The Effect of HIV-1 Superinfection on the Antibody Response

*Lessons for Vaccine Design*

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1. Correlates of protection

2. Immunodominance and immune modulation
Dual infection can be considered a natural equivalent of polyvalent/prime-boost vaccines

Caveat: HIV replication and immune dysfunction that would not be present in vaccine setting

How does the human immune system respond to multiple diverse HIV variants?

Immunodominance vs Additive vs Synergistic

Can this be exploited with vaccination?
Superinfection and cross-neutralizing antibodies

Change in breadth

“Superinfection” No superinfection

P = 0.011


Broadly neutralizing antibodies in a superinfected woman from RSA

Superinfection and the nAb response

- Did superinfection promote the broad, and extremely potent neutralizing antibody (nAb) response in CAP256?

- Mechanism
  - Indirectly via higher viral loads
  - Increase the number of antibody specificities
  - Promote/boost nAb responses to a conserved epitope
  - Modulate the maturation of the nAb response
  - Primary infection modulates subsequent immune responses
CAP256: ontogeny of breadth

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Detection of additional cases of superinfection in the CAPRISA 002 cohort

- CAP237
- CAP256
- CAP281

weeks post infection

5 10 15 20 25 30 35 40 45 50
1 year
Superinfection is not sufficient to broaden the neutralizing antibody response

Heterologous

Autologous

Breadth (% panel neutralized)

Singly Infected  Dual infection

Titer (ID_{50})

weeks post infection/superinfection

CAPRISA participants  CAP281  CAP256  CAP237

L Morris, P Moore
Boosting of non-neutralizing antibody responses following superinfection

CAP237

CAP281

CAP256

J. Bhiman
Onset of nAbs to superinfection was not associated with a boost in primary nAb titers.
Coinfected individual: CAP267

Virus 1  Virus 2

6 weeks
10 weeks
20 weeks
52 weeks
Preferential neutralization of variants in CAP267
Summary: Humoral response to dual infection

• Superinfection boosted titers of non-neutralizing and neutralizing antibody responses

• However, did not seem to alter the specificity/epitopes targeted

• The neutralizing antibody response to multiple Envelopes may be subject to immunodominance/interference
  – Has implications for the use of polyvalent HIV vaccines
Acknowledgements

**NICD**
Lynn Morris
Penny Moore
Molati Nonyane
Jinal Bhiman
Maphuti Madiga

**UCT**
Carolyn Williamson
Zenda Woodman
Roman Ntale

**UKZN**
Salim Abdool Karim
Koleka Mlisana
Nigel Garrett
CAPRISA 002 Study Team

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**CAPRISA**
**HIVRAD**
**National Institute of Allergy and Infectious Diseases**