Martin Delaney Collaboratories for HIV Cure Research 3.0

Investment and Engagement in HIV Cure Research: Looking Ahead

October 27, 2021

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Division of AIDS, NIAID
Reasons Why We Need Optimized Treatments and a Cure for HIV Infection

- It is likely not economically nor logistically feasible to deliver daily antiretroviral therapy (ART) to >37 million people with HIV for their entire lives.

- Challenges of adherence, retention in care, and negotiating the HIV “care continuum”

- Drug resistance, cumulative toxicities, and stigma associated with daily ART
NIAID HIV/AIDS Funding

Fiscal Year

Dollars in billions

HIV Cure-Related Publications in PubMed, 2000 and 2020

HIV and Cure or Remission

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of papers</th>
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<tbody>
<tr>
<td>2000</td>
<td>85</td>
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<tr>
<td>2020</td>
<td>546</td>
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HIV and Reservoir or Latency

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<th>Year</th>
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<tr>
<td>2000</td>
<td>131</td>
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<td>2020</td>
<td>544</td>
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92 interventional trials and 38 observational studies (TAG data as of July 2021)

Approaches include:
- adoptive immunotherapy
- antibodies
- antiretroviral therapy
- broadly neutralizing antibodies
- combinations
- cytokines
- DART molecules
- gene therapy
- immune checkpoint inhibitors
- latency-reversing agents
- stem cell transplantation
- therapeutic vaccines
- treatment intensification/early treatment
- etc.
Stem Cell Transplantation as Proof-of-Concept for Eradication

- HIV-free 2007-2020

Adam Castillejo (a.k.a. “The London Patient”)
- HIV-free 2016-present
The Control of HIV After Antiretroviral Medication Pause (CHAMP) Study: Posttreatment Controllers Identified From 14 Clinical Studies

G Nomazi, JZ Li et al.

- 67 posttreatment controllers in 14 studies enrolling > 700 participants

- Posttreatment control more common in pts treated during early versus chronic infection (13% vs. 4%, P < .001)

- 55% maintained HIV control for 2 years; ~20% for ≥5 years.
Exceptional Elite Control as Proof-of-Concept for Sustained Virologic Remission

Loreen Willenberg (San Diego)
- Controlled HIV for 24 years with no ART
- No intact provirus in 1.5 billion PBMCs


“The Esperanza Patient” (Argentina)
- Controlled HIV for 14 years after stopping ART
- No intact provirus in 1.15 billion PBMCs

XG Yu. Abstract 57, CROI 2021
Martin Delaney Collaboratories for HIV Cure Research

- The flagship NIH program on HIV cure, spanning basic, applied, and clinical research
- Goal: Foster collaboration among academic, industry, government, and community partners to accelerate the pace of HIV cure research
- 3-pronged approach:
  - HIV Reservoir Biology
  - Durable Control of HIV Rebound
  - Reservoir Reduction and Eradication
Martin Delaney Collaboratories
2011-2021

**BELIEVE:** Bench to Bed Enhanced Lymphocyte Infusions to Engineer Viral Eradication
Douglas Nixon
(Weill Cornell Medicine, NYC)

**BEAT-HIV:** Delaney Collaboratory to Cure HIV-1 Infection by Combination Immunotherapy
Luis Montaner & James Riley
(Wistar Institute, Philadelphia)

**I4C:** Combined Immunologic Approaches to Cure HIV-1
Dan Barouch, John Mellors, Nelson Michael (Beth Israel Deaconess, Boston)

**defeatHIV:** Cell and Gene Therapy for HIV Cure
Keith Jerome & Hans-Peter Kiem
(FHCRC, Seattle)

**DARE:** Delaney AIDS Research Enterprise to Cure HIV
Steven Deeks & Louis Picker
(UCSF, San Francisco)

**CARE:** Collaboratory of AIDS Researchers for Eradication
David Margolis
(UNC, Chapel Hill)

Funded 2011-2016
NIH Makes Substantial New Investment in HIV Cure Research

Additional Funding Includes Effort Focused on Pediatric Populations

“June marked the 40th anniversary of the first reported U.S. cases of what would later be recognized as HIV/AIDS. Remarkable progress has been made in the areas of HIV treatment and prevention since that time. However, we must continue to press for a cure”

– Anthony S. Fauci, M.D.
Martin Delaney Collaboratories for HIV Cure Research: Program Funding (Millions)

Total Funding over 5 Years (Millions)

- 2011-2015: $70
- 2016-2020: $154
- 2021-2025: $269

Number of Grant Awards:

- 2011-2015: 0
- 2016-2020: 1
- 2021-2025: 1
Martin Delaney Collaboratories for HIV Cure Research

Academia  Industry  Community  Government
MDC Program Co-Funded by Seven Institutes

(*New Partners)

- National Institute of Allergy and Infectious Diseases (NIAID)
- *Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
- National Institute on Drug Abuse (NIDA)
- National Institute of Mental Health (NIMH)
- *National Heart, Lung, and Blood Institute (NHLBI)
- *National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
- National Institute of Neurological Disorders and Stroke (NINDS)
Martin Delaney Collaboratories for HIV Cure Research (2021-2026)

* New Collaboratory
Awardee Institutions & Principal Investigators

- **BEAT-HIV** (Wistar) – *Montaner, Riley, Siliciano*
- **CARE** (UNC) – *Margolis*
- **CRISPR for Cure** (Temple) – *Khalili, Burdo*
- **DARE** (UCSF) – *Deeks, Lewin, Picker*
- **ERASE-HIV** (Emory) – *Paiardini, Kulpa, Silvestri*
- **HOPE** (Gladstone) – *Ott, Ndholovu, Valente*
- **I4C** (BIDMC) – *Barouch, Mellors, Vasan*
- **PAVE** (JHU) – *Persaud, Chahroudi*
- **REACH** (Weill Cornell) – *Jones, Caskey*
- **RID-HIV** (Scripps) – *Chanda, Cannon, Sekaly*

15 Male
10 Female

*Contact PI*
MDC 3.0 Key Changes

- Clinical trials not allowed; partnership with ACTG
- “Back to basics” Research Focus
- Must pursue distinct strategies for eradication and durable control of rebound
- Require formal community partnerships
- One MDC devoted to pediatric HIV cure research
Thank you!