.00109-22](https://doi.org/10.1128/jvi.00109-22)

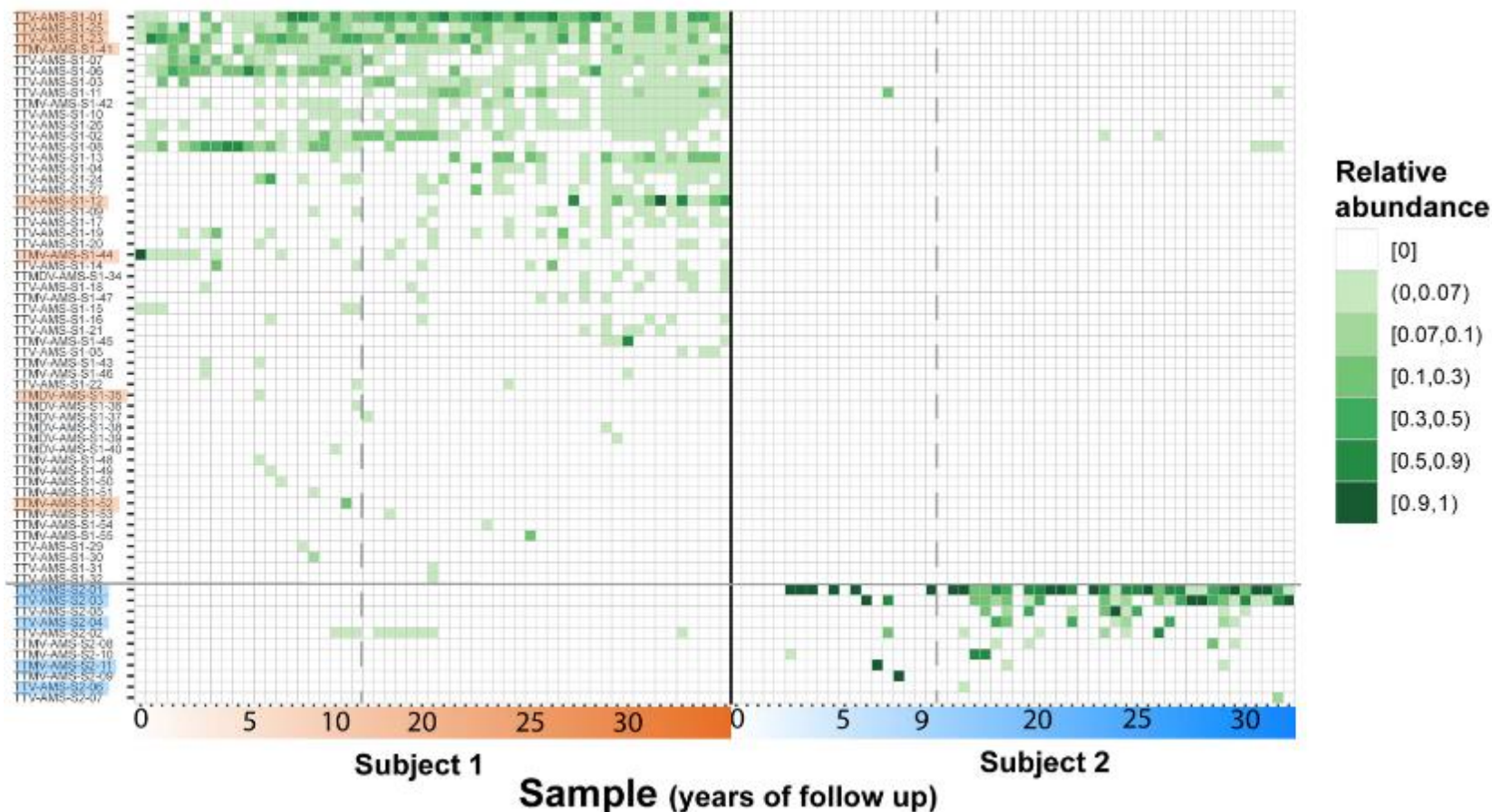
Anellome diversity

- Collected every 6 months serum samples of 2 healthy males
 - Subject 1: 55 samples, age 41 at start
 - Subject 2: 52 samples, age 35 at start
- Missing samples between 1996-2003
- Both participants: Amsterdam Cohort Studies of HIV infection and AIDS
 - Lived in Amsterdam area
 - Both remained HIV-1 negative
 - Subject 2: hepatitis B virus infection in 1998



Loss of existing lineages and introduction of new ones were rare

- 44 viral lineages were detected multiple times
- Persistent lineages dominated
- Most lineages were persistent throughout the study
 - Subject 1: 24/35
 - Subject 2: 5/9





Global genome analysis reveals a vast and dynamic anellovirus landscape within the human virome

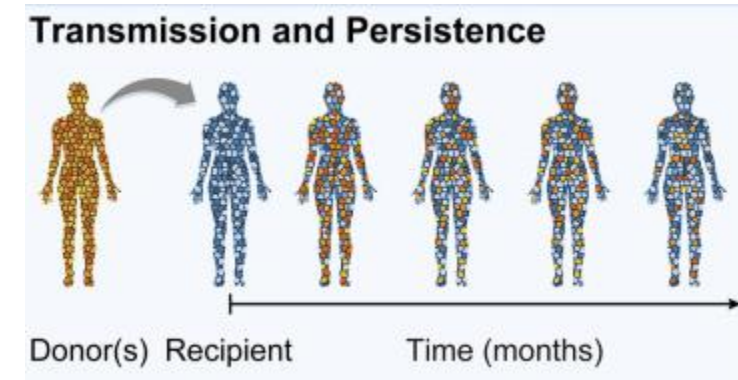
Cesar A Arze¹, Simeon Springer¹, Gytis Dudas², Sneha Patel¹, Agamoni Bhattacharyya¹, Harish Swaminathan¹, Carlo Brugnara³, Simon Delagrave¹, Tuyen Ong¹, Avak Kahvejian⁴, Yann Echelard⁴, Erica G Weinstein⁴, Roger J Hajjar⁴, Kristian G Andersen⁵, Nathan L Yozwiak⁶

Affiliations + expand

PMID: 34320399 DOI: [10.1016/j.chom.2021.07.001](https://doi.org/10.1016/j.chom.2021.07.001)

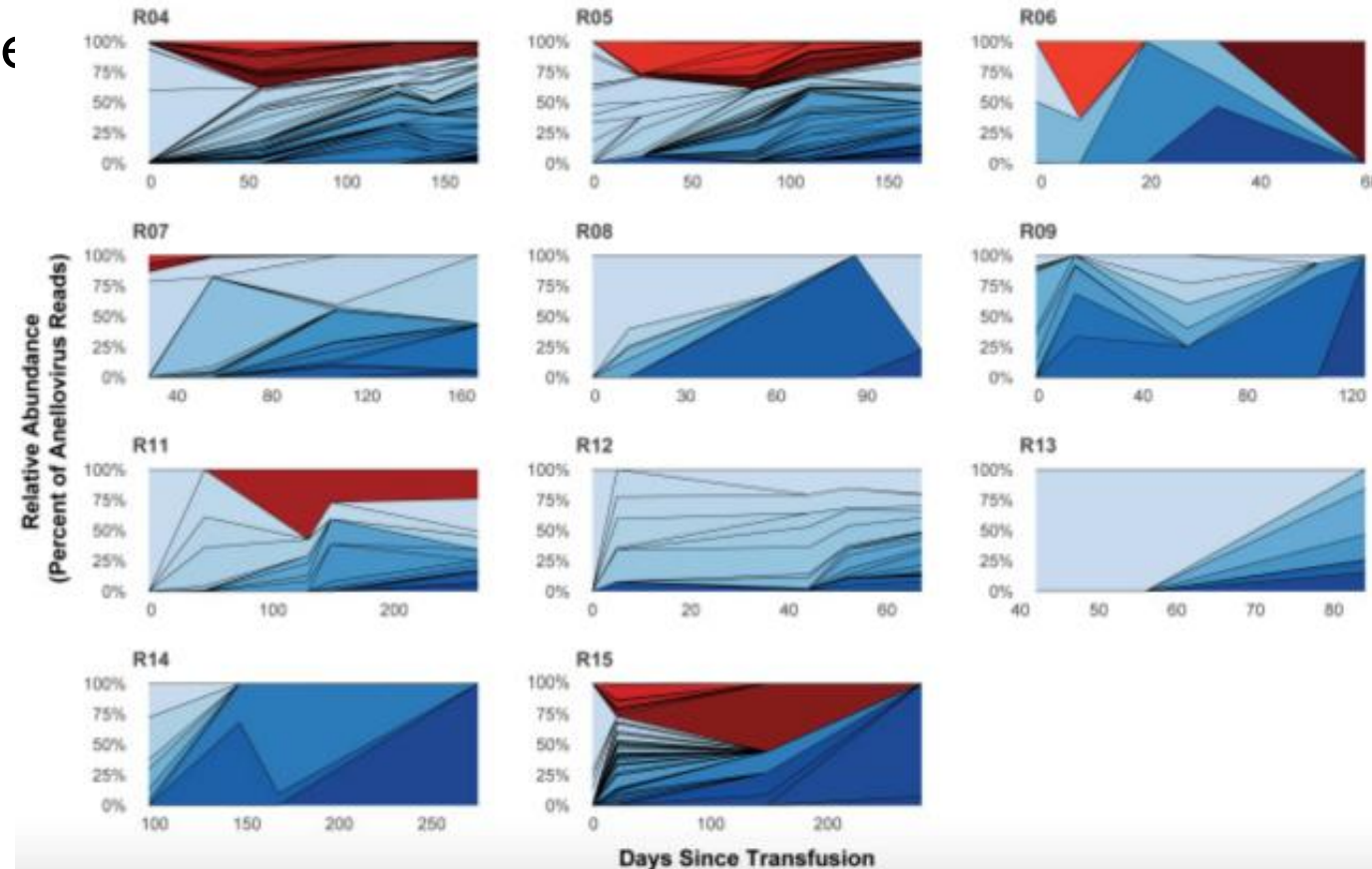
Transmission via blood transfusion

- 15 surgical patients → received blood transfusions from one or more unique donor pools
- Blood samples: before and after transfusion over 280 days
- Pan-anellovirus PCR → detection and tracking of lineages



Donor-derived anellovirus lineages persist and can become dominant after transfusion

- Donors and recipients carried multiple diverse anellovirus lineages
- Transmission was common
 - Donor-derived lineages in 8/15 recipients
 - Sometimes > 100 days after transfusion
- Transmitted lineages can become dominant
- Sequence similarity did not predict transmission





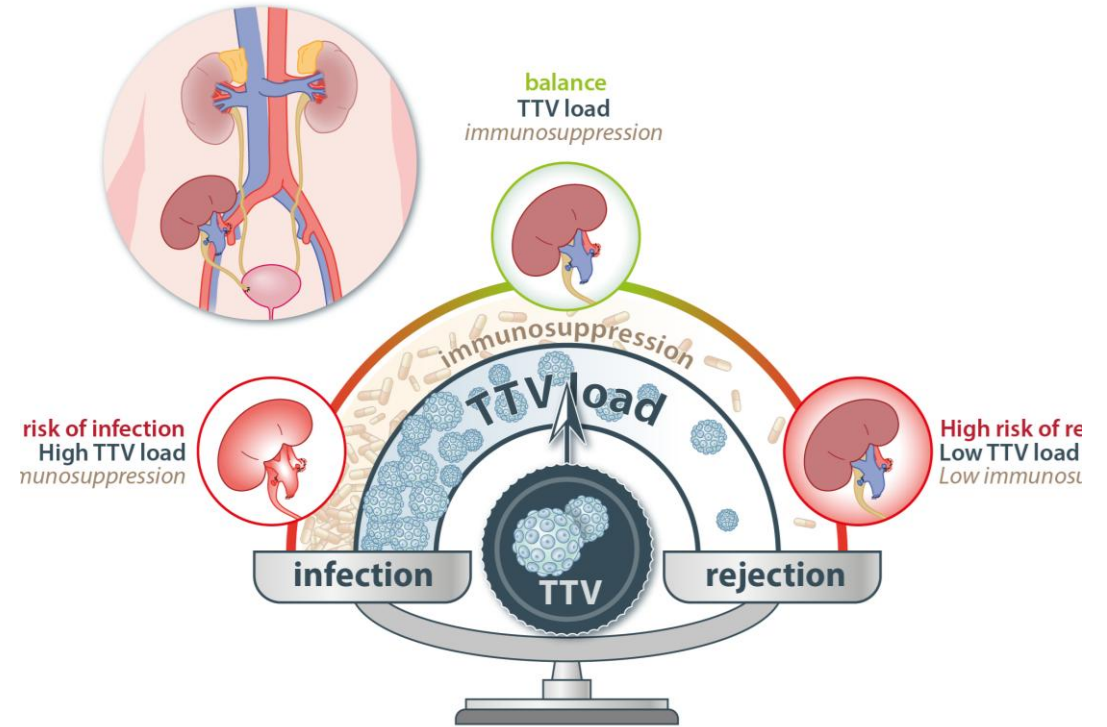
Anelloviruses and immune function

- Consequences TTV transmission unclear
- No proven pathogenicity
- Immune controlled replication
- Higher levels in:
 - HIV-1 infection
 - Pregnant women
 - Elderly
 - Males
 - Obese
 - Frail
 - Organ transplant recipients



Organ transplantation

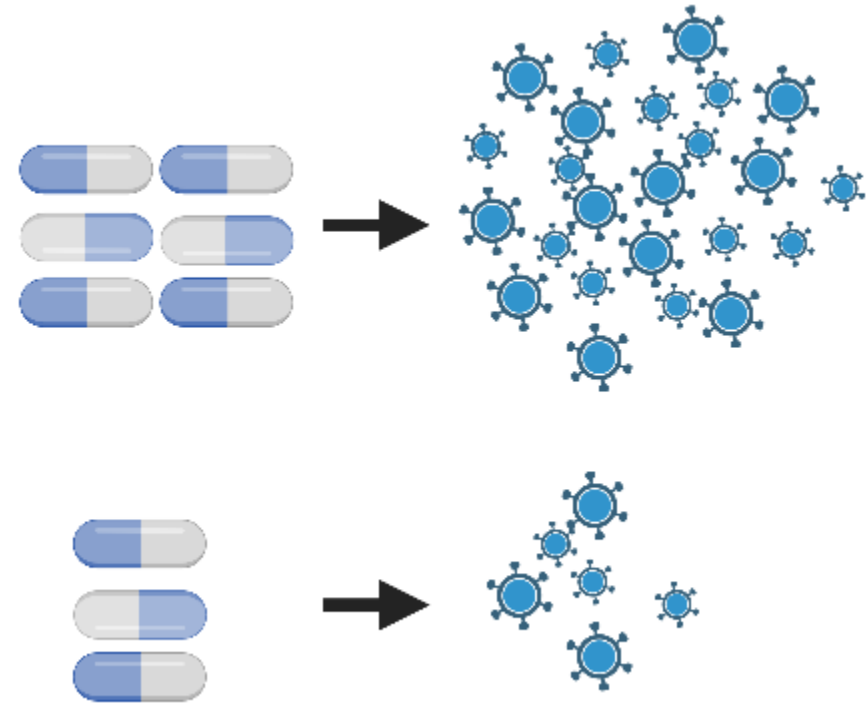
- Need for lifelong immunosuppressive drugs
- Dosage based on blood drug levels
 - Optimal window based on time after transplantation
- Challenge in transplant recipients: balance between infection and rejection





TTV as biomarker of immune competence

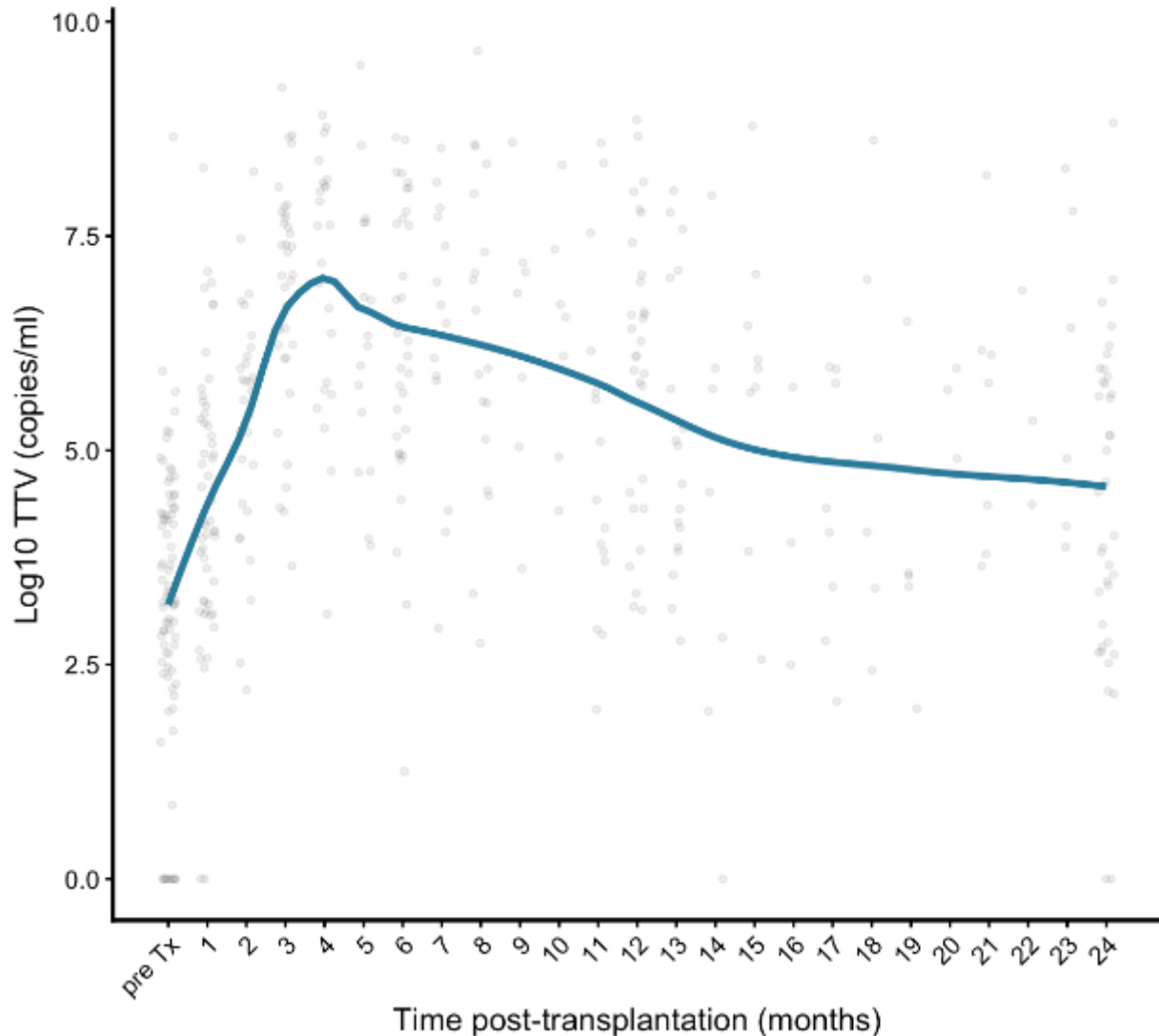
- TTV most abundant
- Viral expansion under immunosuppression
 - High viral loads → low immunity
 - Low viral loads → high immunity
- TTV loads rise after transplantation





Higher TTV loads after transplantation

TTV Load dynamics after pediatric kidney transplantation



- Is the increase of TTV post transplant entirely autologous? Or is it donor derived?

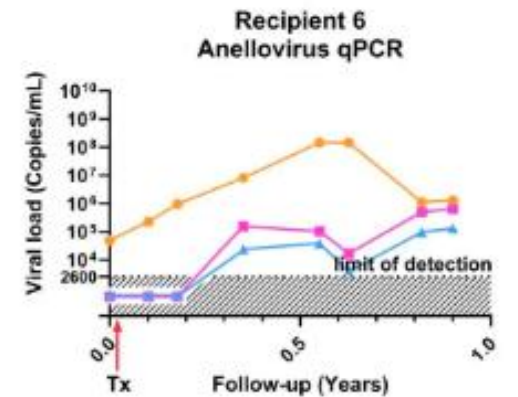
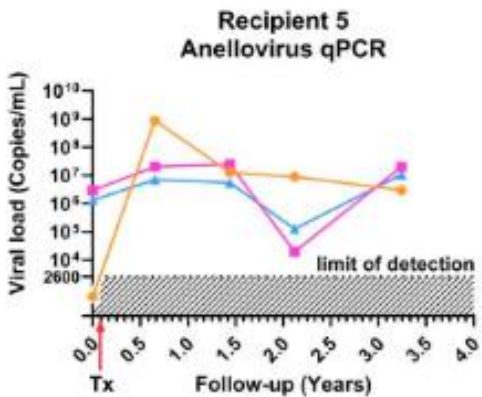
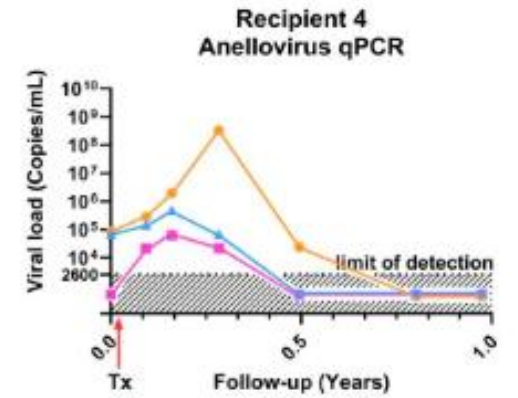
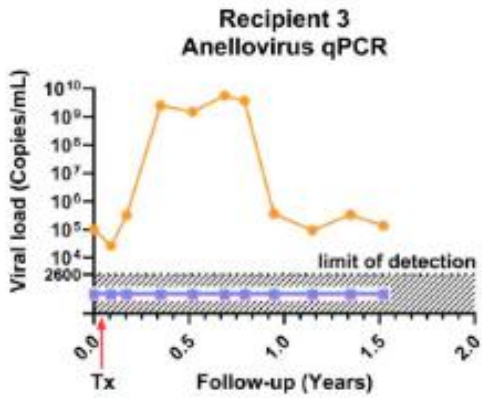
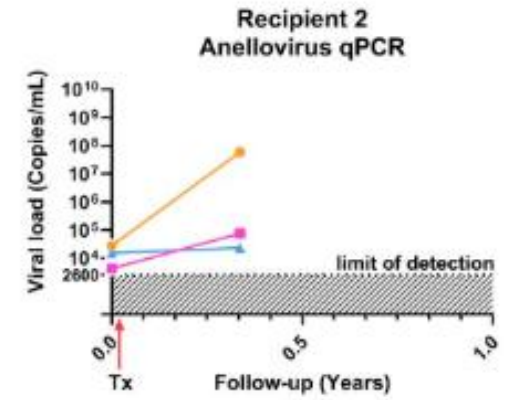
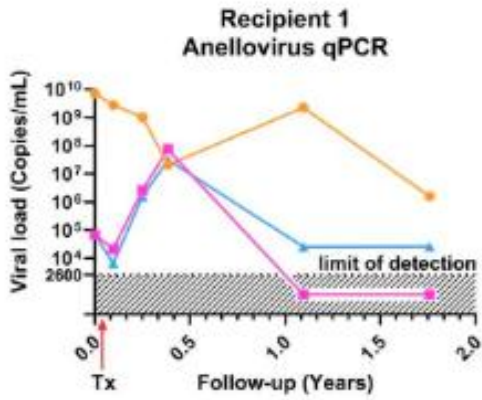
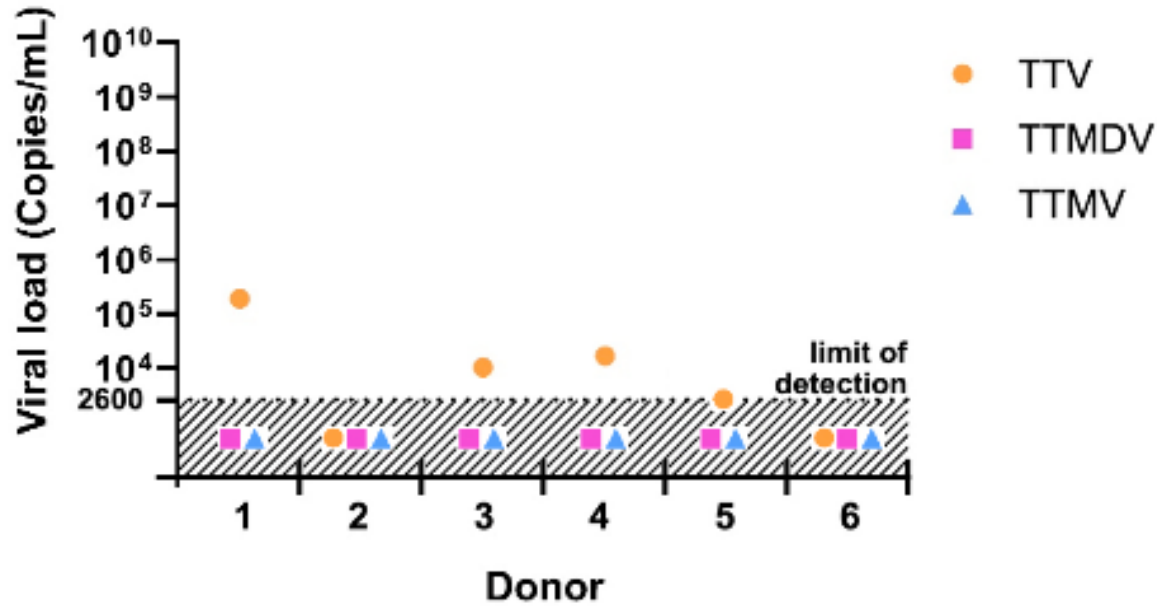


TTV introduced with donor organ?

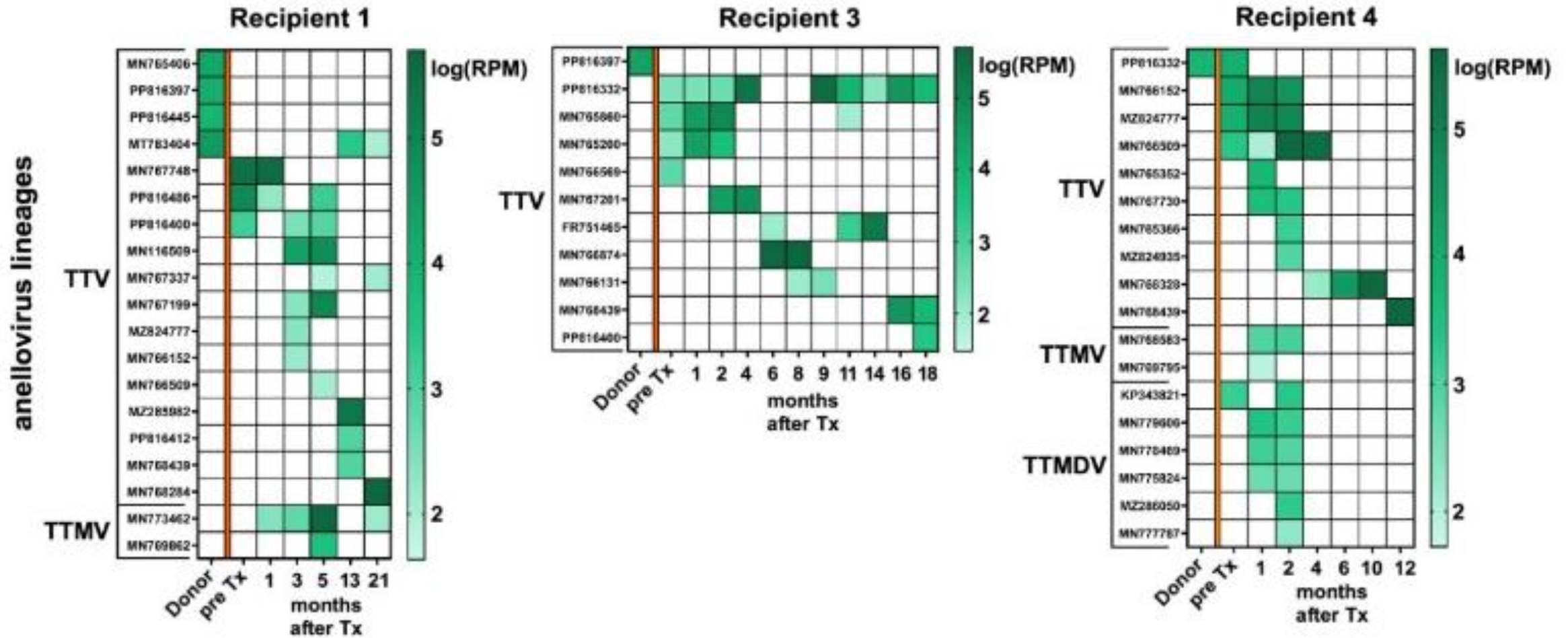
- What are the dynamics of the anelome in pediatric kidney transplant recipients?
 - 6 donor-recipient pairs (living donors)
 - NGS approach to determine anelome
 - Donor: one sample
 - Recipient: one sample prior transplantation, multiple samples after transplantation

Viral loads in 6 kidney donors and recipients

Donors Anellovirus qPCR



Anellome in 3 donor-recipient pairs





Conclusion

- 4 out of 6 donors tested positive for TTV, non for TTMV or TTMDV
- All recipients tested positive for TTV, usually peaking in the first six months
- TTMV and TTMDV loads were generally lower
- Recipient 1 acquired an *Alphatorquevirus* lineage matching the donor lineage (13- and 21-months post transplantation)
 - Genome comparison: >99% identity

Anelloviruses are transmitted not only through blood transfusion, but also from kidney donors to pediatric transplant recipients.



Take home messages



At least 70% of healthy blood donors carry one or more anelloviruses in their blood



Transmission via blood transfusion can change a person's 'core' anellome



Majority of blood transfusions transmit TTV



TTV may function as a biomarker for the level of immunity



Transmission via (pediatric) kidney transplantation occurs



Thank you for listening

- *Emma Children's Hospital: department of pediatric nephrology*
 - Antonia Bouts
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 - Margreet Bakker
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