

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 latent
infectious cells

HDAC inhibitors

BET inhibitors

PKC activators

KILL

Immune clearance by the
immune system

Broadly neutralizing antibodies

Attenuated HIV vaccines

Anti PD1, Anti PDL1

Combination
Cure

HIV RESISTANT CELLS

Transfusing cells without CCR5 gene

Gene-editing therapy

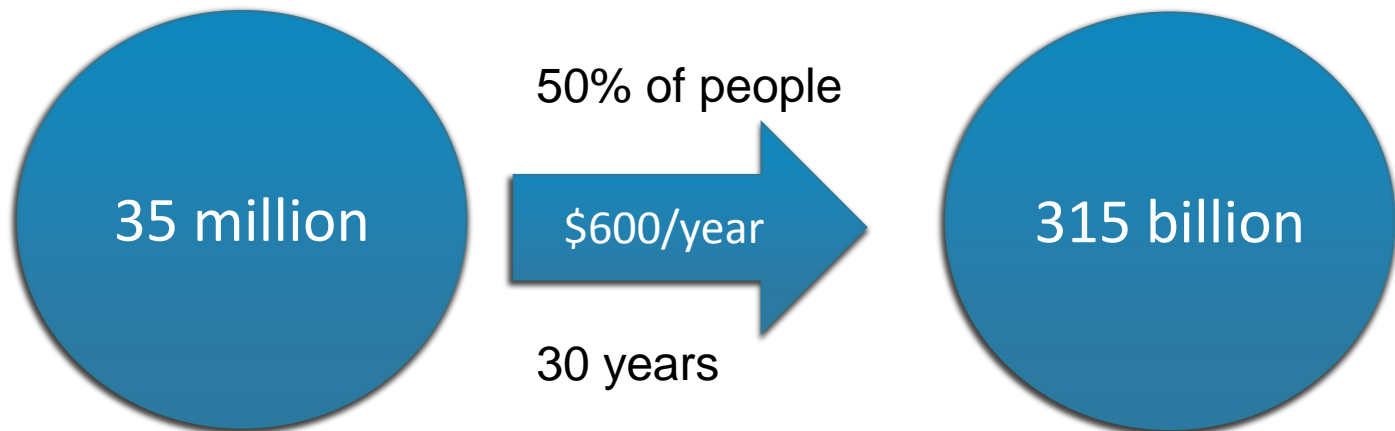
Bone marrow or cord blood transplantation

HIV cure research is relevant in RLS NOW

Response and complications may be different in RLS

Host and environmental factors

HIV clades



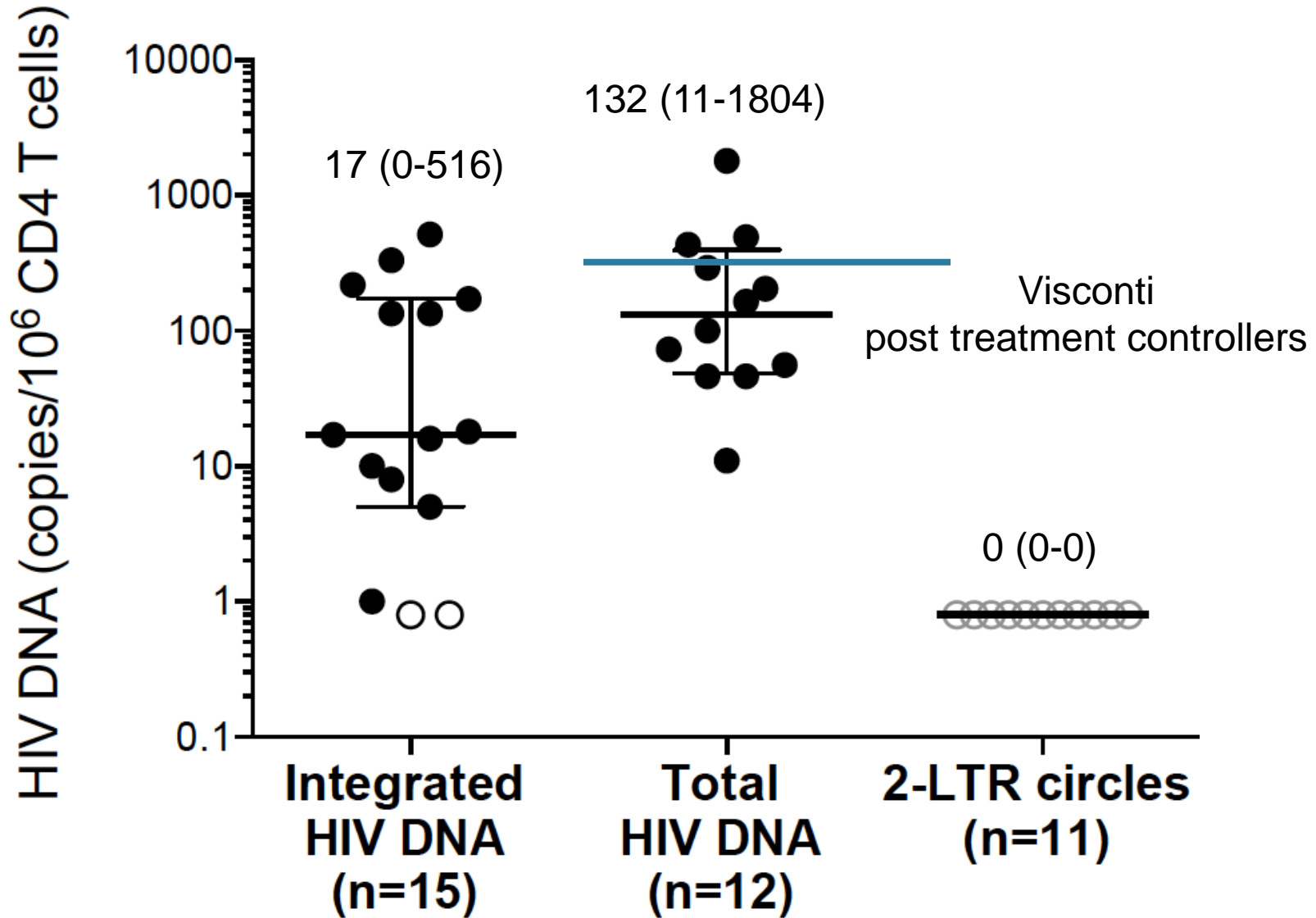
Therapy for HIV remission/cure

Limited period of ART \pm other intervention

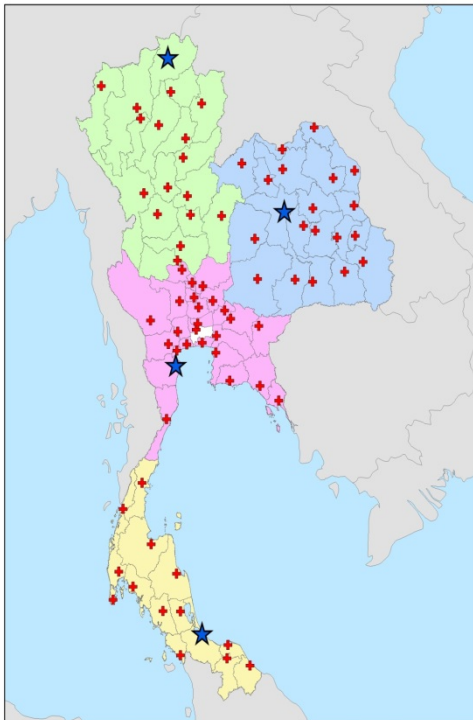
How can RLS contribute to HIV cure research?

- Limiting HIV seeding of the reservoir
 - Early diagnosis
 - Early treatment
 - Keeping patients virally suppressed

Restricted Reservoir Size in Early Treated Thai Children



Components of Participating Organizations	<i>Eunice Kennedy Shriver</i> National Institute of Child Health and Human Development (NICHD) National Institute of Allergy and Infectious Diseases (NIAID)
Funding Opportunity Title	Evaluation of the Latent Reservoir in HIV-Infected Infants and Children with Early Antiretroviral Treatment and Virologic Control (R01)
Activity Code	R01 Research Project Grant
Announcement Type	New
Related Notices	None
Funding Opportunity Announcement (FOA) Number	RFA-HD-14-026



Data	2012
N of infants infected with HIV	90
ART by first year of life	55%
MTCT rate	
- All HIV-exposed (n=4716)	3%
- High-risk (n=1179)	12%

Stakeholders engagement: Synergistic public health and research goals

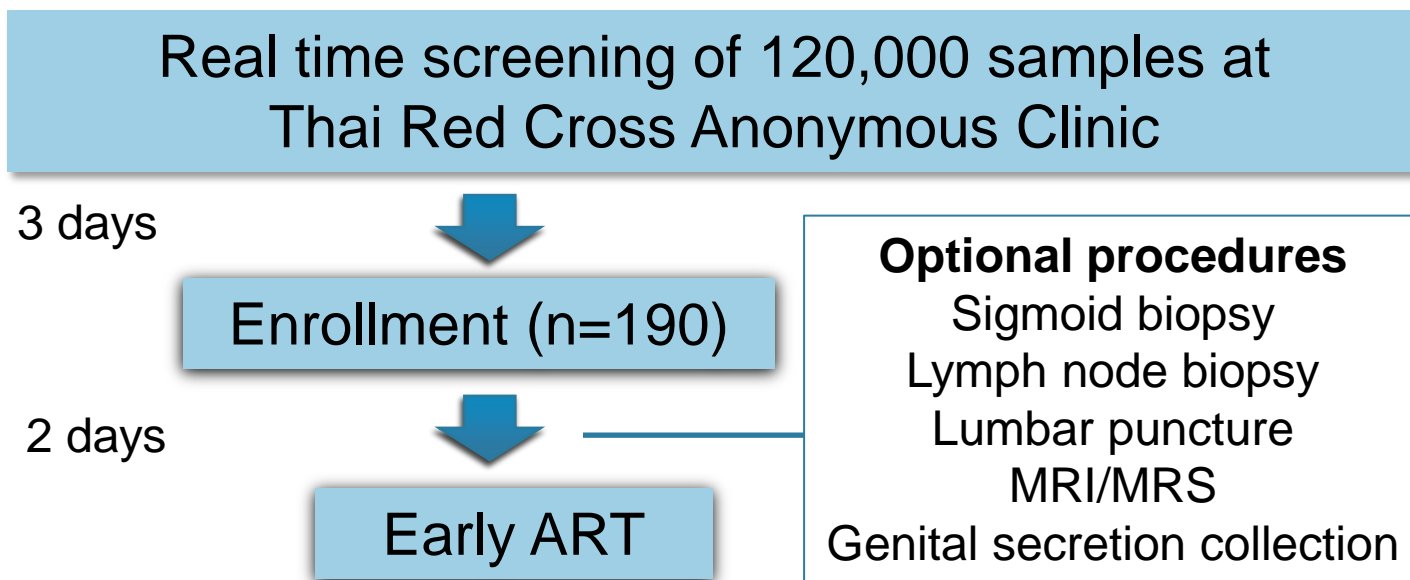
2014 Thai MOPH Guideline

- ART at birth in all high-risk infants
- Earlier HIV DNA PCR
- Case management system

R01 AI 114236 (2014-2019)

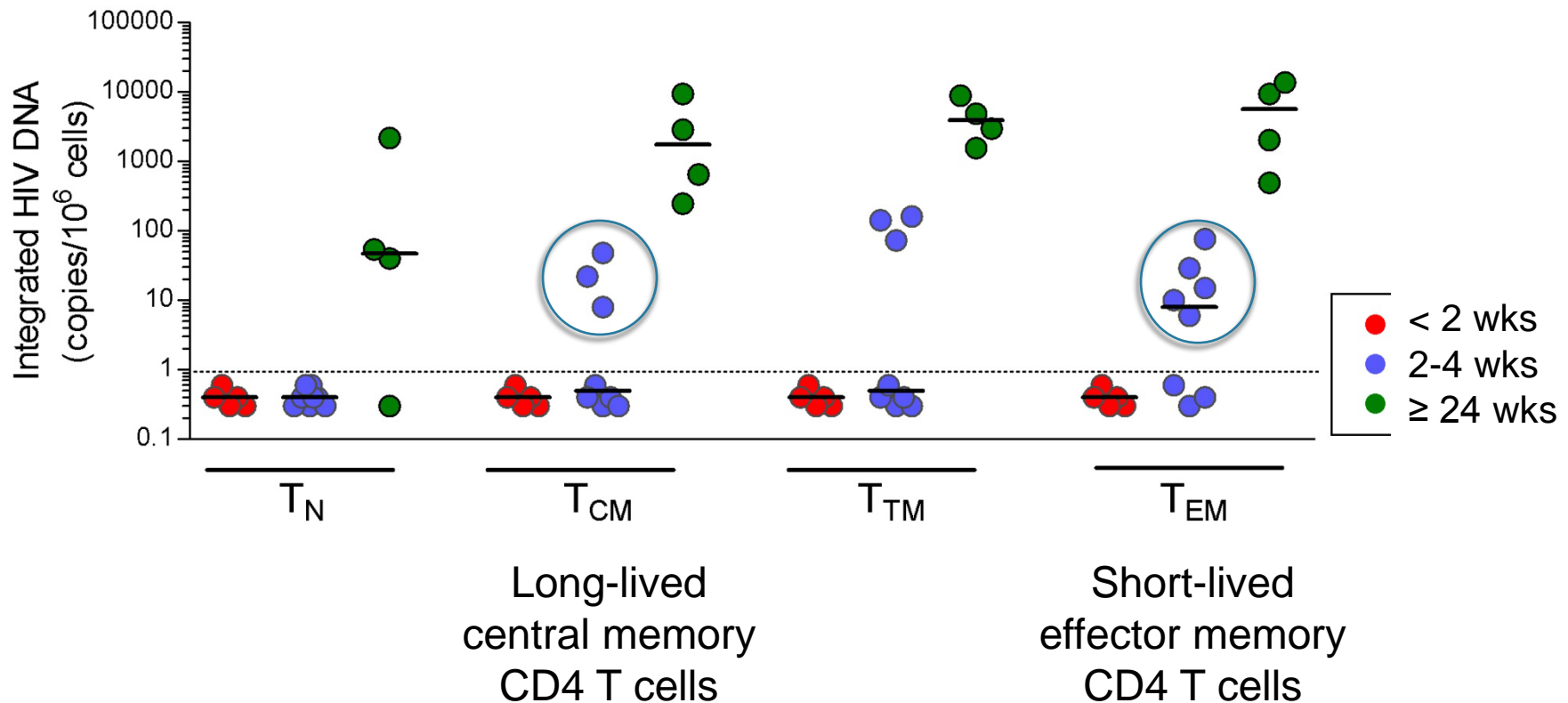
- Measure reservoir, low level viremia and immune activation
- 260 newly infected infants (80 treated at birth)
40 early-treated long-term VL suppressed children

Early ART in Thai Adults: RV254/SEARCH010 Study



Characteristics	Values
Median duration of infection	18 days
Fiebig I/II (< 2 weeks)	51%
Fiebig III (2-4 weeks)	40%

Early ART limits persistence of HIV reservoir in all CD4+ T cell subsets



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

Cost efficient

Financial contribution

In-country grants

Antiretroviral treatment

Human resources

Infrastructure