Introduction to HIV Cure-Related Research

Presented by Laurie Sylla

CUREiculum

This research training curriculum is a collaborative project aimed at making the science of HIV cure-related research saccessible to the community and the HIV research field.

A Whirlwind Tour

- What do we mean by cure
- Why an HIV cure is needed
- Why we believe an HIV cure is possible
- Path to a cure
- Why is curing HIV so difficult
- Cure strategies being pursued
- Ethical Issues

What Would an HIV Cure **Mean**?

"Cure"

A complete or permanent solution or remedy
To bring about recovery from
To permanently restore health

Two main pathways being investigated:

- **"Complete" or "classic" cure** = *complete elimination of the virus from the body*
- **ART-free durable suppression** (or **control**) = *the ability to control HIV replication without HIV treatment*

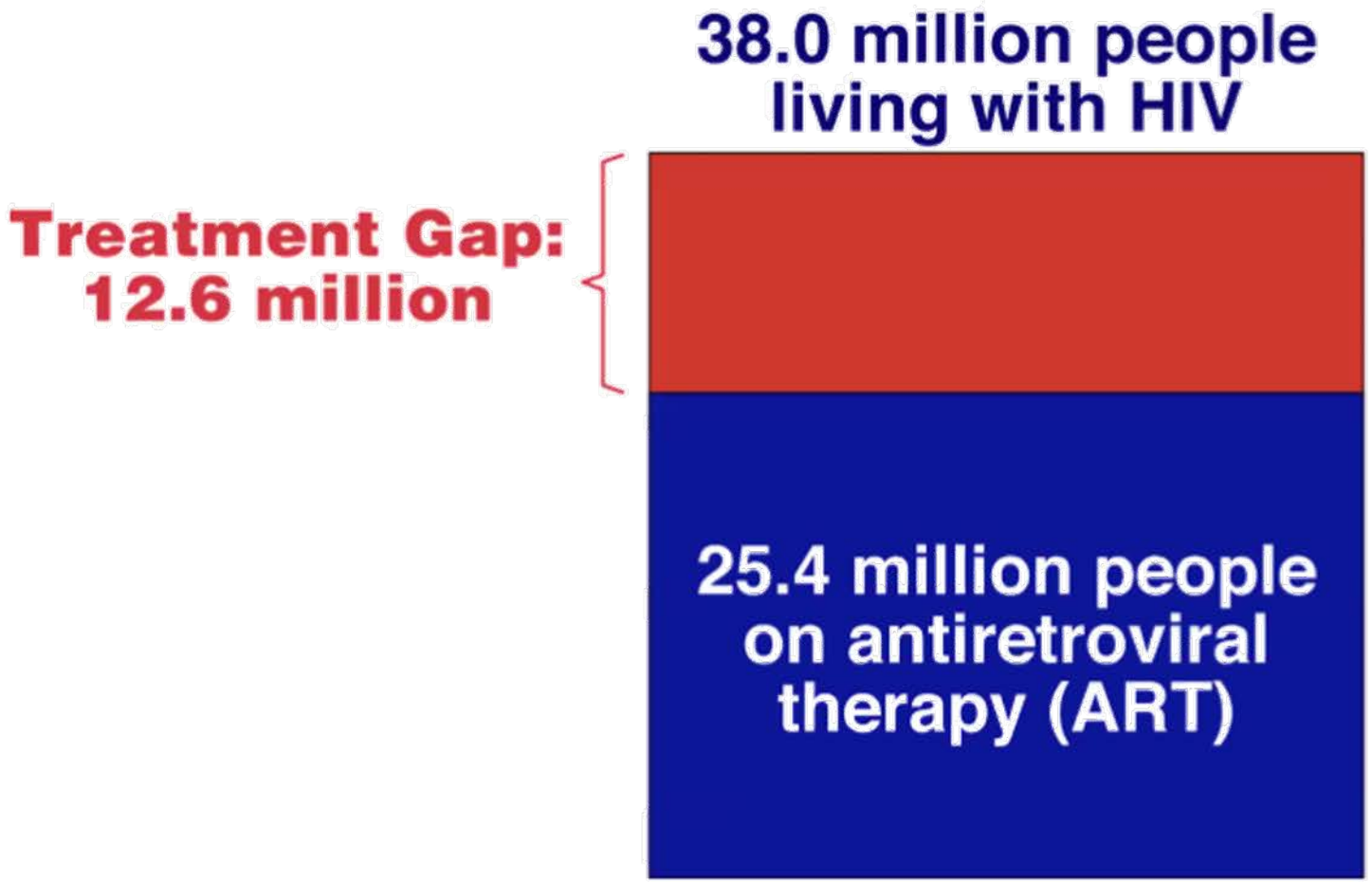
What Kind of Cure Do PWH Want?

- Safe
- Simple
- Affordable
- Scalable
- Complete
- Durable
- Prevents Transmission

  (ideally both ways)

Why do we need a cure?

The Global HIV Treatment Gap



Source: UNAIDS, 7/2020.
Data for 2019.

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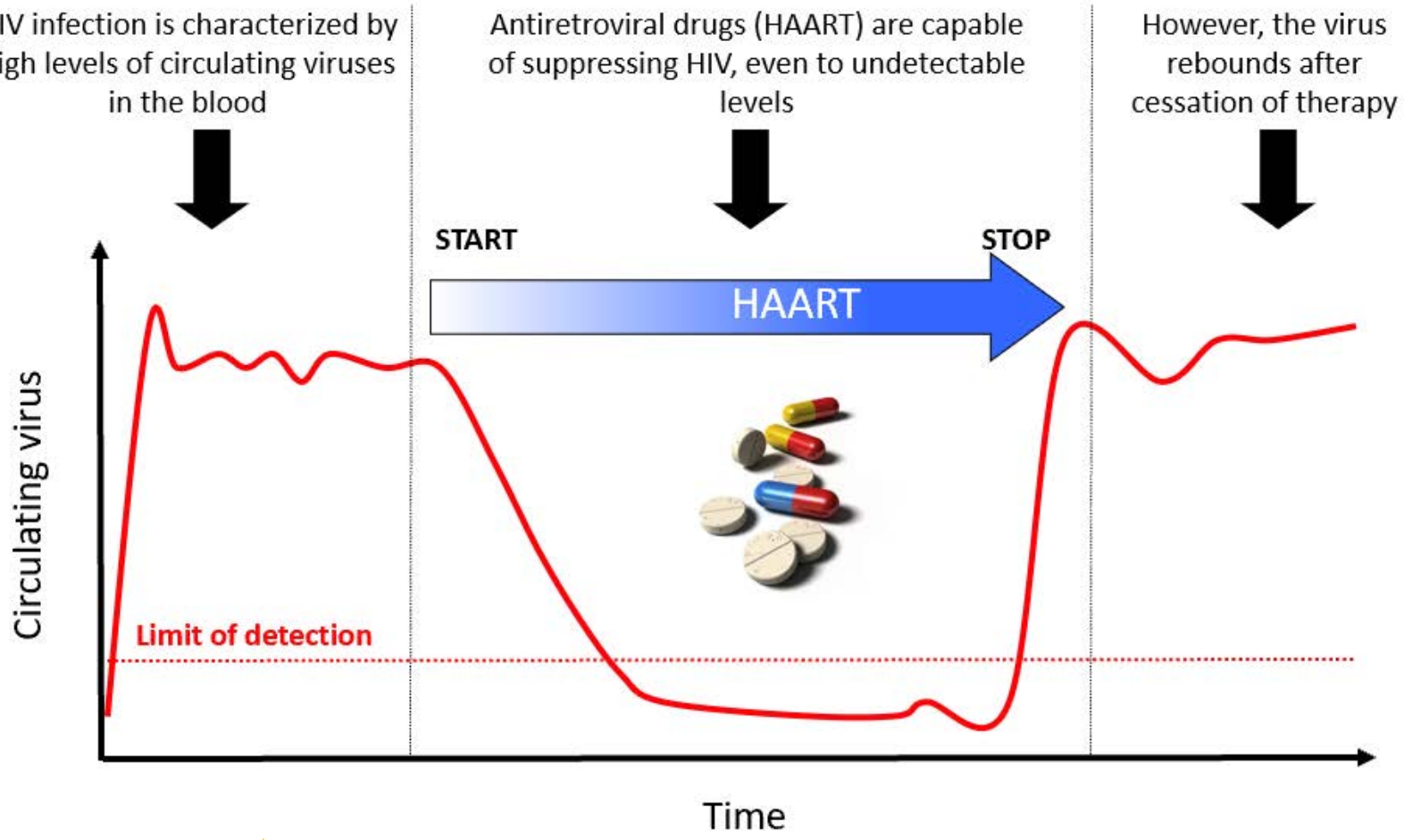
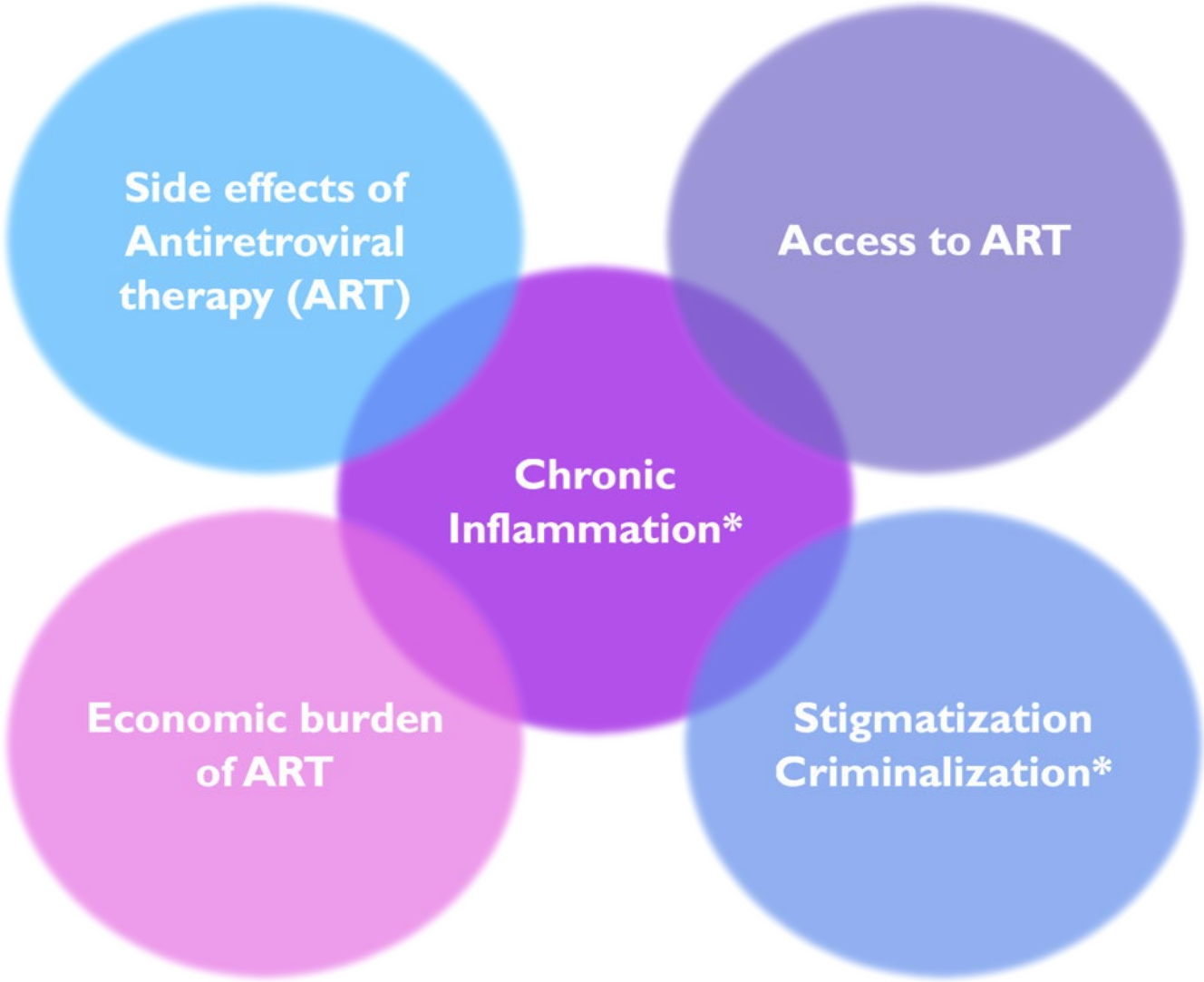
Sylla L et al. What would an HIV cure mean to you? Ascribing meaning through an HIV cure tree. Poster abstract WEPEC1047, IAS 2017.

Current anti-HIV drugs do not eliminate HIV

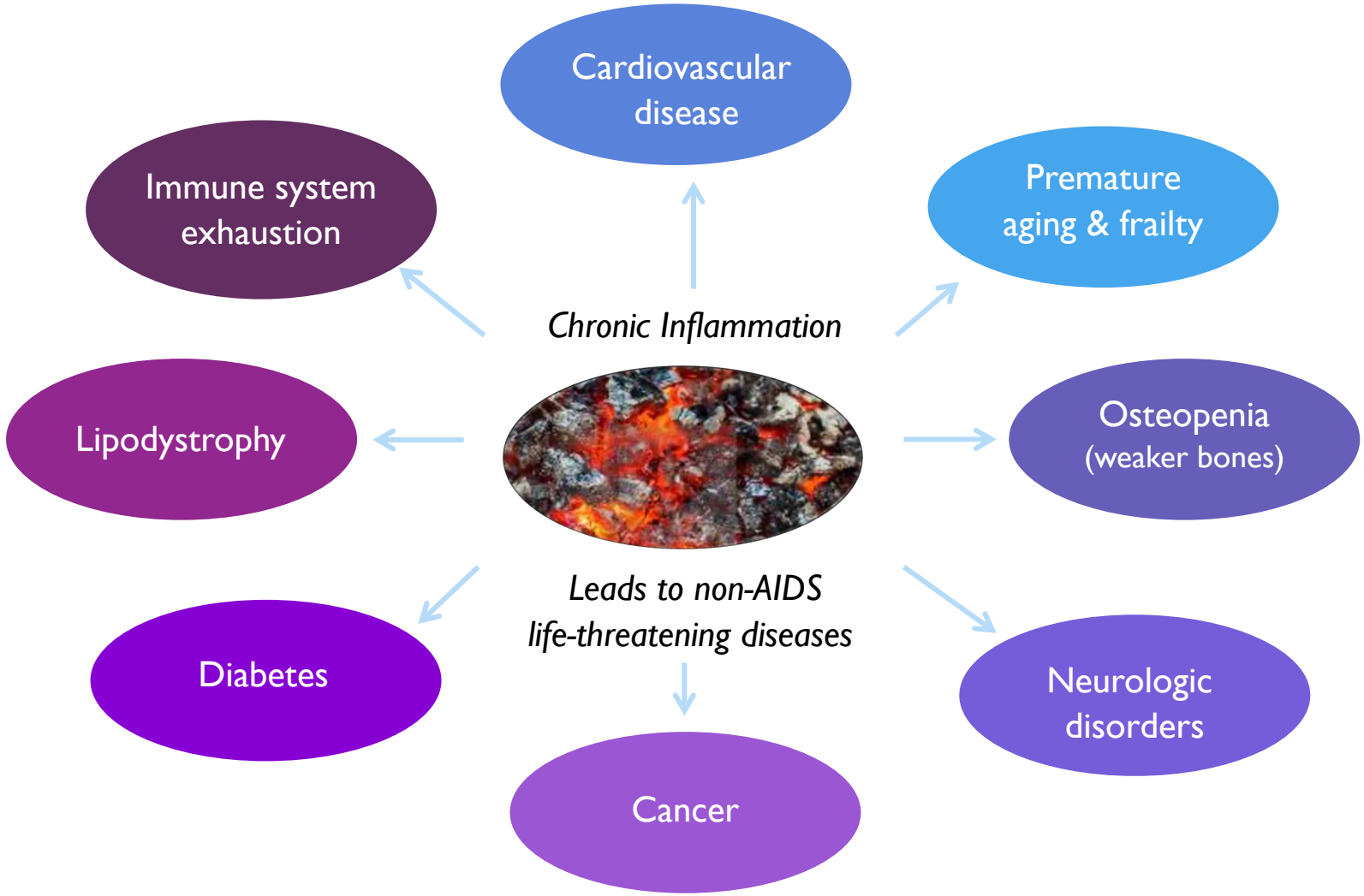


HIV hides in places that are not sensitive to current therapies

Why Do We Need an HIV Cure?



Why Do We Need an HIV Cure?



Inspired from: https://www.cryophiladelphia.com/what-is-chronic-inflammation-how-can-it-damage-your-body/

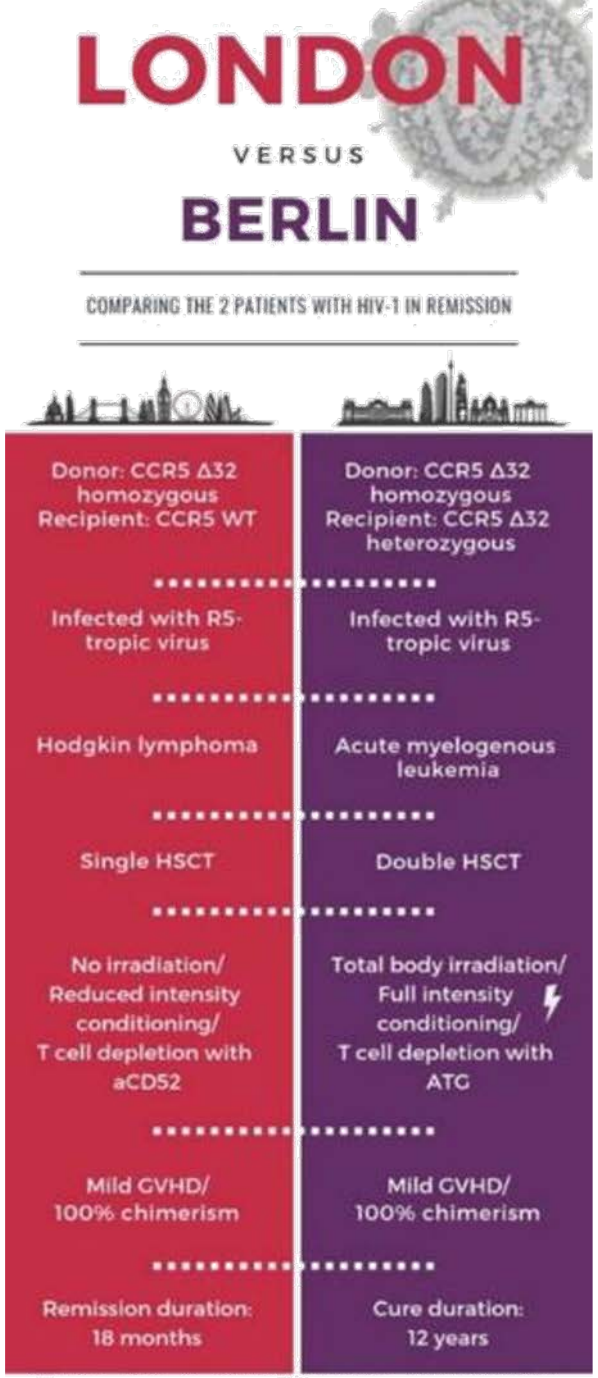
Why do we think a cure for HIV is possible?

Introduction

Why We Believe a Cure Might be Possible

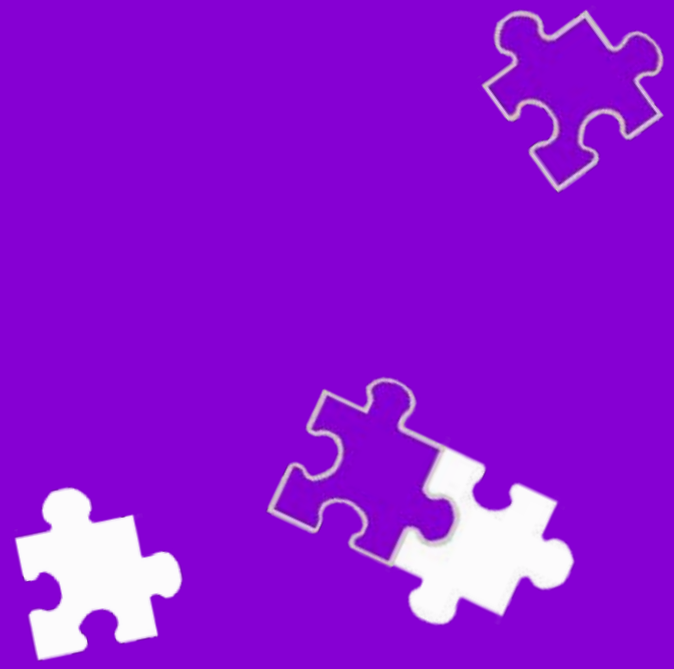
Timothy Ray Brown
"The Berlin Patient"
March 11, 1966 – September 29, 2020

Adam Castillejo
"The London Patient"

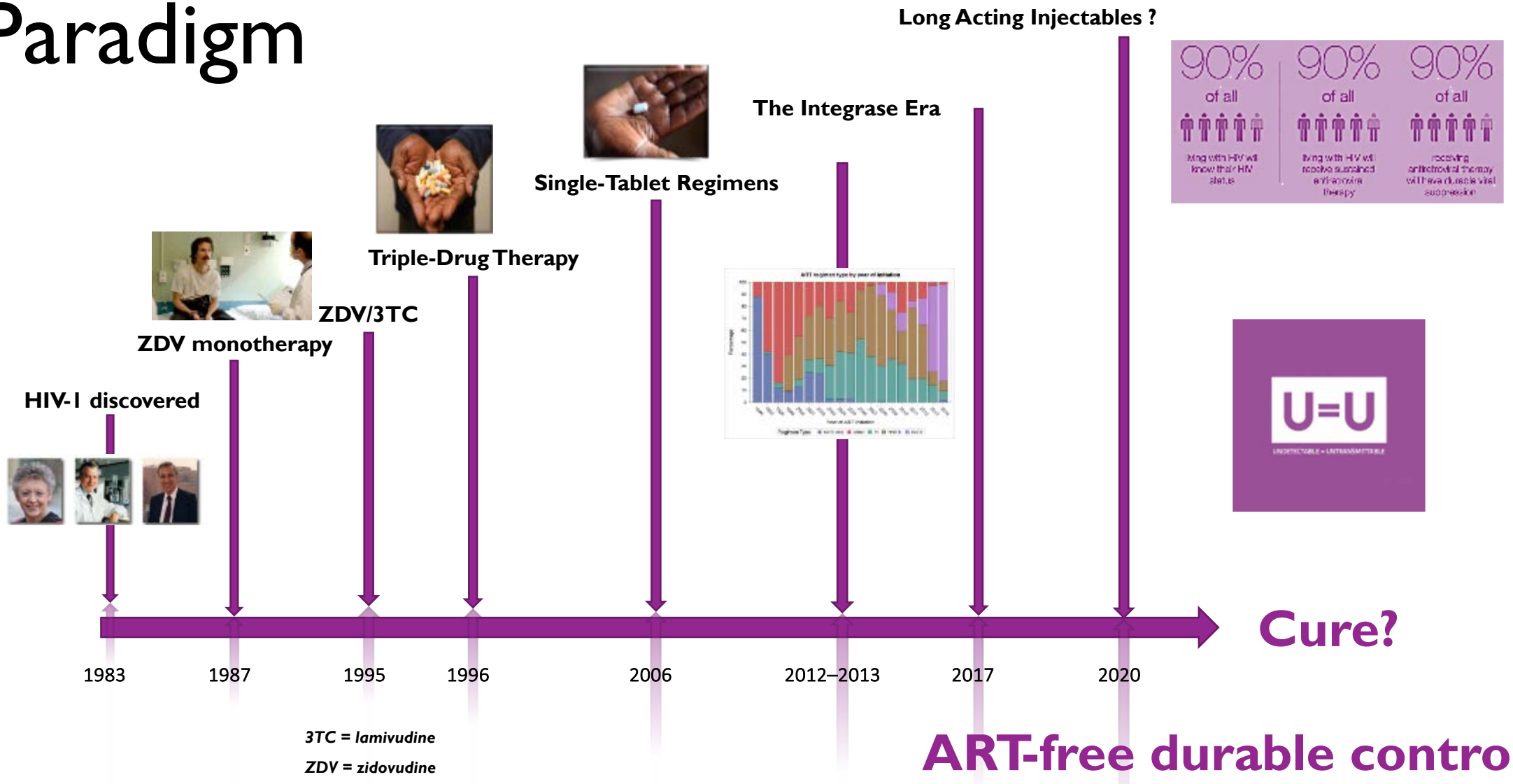


Adapted from Gupta et al. CROI 2019, Seattle, WA.
Infographic: @taliaswartz

What is the pathway to an HIV cure?



Evolving HIV Treatment Paradigm



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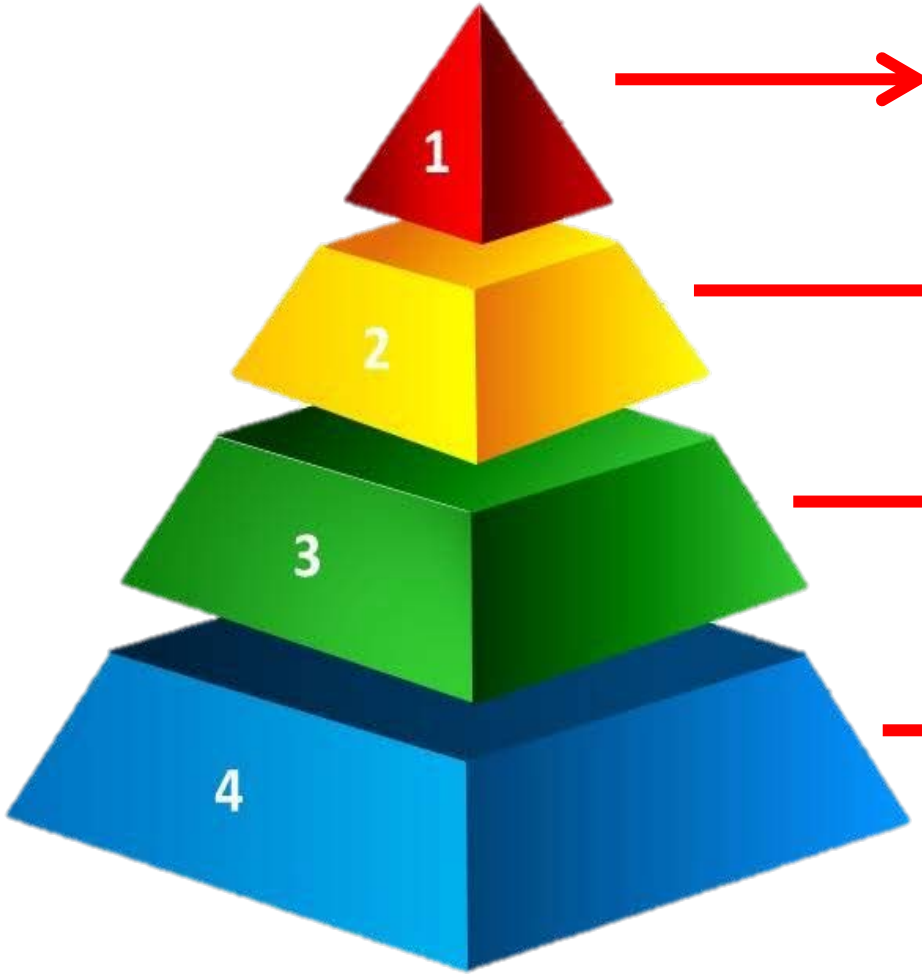
Stages of Clinical Research

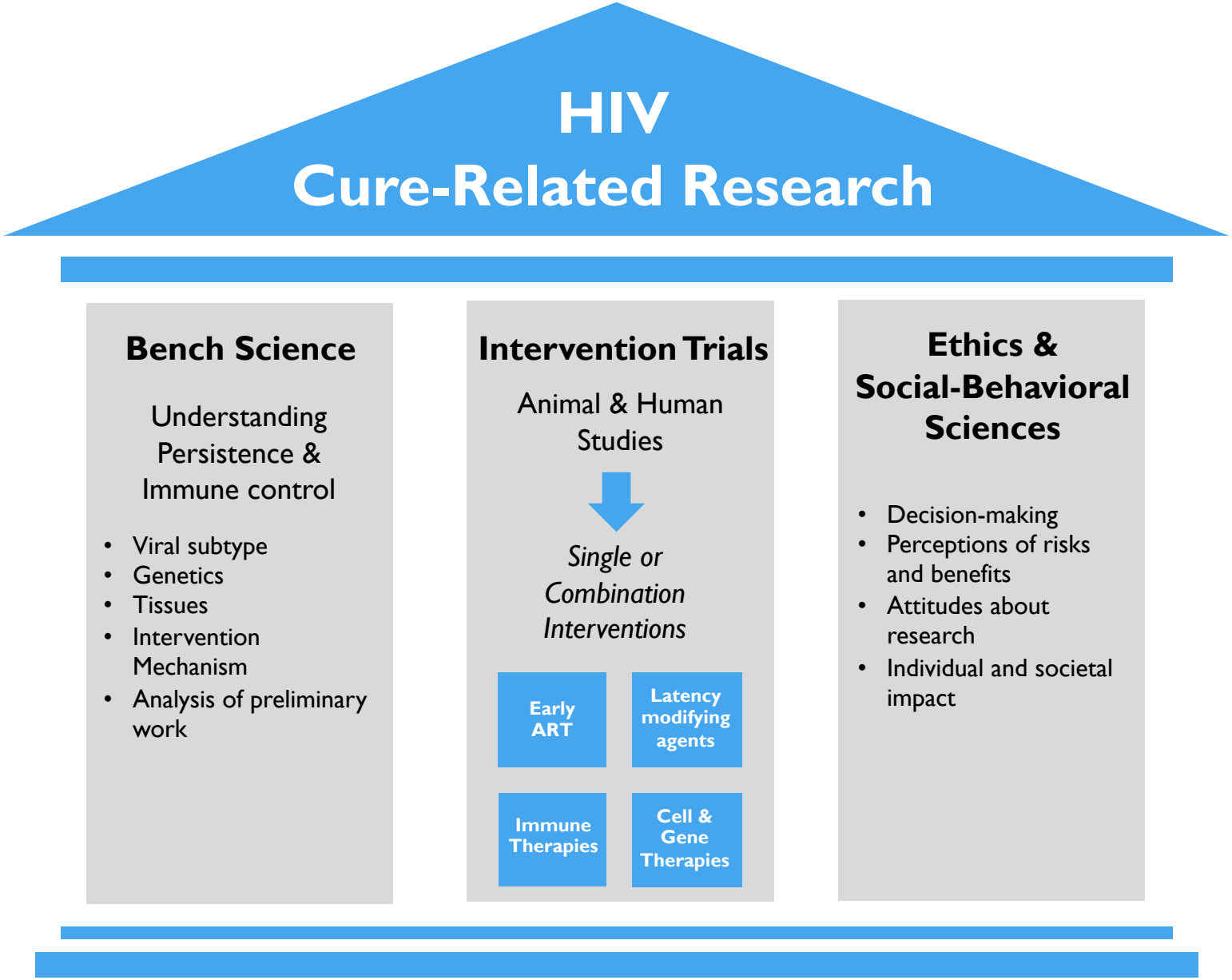


Studies with cells in culture.

Studies in animal models.

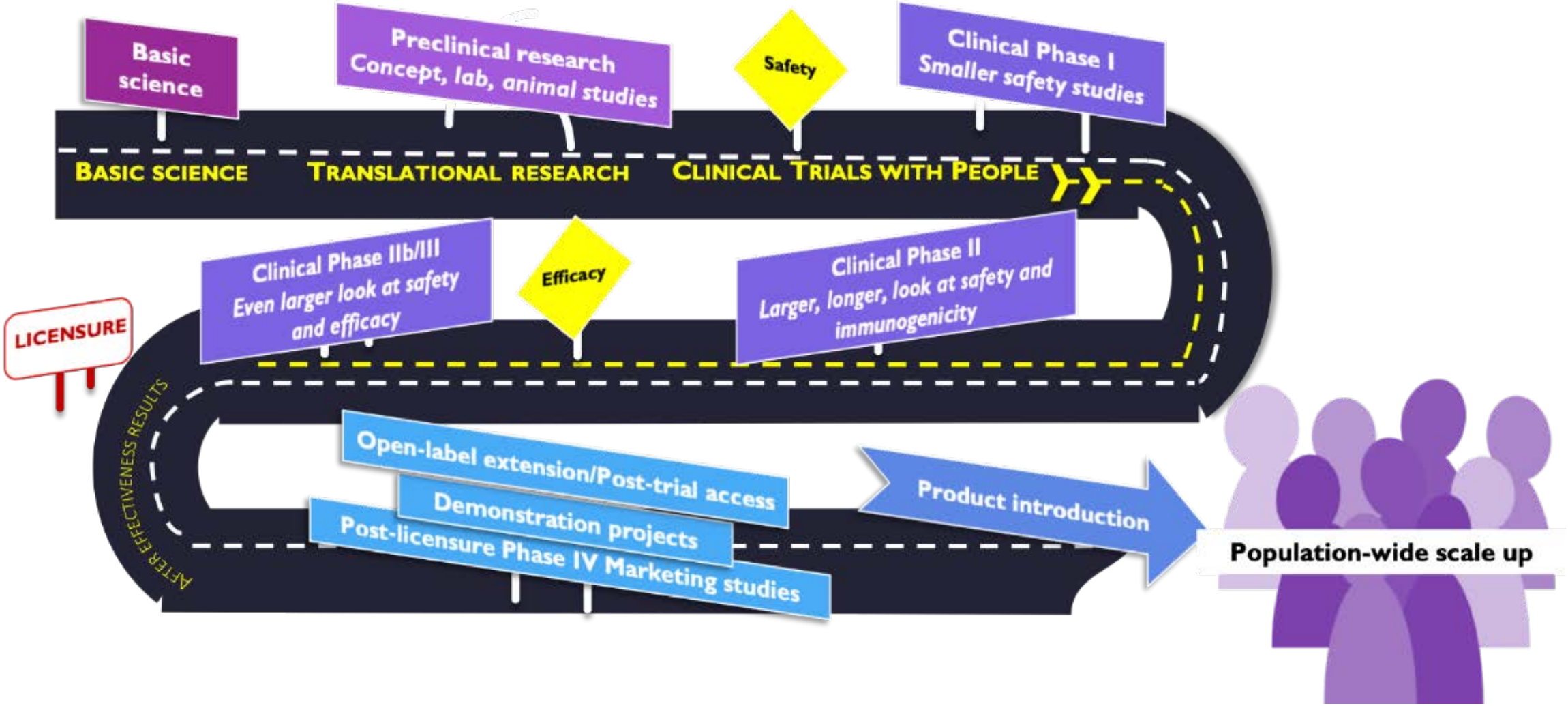
Clinical studies looking at safety.

Larger clinical studies looking at efficacy.



Adapted from Jintanat Ananworanich, Community HIV Cure Workshop, AIDS 2018

Overview of Research Process



Courtesy of AVAC

Antiretroviral Treatment Interruptions (ATIs) to evaluate cure interventions

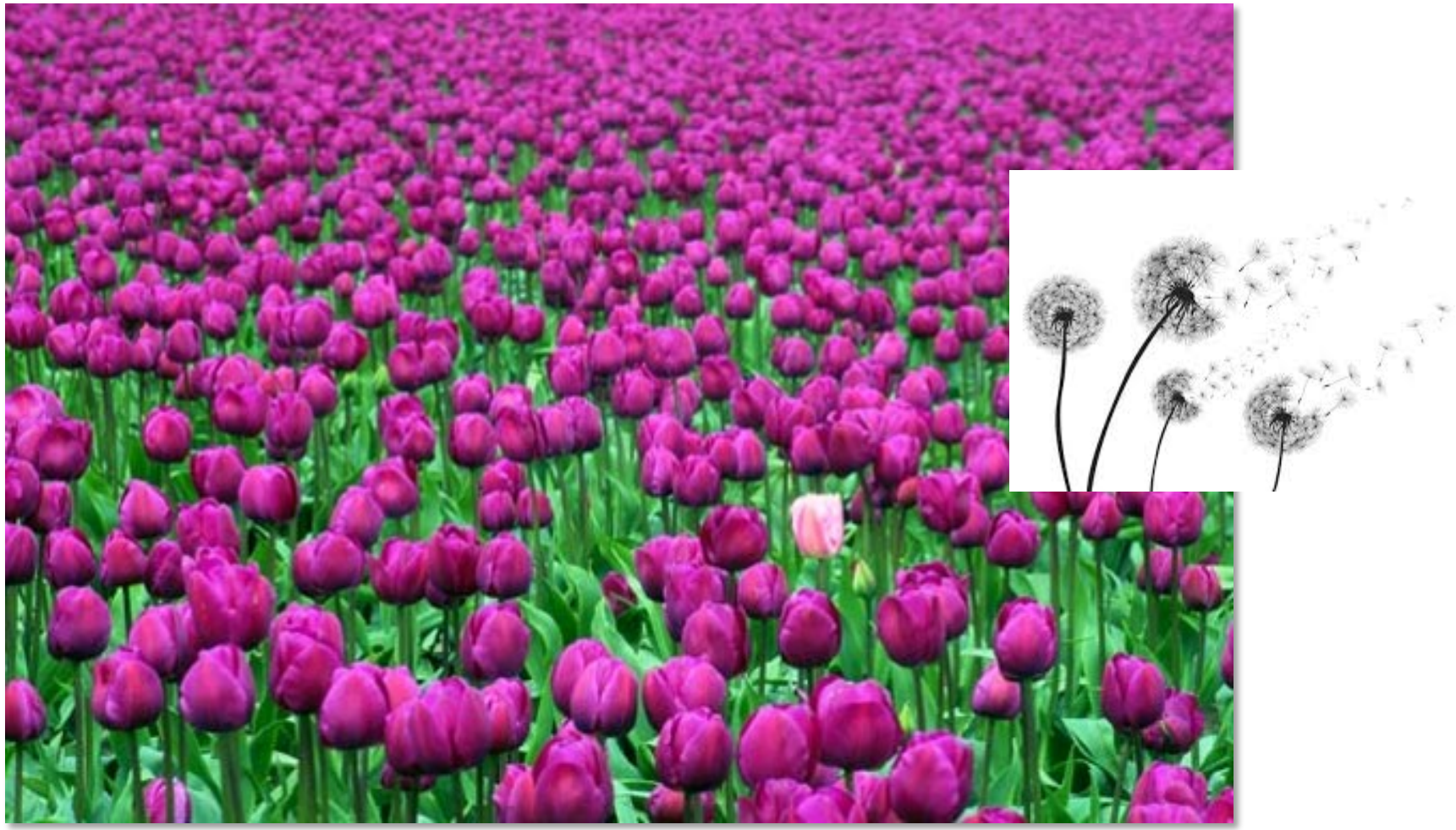
temporarily interrupting or pausing ART in someone who has HIV

Image credit: Michael Louella

- **Other terms:**
  - Structured treatment interruptions (STI)
  - Intensively Monitored Antiretroviral Pause (IMAP)
- **Why pause ART?**
  - We cannot easily measure the HIV reservoir
  - We need to "jump start" the immune system

Why is it difficult to cure HIV?

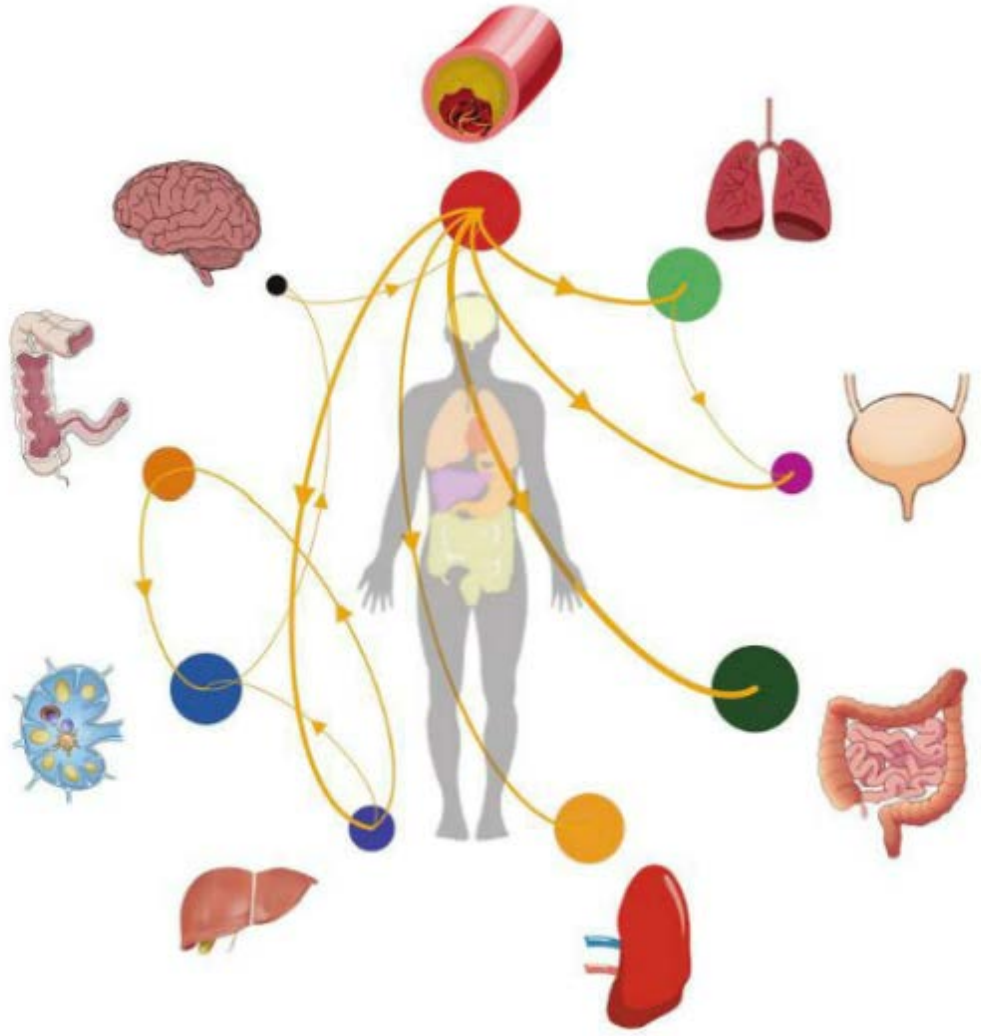
Why is HIV so hard to cure?



So few cells harbor HIV in people on antivirals medications and these cells appear normal to our immune system.

Where is the HIV Reservoir?

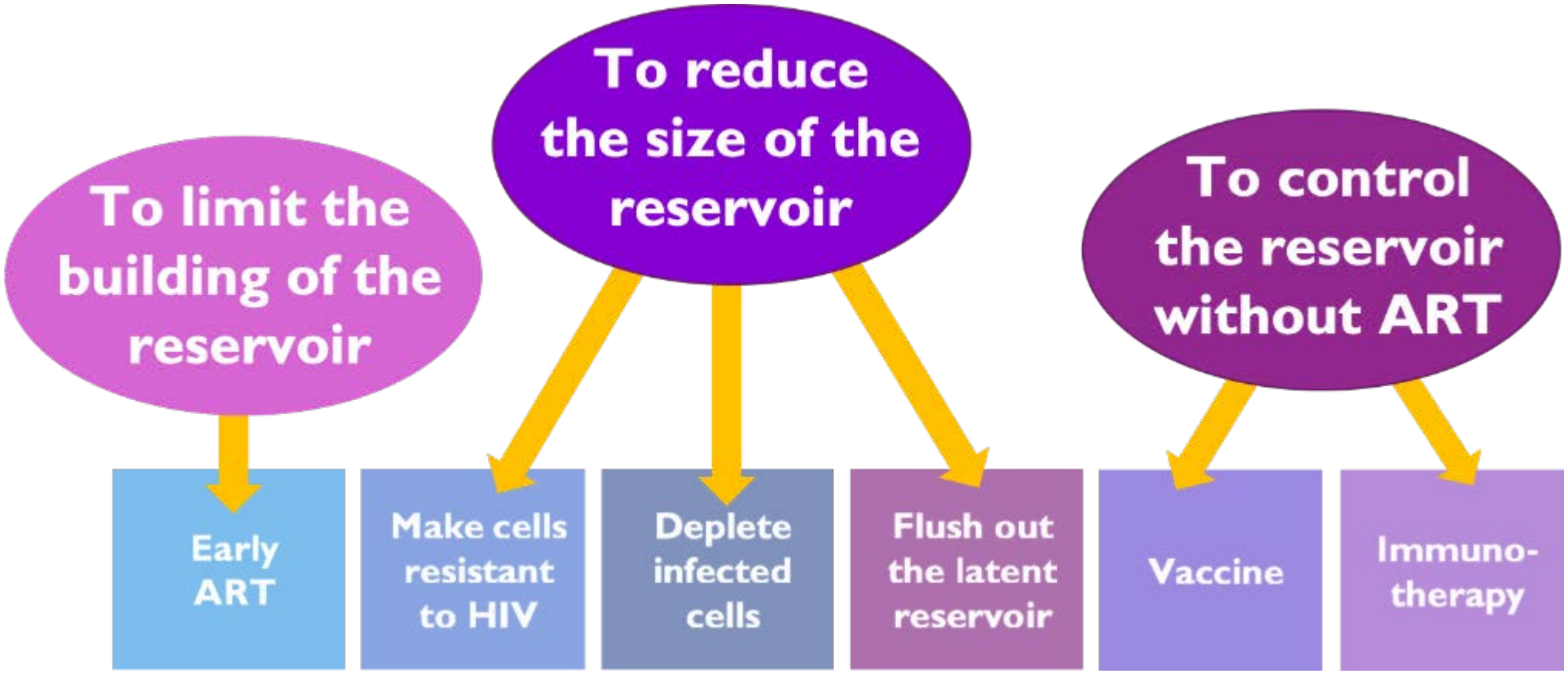
- Brain
- Lymph nodes
- Peripheral blood
- Gut
- Bone marrow
- Genital tract



Chaillon A, Gianella S, Dellicour S, Rawlings SA, Schlug TE, De Oliveira MF, et al. HIV Persists Throughout Deep Tissues with Repopulation from Multiple Anatomical Compartments. *Journal of Clinical Investigation* 2020.

What pathways are currently being explored?

HIV Cure-Related Research Strategies Under Investigation



Slide Credit: Nicolas Chomont

Latency Reversing Agents

Image credit: The Economist, July 11

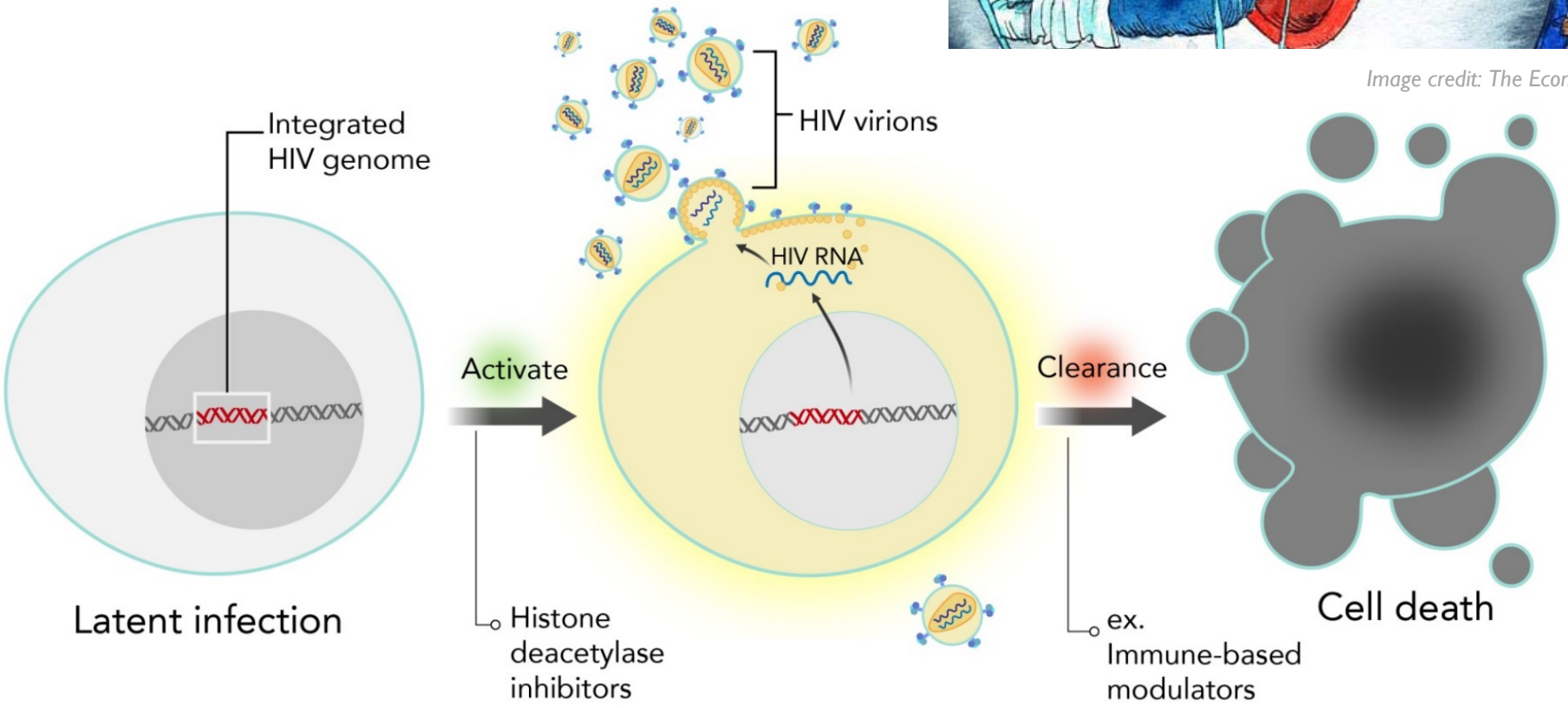
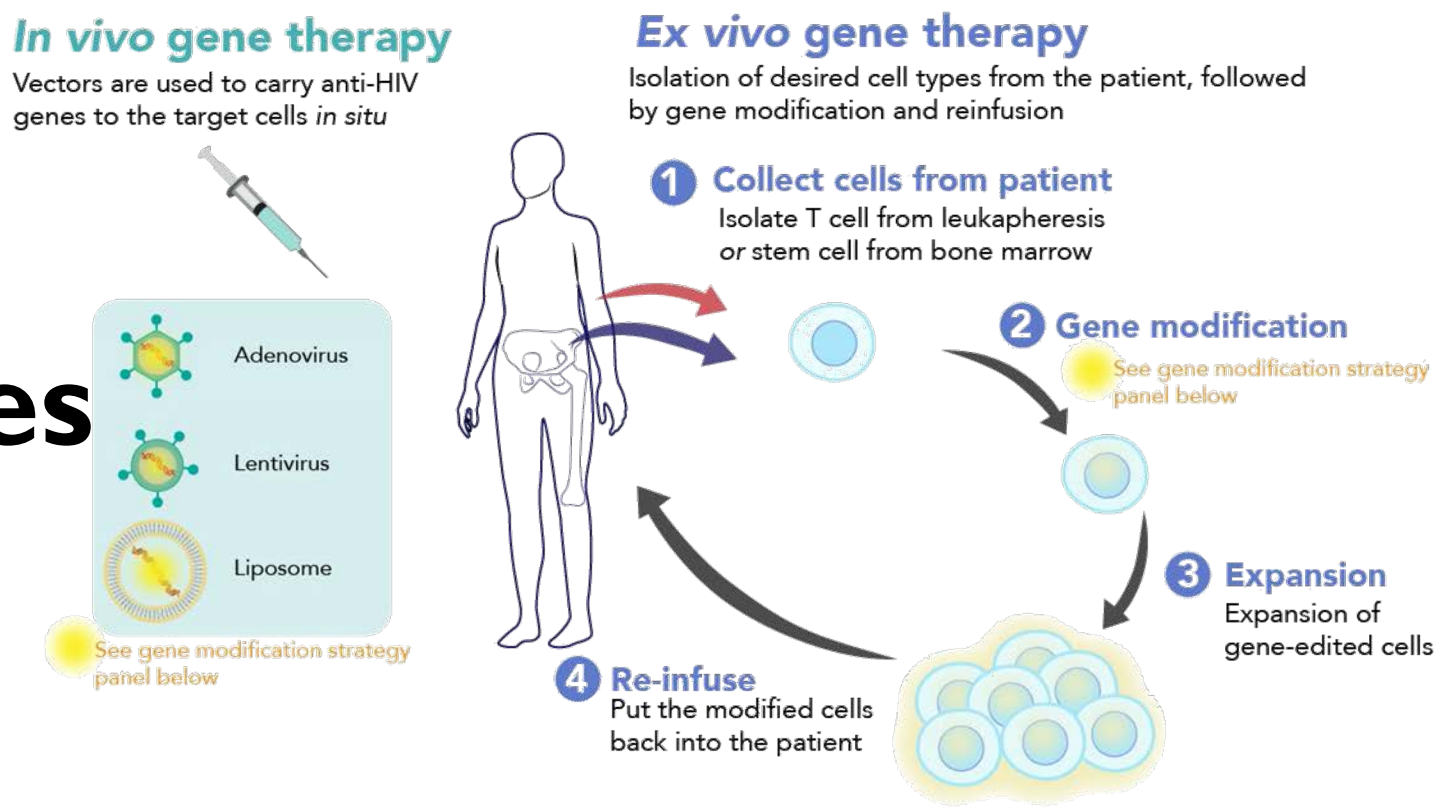
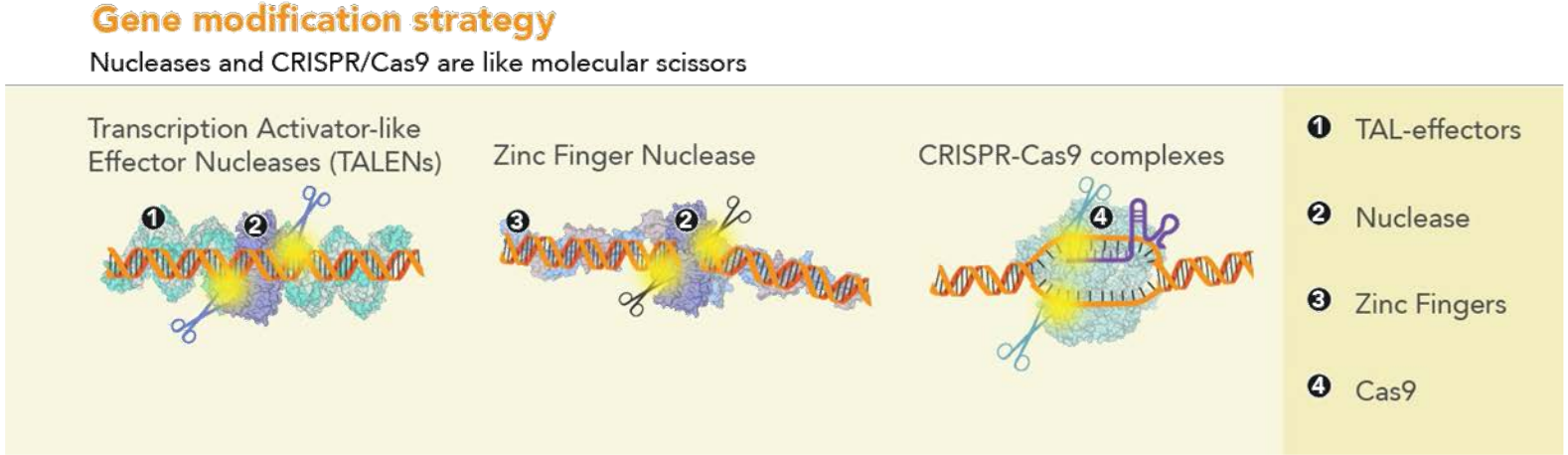


Illustration Credit: Grace Hsu, MS, CMI, Scientific Animation, Animation Lab: https://animationlab.utah.edu/

Cell & Gene Approaches





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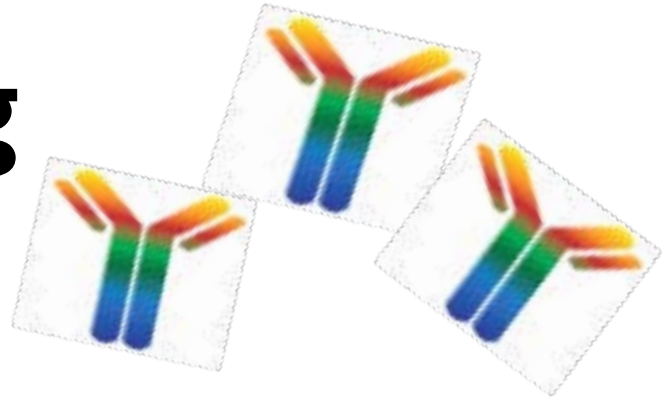
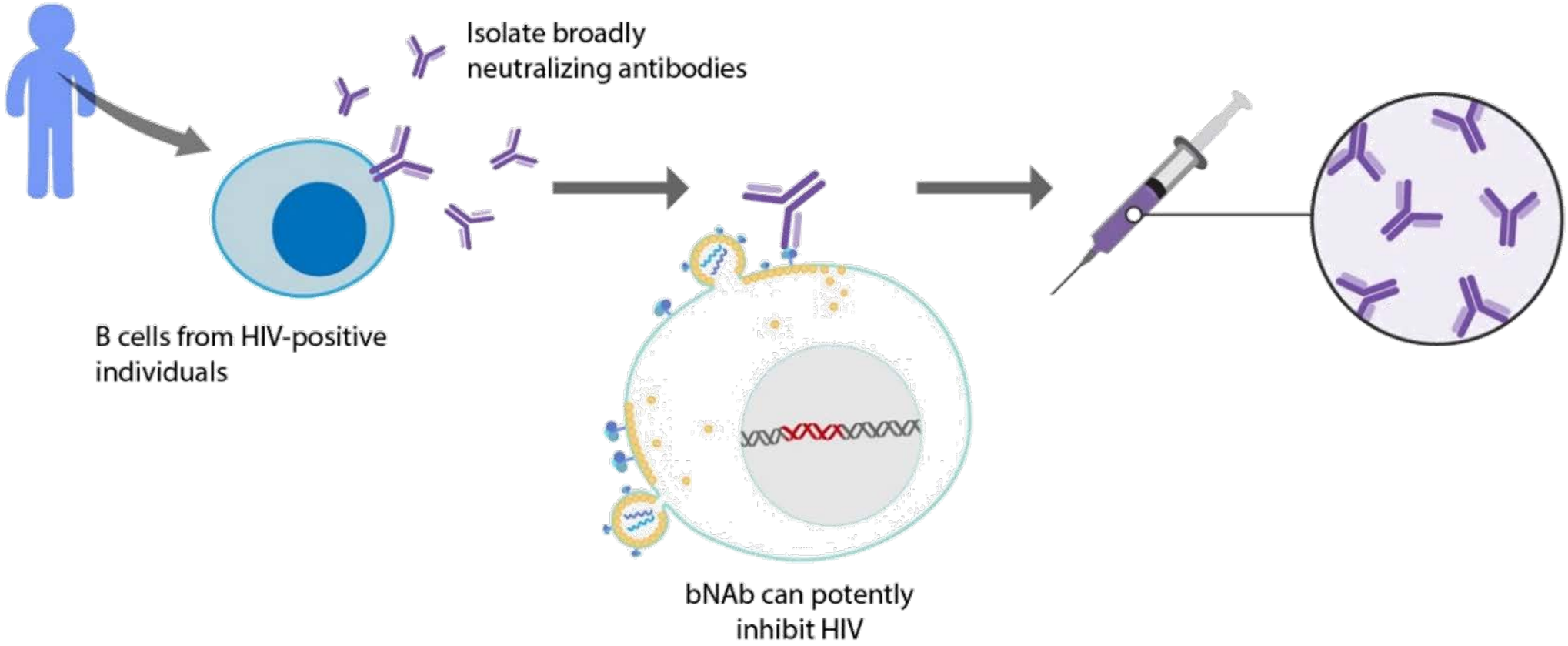
Broadly Neutralizing Antibodies





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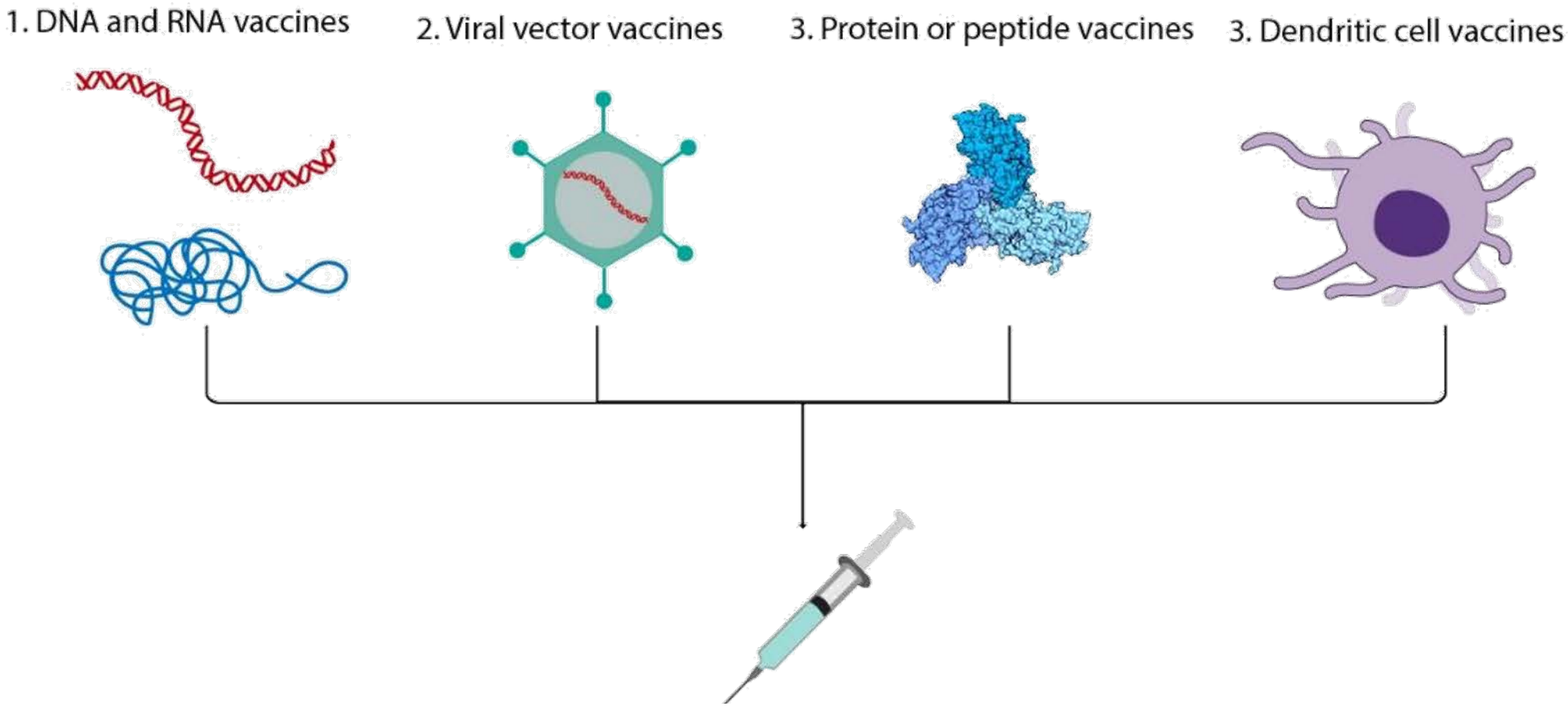
Immune-Based Strategies



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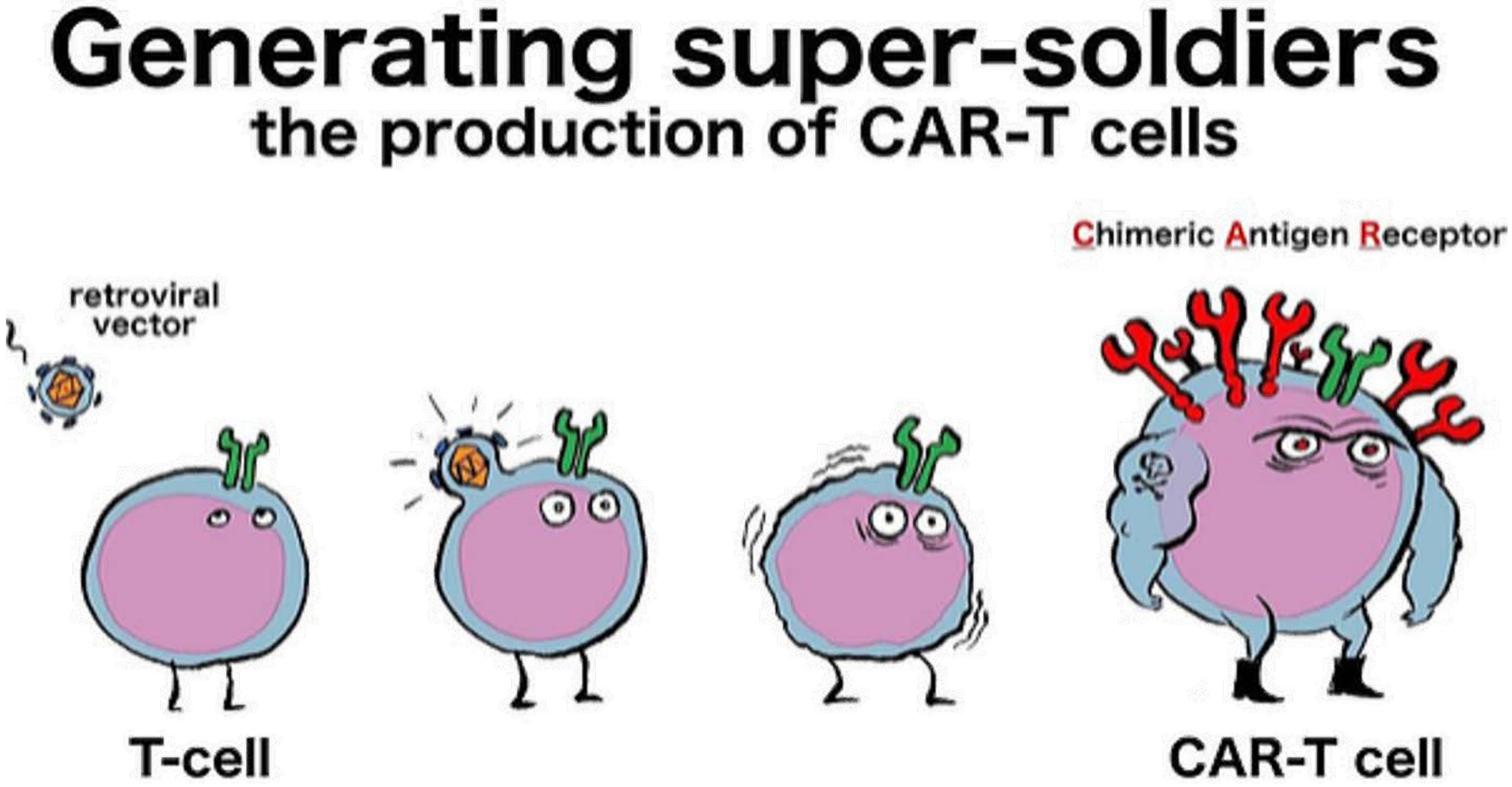
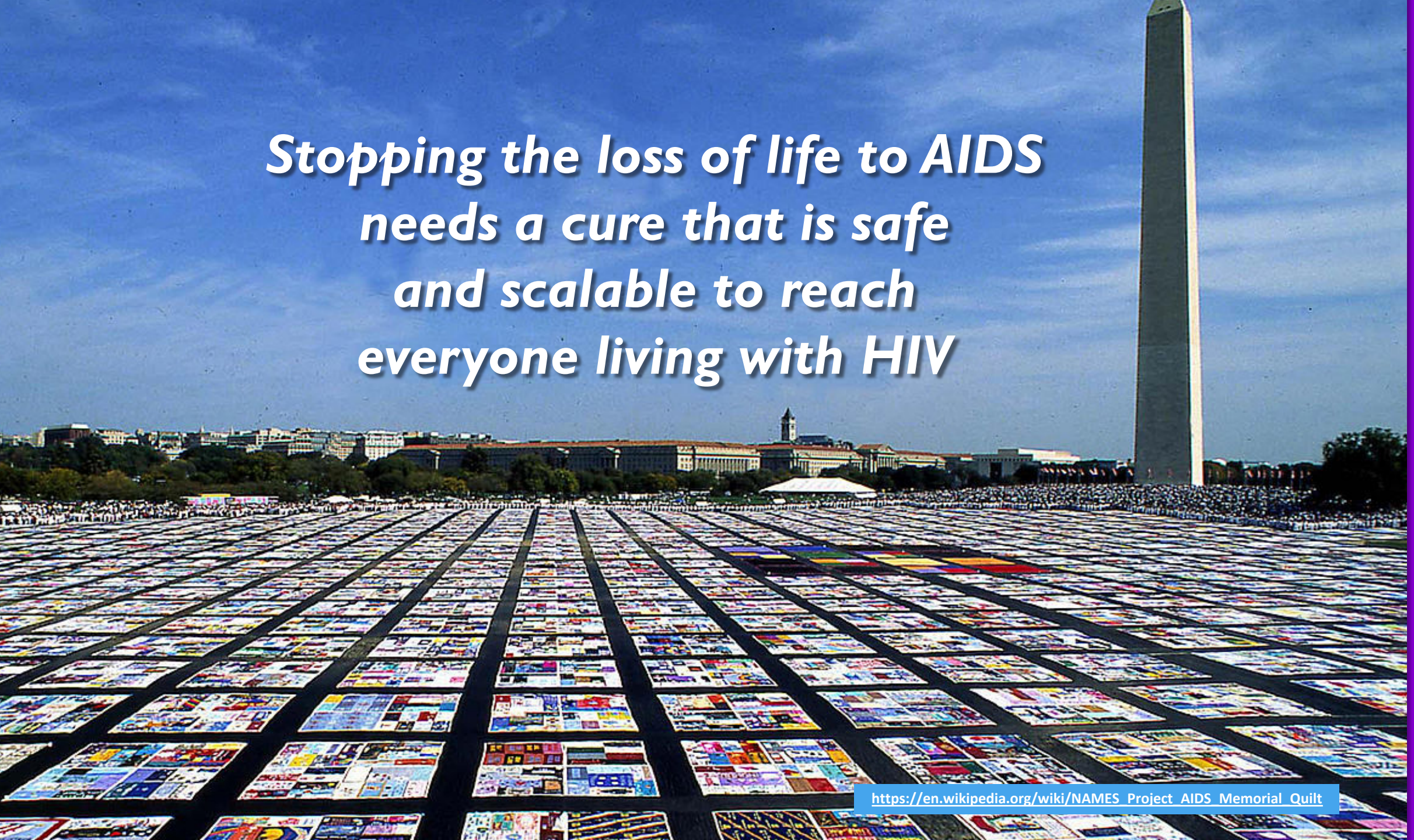
Chimeric Antigen Recptor - T cells (CAR-T cell)



https://blog.seracare.com/ngs/aacr-2019-day-one-highlights-next-generation-car-t-cells?utm_medium=social&utm_source=facebook

Ethical Challenges to HIV Cure-Related Research

- Language of HIV cure-related research
- Participation of people living with HIV
  - Informed consent
  - Background standard of care and U = U
    - Biological and social context of HIV cure-related research
  - Risks and benefit
  - Representation in research
- ATIs and partner protections
- Scalability of interventions
- Access and affordability
- Structural inequities


Stopping the loss of life to AIDS
needs a cure that is safe
and scalable to reach
everyone living with HIV
https://en.wikipedia.org/wiki/NAMES_Project_AIDS_Memorial_Quilt

ACKNOWLEDGMENTS

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Their caring support of the CUREiculum 2.0. will make a difference in the lives of thousands of people living with HIV

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