Early Antiretroviral Therapy

HIV Cure Research Training Curriculum

HIV and Cure Early ART

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The HIV CURE research training curriculum is a collaborative project aimed at making HIV cure research science accessible to the community and the HIV research field.

Objectives

- Understand the current state of the HIV cure research field
- Summarize how early treatment could play a role in HIV cure research
- Explain the major cohorts involved in HIV cure research

What is an

HIV Cure?

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What is an HIV Cure?

- Key elements of any cure:
  - NO Transmission
  - NO Disease Progression
  - NO Medications

How Do We

Define “Cure”?

How Do We Define “Cure”?

- **Sterilizing/Eradication-**
  - HIV is completely removed from every cell in the body
  - Person is HIV-free (virus free)
  - No need for medication

- **Functional/Remission-**
  - HIV is NOT completely gone from the body
  - All requirements from previous slide met
  - No need for medication
  - *HIV has potential to resurface*

Why is

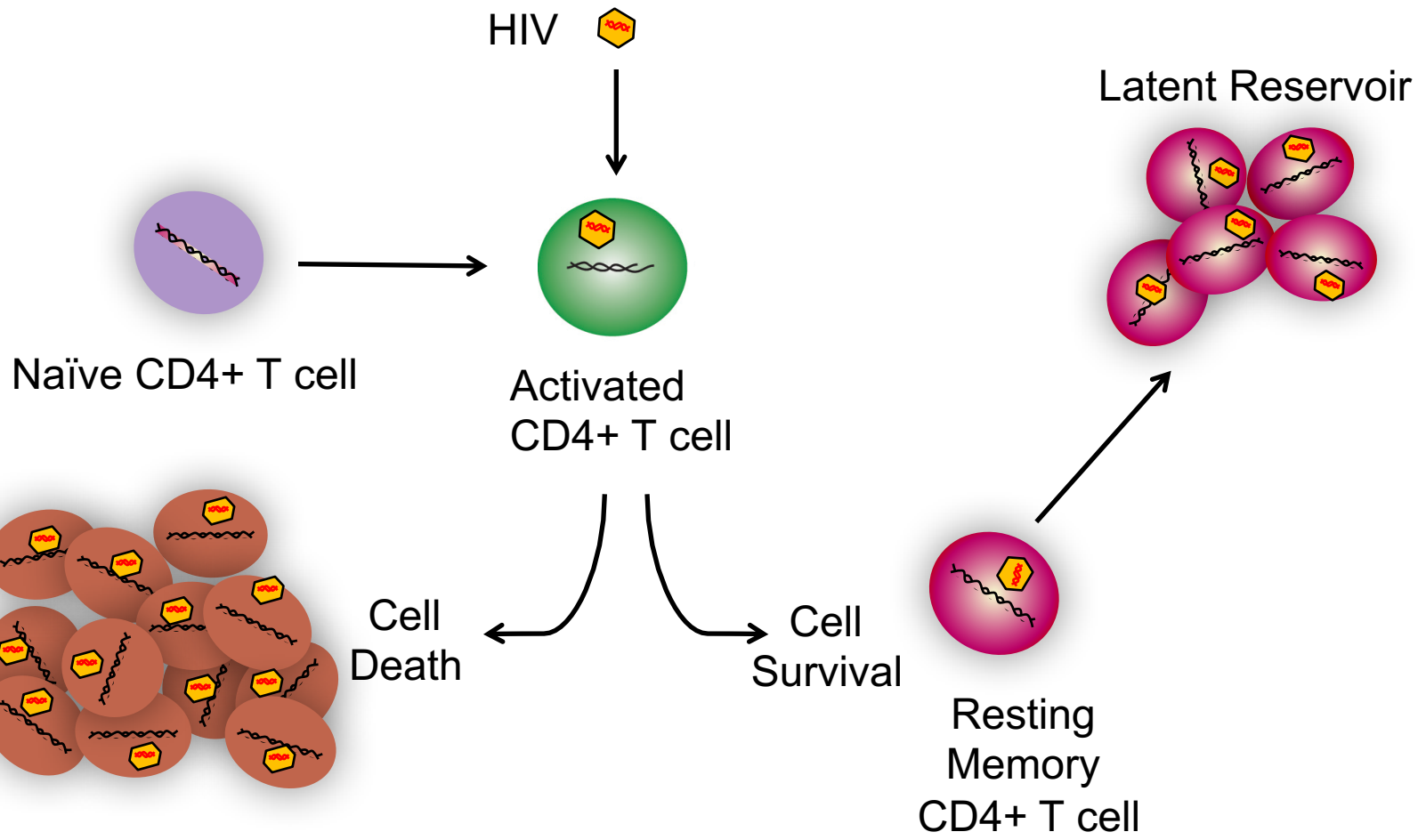
HIV so Hard to Cure?

Why is HIV so Hard to Cure?

- HIV enters a cell and integrates into the cell's DNA
- **Most** cells recognize infection - causing cell death
- **A few** infected cells become "long-lived" memory cells or "resting memory" cells
- The collection of long-lived memory cells is called the **Latent Reservoir**

Why is HIV so Hard to Cure?

Why is it so Hard to Cure HIV: Establishing the Latent Reservoir



Adapted from D. Persaud

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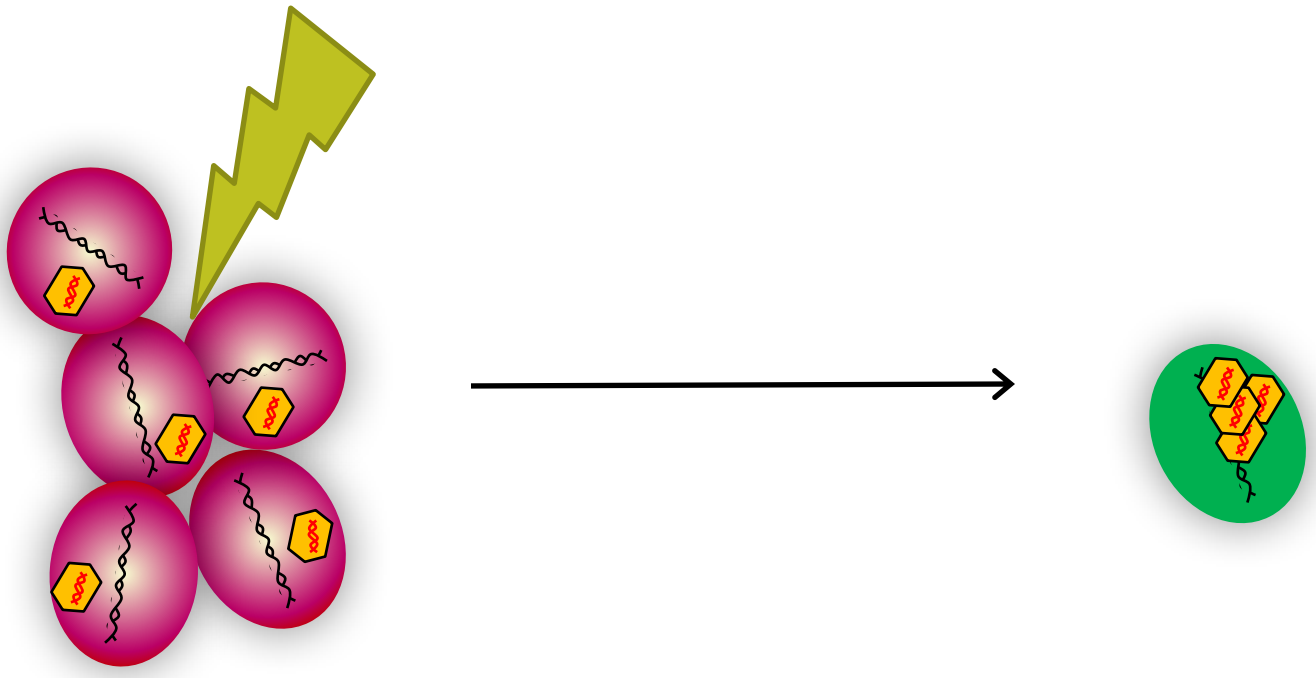


Latent Reservoir

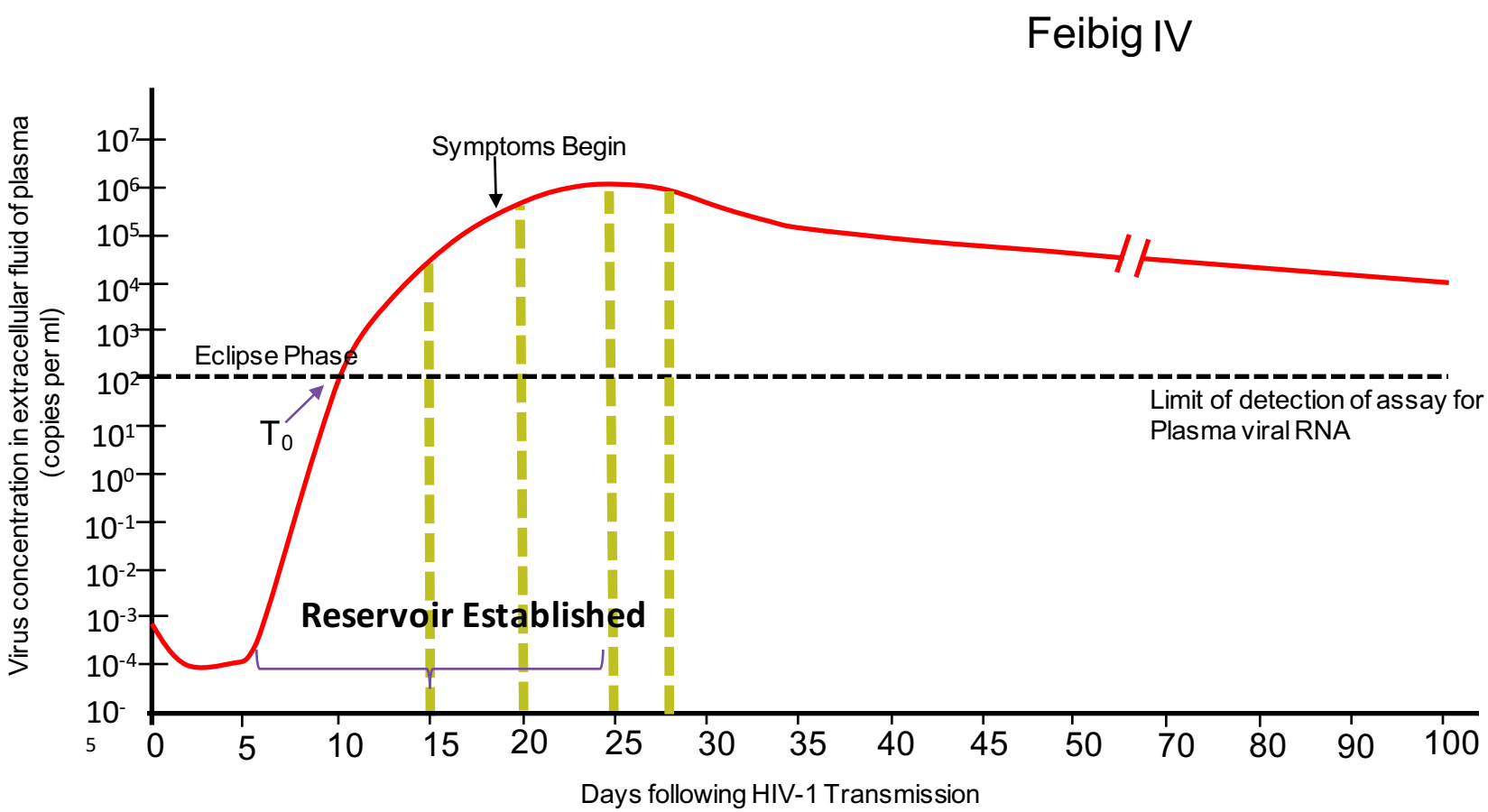
Reactivated CD4+ T cell

Adapted from D. Persaud

What is the Definition of Early?

- There is NO consistent definition of early
- Researchers do not know when the latent reservoir forms
- Most researchers define “early ART” as 14-90 days post infection.
- Some protocols use the term early to describe treatment initiation within six months.

What is the Definition of Early?



Adapted from McMichael AJ, *Nature Reviews Immunology*, 2010

How is PEP Different From Early ART

- Post Exposure Prophylaxis is a regimen of drugs taken within 72 hours of HIV expected exposure
- The closer PEP is taken to exposure increases efficacy
- Early ART is ONLY given with a positive HIV test
  - The earliest HIV tests are RNA and can be administered between 3-7 days post infection

New antibody tests take 2-3 weeks to return results

Why is Early ART Important?

- Preservation of Immune cells
  - Early ART= early protection of non-infected cells
  - This preserves the number of immune cells
- Smaller reservoirs
  - Early treatment = less seeding of the reservoir

VISCONTI Cohort

Visconti Cohort

- French cohort of 14 men and women
- Treated within 10 weeks of infection
- On treatment for at least 3 years
- Able to control virus off treatment for an average of 7.5 years
- **NO** pre-existing markers for control

Innate Ability to Control HIV

Elite Controllers

- Individuals who can:
  - control their virus- sometimes to undetectable levels- without antiretroviral treatment
  - They generally have regular CD4 and CD8 counts.

Long Term Non-Progressors

- Individuals who may:
  - have low levels of virus but maintain normal T-cell counts with no disease progression

VISCONTI Cohort- An Unsolved Puzzle

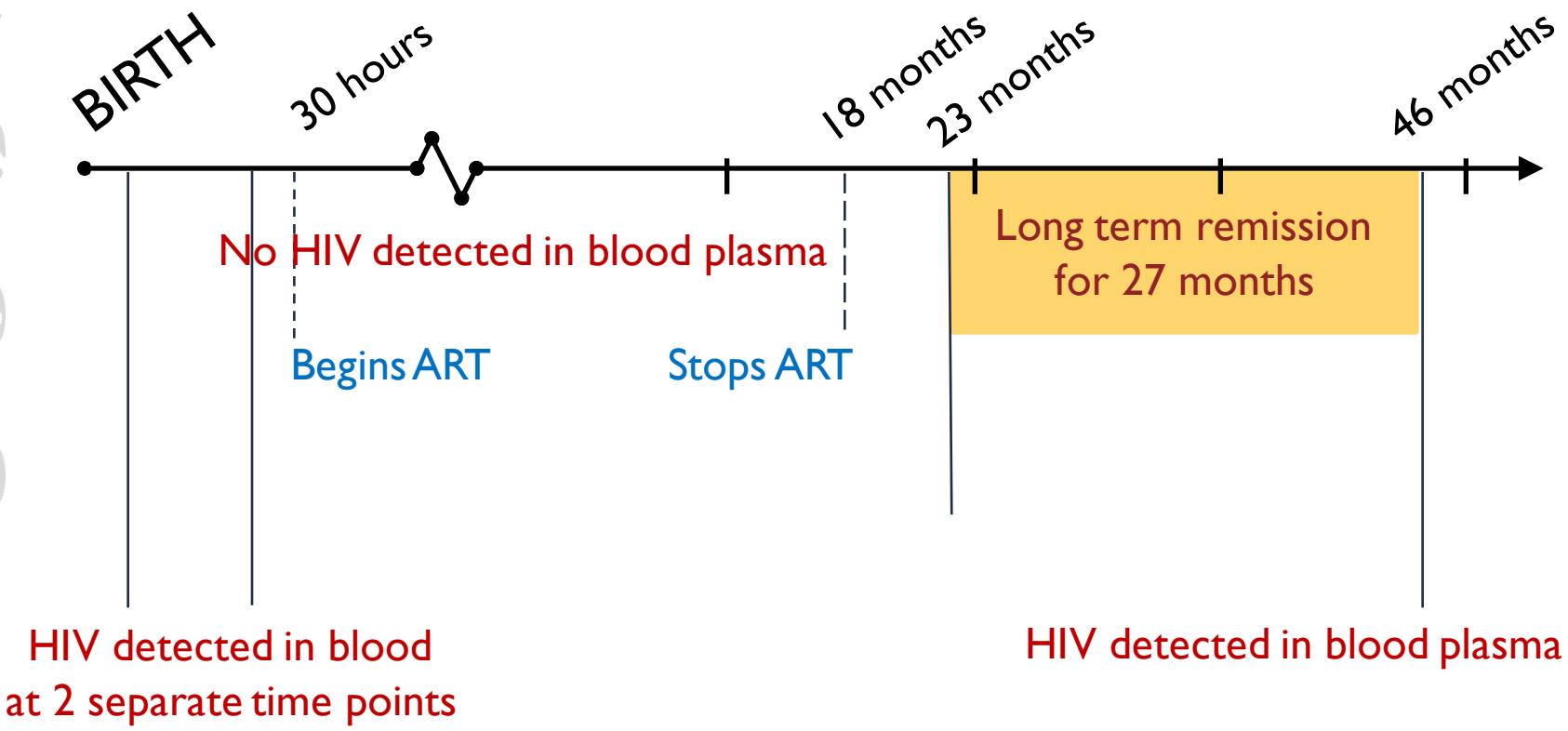
- Researchers are not sure what caused the control of the virus
- Most people who begin treatment early do not demonstrate spontaneous control
- Spontaneous control does not translate to life-long control
- Virus is still known to be present in the body

Mississippi Child

Mississippi Child

- HIV-positive at birth
- Started triple drug therapy 30 hours after birth
- Lost to follow-up and returned into care after 18 months off treatment
- Remained off treatment with no detectable virus for 27 months
- Rebounded and successfully restarted treatment at 28 months post-treatment

Mississippi Child



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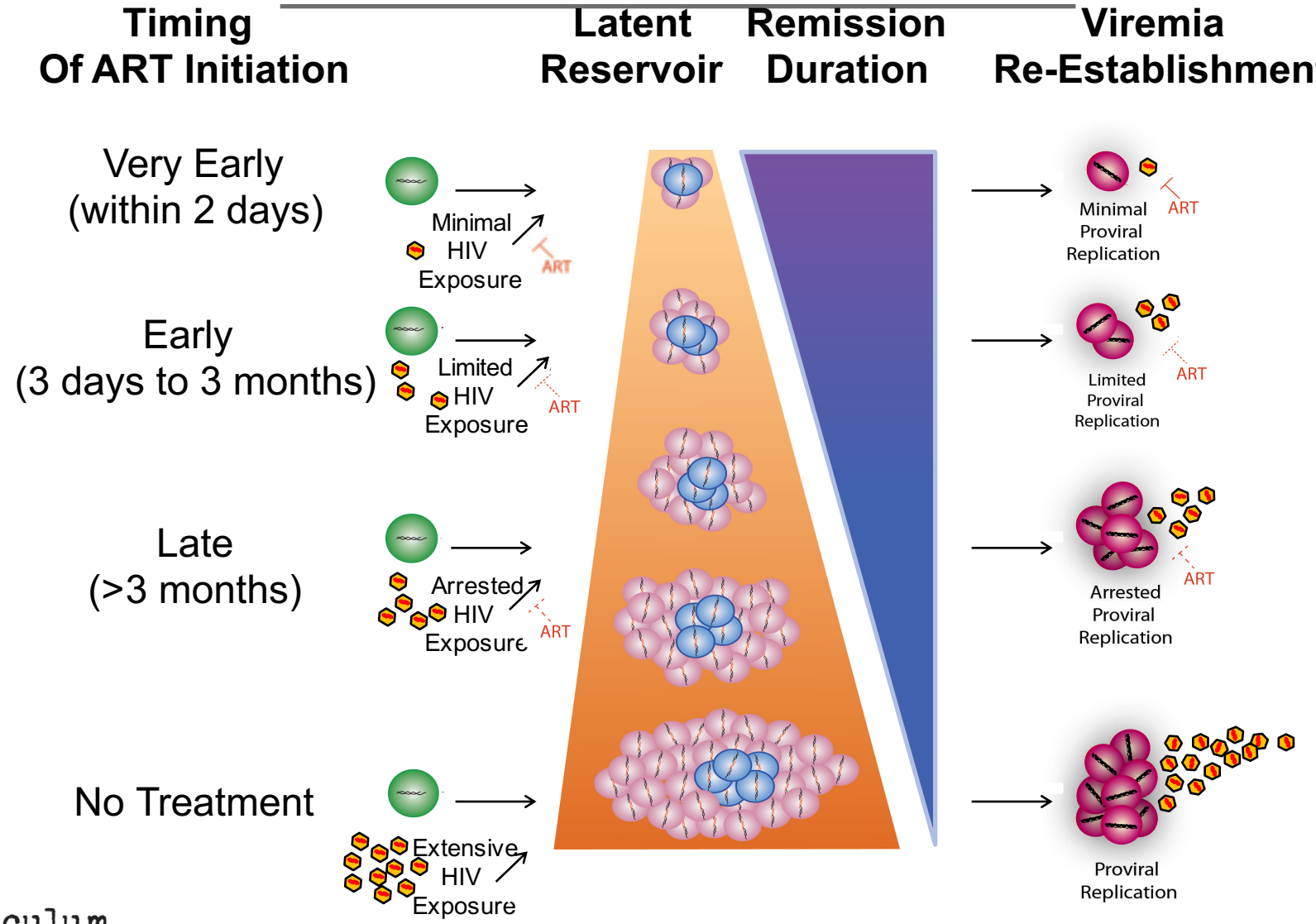
Persaud et al 2013 NEJM; Luzuriaga et al 2015 NEJM

What Can We Learn From the Mississippi Child?

- Proof that sustained viral remission is possible
- Early treatment prevented a large viral reservoir from seeding
- Even a small amount of virally infected cells can reestablish the reservoir

Early ART in Infants



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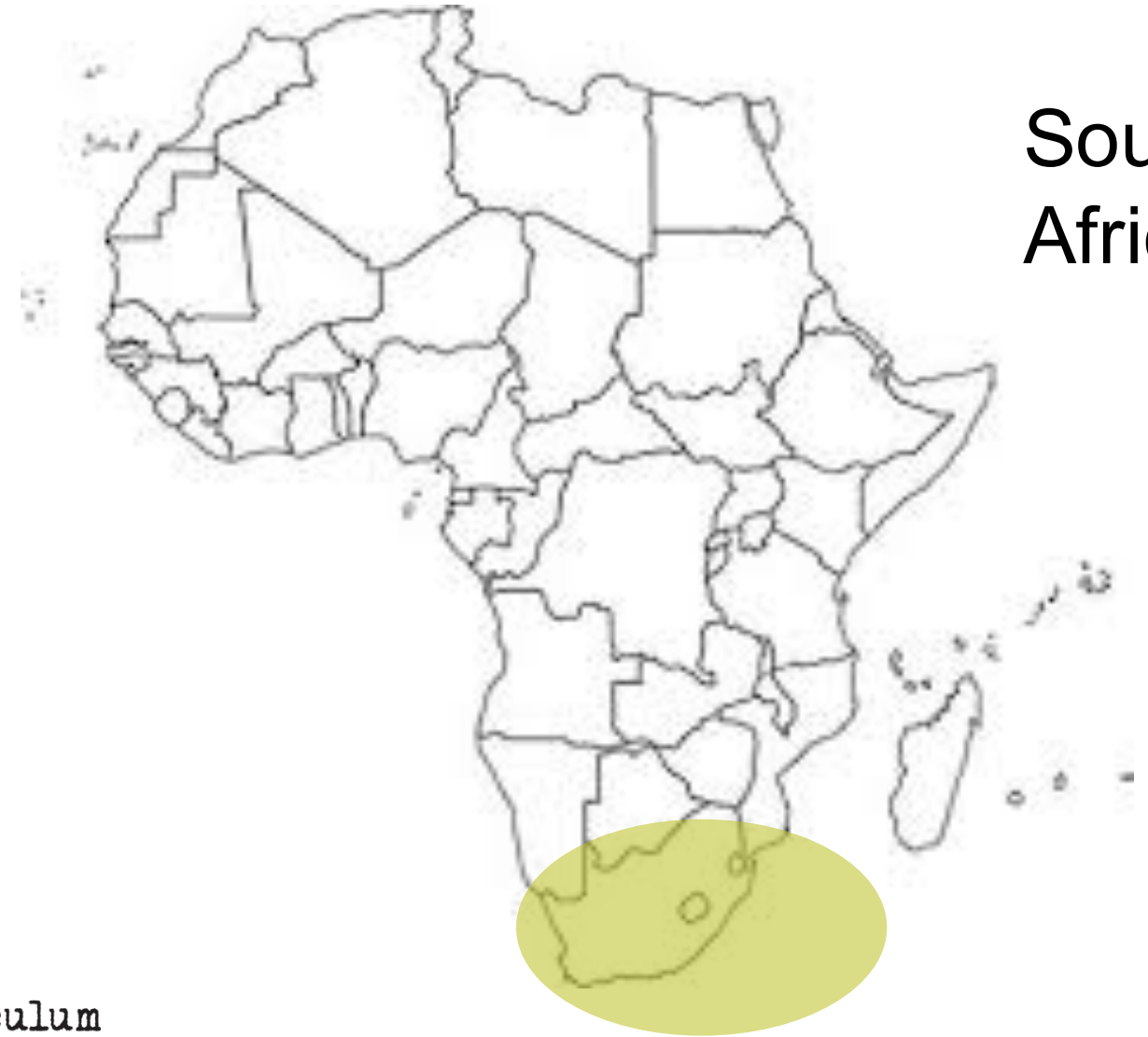
Rainwater-Lovett et al 2015 Curr Opin HIV AIDS

Early Capture Cohorts

The FRESH Cohort

- Young women (18-25) diagnosed within 14 days post-infection
- Biweekly clinic visits that include an intensive educational component
- Treated as soon as infection becomes detectable
- Samples being used to determine how early immune system functions

The FRESH Cohort



South Africa

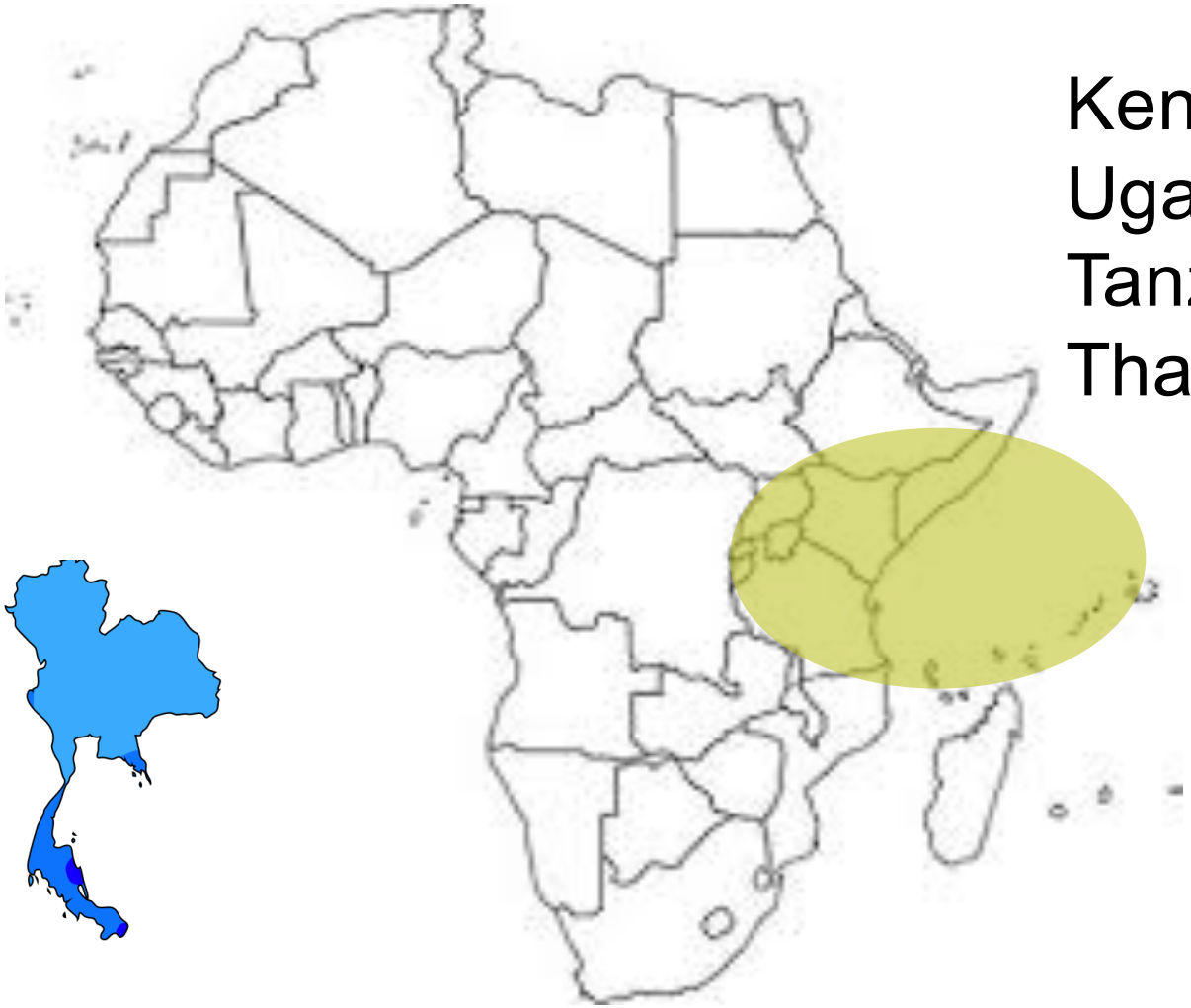
Early Capture HIV Cohort Study (RV217)

- MHRP began enrolling high risk individuals into the study in 2009
- Located in East Africa and Thailand
- As of 2016
  - 2000 participants enrolled
  - 115 early incidence cases captured
  - Some captured within days after infection
- Researchers are studying how the genes of the virus change after infection and early immune markers

What Can We Learn From Early Capture Cohorts?

- A better understanding of the immune system may contribute:
  - To tests for latency
  - To developing immune killing strategies
  - To better ways to preserve or restore immune function
  - To a preventive vaccine
- Individuals in these cohorts may be asked to participate in cure related trials in the future

Early Capture HIV Cohort Study (RV217)



Kenya
Uganda
Tanzania
Thailand

Challenges of Identifying Acute Infection

- Difficult to implement outside of a research center
  - Testing technologies
  - Testing frequency
  - Drug availability
- The urgency of starting treatment very early is not widely understood

Challenges of HIV Cure Trials

- Therapeutic Misconception
  - Participants who are in early capture cohorts may believe a cure related trial will offer them direct benefit
- Participant Selection
  - Participants are otherwise healthy and taking them off treatment could bring more risks then rewards

Conclusions

Early treatment can:

- Preserve the immune system function
- Reduce long term inflammation
- Limit the size of the reservoir

Acknowledgements

Questions

For additional information visit: **www.avac.org/CUREiculum**

Next Webinar

Join us on

Wednesday June 29th at 10am ET

for the Ethics of HIV Cure Research!

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