HIV Cure in the News: The South African child

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Session: Let's talk about HIV Cure
Conflict of interest disclosure

*I have no relevant financial relationships with ineligible companies to disclose*
**Children with HIV Early Antiretroviral Therapy (CHER) Trial: 2005-2011**

**Drug Regimen**
- zidovudine + lamivudine + lopinavir/ritonavir

**Treatment-naive HIV+ infants (N=411):**
- ≤ 12 weeks of age with CD4% ≥ 25%

1. **Deferred Therapy**
   - initiated when met WHO immunologic or clinical criteria
   - N=125

2. **Early Therapy: 40 weeks**
   - initiated immediately, continued to 1 year of age
   - N=143: 122 stopped ART

3. **Early Therapy: 96 weeks**
   - initiated immediately, continued to 2 years of age
   - N=143: 105 stopped ART

**ART was re-initiated:**
- CD4% <20% and clinical criteria were met

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A very unique child...

Born in 2007

32 days – HIV+ve PCR

Child maintained healthy CD4 T cell count

39 days – VL > 750,000

61 days – started ART

60 days – VL = 151,000

Treatment cessation – 1yr

40 weeks treatment

Child has undetectable VL > 13 yrs

Only 1/227 children to achieve this!!

At 9.5 years of age....

Standard Diagnostic tests

- HIV Qualitative PCR: Negative
- ELISA: HIV-specific antibodies: Negative
- Viral Load: Target not detected
- Western Blot: HIV-specific antibodies: Indeterminate

**SA CHILD**

**Controls**

**High Pos**

**Low Pos**

**Neg**

- gp160
- gp120
- p65
- P55/51
- gp41
- p40
- p31
- p24
- p18

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Can we detect any sign of HIV infection?
- proviral reservoir and detectable viral load (10ml plasma)

Can we detect a HIV-specific immune response?
- weak CD4+ T cell GAG response and HIV-Abs using luminex

Does the child have any features that may explain control?
- low CCR5 and high PD-1

Are there any signs of replication-competent HIV?
- ?….ongoing work
Proviral Landscape (FLIPS)

- No detection of intact proviral sequence
- Proviral reservoir is composed of defective HIV DNA dominated by a ≈3200bp provirus (containing intact \textit{gag} gene): indicative of cellular proliferation
- Have identified intact \textit{gag}, \textit{vpr}, \textit{vif} and \textit{nef} genes in provirus sequenced to date and \textit{env} shows evidence of considerable hypermutation
Further searches for replication competent virus

- Viral Outgrowth Assay
- Unspliced HIV RNA
- Multiply-SPLICED HIV RNA
- Episomal DNA (2-LTR)
- RNA-Flow FISH Assay

Int: 6/20 (30%) reps positive
GAG: 12/24 (50%) reps positive
TILDA: 13/16 (81%) reps positive
Hot off the press….

10x Single cell RNA sequencing PBMCs from the SA child and three control (HIV-negative) male children
In summary, this unique child maintains a healthy CD4:CD8 ratio and undetectable viral load by standard assays 14 years post treatment cessation.

Although we can detect signals of transcriptionally active HIV we have no evidence to support replication competent HIV thus far.

The child has some interesting features, including high PD-1 expression despite low immune activation, that warrant further investigation.

Continued intense studies using a platform of new technologies will be conducted to try and understand how this child has managed to achieve what appears to be a ‘cure’ – may offer insights into cure strategies.
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