

HIV Controllers: A model for T cell vaccination?

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HIV elite controllers

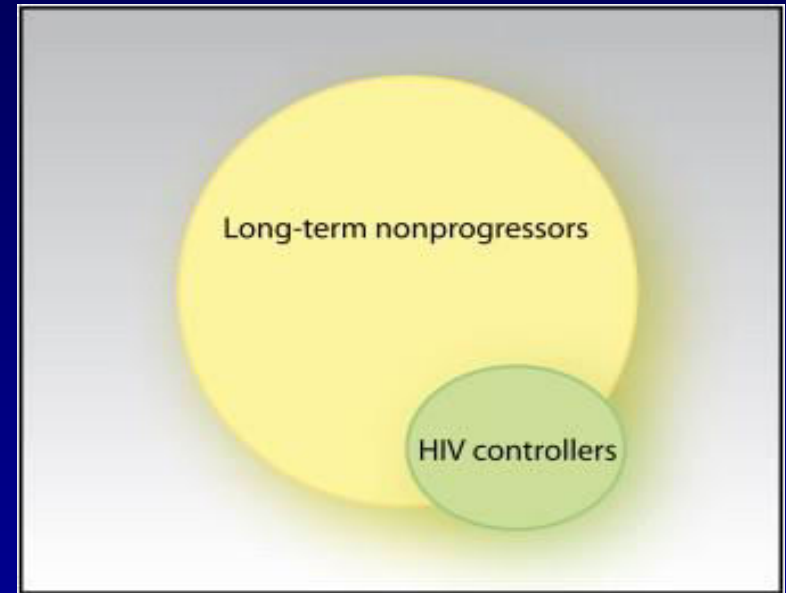
- Most HIV-infected individuals have continuous viral replication and if left untreated, eventually progress to AIDS
- Durable control of HIV replication does occur in about 1% of infected people
 - HIV antibody positive with no measurable virus in plasma by standard clinical assays
- Some have remained untreated for more than 25 years
 - Clear evidence that durable containment of HIV in the absence of therapy is possible

Definition of HIV Controllers

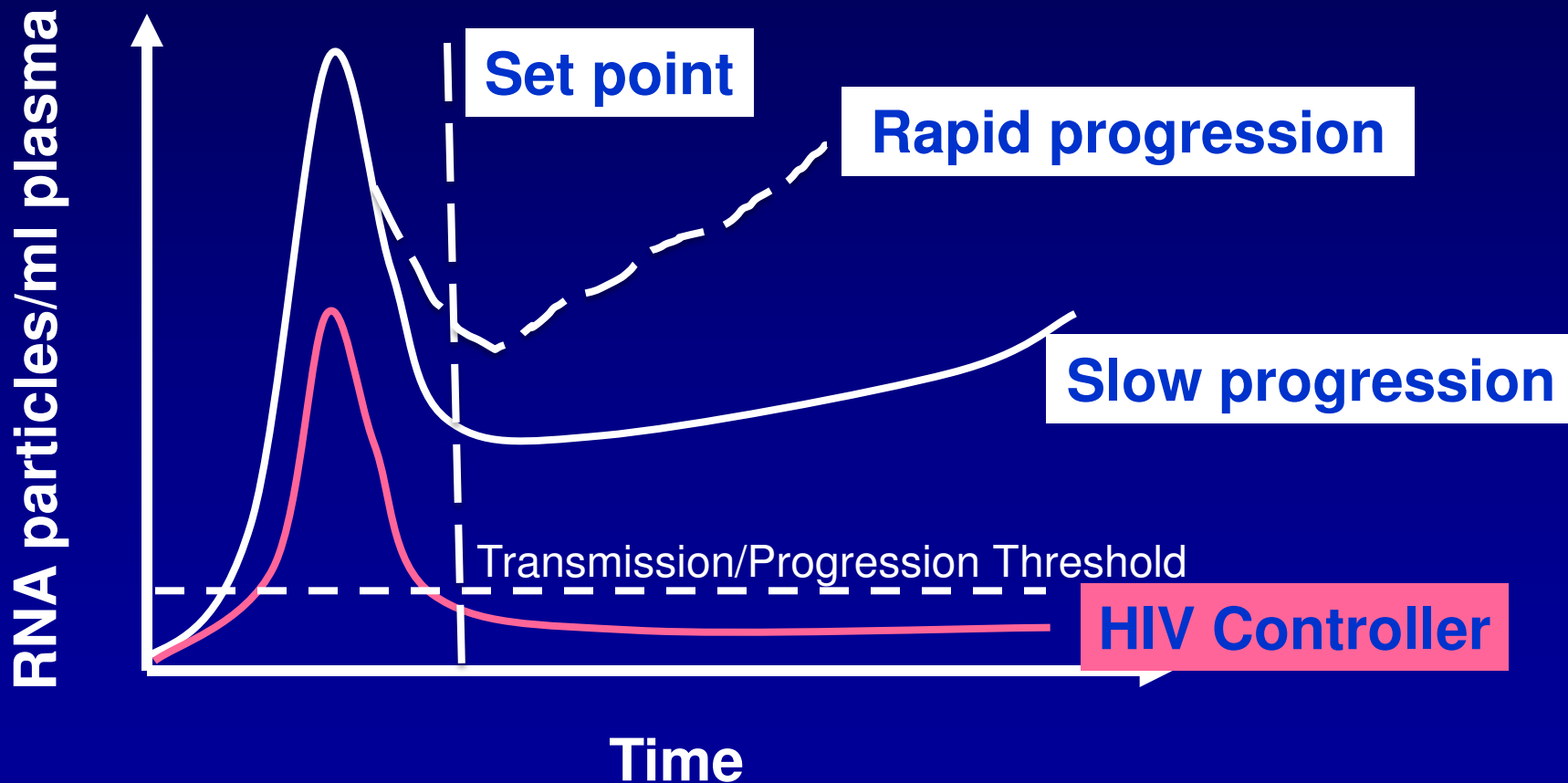
- Plasma HIV RNA levels below 50 copies in the absence of antiretroviral therapy
- Maintain undetectable viral load for 10 years
- Maintain stable CD4 counts for the duration of follow up
- No AIDS defining illness for the duration of follow up

Distinction between elite controllers and Long-term non-progressors

- EC defined by $VL < 50 \text{ cop/ml}$
- 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

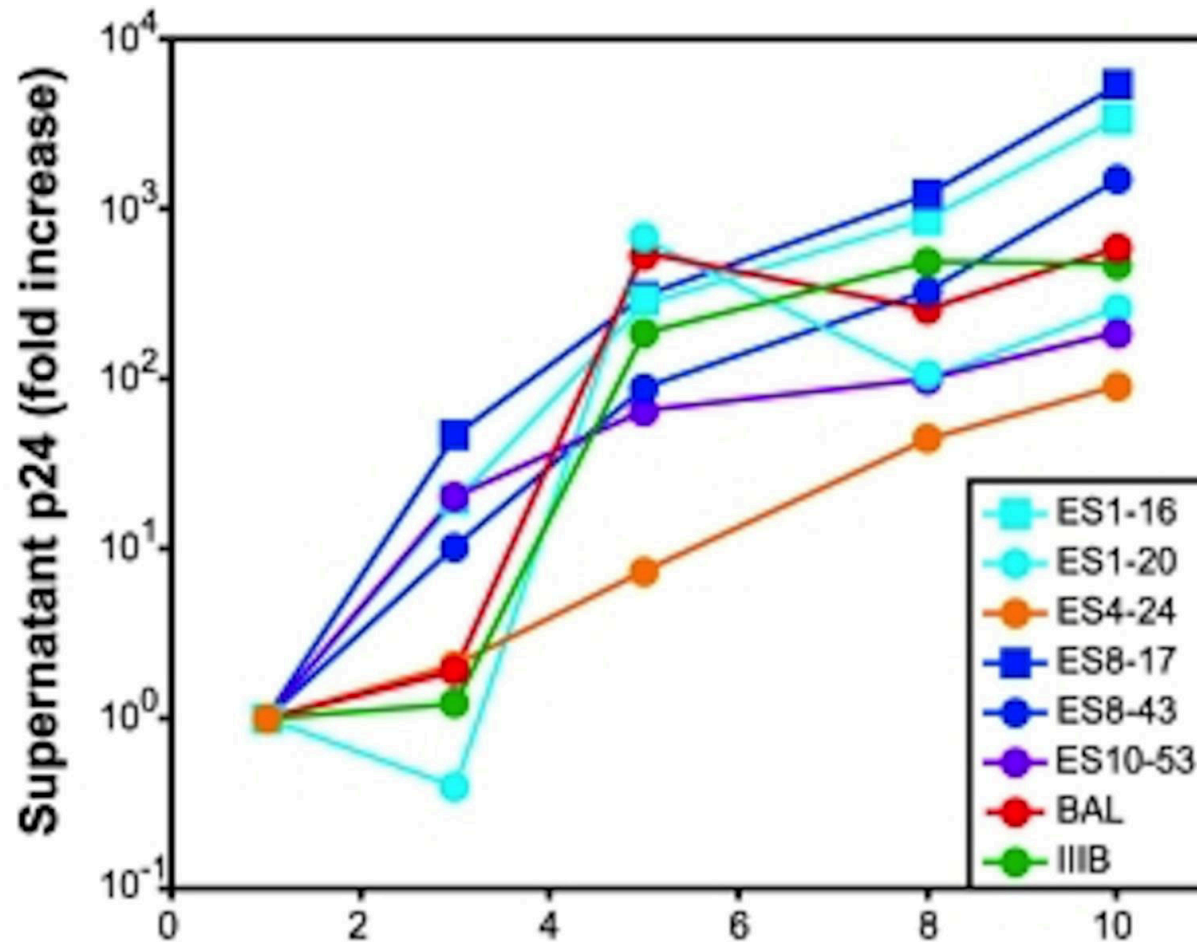
Factors NOT associated

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

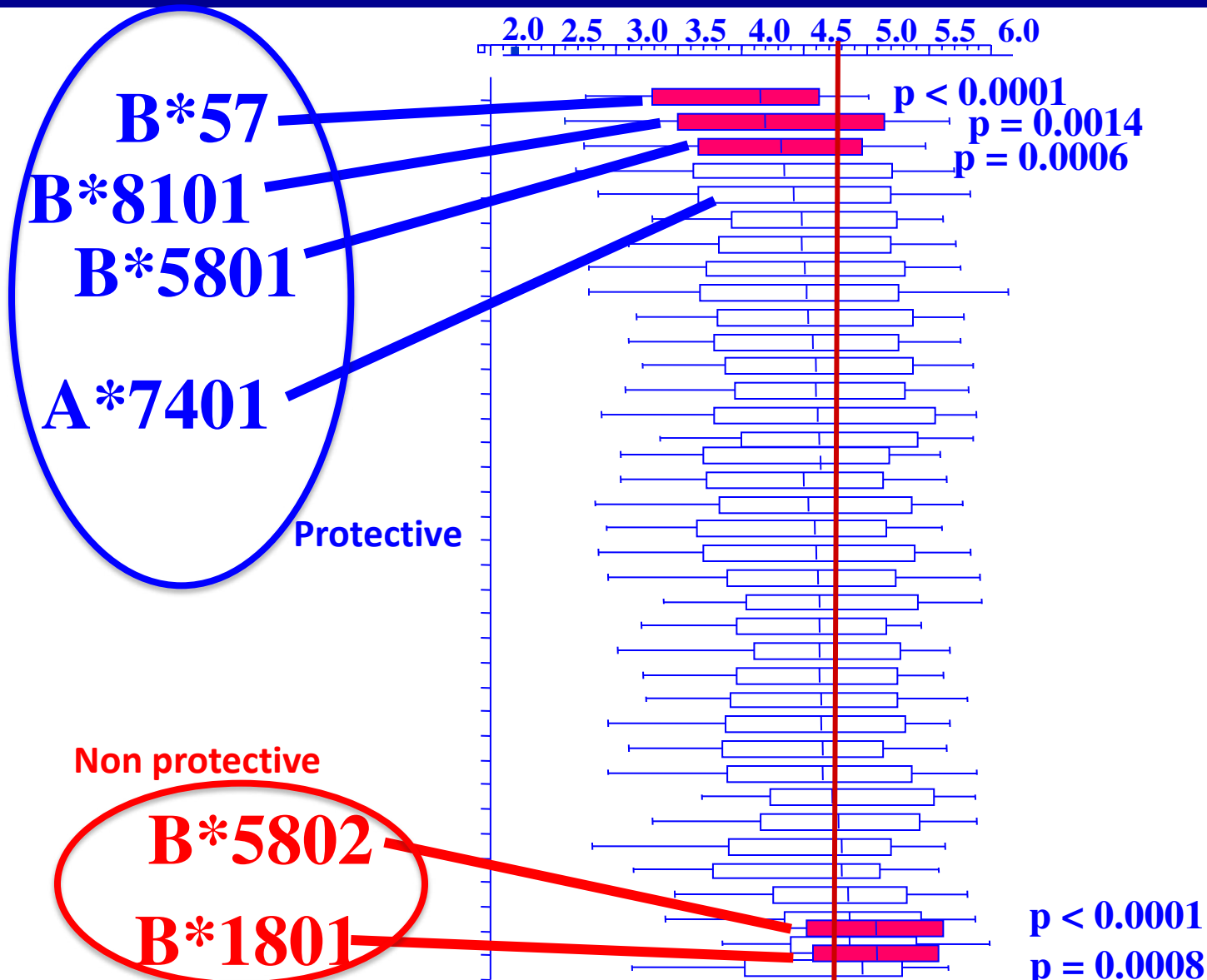
Factors Associated

- 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

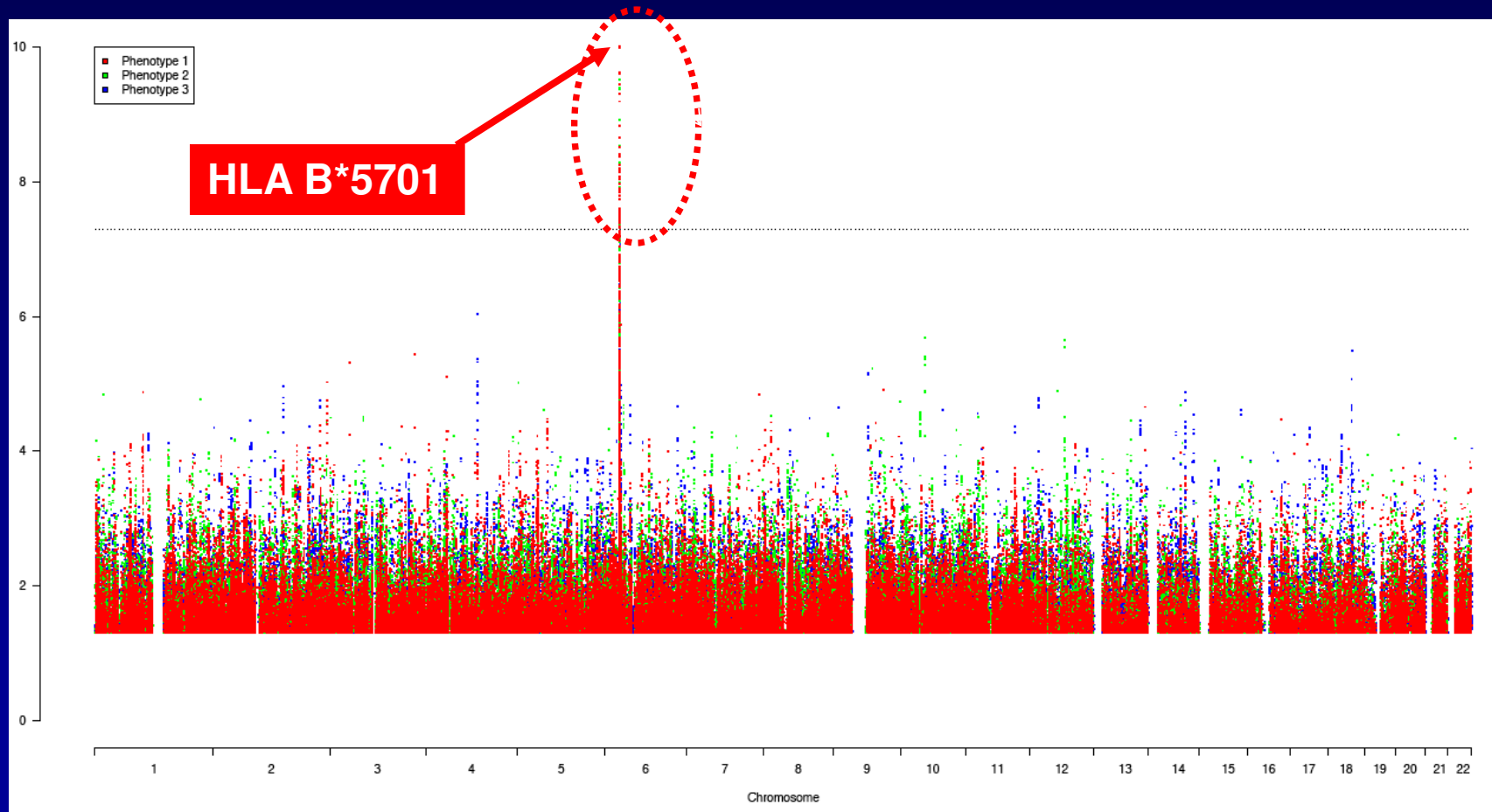


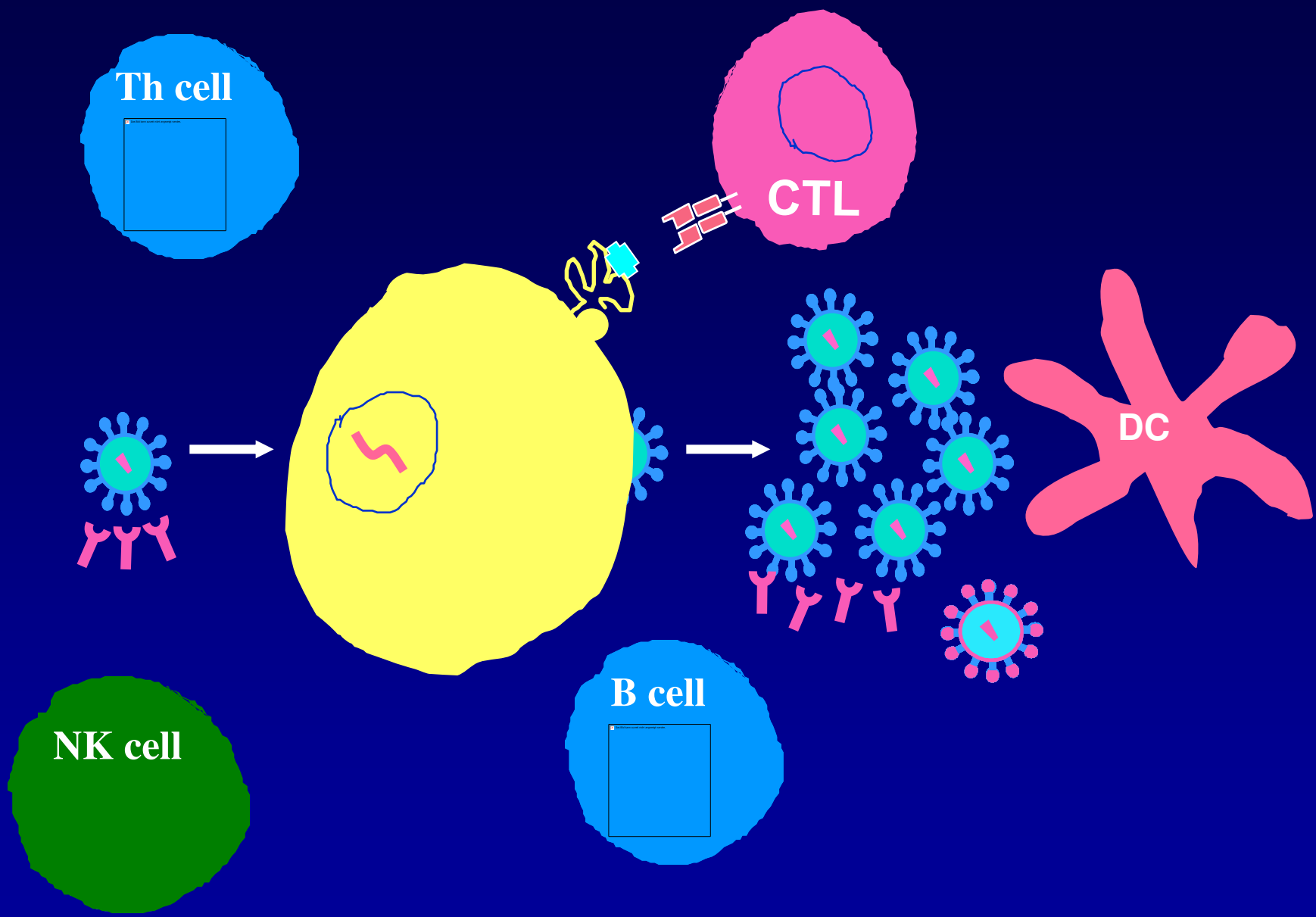
The impact of HLA on HIV disease progression



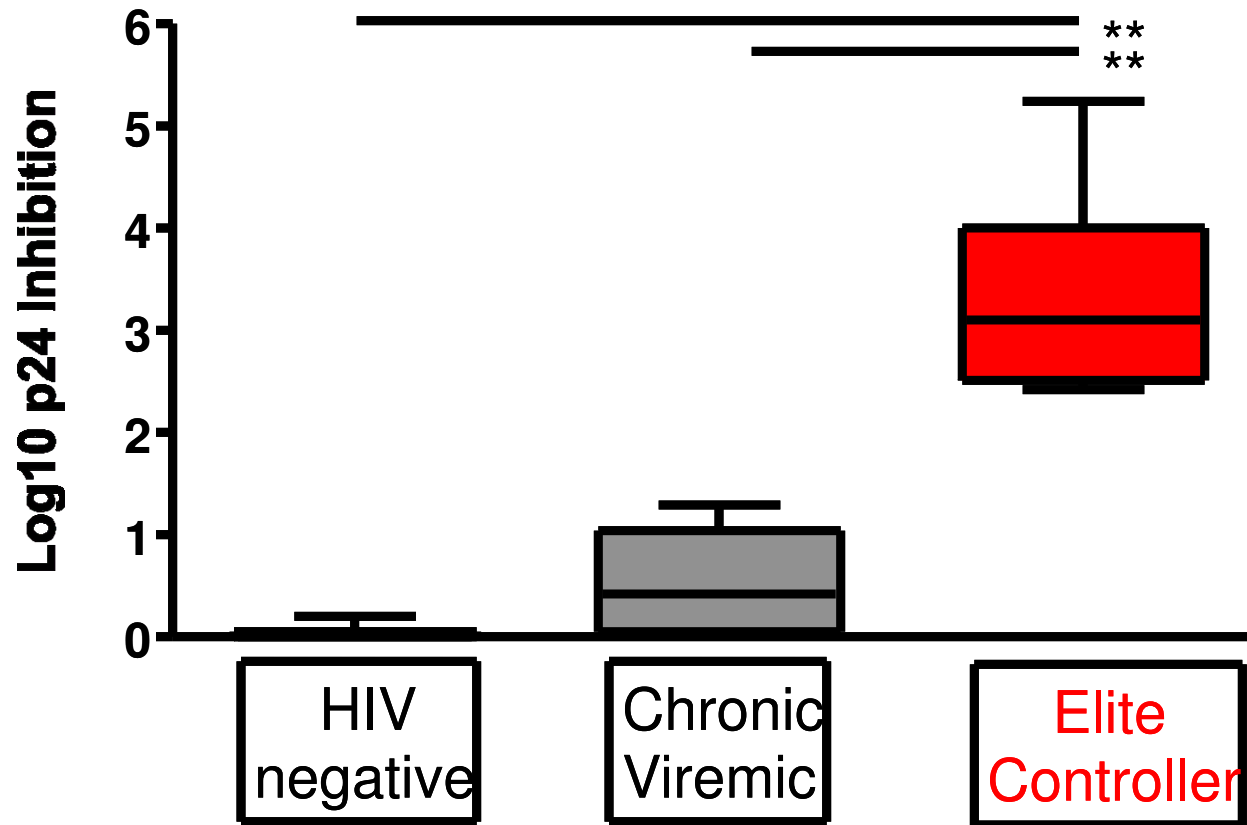
Genome-wide results in Whites

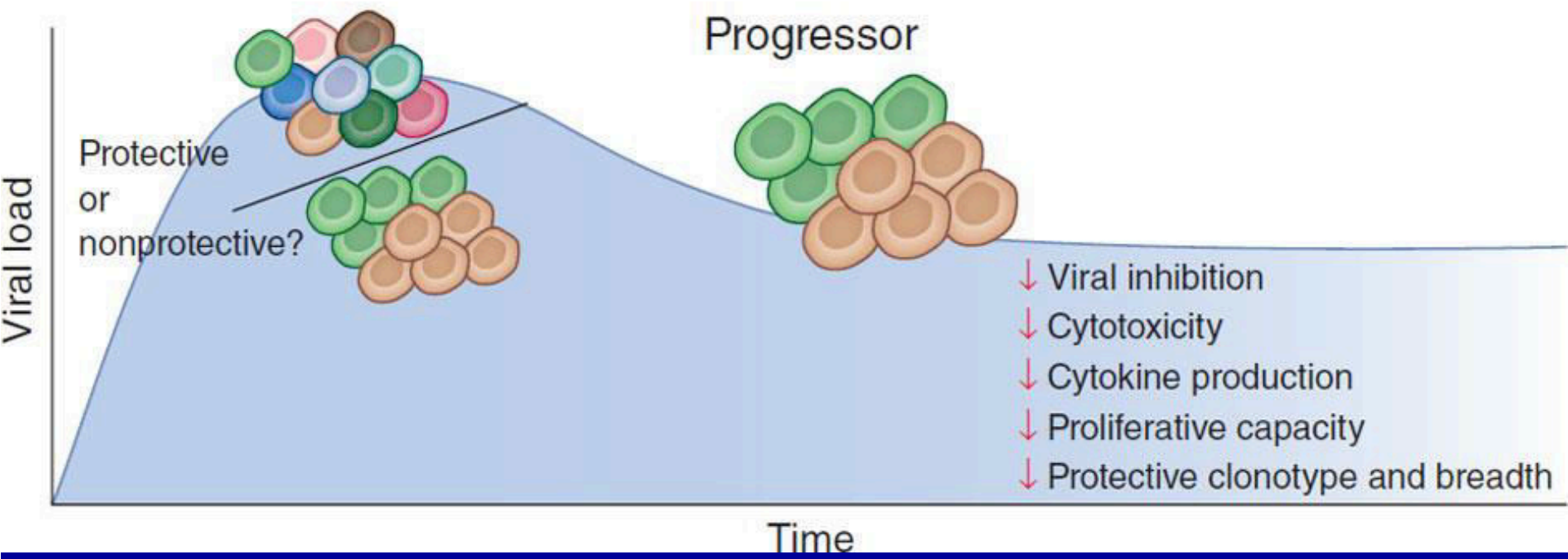
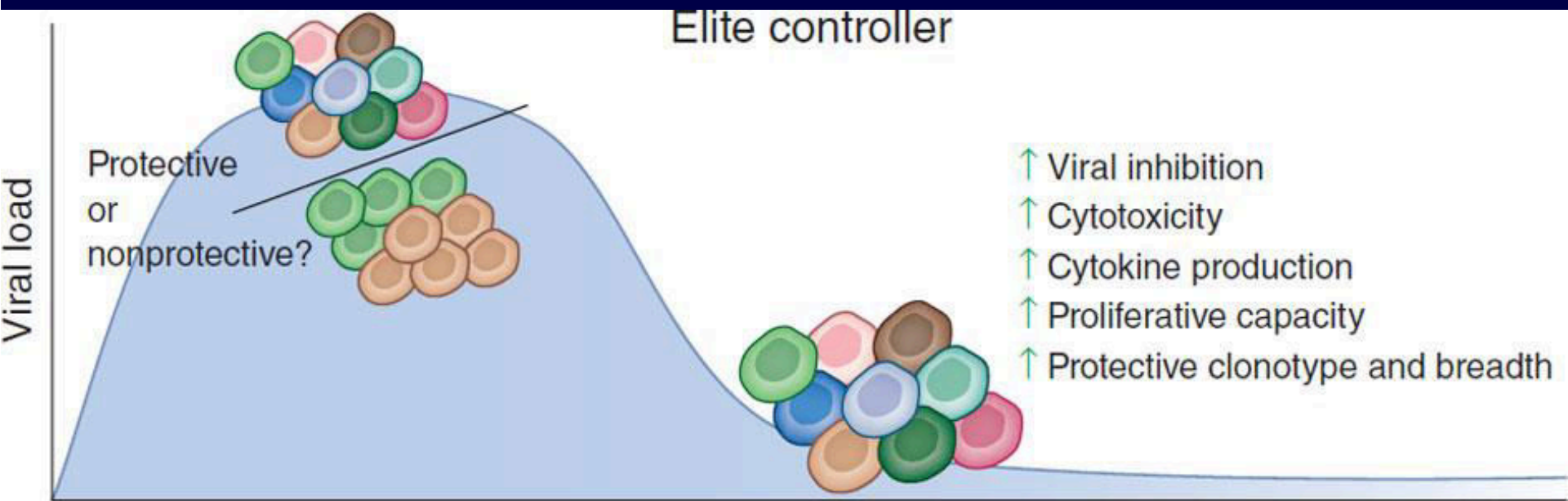
statistical significance (p-value)



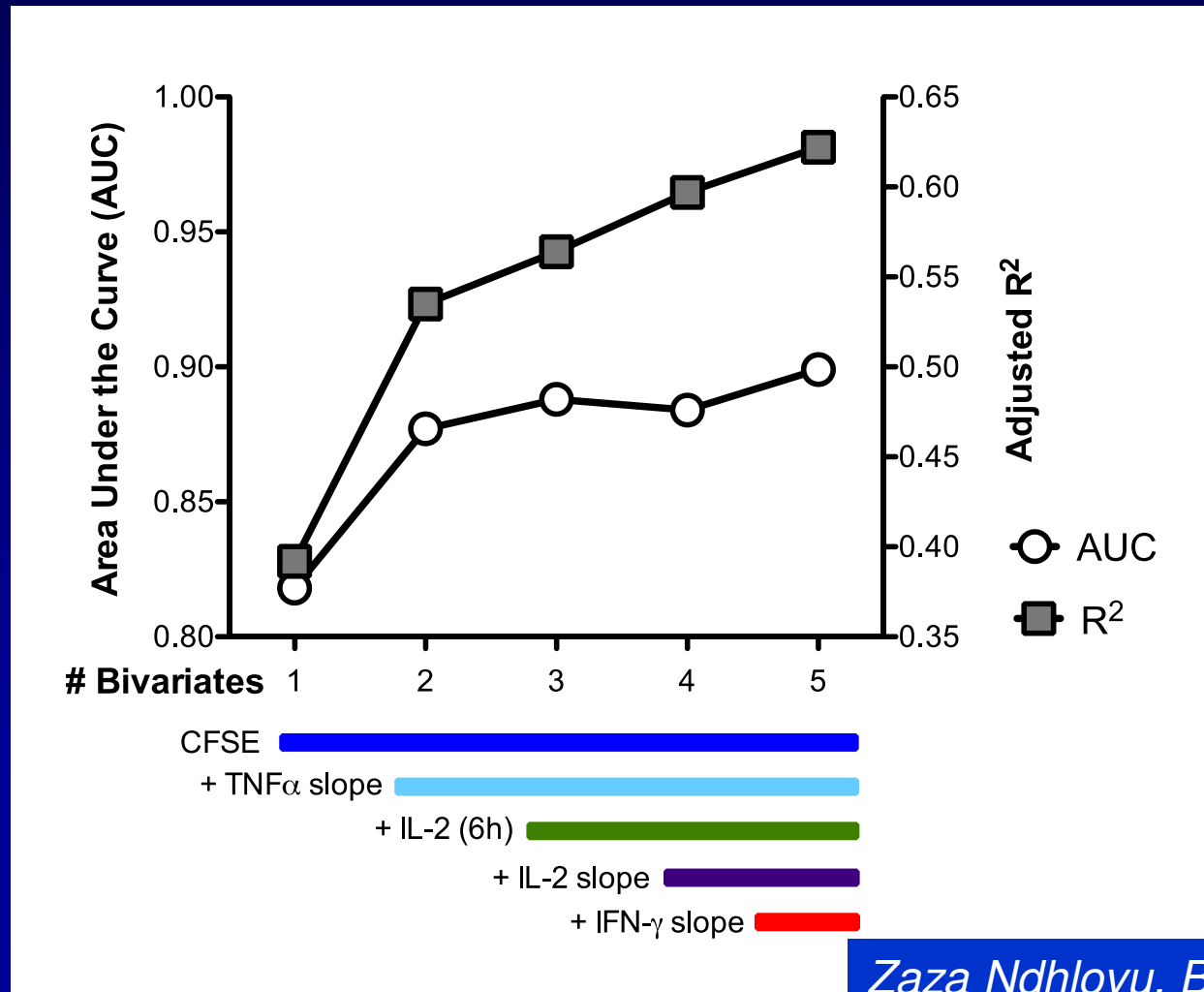


Viral Inhibition in HIV negative, chronic viremic and elite controllers





Differential impact of increasing variables in the model



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

Contact information

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