

Perinatal Transmission of Hepatitis C Virus

Vienna, 1 June 2017

VHPB MEETING

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Perinatal Transmission of Hepatitis C Virus

Outline

- ❖ definition and timing
- ❖ transmission rates
- ❖ risk factors
- ❖ the *Trojan horse hypothesis*
- ❖ conclusion

Global Burden of HCV in Children and Adolescents

- ❖ **13.2 (11.5-21.2) million** children between 1 and 15 years are infected with HCV worldwide
- ❖ **6.6 (6.1-11.6) million viraemic** infections

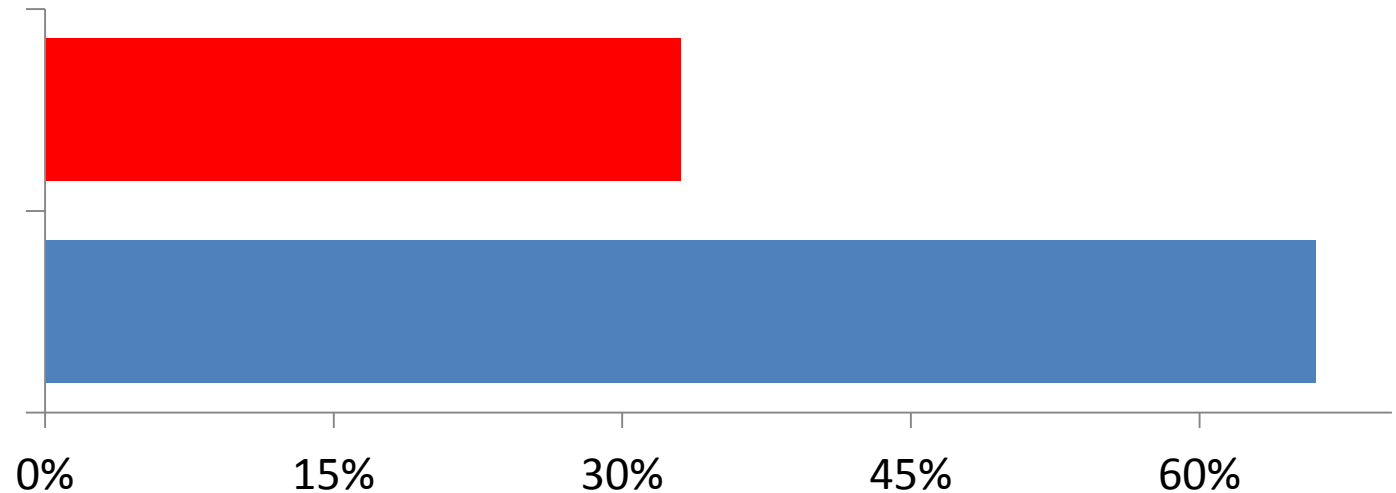
Vertical Transmission of Hepatitis C Virus

Timing

**HCV RNA detected by PCR in
serum of the neonate/infant**

first 24 hours of life

weeks after birth



Resti et al. BMJ 1998

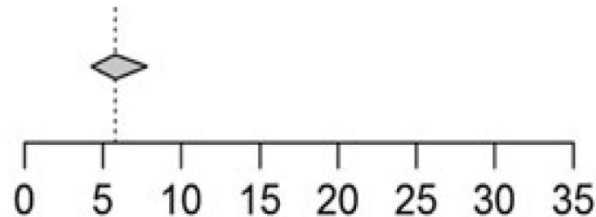
Vertical Transmission of Hepatitis C Virus

HCV antibody and RNA-positive women

HIV-negative women

Random effects model

Heterogeneity: $I^2=45.9\%$, $P = .0203$

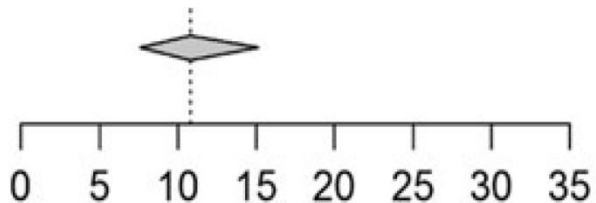


5.8 [4.2; 7.8] 100%

HIV-positive women

Random effects model

Heterogeneity: $I^2=28.8\%$, $P = .1982$



10.8 [7.6; 15.2] 100%

Vertical Transmission

Risk factors

- ❖ maternal
- ❖ obstetric procedures
- ❖ factors **NOT** associated with an increased risk

Vertical Transmission

Maternal risk factors

- ❖ **HCV viraemia**
- ❖ **HIV co-infection**
- ❖ **previous or ongoing history of IVDU**
- ❖ **sexual partner HCV-infected**
- ❖ **active hepatitis**
- ❖ **infection of **maternal PBMCs****
- ❖ **presence of the negative strand of HCV inside the PBMC**
- ❖ **HLA class II mother-child concordance**

Vertical Transmission

Obstetric procedures

- ❖ **invasive internal fetal monitoring**
- ❖ **vaginal or perineal laceration during vaginal delivery**
- ❖ **>6 hours duration of the rupture of membranes**
- ❖ **episiotomy**
- ❖ **amniocentesis**

- ❖ **conditions increasing the intrapartum exposure to maternal blood**

- ❖ **being second twin**

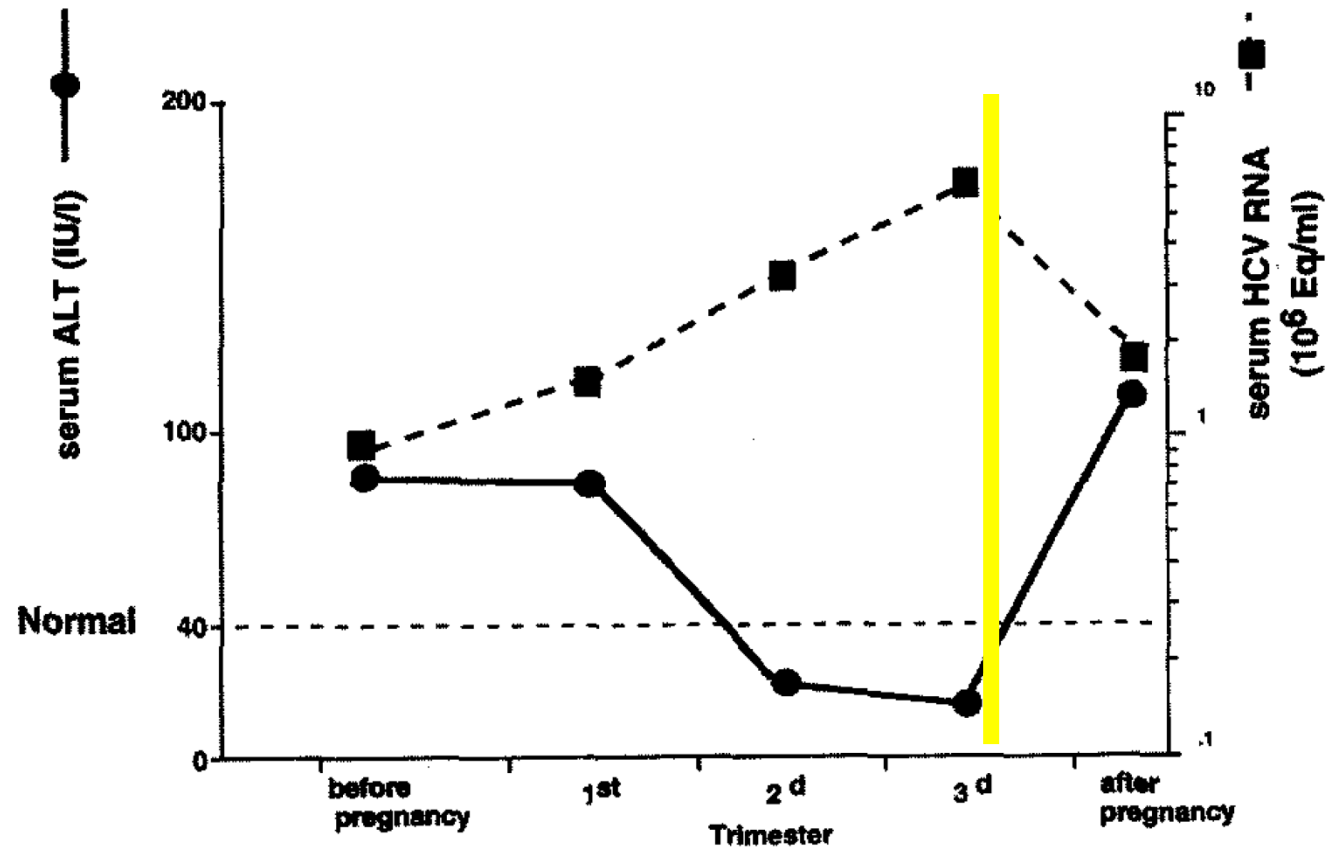
Vertical Transmission

Factors **NOT** associated with an increased risk

- ❖ HCV genotype
- ❖ *IL28B (IFNL4)* genotype
- ❖ mode of delivery (Caesarean *versus* vaginal)
- ❖ type of feeding
- ❖ **level of viraemia**

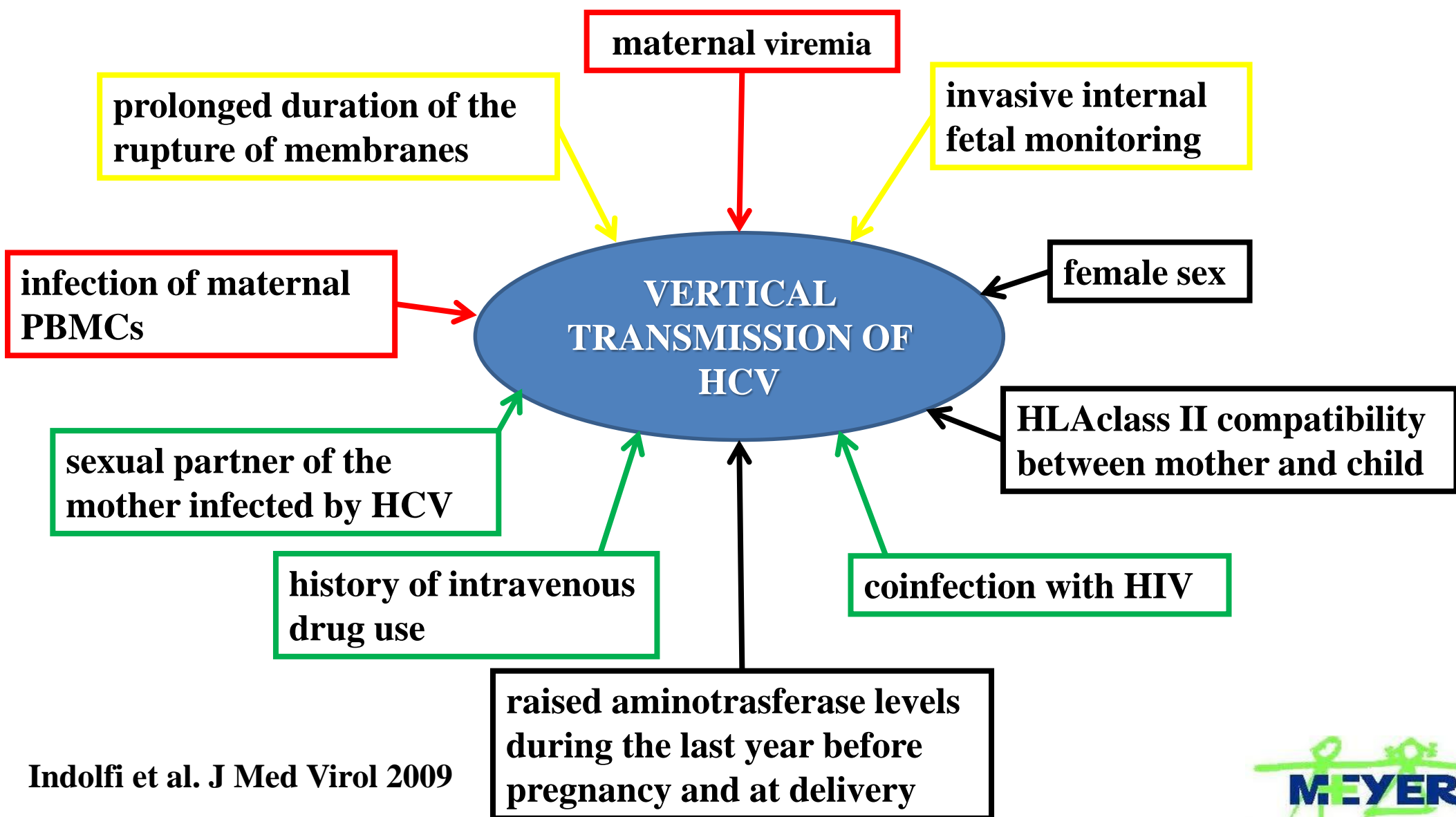
HCV Infection in Pregnancy

Viraemia and Transaminases

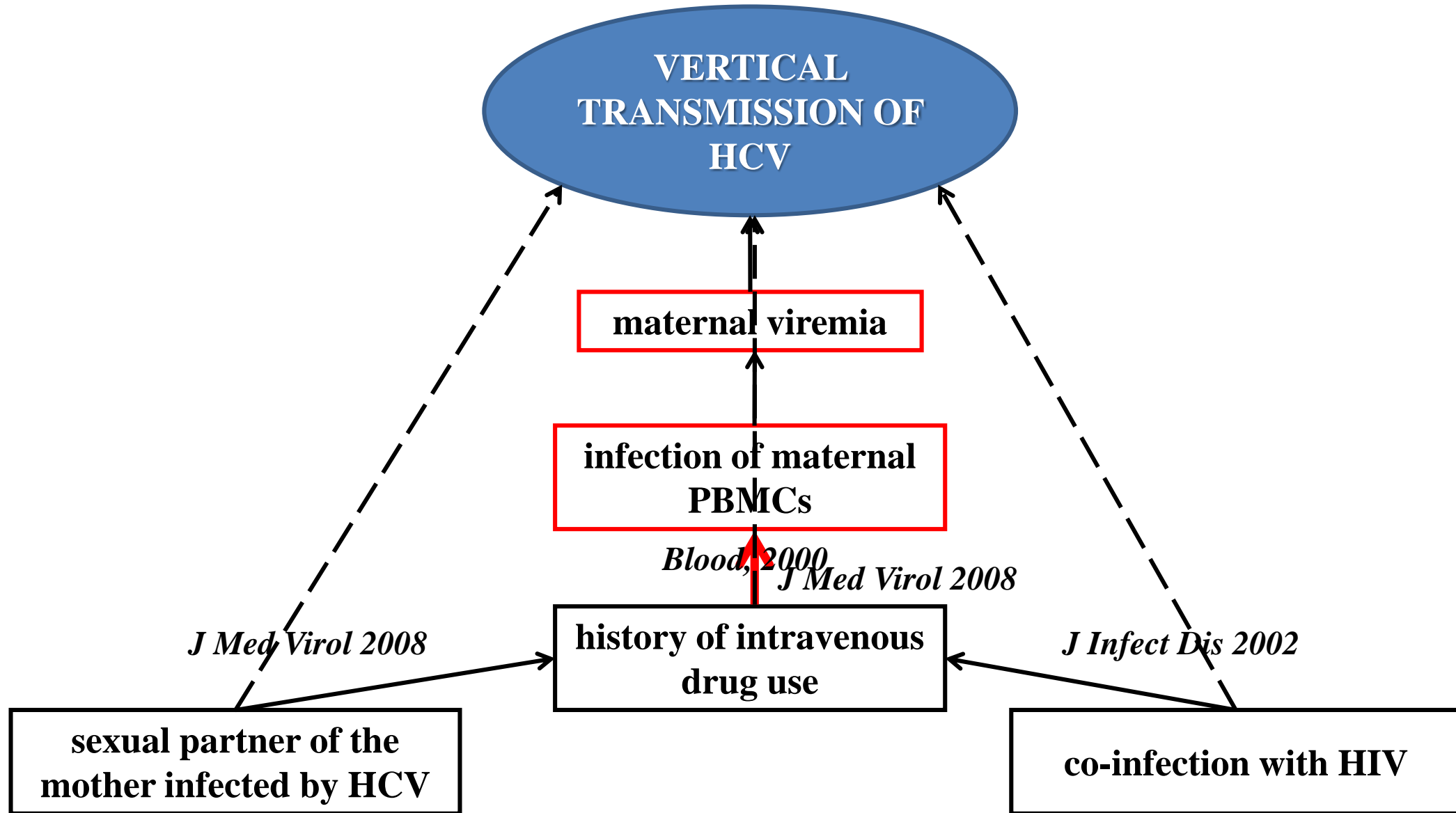


Gervais et al. J Hepatol 2000

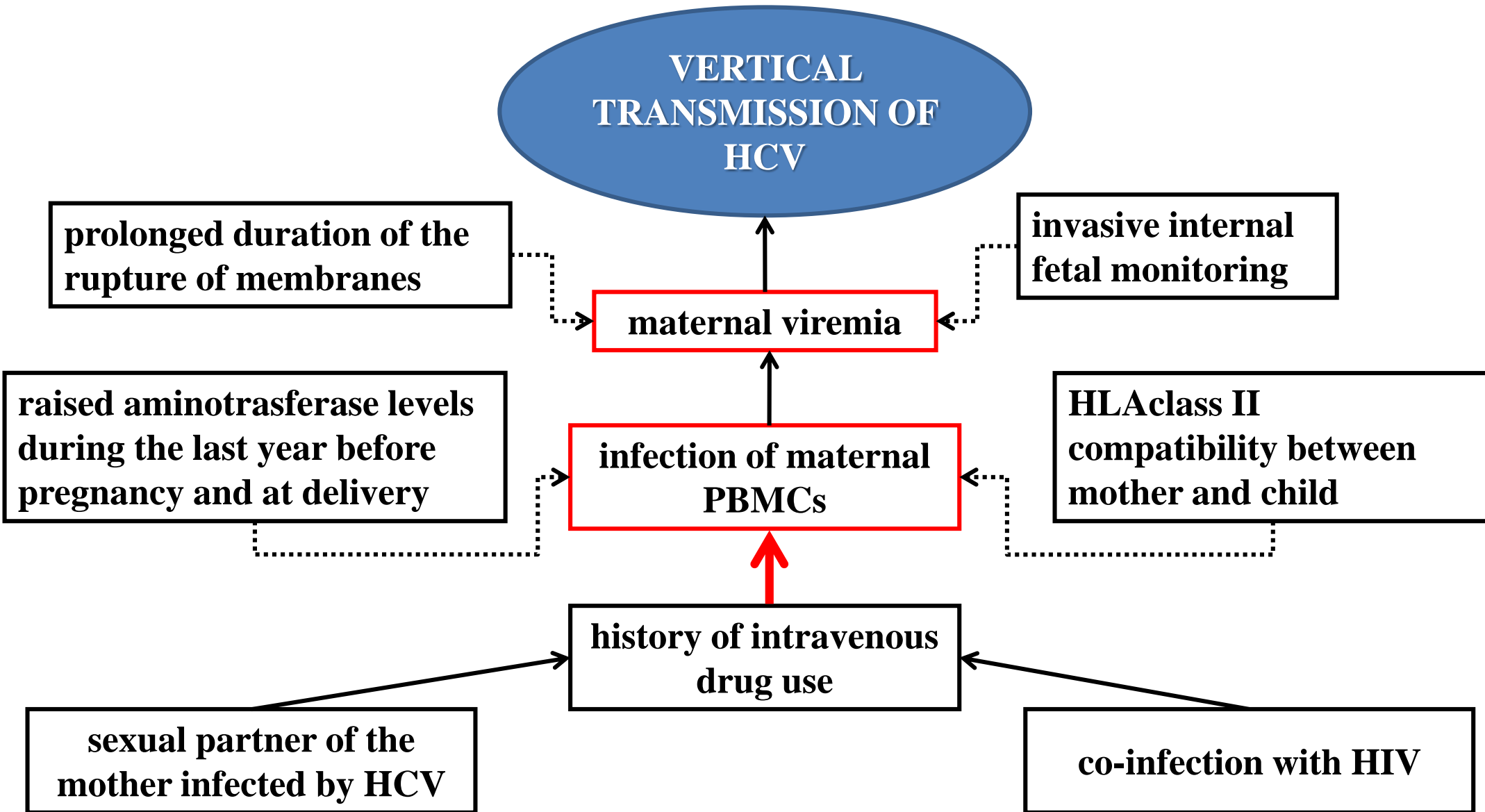
Results of Epidemiological Studies



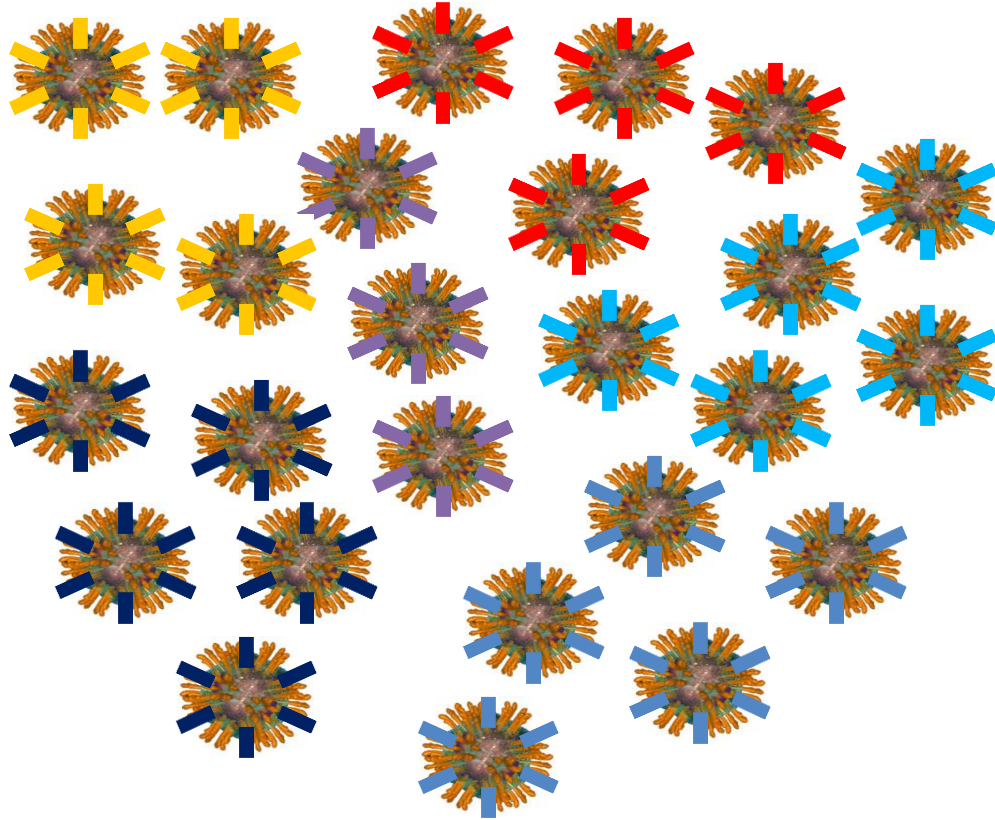
Results of Multivariate Analyses and Possible Logical Interpretation



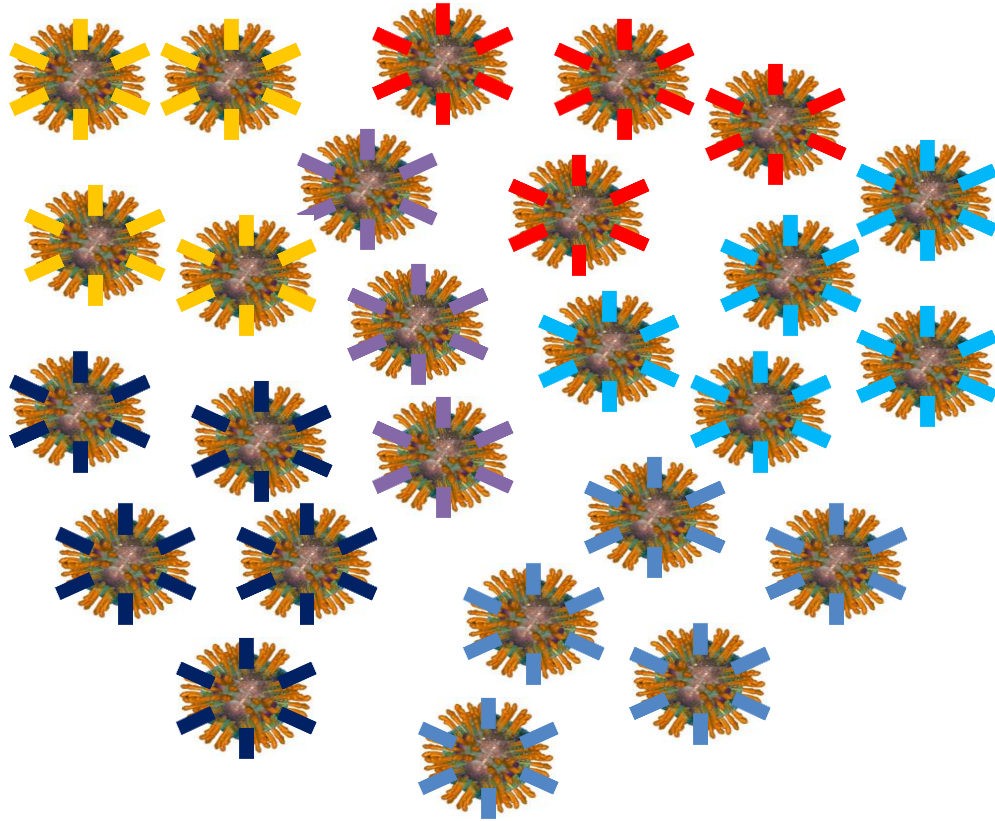
Results of Multivariate Analyses and Possible Logical Interpretation



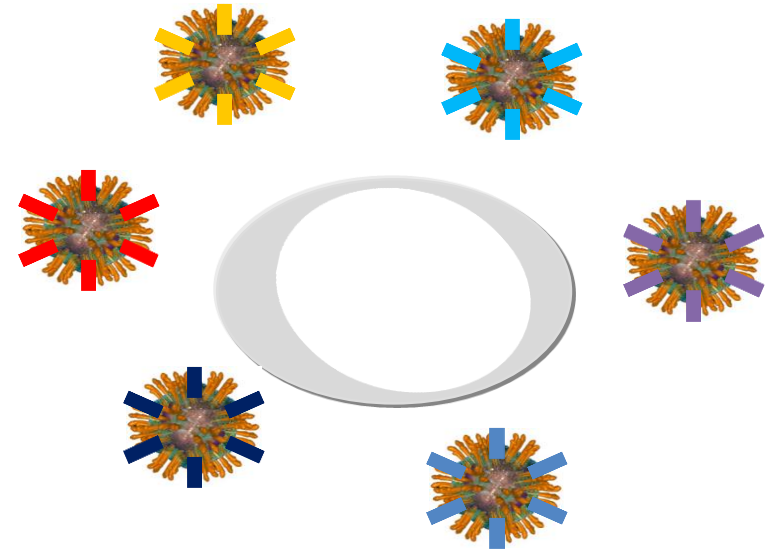
HCV MATERNAL QUASISPECIES



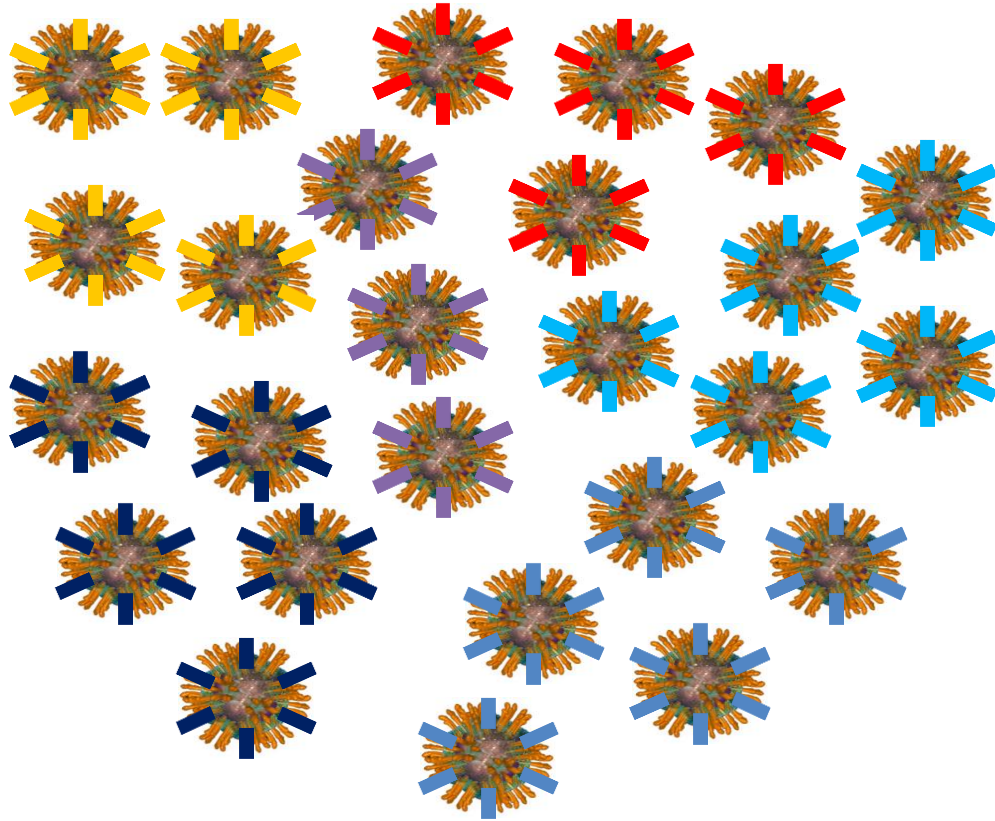
HCV MATERNAL QUASISPECIES



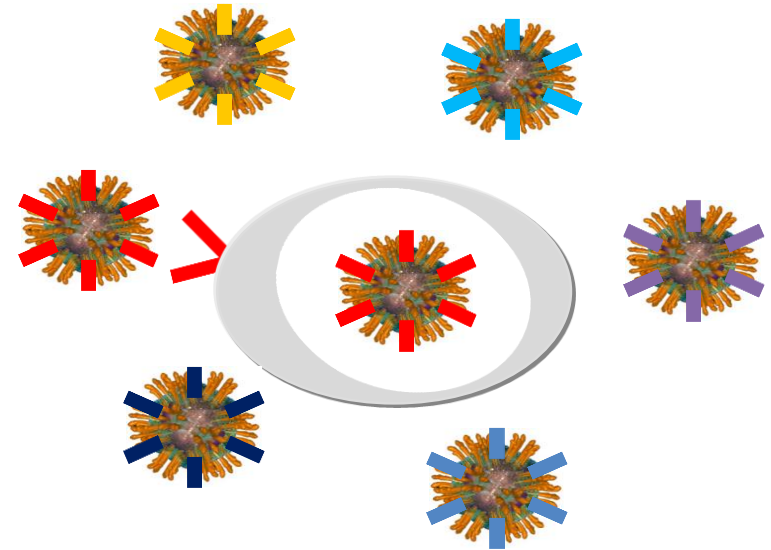
MATERNAL PBMC



HCV MATERNAL QUASISPECIES

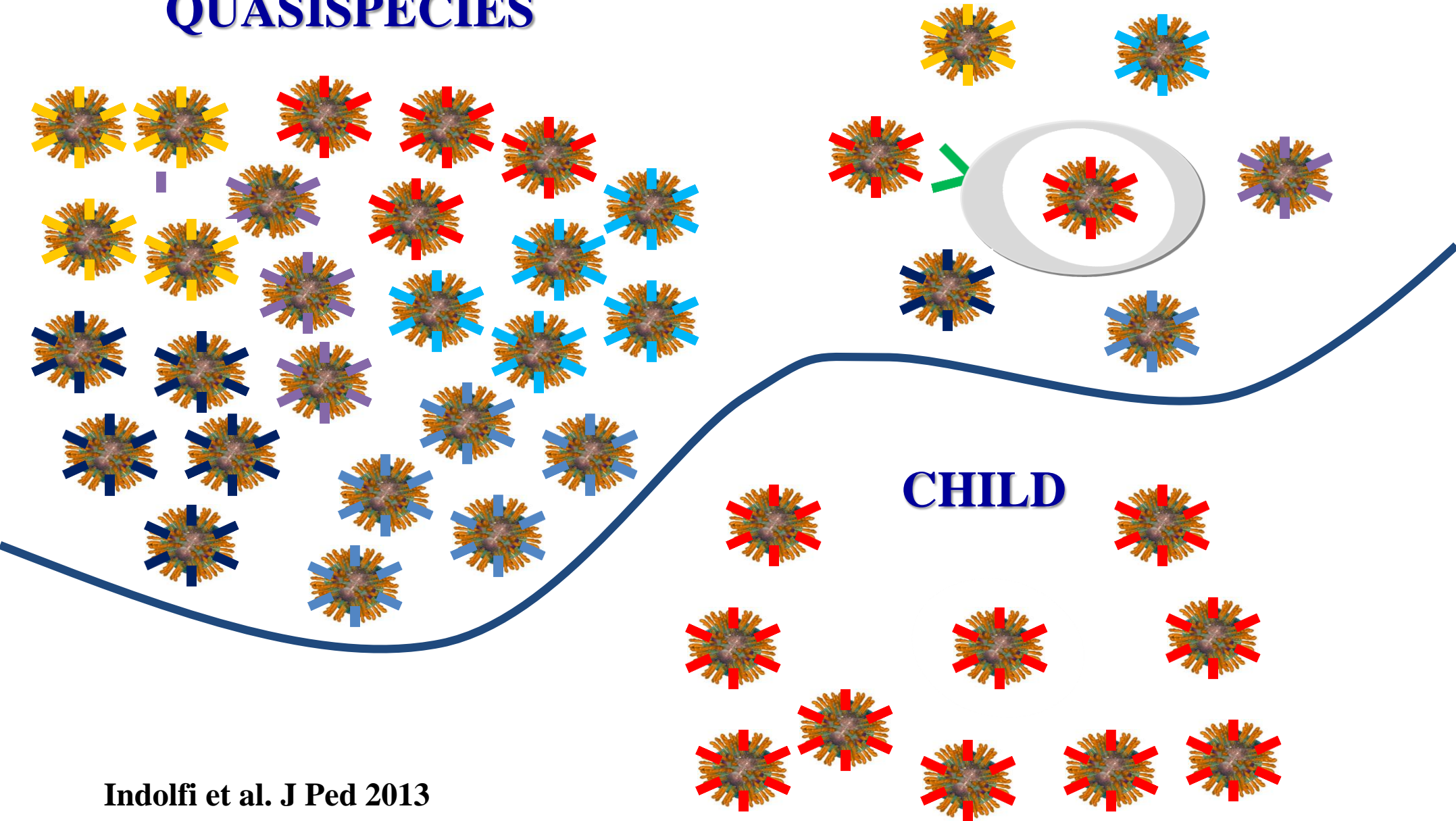


MATERNAL PBMC



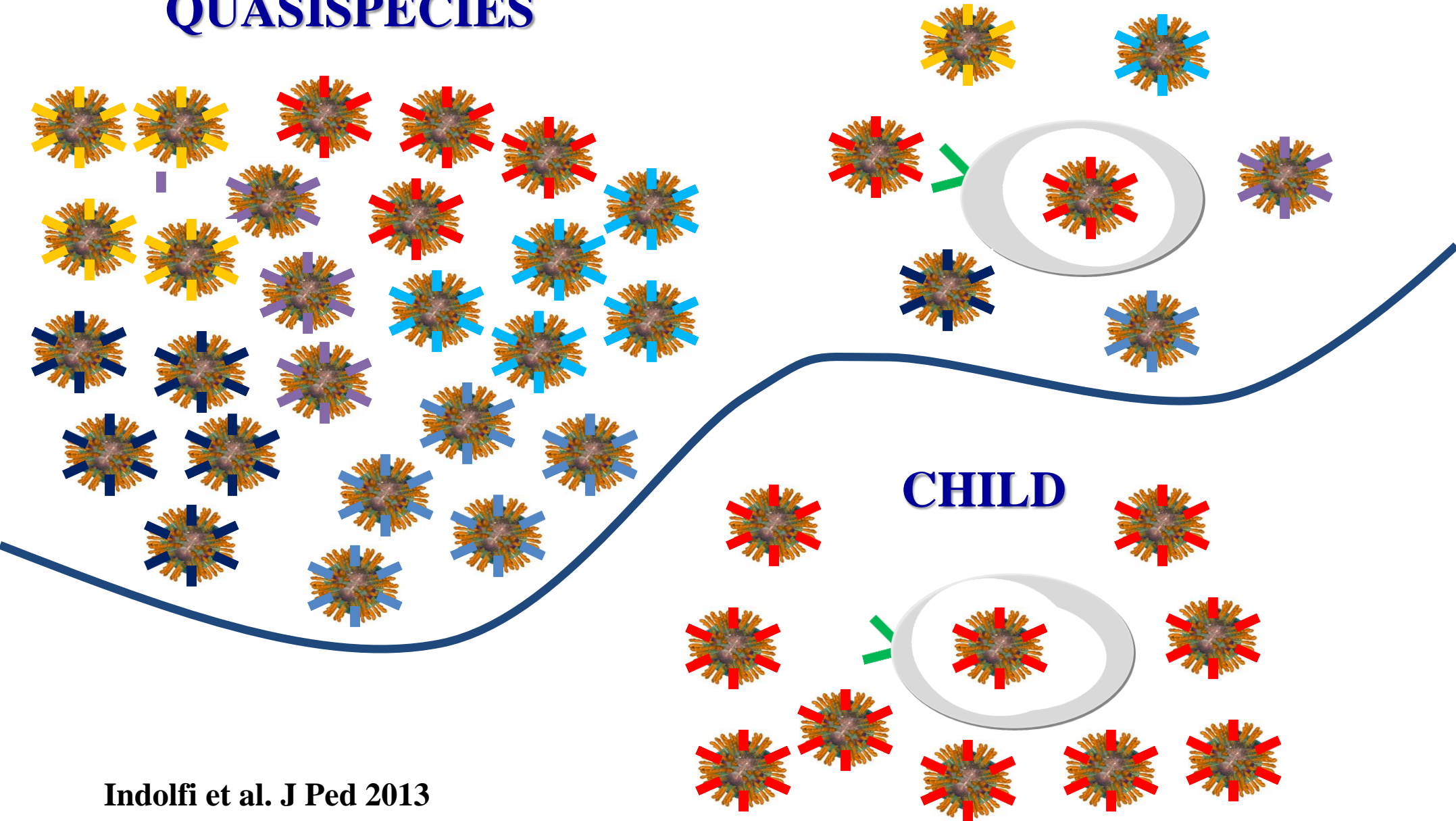
HCV MATERNAL QUASISPECIES

MATERNAL PBMC



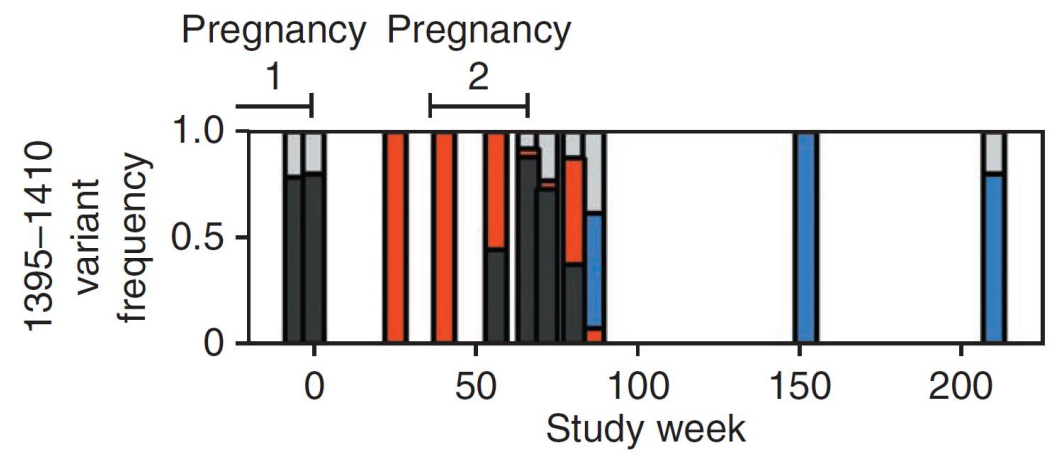
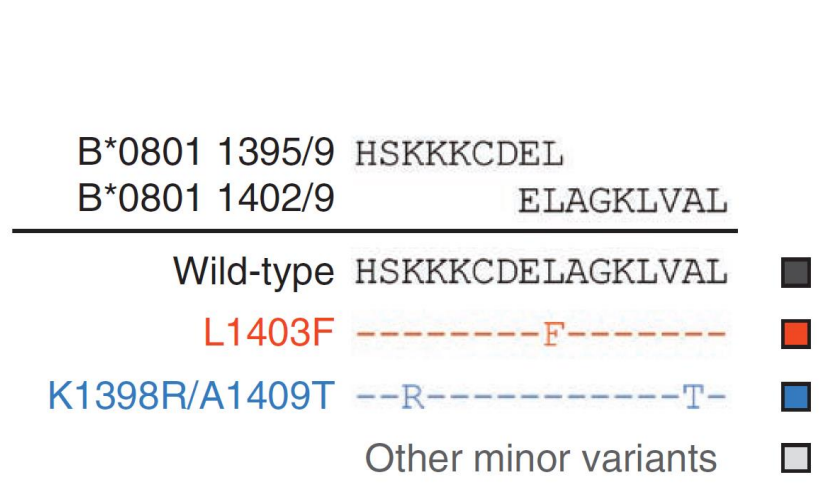
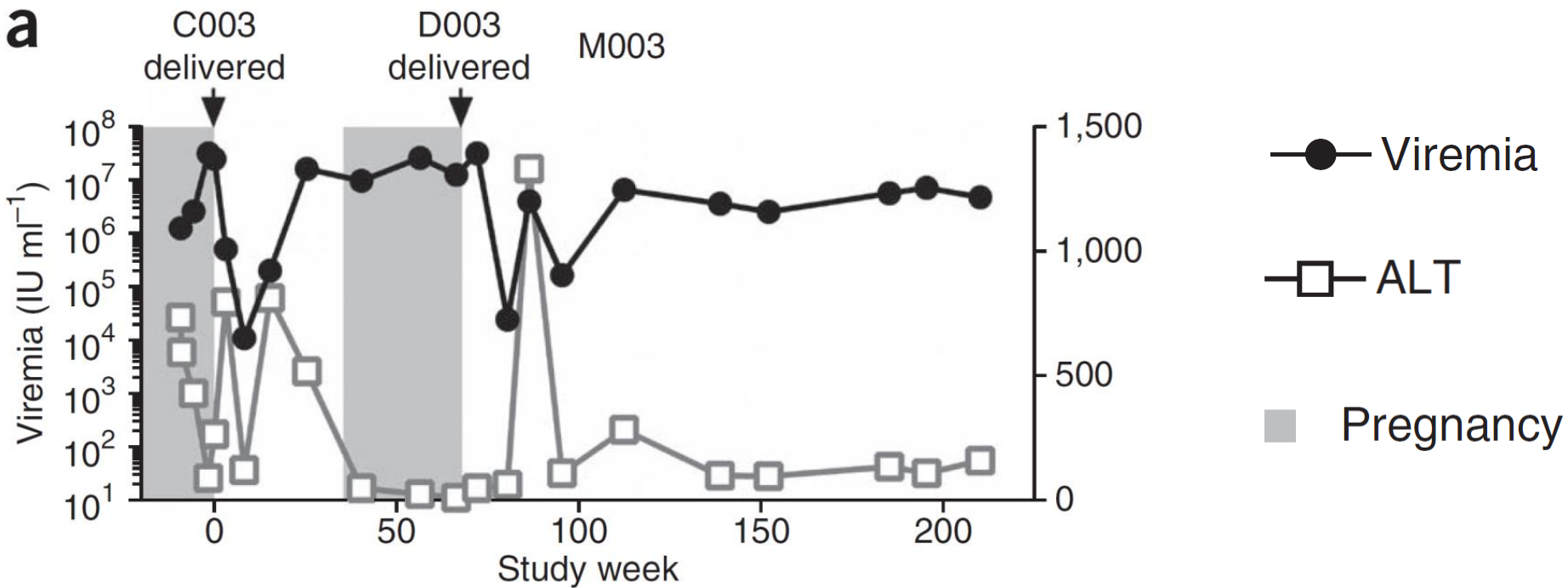
HCV MATERNAL QUASISPECIES

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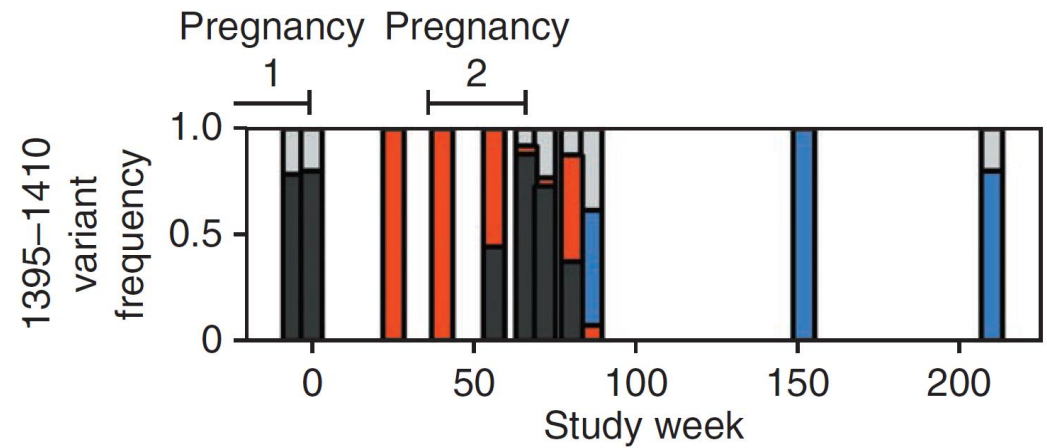


Loss of immune escape mutations during persistent HCV infection in pregnancy enhances replication of vertically transmitted viruses

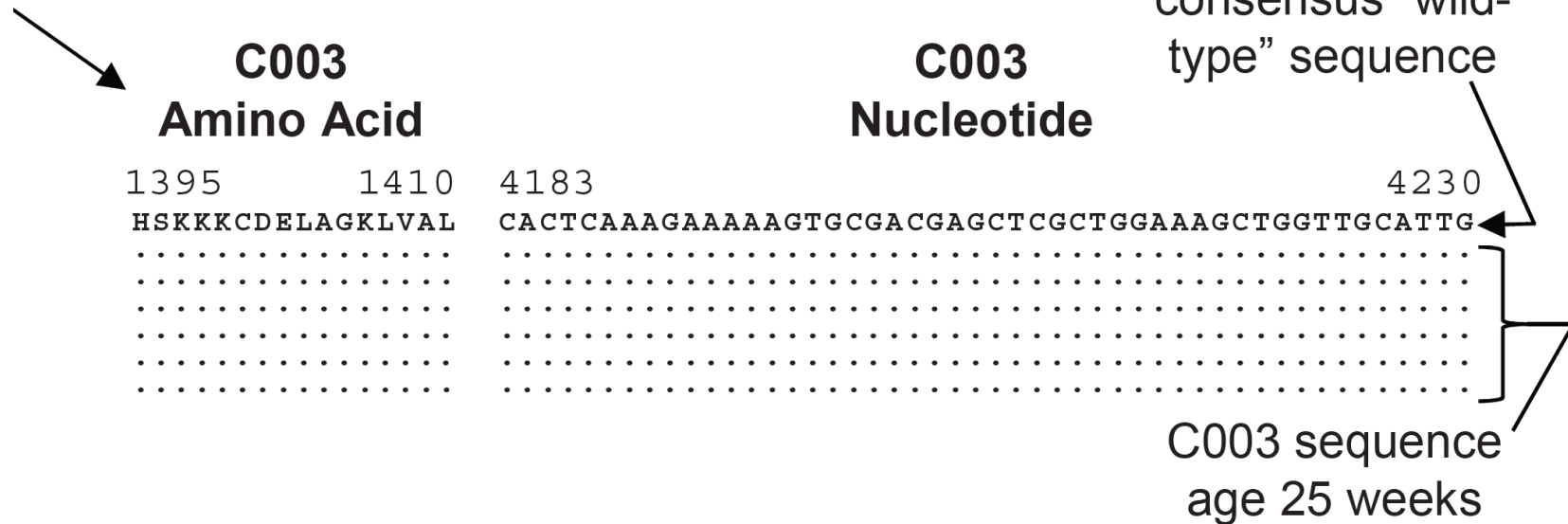
Jonathan R Honegger^{1,2}, Seungtaek Kim^{3–5}, Aryn A Price⁶, Jennifer A Kohout¹, Kevin L McKnight³,
Mona R Prasad⁷, Stanley M Lemon^{3,8,9}, Arash Grakoui^{6,10} & Christopher M Walker^{1,2}

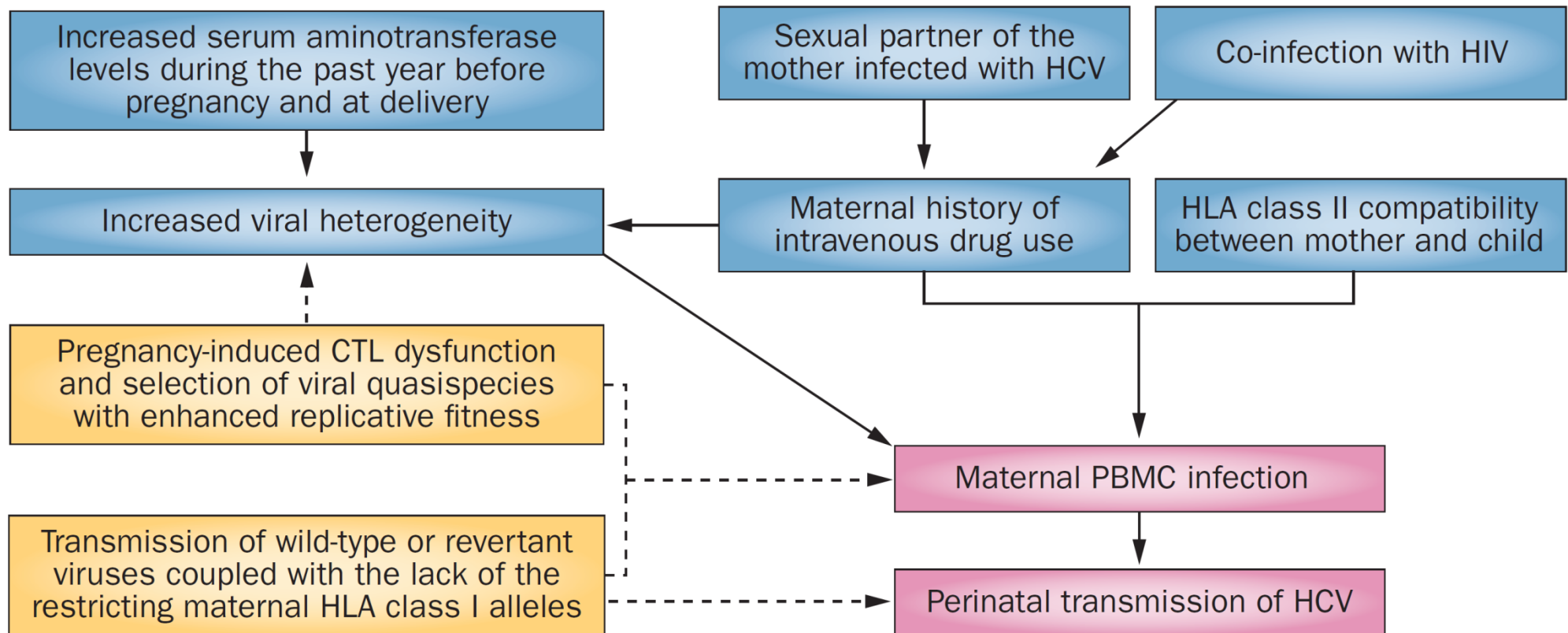
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B*0801 1395/9	HSKKKCDEL	
B*0801 1402/9	ELAGKLVAL	
<hr/>		
Wild-type	HSKKKCDELAGKLVAL	■
L1403F	-----F-----	■
K1398R/A1409T	--R-----T--	■
	Other minor variants	■



C003 delivery at study week 0





Vertical Transmission of Hepatitis C Virus

Conclusion

- ❖ maternal HCV viraemia is the limiting condition for vertical transmission
- ❖ the use of DAAs **during** or **at the end of pregnancy** could significantly impact **intrauterine** and **perinatal** transmission of the virus, respectively
- ❖ the ultimate mechanism of vertical transmission is still unknown

Acknowledgments

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- Elisa Bartolini
- Daniele Serranti
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- Massimo Resti

PENTA

- Claire Thorne
- Carlo Giaquinto





Vertical Transmission of Hepatitis C Virus

PBMC Infection

- ❖ HCV RNA in maternal **PBMC** is highly associated with transmission of HCV to the newborn
- ❖ the presence of **negative-strand HCV RNA** (a marker of HCV replication) in maternal PBMC is associated with perinatal transmission

HCV strand	Infants infected (n = 13), no.	Infants not infected (n = 53), no.	<i>P</i>
Positive	13	13	< .000001
Negative	5	0	.0001