

# *Understanding the evolution of HIV using next generation sequencing technologies*

**Silvana Gaudieri**

**School of Human Sciences, UWA**

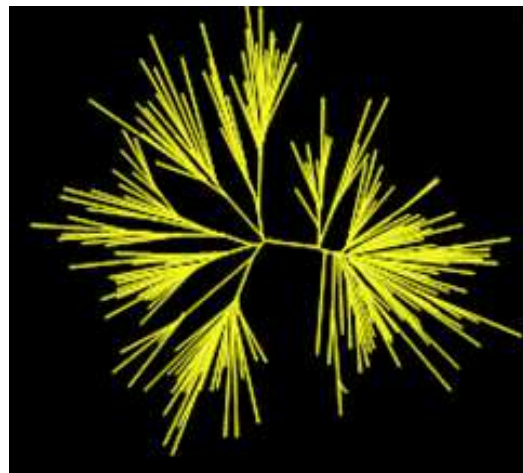
**Division of Infectious Diseases, Department of  
Medicine, Vanderbilt University Medical Center**

---

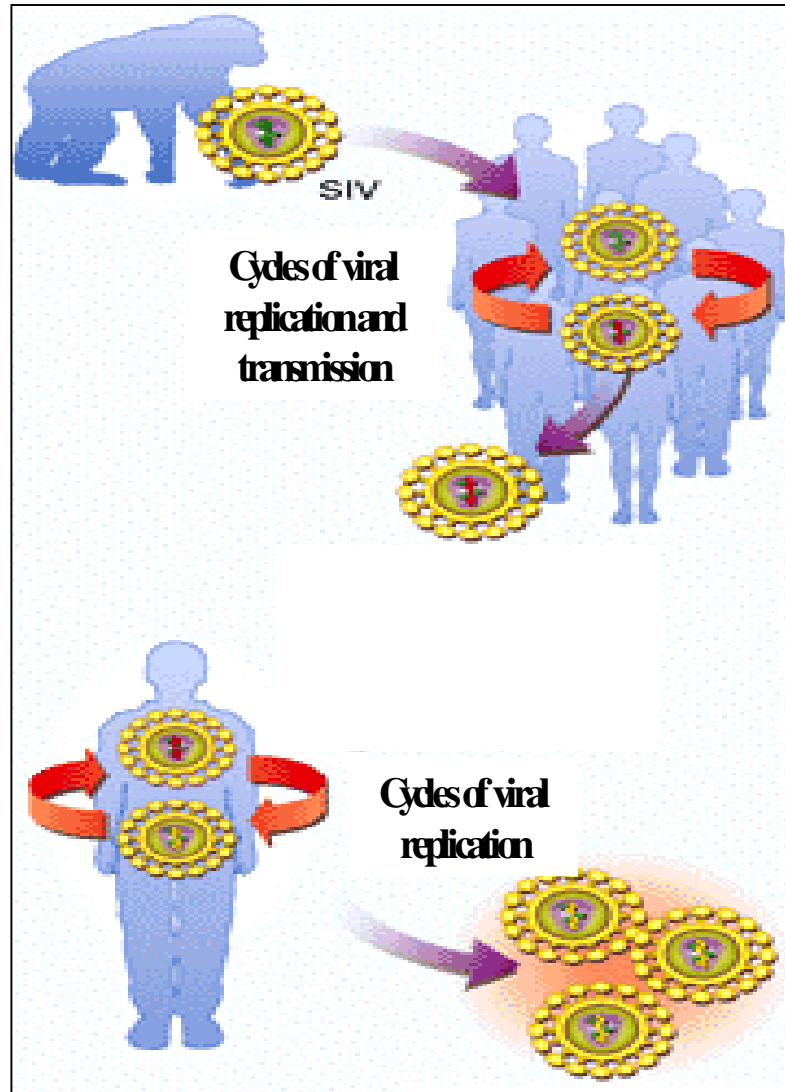
**Institute for Immunology and Infectious Diseases,  
Murdoch University**

# HIV diversity and continuing evolution is an impediment to vaccine design

## HIV diversity



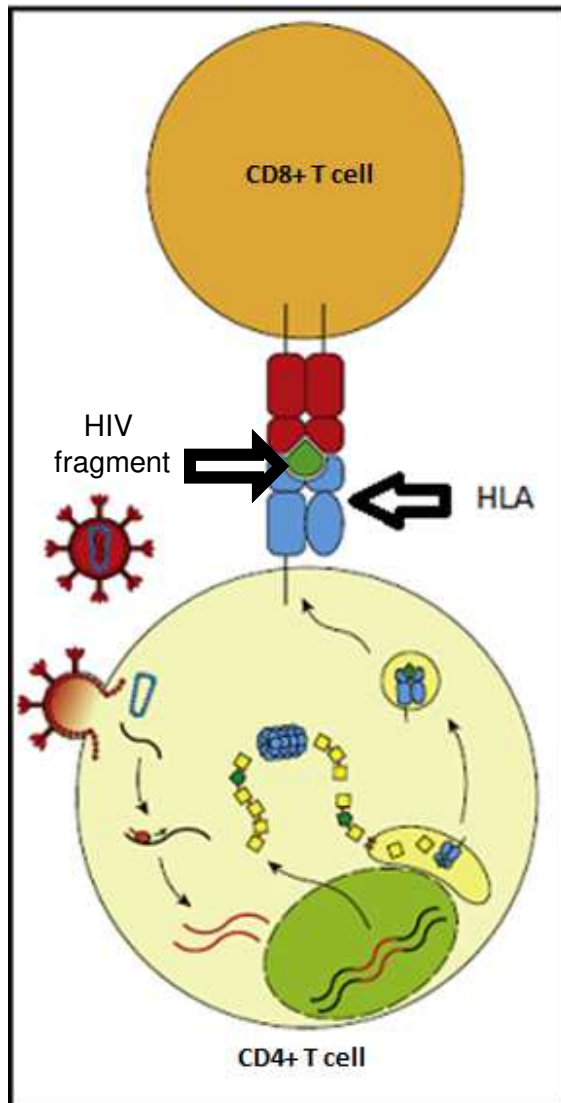
1996 global H3N2 viruses



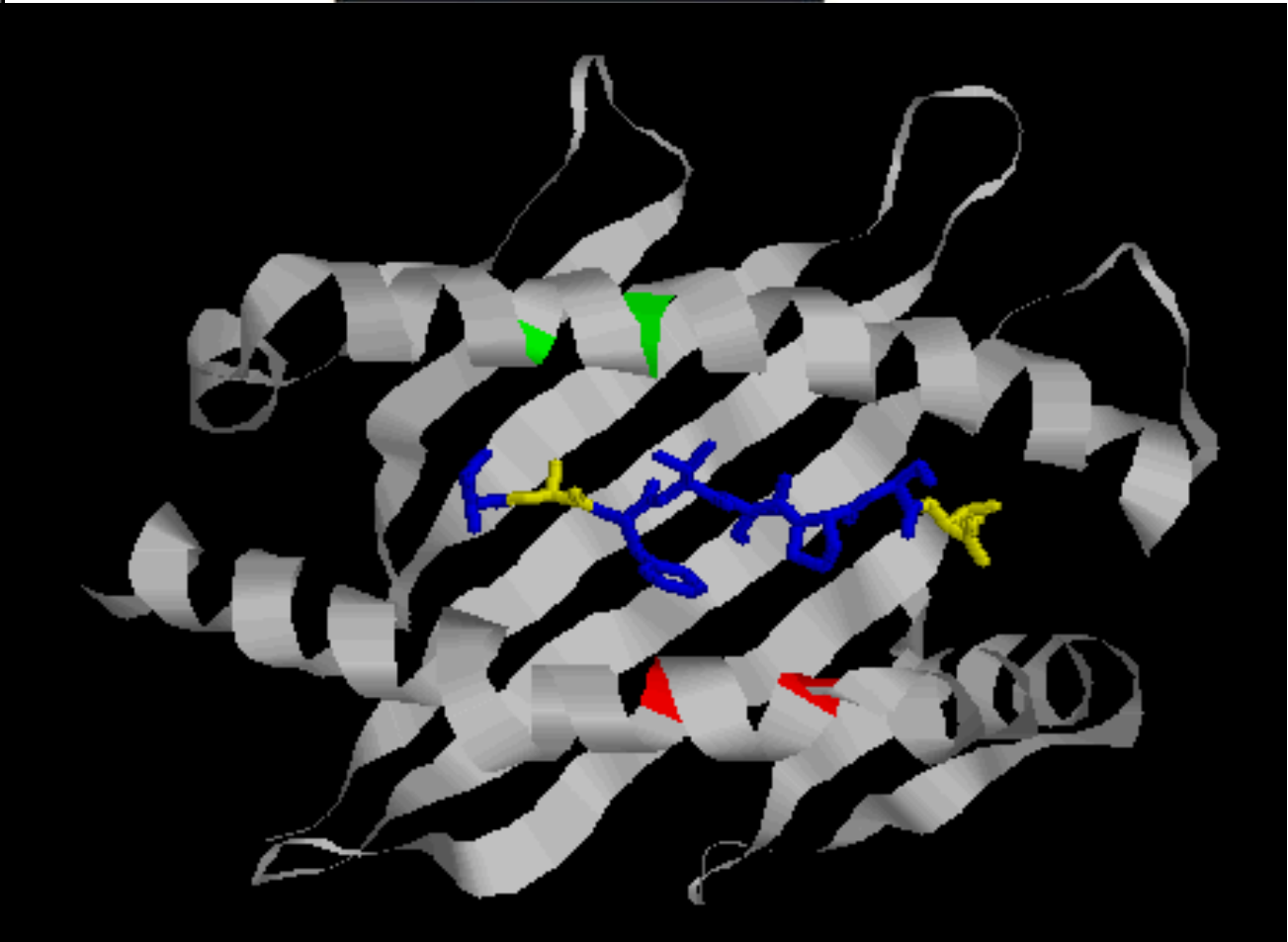
What are the selection pressures driving evolution of HIV?

Host's immune response ("immune drug") known correlate of outcome

# Mutations in HIV genome allow immune escape (adaptations)

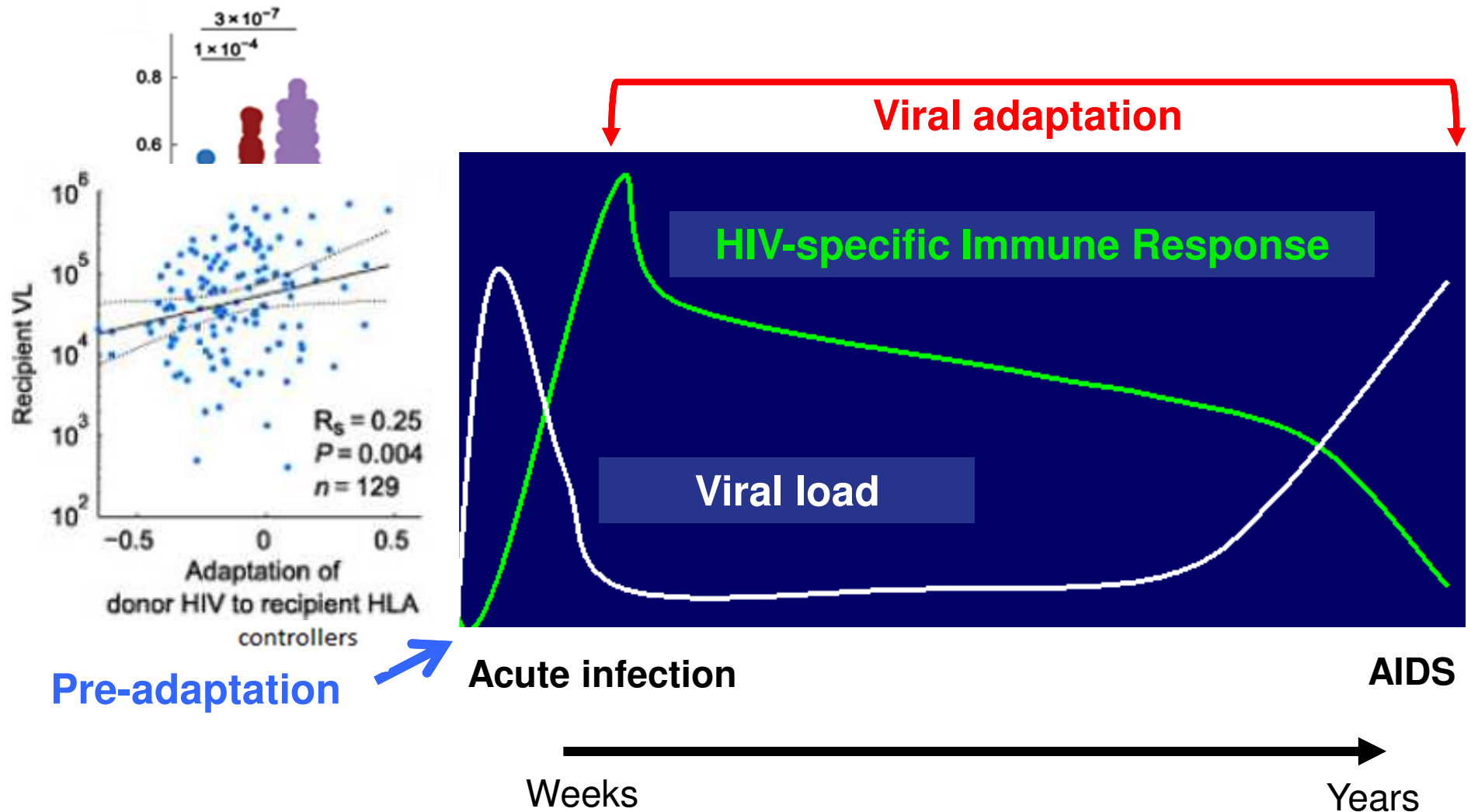


Adaptive immunity



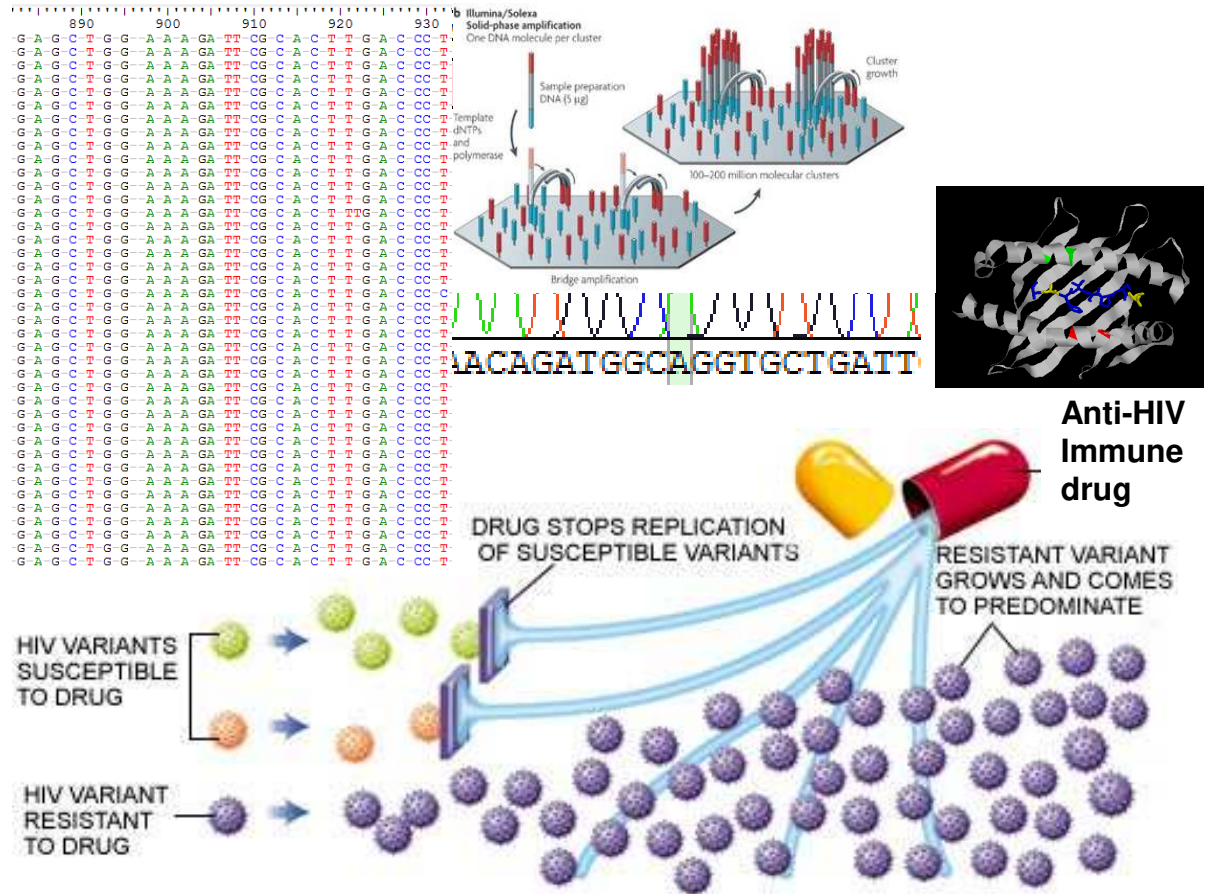
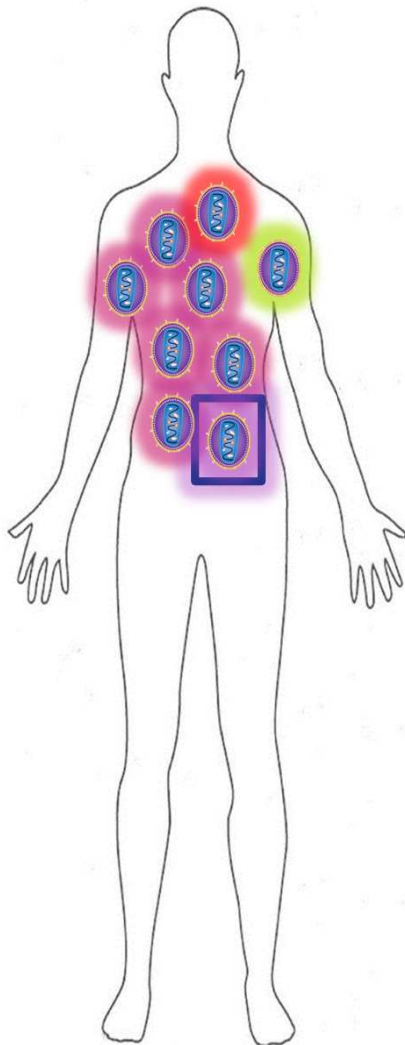
(Image from Carlson et al., 2015)

# Adaptation an important factor influencing HIV evolution and outcome



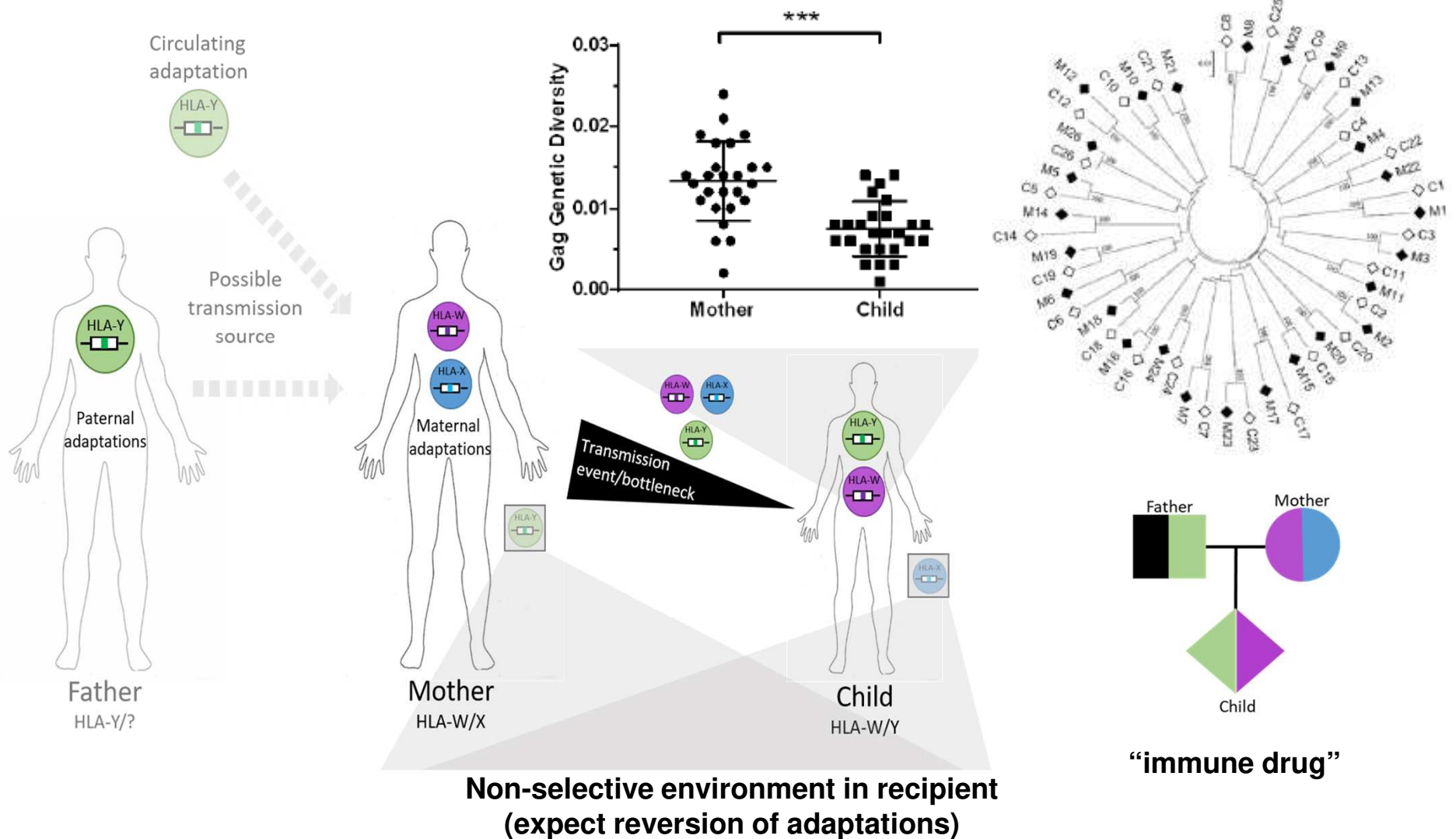
# How can we understand dynamics of these HIV mutations (adaptations) and how they contribute to HIV evolution?

*Next generation sequencing provides high-resolution snapshot of HIV quasispecies*

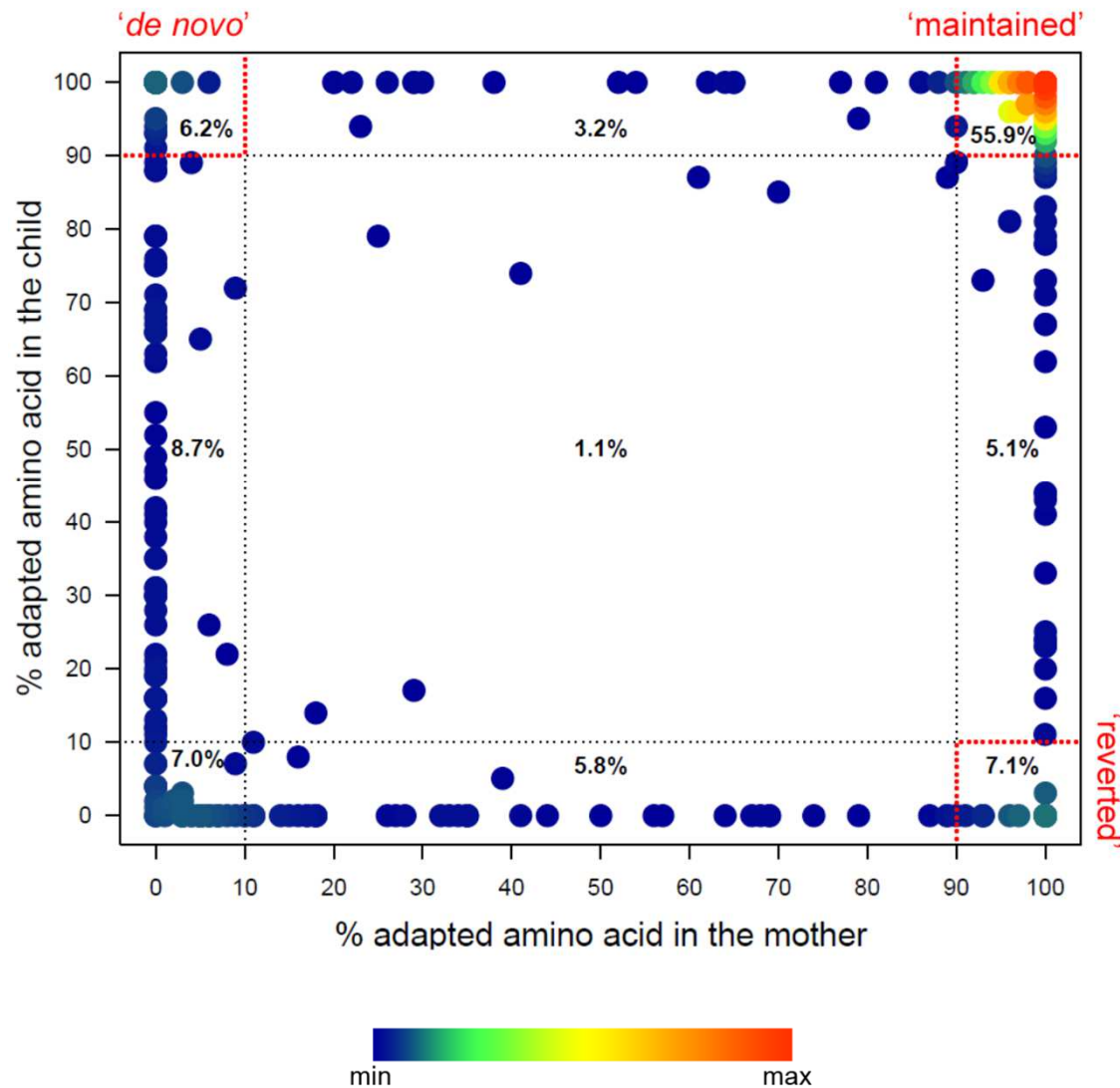


**Adaptation can become dominant strain but if drug is removed could go back to wildtype (reversion)**

# Understanding dynamics of adaptations using samples from *26 Mother-child pairs* – *known source and child at least 50% haplo-identical with mother*



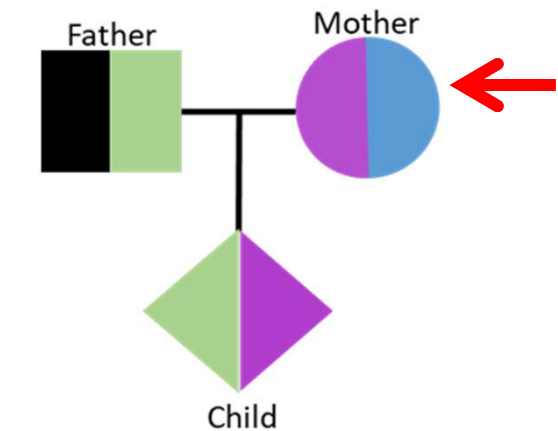
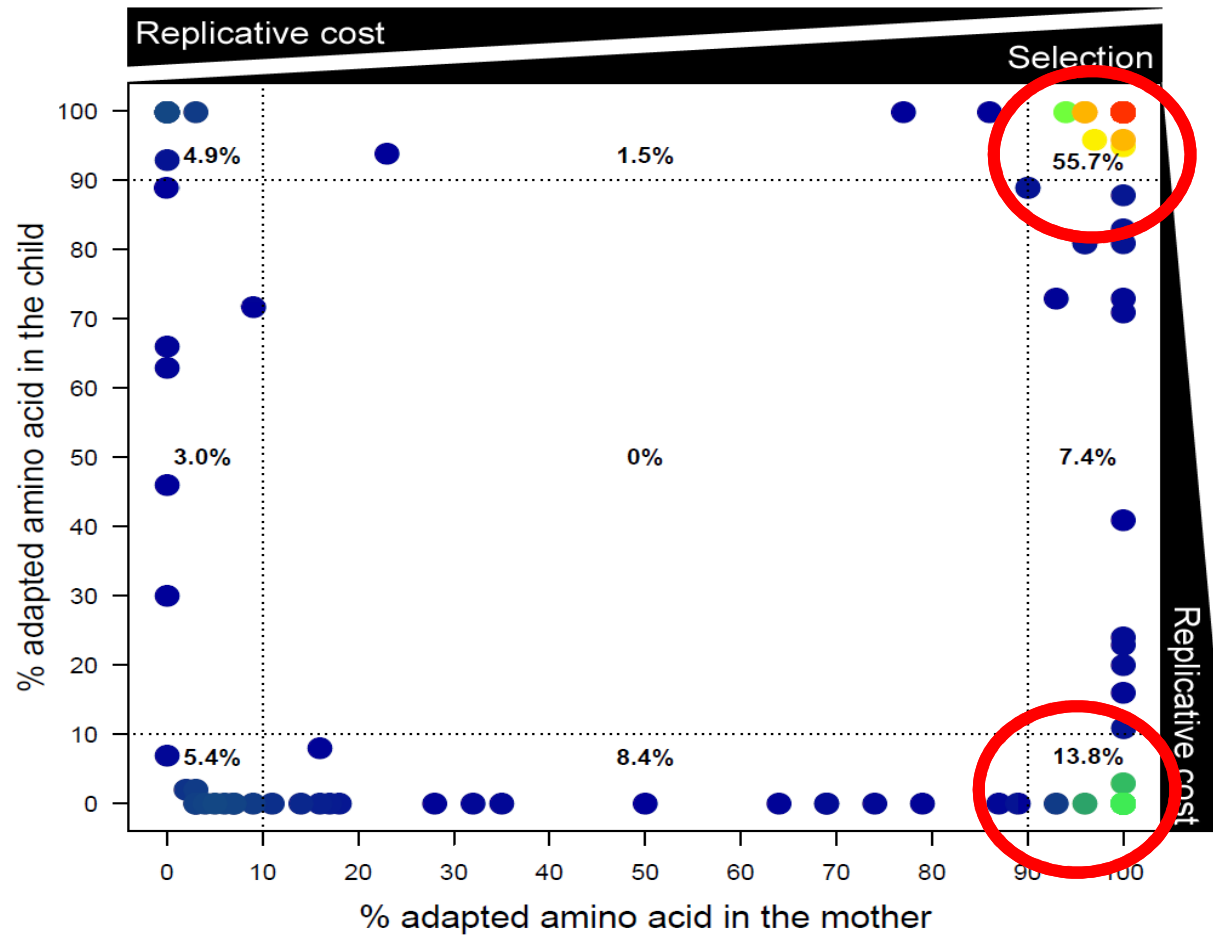
# Maintenance or reversion of adaptations reflects immune environment of new host



- More maintenance of adaptations in the child for adaptations in a selective environment
- More reversion of adaptations in the child when not in a selective environment
- More de novo adaptations in the child at sites under selection pressure in the child only

# Lack of reversion suggests low fitness cost and/or compensatory mutations

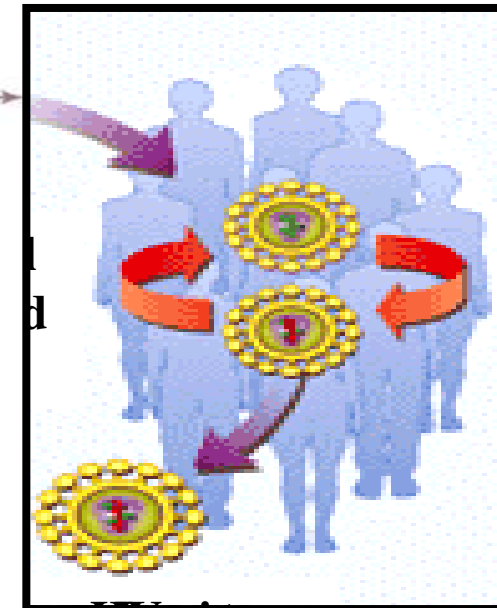
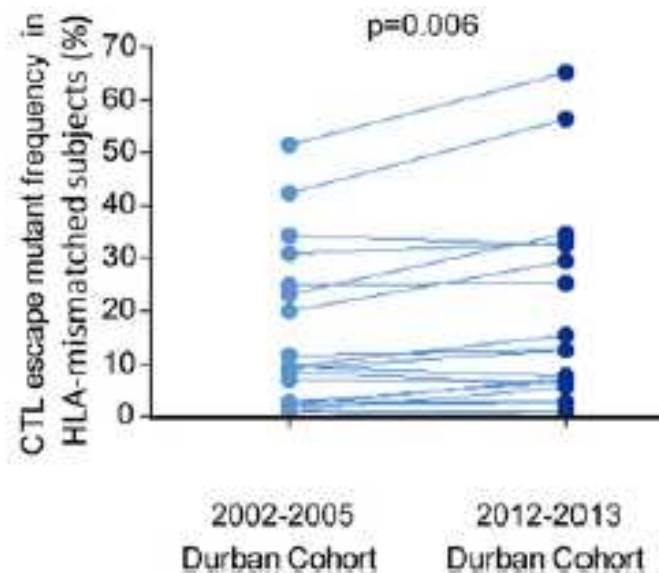
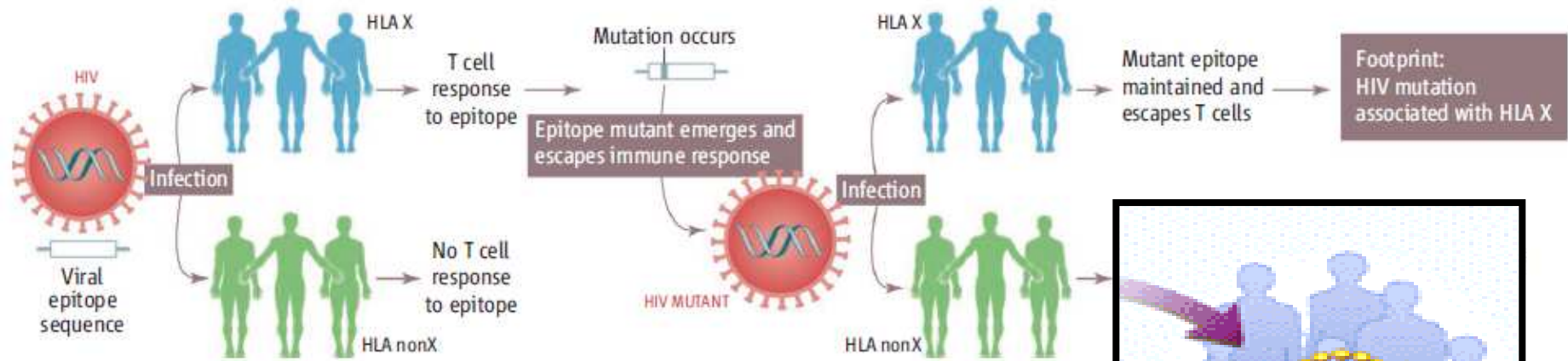
Mother only HLA allele (blue allele; no immune pressure in child – expect reversion in child)



Reversion



# Accumulation of adaptations in circulating viruses: implications for future vaccine designs



**Circulating virus becomes more adapted to host population**

# Acknowledgements



## ***IIID Murdoch, Western Australia***

Simon Mallal	Abha Chopra
<b>Jennifer Currenti*</b>	Mina John
Ian James	Shay Leary
Linda Choo	Bethy McKinnon
Eric Alves*	Pooja Deshpande
Michaela Lucas*	Ramesh Ram
Becker Law*	Yueran Li*

## ***VUMC, USA***

<b>Spyros Kalams</b>	Mark Pilkinton
Louise Barrett	Rama Gangula
Wyatt McDonnell	Cindy Hager
Rita Smith	<b>Joseph Conrad</b>

***GHESKIO Centre, Port-au-prince, Haiti***  
Francine Noel



\* UWA student/staff



VANDERBILT  
UNIVERSITY  
MEDICAL  
CENTER



**Patients and support staff**