HIV Controllers:
A model for T cell vaccination?

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HIV elite controllers

• Most HIV-infected individuals have continuous viral replication and if left untreated, eventually progress to AIDS

• Durable control of HIV replication does occur in about 1% of infected people
  • HIV antibody positive with no measurable virus in plasma by standard clinical assays

• Some have remained untreated for more than 25 years
  • Clear evidence that durable containment of HIV in the absence of therapy is possible
Definition of HIV Controllers

- Plasma HIV RNA levels below 50 copies in the absence of antiretroviral therapy
- Maintain undetectable viral load for 10 years
- Maintain stable CD4 counts for the duration of follow up
- No AIDS defining illness for the duration of follow up
Distinction between elite controllers and Long-term non-progressors

- EC defined by VL < 50 cop/ml
- LTNP defined by ability to maintain normal CD4 counts for long period
- 5%-15% of infected persons are LTNP
- Less than 0.15% of infected individuals are elite controllers
HIV Controllers: A human model for successful T cell vaccination?
What are the mechanisms underlying elite control of HIV infection?
Factors associated with elite control of HIV

Factors NOT associated

- Route of HIV acquisition
- Gender
- Virus subtype/Clade?
- Ethnicity?
- Intrinsic Host factors?
- Neutralizing antibodies

Factors Associated

- Immune mediated factors
  - Durable anti HIV cellular immune response
- Host genetic factors
  - Protective class I HLA
- Viral factors,
  - Fitness, Nef deleted viruses
Replicative competent viruses can be isolated from EC

![Graph showing supernatant p24 (fold increase) against time (days).](image-url)

Alireza Rabi et al, JV 2010
The impact of HLA on HIV disease progression

Protective

Non protective

B*57
B*8101
B*5801
A*7401

p < 0.0001
p = 0.0006
p < 0.0001
p = 0.0014
p = 0.0006

Nature, 2004
Genome-wide results in Whites

>60 associated SNPs in MHC with genome-wide significance (p<5x10^{-8})

HLA B*5701

Pererya et al, Science 2011
Viral Inhibition in HIV negative, chronic viremic and elite controllers

B Juelg et al, unpublished

![Graph showing viral inhibition in HIV negative, chronic viremic, and elite controllers.](image)
Differential impact of increasing variables in the model

Zaza Ndhlovu, Blood 2012
What have we learned

- No single factor identified so far confers complete protection
- No one factor is strictly required.
- Large well-designed studies are needed to define which combinations of host factors are most likely to result in such remarkable virus control.
- Efforts are now underway to develop the large cohorts necessary to initiate such work here in Durban.
The role of ethnicity clade and Geographical location in natural control of HIV

- Establish a prospective cohort of elite controllers in Durban South Africa
- We have already secured funding for the project
- We already have IRB approval
- Preliminary evidence of EC being referred to by several clinicians
- We need more physicians to partner with us to help identify and recruit potential elite controllers
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