HIV Cure Research in Resource-limited Settings

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The views expressed are those of the authors and should not be construed to represent the positions of the U.S. Army or the Department of Defense.
Outline

- Relevance of HIV cure research in RLS
- How can RLS participate in HIV cure research?
  - Examples from Thailand
- Ethical and social considerations

*Short video on a Thai teenager’s perspective on cure*
Strategies currently in human studies

**MINIMIZE RESERVOIR**
Limit reservoir with early treatment
- Antiretroviral therapy
- Broadly neutralizing antibodies

**SHOCK**
- Reactivating latently-infected cells
- HDAC inhibitors
- BET inhibitors
- PKC activators

**KILL**
- Clearance by the immune system
- Broadly neutralizing antibodies
- Therapeutic HIV vaccines
- Anti PD1, Anti PDL1

**HIV RESISTANT CELLS**
- Transfusing cells without CCR5 gene
- Gene-editing therapy
- Bone marrow or cord blood transplantation

**Combination Cure**
HIV cure research is relevant in RLS NOW

Response and complications may be different in RLS
  Host and environmental factors
  HIV clades

- 35 million
- 50% of people
- $600/year
- 315 billion
- 30 years

Therapy for HIV remission/cure
Limited period of ART ± other intervention
How can RLS contribute to HIV cure research?

- Limiting HIV seeding of the reservoir
  - Early diagnosis
  - Early treatment
  - Keeping patients virally suppressed
Restricted Reservoir Size in Early Treated Thai Children

HIV DNA (copies/10^6 CD4 T cells)

- Integrated HIV DNA (n=15)
- Total HIV DNA (n=12)
- 2-LTR circles (n=11)

Visconti post treatment controllers

HIV-NAT 194 study (Ananworanich J, AIDS 2014)
<table>
<thead>
<tr>
<th>Components of Participating Organizations</th>
<th>Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) National Institute of Allergy and Infectious Diseases (NIAID)</th>
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<tr>
<td>Funding Opportunity Title</td>
<td>Evaluation of the Latent Reservoir in HIV-Infected Infants and Children with Early Antiretroviral Treatment and Virologic Control (R01)</td>
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<td>Activity Code</td>
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<td>RFA-HD-14-026</td>
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<table>
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<tr>
<th>Data</th>
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<tr>
<td>N of infants infected with HIV</td>
<td>90</td>
</tr>
<tr>
<td>ART by first year of life</td>
<td>55%</td>
</tr>
<tr>
<td>MTCT rate</td>
<td></td>
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<tr>
<td>- All HIV-exposed (n=4716)</td>
<td>3%</td>
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<tr>
<td>- High-risk (n=1179)</td>
<td>12%</td>
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### Stakeholders engagement:
**Synergistic public health and research goals**

#### 2014 Thai MOPH Guideline
- ART at birth in all high-risk infants
- Earlier HIV DNA PCR
- Case management system

#### R01 AI 114236 (2014-2019)
- Measure reservoir, low level viremia and immune activation
- 260 newly infected infants (80 treated at birth)
- 40 early-treated long-term VL suppressed children
Real time screening of 120,000 samples at Thai Red Cross Anonymous Clinic

Enrollment (n=190)

Optional procedures
- Sigmoid biopsy
- Lymph node biopsy
- Lumbar puncture
- MRI/MRS
- Genital secretion collection

Characteristics

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<tr>
<td>Median duration of infection</td>
<td>18 days</td>
</tr>
<tr>
<td>Fiebig I/II (&lt; 2 weeks)</td>
<td>51%</td>
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<tr>
<td>Fiebig III (2-4 weeks)</td>
<td>40%</td>
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</table>
Early ART limits persistence of HIV reservoir in all CD4+ T cell subsets

Long-lived central memory CD4 T cells

Short-lived effector memory CD4 T cells

Nicolas Chomont (VGTI-Florida)
Thailand – US Collaboration for RV254/SEARCH 010 Study (2007 to now)

- High HIV prevalence in clients of Thai Red Cross
- Testing of stored samples showed 2.7% acute HIV
- Grant and protocol for acute HIV cohort
- ARV protocol and drug support from Thai Gov and companies
- Thai, US and international collaborators
- Training and technology transfer
- Campaign to increase awareness of early diagnosis and treatment
- Enrollment increase 0-1/month to 10-20/month
- Additional funding Thai Gov, US Gov, amfAR
- HIV cure-related protocols
- ART interruption in early treated Fiebig I
- Broadly neutralizing antibody
- Therapeutic HIV vaccine
- Immune modulators
- Latency reversing agents
Ethical and social considerations of HIV cure research

- Consequences of cure
  - HIV complications
  - Stigma and discrimination

- Equity enrollment in trials

- Cost and accessibility
  - Cure strategies
  - Monitoring

Contribution of RLS in HIV Cure Research

**Scientific contribution**
- Local knowledge and connections
- Find in-country funds for pilot projects
- Publish findings
- Co-design/write grants and protocols
- Mentored young/early career scientists

**Trial conduct contribution**
- Rapid enrollment of volunteers
- High willingness to participate in research
- Fewer sites required
- Conduct complicated protocol procedures
- Laboratory capability

**Financial contribution**
- In-country grants
- Antiretroviral treatment
- Human resources
- Infrastructure

- Cost efficient