The Basics of HIV Cure Research

HIV Cure Research Training Curriculum

HIV and Cure Basics Module Presented by:

May 2016

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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

Describe:

- Different ways to conceptualize an HIV cure
- Why it is difficult to cure HIV
- Rationale for exploring a cure
- Current cure strategies being researched

What Does

HIV Cure Mean?

What Does HIV Cure Mean?

- No need for on-going medication (ARV treatment)
- No symptoms
- No viral progression/immune damage
- No risk of transmission

The Language of “Cure”

- **Sterilizing/Eradication-**
  - HIV is completely removed from every cell in the body
  - Person is HIV-free (virus free)

- **Functional/Remission-**
  - HIV is NOT completely gone from the body
  - All requirements from previous slide met
  - HIV has potential to resurface.

Why is an HIV Cure Important?

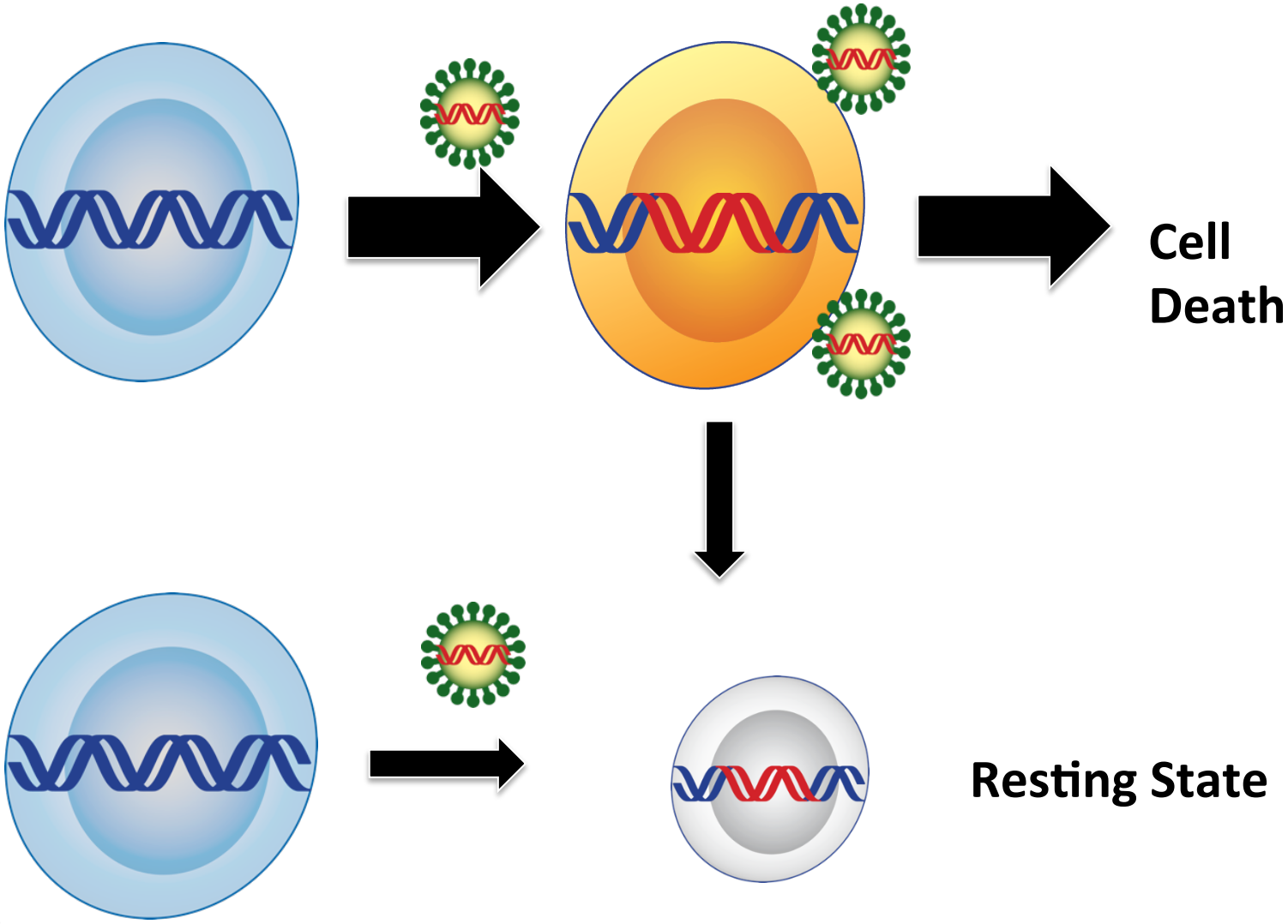
- Disparity of access to care/HIV treatment globally
- Medication burden
- Medication side effects
- Expense

Why is HIV so Hard to Cure?

Why is HIV so Hard to Cure?

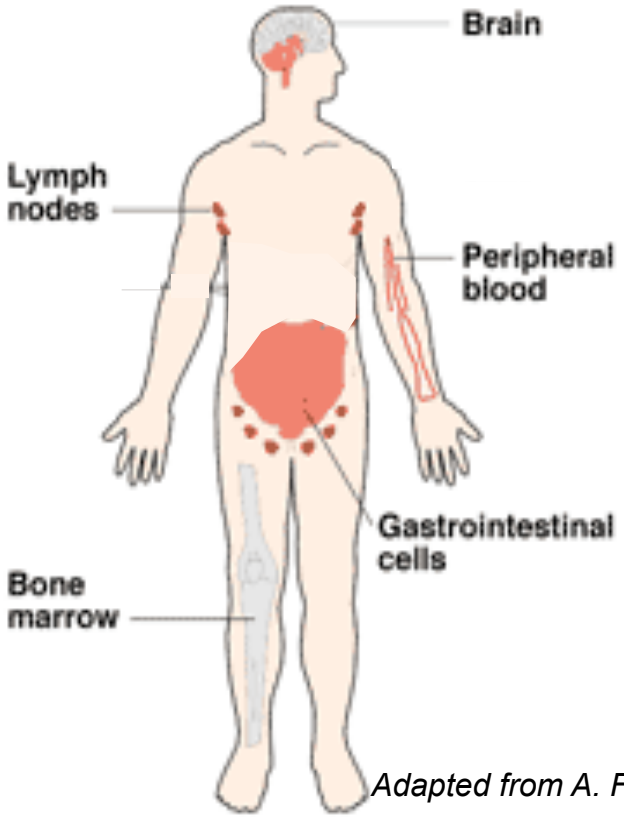
- HIV enters a cell and integrates into the cell's DNA
- **Most** cells recognize infection- causing cell death
- **A few** infected cells become "long-lived" memory cells or "resting memory" cells
- The collection of long-lived memory cells is called the **Latent Reservoir**

Establishing the Latent Reservoir



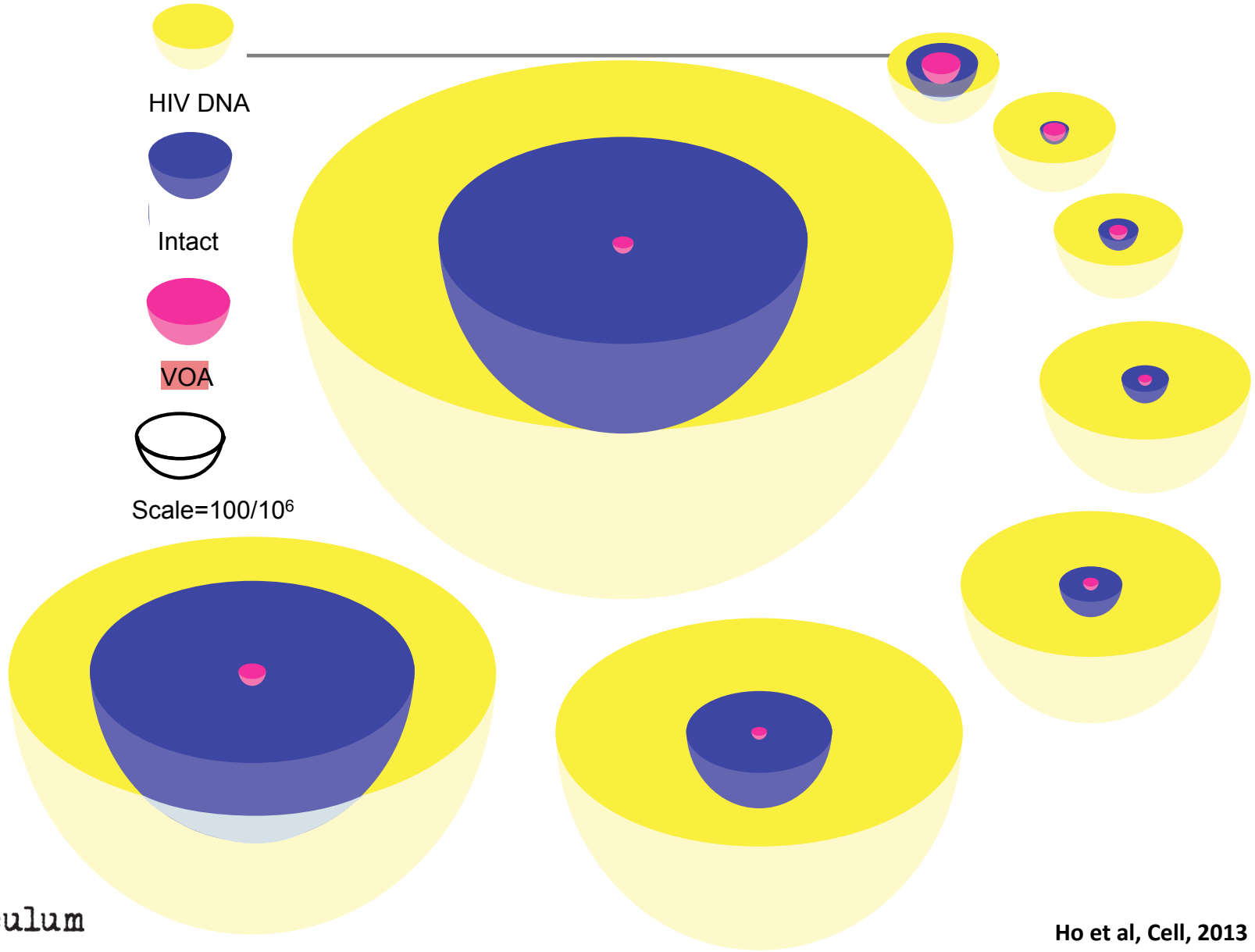
Where is the HIV Reservoir?

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



Adapted from A. Fauci

How Can the Reservoir be Measured?



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Ho et al, Cell, 2013

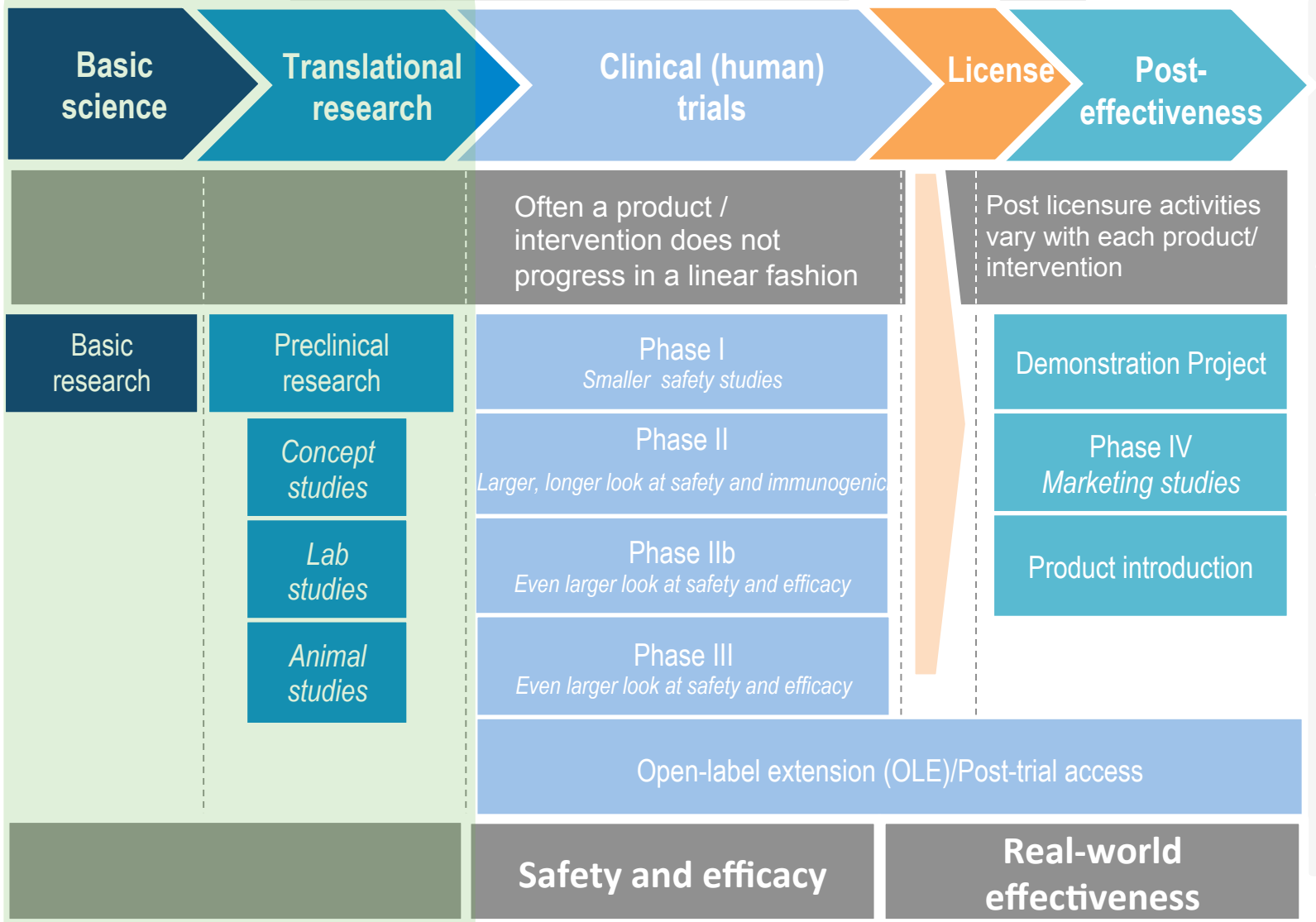
HIV Cure: Proof of Concept

- HIV+ Acute Myeloid Leukemia Patient
- Identification of HLA-identical, CCR5Δ32 homozygous bone marrow donor
- Chemo- and Radiotherapy Conditioning
- Allogeneic stem cell transplant
- 10 years later: remains cured

New Hope of a Cure for H.I.V.

Heidi Schumann for The New York Times

What are the Research Stages?



Current Strategies

Kick and Kill

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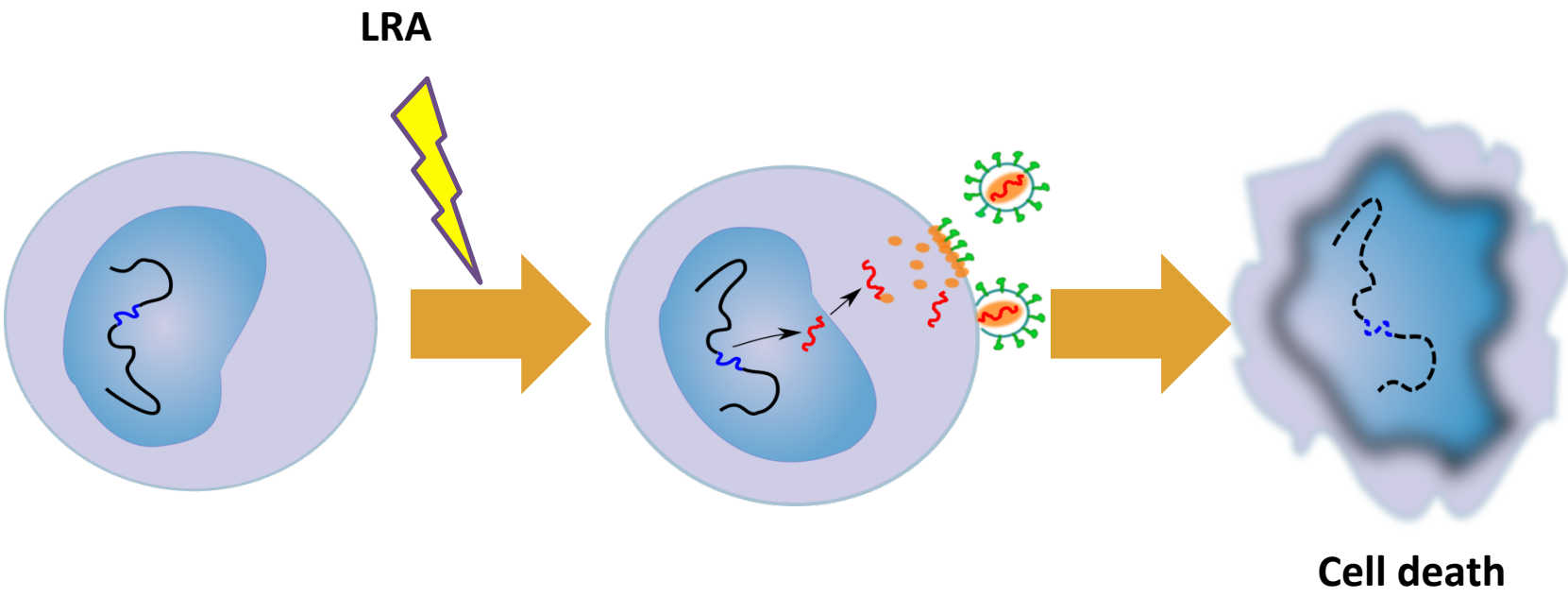
The Economist, July 17, 2011

What is kick and kill?



Latency Reversing Agents

- A category of drugs that stimulate HIV-positive long-lived memory cells to begin producing virus
- **HDAC Inhibitors**- Histone Deacetylase Inhibitors have been one of the class of drugs being pursued in the field

Notable LRAs

- TLR7- Agonist
- Bromodomains
- Ingenol

Current Challenges of Kick and Kill

- Measurement of reservoir size/Getting it all
- New reservoirs
- Medication side effects

What are Immune Modulators?

- Harness the innate and adaptive immune system to better recognize and/or fight HIV
- All immune modulators would likely need to be used in combination with each other or other approaches

Innate immunity- No specific response; first line of defense like skin

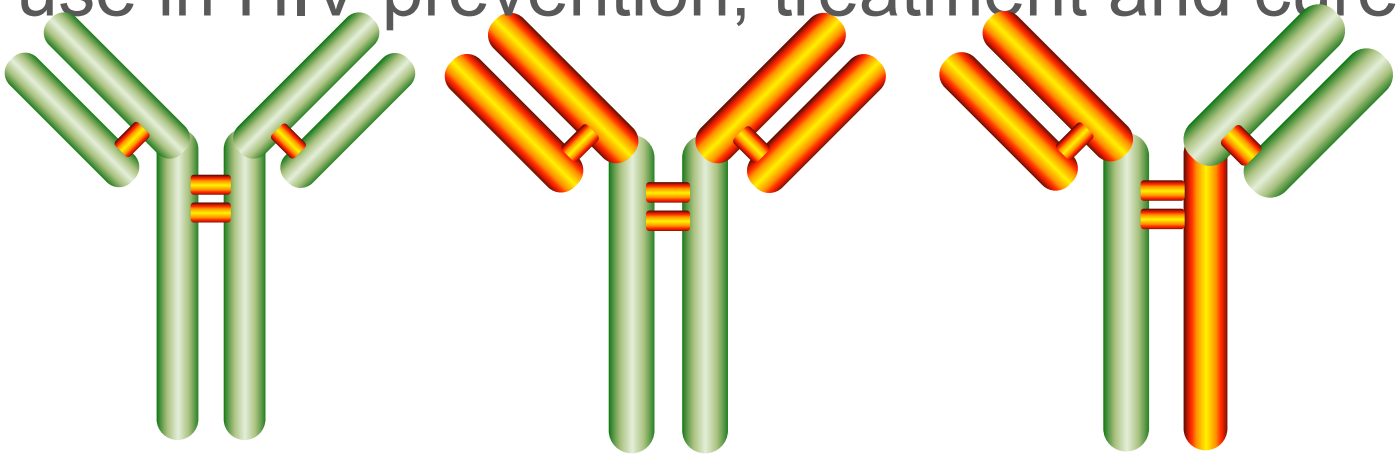
Adaptive immunity- Targeted responses to specific pathogens- creating a whole army dedicated to attacking one enemy

Therapeutic Vaccines

- **Rationale: Strengthen or create new and more effective immune responses to HIV in people living with HIV**
- Generate long-lived adaptive immune responses to HIV that can continue to control the virus without medication

Broadly Neutralizing Antibodies

- Broadly Neutralizing Antibodies (bNAbs) are able to make many different mutations of HIV harmless by binding to 1 of 3 places on HIV
- bNAbs are currently being explored for use in HIV prevention, treatment and cure



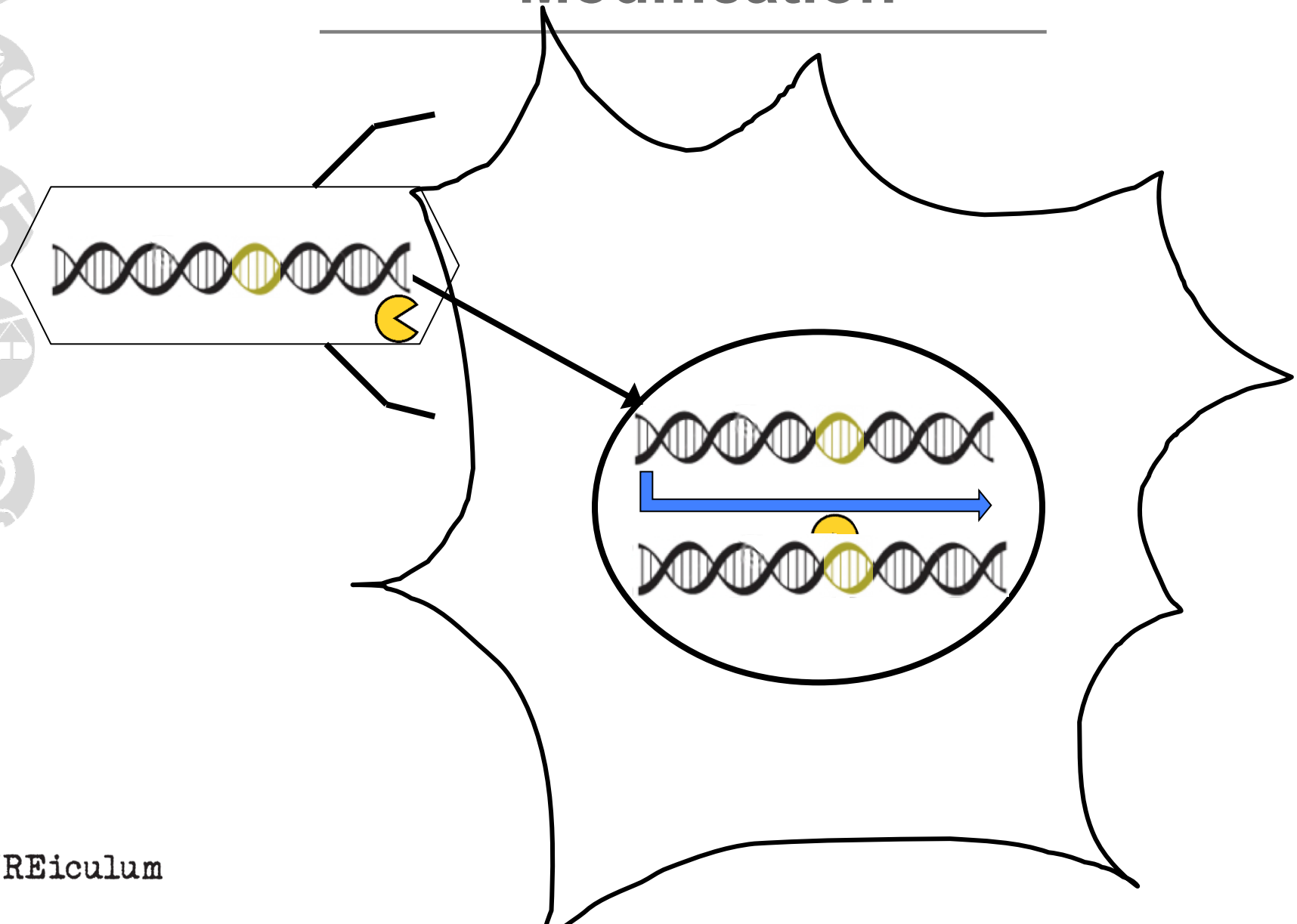
Current Challenges of Immune Modulation

- There is a potential for therapeutic misconception- people thinking there is a benefit where there is none
- Complex regulatory issues because each vaccine component will need to be evaluated separately and in combination
- Animal models do not always translate to humans
- Proving that strict immune control of HIV is clinically equivalent or better than ART

What is Gene Alteration/ Modification?

- A process to edit the DNA inside immune cells in some way to make the cell less susceptible to HIV
- A process to edit the DNA inside immune cells to increase the killing potential of the cells
- A process to edit the DNA inside the virus to reduce it's ability to impact people

What is Gene Alteration/ Modification



What Are the Social & Ethical Challenges

- Balancing resources
- Risk versus reward
- Participant selection
- Trial design
- Cost
- Scalability

What Does an HIV Cure Need to be?

- Safe
- Effective
- Durable
- Affordable
- Accessible

Questions

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

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