

Milestones of HIV Cure

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Engagement

September 23rd, 2024



IMPAACT

International Maternal Pediatric Adolescent
AIDS Clinical Trials Network

ANNUAL MEETING

2024

Key Messages

- HIV cure science has experienced a number of advances in the last decade that lead to hope for an eventual HIV cure
- Communities play a key role moving the scientific agenda forward and preparing for introduction of research

Language Check

- **HIV Eradication:** the complete removal of virus that can cause harm
- **HIV Control:** virus remains but is kept below detection without ARVs
- **HIV Remission:** the presence of the virus is unknown but cannot be found using the most sensitive assays available
- **HIV Cure:** umbrella term that includes ‘control’ and ‘eradication’

JOURNAL ARTICLE

Identification of a Reservoir for HIV-1 in Patients on Highly Active Antiretroviral Therapy

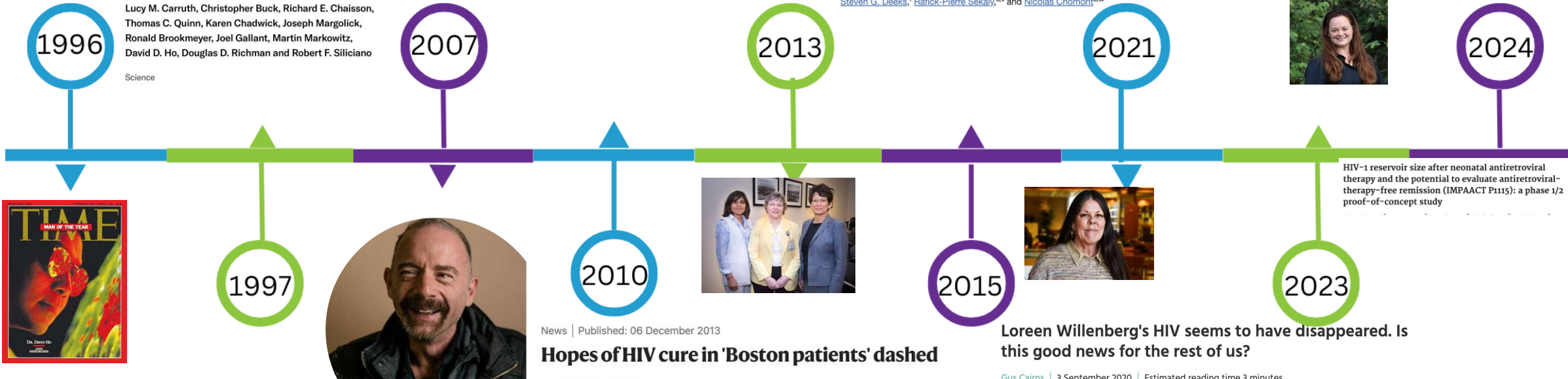
Diana Finzi, Monika Hermankova, Theodore Pierson, Lucy M. Carruth, Christopher Buck, Richard E. Chaisson, Thomas C. Quinn, Karen Chadwick, Joseph Margolick, Ronald Brookmeyer, Joel Gallant, Martin Markowitz, David D. Ho, Douglas D. Richman and Robert F. Siliciano

Science

Martin Delaney Collaboratories for HIV Cure Research (MDC)

A Novel Assay to Measure the Magnitude of the Inducible Viral Reservoir in HIV-infected Individuals

Francesco Andrea Procopio,^a Rémi Fromentin,^a Deanna A. Kulpa,^a Jessica H. Brehm,^a Anne-Gaelle Bebin,^a Matthew C. Strain,^b Douglas D. Richman,^b Una O'Doherty,^c Sarah Palmer,^{d,e} Frederick M. Hecht,^f Rebecca Hoh,^f Richard J.O. Barnard,^g Michael D. Miller,^g Daria J. Hazuda,^g Steven G. Deeks,^f Rafick-Pierre Sékaly,^{a,*} and Nicolas Chomont^{a,**}



HIV-1 reservoir size after neonatal antiretroviral therapy and the potential to evaluate antiretroviral-therapy-free remission (IMPAACT P1115): a phase 1/2 proof-of-concept study

News | Published: 06 December 2013

Hopes of HIV cure in 'Boston patients' dashed

Erika Check Hayden

Loren Willenberg's HIV seems to have disappeared. Is this good news for the rest of us?

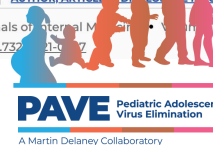
Gus Cairns | 3 September 2020 | Estimated reading time 3 minutes

Original Research | 16 November 2021

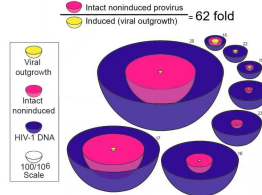
A Possible Sterilizing Cure of HIV-1 Infection Without Stem Cell Transplantation

Authors: Gabriela Turk, PhD, Kyra Seiger, BSc, Xiaodong Lian, PhD, Weiwei Sun, PhD, Elizabeth M. Parsons, BSc, Ce Gao, PhD, Svetlana Rassadkina, BSc, ... SHOW ALL ... and Xu G. Yu, MD, MSc | AUTHOR ARTICLE | DOWNLOAD | INFORMATION

Publication: Annals of Internal Medicine, Volume 175, Number 1, February 1, 2021. <https://doi.org/10.7326/00002933-202102010-00007>



The frequency of intact HIV-1 proviruses is a closer estimate of the true size of the latent reservoir



Ho et al., Cell 2013

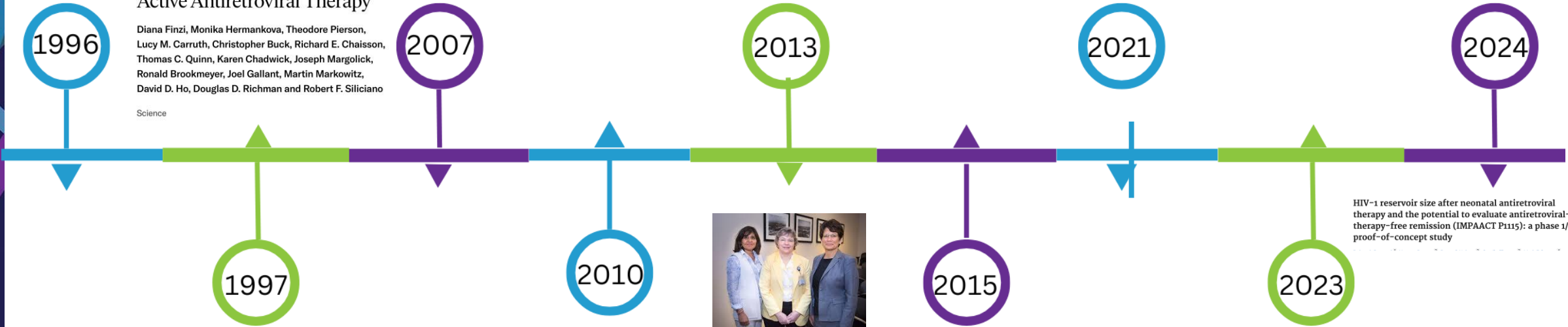


JOURNAL ARTICLE

Identification of a Reservoir for HIV-1 in Patients on Highly Active Antiretroviral Therapy

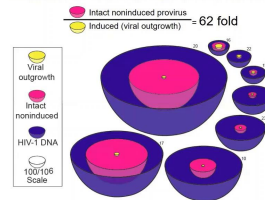
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Science



HIV-1 reservoir size after neonatal antiretroviral therapy and the potential to evaluate antiretroviral-therapy-free remission (IMPAACT P1115): a phase 1/2 proof-of-concept study

The frequency of intact HIV-1 proviruses is a closer estimate of the true size of the latent reservoir

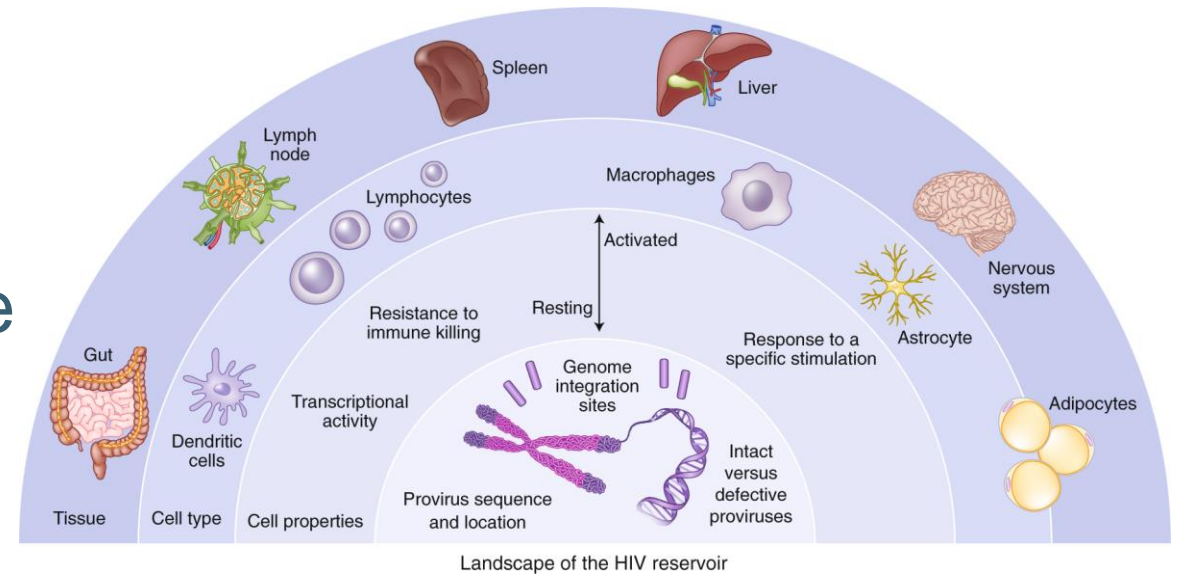


Ho et al., Cell 2013

The Challenge with HIV Persistence

The Challenge with Persistence

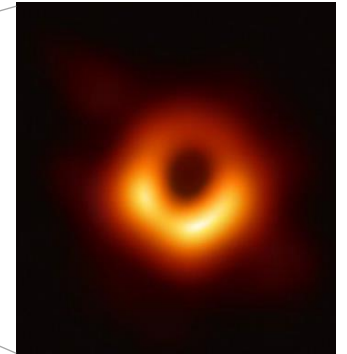
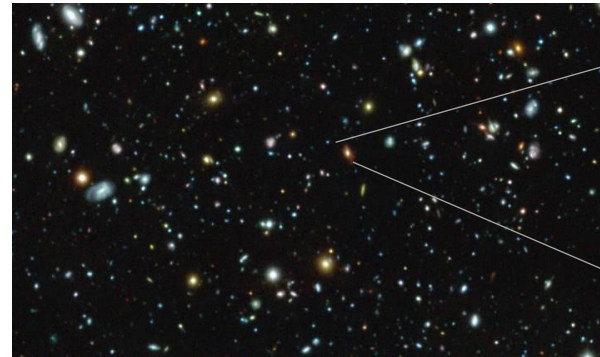
- The reservoir is the major challenge to curing HIV
- Some latent cells harbor HIV and remain undetectable by the body
- When these cells reactive, HIV circulates
- Latent cells are **rare**, but can be found throughout the body



Source:

Research Priorities for an HIV Cure:
International AIDS Society Global
Scientific Strategy 2021

The Challenge with Persistence

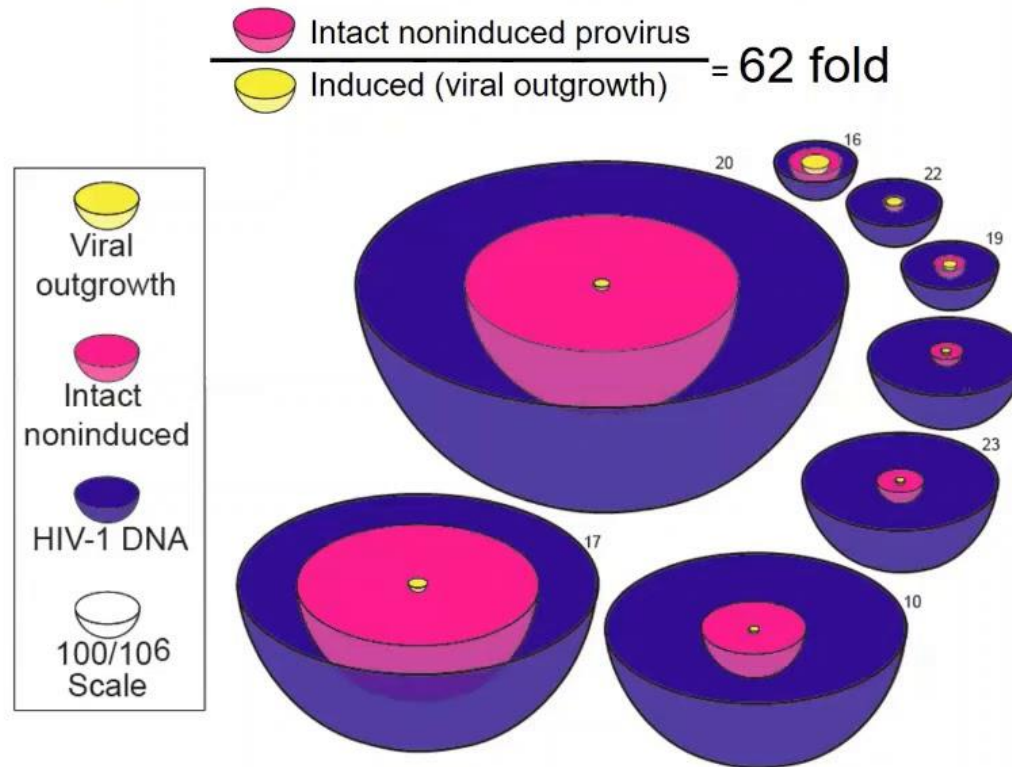


Heterogeneous

Rare

Measuring the HIV Reservoir

The frequency of intact HIV-1 proviruses is a closer estimate of the true size of the latent reservoir



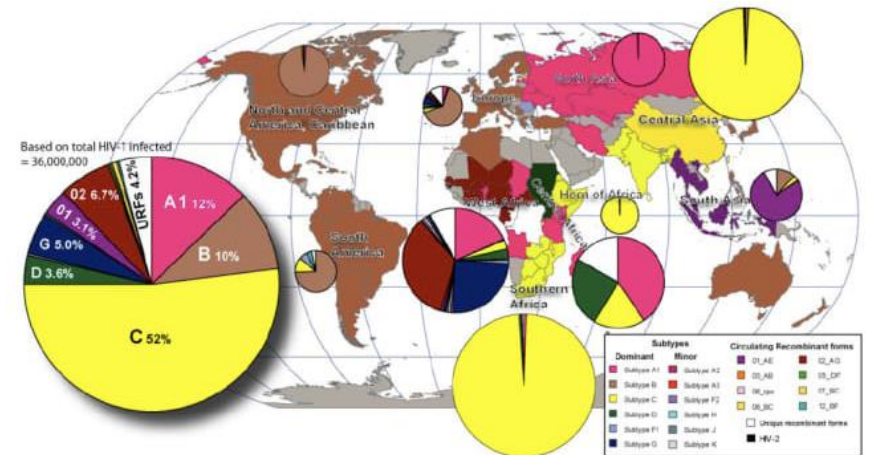
Ho *et al.*, Cell 2013

Measuring the HIV Reservoir

The **quantitative viral growth assay (QVOA)** is the gold standard for measuring the reservoir. It is labor intensive, requires a large blood volume and expertise

New assays like the **Intact Proviral DNA Assay** require less blood and more readily available equipment

Assays are being adapted to new clades



Early ART Limits Reservoir Size

The transient HIV remission in the Mississippi baby: why is this good news?

[Jintanat Ananworanich](#)^{§,1,2} and [Merlin L Robb](#)^{1,2}

[https://www.sciencedirect.com/science/article/pii/S2352301816300011](#)

- In 2013, both the Mississippi Child and Visconti cohort provided evidence that starting ART shortly after acquisition limits the formation of the reservoir

Post-treatment HIV-1 controllers with a long-term virological remission after the interruption of early initiated antiretroviral therapy ANRS VISCONTI Study

Evidence Toward an HIV Cure

Early intervention with 3BNC117 and romidepsin at antiretroviral treatment initiation in people with HIV-1: a phase 1b/2a, randomized trial

Jesper D. Gunst, Marie H. Pahun, Miriam Rosás-Umbert, I-Na Lu, Thomas Benfield, Henrik Nielsen, Isik S. Johansen, Rajesh Mohey, Lars Østergaard, Vibeke Klastrup, Maryam Khan, Mariane H. Schleimann, Rikke Olesen, Henrik Støvring, Paul W. Denton, Natalie N. Kinloch, Dennis C. Copertino, Adam R. Ward, Winiffer D. Conce Alberto, Silke D. Nielsen, Maria C. Puertas, Victor Ramos, Jacqueline D. Reeves, Christos J. Petropoulos, ... Ole S. Søgaard  [+ Show authors](#)

Original Research | 16 November 2021

A Possible Sterilizing Cure of HIV-1 Infection Without Stem Cell Transplantation

Authors: Gabriela Turk, PhD , Kyra Seiger, BSc , Xiaodong Lian, PhD , Weiwei Sun, PhD, Elizabeth M. Parsons, BSc , Ce Gao, PhD , Yelizaveta Rassadkina, BSc , ... [SHOW ALL](#) ..., and Xu G. Yu, MD, MSc  | [AUTHOR, ARTICLE, & DISCLOSURE INFORMATION](#)

Publication: Annals of Internal Medicine • Volume 175, Number 1
<https://doi.org/10.7326/L21-0297>

Loreen Willenberg's HIV seems to have disappeared. Is this good news for the rest of us?

Gus Cairns | 3 September 2020 | Estimated reading time 3 minutes

The Control of HIV After Antiretroviral Medication Pause (CHAMP) Study: Posttreatment Controllers Identified From 14 Clinical Studies

Golnaz Namazi,¹ Jesse M Fajnzylber,¹ Evgenia Aga,² Ronald J Bosch,² Edward P Acosta,³ Radwa Sharaf,¹ Wendy Hartogensis,⁴ Jeffrey M Jacobson,⁵ Elizabeth Connick,⁶ Paul Volberding,⁴ Daniel Skiest,⁷ David Margolis,⁸ Michael C Sneller,⁹ Susan J Little,¹⁰ Sara Gianella,¹⁰ Davey M Smith,¹⁰ Daniel R Kuritzkes,¹ Roy M Gulick,¹¹ John W Mellors,¹² Vikram Mehraj,¹³ Rajesh T Gandhi,¹⁴ Ronald Mitsuyasu,¹⁵ Robert T Schooley,¹⁰ Keith Henry,¹⁶ Pablo Tebas,¹⁷ Steven G Deeks,⁴ Tae-Wook Chun,⁹ Ann C Collier,¹⁸ Jean-Pierre Routy,¹³ Frederick M Hecht,⁴

The search for a cure

Barcelona woman controls HIV for over 15 years without treatment

HIV-1 reservoir size after neonatal antiretroviral therapy and the potential to evaluate antiretroviral-therapy-free remission (IMPAACT P1115): a phase 1/2 proof-of-concept study

Yrah Persaud¹, Yvonne Bryson², Bryan S Nelson³, Camlin Tierney³, Mark F Cotton⁴, ... Coletti⁵, Jennifer Jao⁶, Stephen A Spector⁷, Mark Mirochnick⁸, Edmund V Capparelli⁷, ... Costello², Joseph Szewczyk⁹, Nicol Nicodimus¹⁰, Lynda Stranix-Chibanda¹⁰, ... data R Kekitiinwa¹¹, Violet Korutaro¹¹, Christina Reding¹², Mary N Carrington¹³, ... faji¹⁴, Dwight E Yin¹⁵, Patrick Jean-Philippe¹⁵, Ellen G Chadwick⁶

Transplant Related HIV Cures

- **Timothy Brown** (“Berlin Patient”)
 - Remained off therapy with non-detectable virus for > 12 years
- **Adam Castillejo** (“London Patient”)
 - ART interruption was initiated in September 2017 and there is no evidence of viral rebound or detectable intact virus.
- **“Dusseldorf Patient”**
 - ART interruption was initiated in November 2018 and there is no evidence of viral rebound or detectable intact virus.
- **“New York Patient”**
 - The only female; received cord blood. ART interruption in 2021
- **Paul Edmonds** (City of Hope Patient)
- The oldest person to be cured; ART interruption was initiated in 2021 and there is no evidence of detectable intact virus



Sex Differences in HIV Cure

Sex differences in HIV-1 persistence and the implications for a cure

[Shringar Rao](#)^{*}

JCI insight

RESEARCH ARTICLE

Reduced HIV-1 latent reservoir outgrowth and distinct immune correlates among women in Rakai, Uganda

Jessica L. Prodger,^{1,2,3} Adam A. Capoferri,³ Katherine Yu,² Jun Lai,³ Steven J. Reynolds,^{3,4,5} Jingo Kasule,⁵ Taddeo Kityamuweesi,⁵ Paul Buule,³ David Serwadda,^{5,6} Kyungyoon J. Kwon,³ Katherine Schlusser,³ Craig Martens,⁷ Eileen Scully,³ Yun-Hee Choi,² Andrew D. Redd,^{3,4} and Thomas C. Quinn^{3,4}

The MOXIE Trial Shows that Women Are Invested in Cure Research

Sustained aviremia despite anti-retroviral therapy non-adherence in male children after in utero HIV transmission

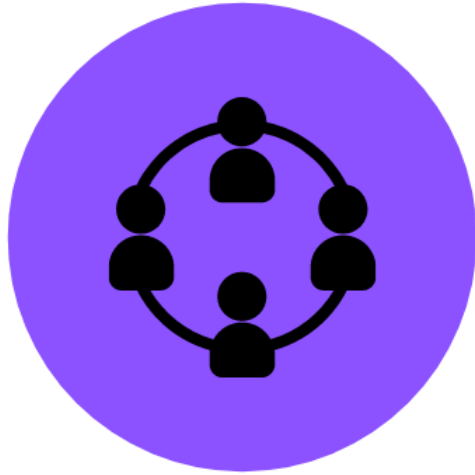
[Nomonde Bengu](#), [Gabriela Cromhout](#), [Emily Adland](#), [Katya Govender](#), [Nicholas Herbert](#), [Nicholas Lim](#), [Rowena Fillis](#), [Kenneth Sprenger](#), [Vinicius Vieira](#), [Samantha Kannie](#), [Jeroen van Lobenstein](#), [Kogielambal Chinniah](#), [Constant Kapongo](#), [Roopesh Bhoola](#), [Malini Krishna](#), [Noxolo Mchunu](#), [Giuseppe Rubens Pascucci](#), [Nicola Cotugno](#), [Paolo Palma](#), [Alfredo Tagarro](#), [Pablo Rojo](#), [Julia Roider](#), [Maria C. Garcia-Guerrero](#), [Christina Ochsenbauer](#), ... [Philip Goulder](#)  [+ Show authors](#)

Transcendendo: A Cohort Study of HIV-Infected and Uninfected Transgender Women in Rio de Janeiro, Brazil

[Ana Cristina Garcia Ferreira](#),^{1,*} [Lara Esteves Coelho](#),¹ [Emilia Moreira Jalil](#),¹ [Paula Mendes Luz](#),¹ [Ruth K. Friedman](#),¹ [Maria Regina C. Guimarães](#),¹ [Rodrigo C. Moreira](#),¹ [Leonardo F. Eksterman](#),¹ [Sandra Wagner Cardoso](#),¹ [Cristiane V. Castro](#),¹ [Monica Derrico](#),¹ [Ronaldo I. Moreira](#),¹ [Biancka Fernandes](#),¹ [Laylla Monteiro](#),¹ [Luciana Kamel](#),¹ [Antonio G. Pacheco](#),² [Valdilea G. Veloso](#),¹ and [Beatriz Grinsztejn](#)¹

The Importance of Community in HIV Cure

Community Milestones



Strengthening networks



Improving communication





Driving ethical research conduct

Shaping the Research Agenda

Review

A partner protection package for HIV cure-related trials involving analytical treatment interruptions

Karine Dubé DrPH^{a b}  , Tia Morton RN^c, Lawrence Fox MD^c, Lynda Dee JD^{d g}, David Palm MS^{h i}, Thomas J Villa^{j k l m}, William Freshwaterⁿ, Jeff Taylor^{d l o q}, Gail Graham^p, William B Carter^{p r}, John A Saucedo PhD^e, Michael J Peluso MD^f, Annette Rid MD^s

Recommendations for Analytical Antiretroviral Treatment Interruptions in HIV Research Trials – Report of a Consensus Meeting

Boris Julg, MD,^{1,#} Lynda Dee,² Jintanat Ananworanich, MD,³ Dan H. Barouch, MD,^{1,4} Katharine Bar, MD,⁵ Marina Caskey, MD,⁶ Donn J. Colby, MD,⁷ Liza Dawson, PhD,⁸ Krista Dong, MD,^{1,9} Karine Dubé, DrPH,¹⁰ Joseph Eron, MD,¹¹ John Frater, MD,^{12,13} Rajesh T. Gandhi, MD,¹⁴ Romas Geleziunas, PhD,¹⁵ Philip Goulder, MD,¹⁶ George J. Hanna, MD,¹⁷ Richard Jefferys,¹⁸ Rowena Johnston, PhD,¹⁹ Daniel Kuritzkes, MD,²⁰ Jonathan Z. Li, MD,²⁰ Udom Likhitwonnawut,²¹ Jan van Lunzen, MD,²² Javier Martinez-Picado, PhD,²³ Veronica Miller,²⁴ Luis J. Montaner, PhD,²⁵ Douglas F. Nixon, MD,²⁶ David Palm, MS,²⁷ Giuseppe Pantaleo, MD,²⁸ Holly Peay, PhD,²⁹ Deborah Persaud, MD,³⁰ Jessica Salzwedel, MA,²¹ Karl Salzwedel, PhD,⁸ Timothy Schacker, MD,³¹ Virginia Sheikh, MD,³²

Language for HIV Cure

Community-preferred language to describe cases of HIV cure

HIV cure research is seeing momentum with new research, discussion and debate happening. This document shares the most up-to-date community-preferred terminology related to cure research to help those presenting new research or sharing information with lay audiences. Terminology was reviewed by global community stakeholders.

Defining HIV Cure

Cure

Definition: Removal of all replication-competent virus.

Preferred Alternative Phrases

"Eradication"

Terminology to Avoid

"Sterilizing cure", "Natural cure"

Examples

Timothy Ray Brown: ("Berlin Patient"): Remained cured with non-detectable virus for > 12 years until his death from a recurrence of cancer in 2020.

Adam Castillejo ("London Patient"): ART interruption was initiated in September 2017 and there is no evidence of viral rebound or detectable intact virus. HIV-specific antibodies have waned.

Marc Franke: ("Dusseldorf Patient"): ART interruption was initiated in November 2018 and there is no evidence of viral rebound or detectable intact virus. HIV-specific antibodies have waned.

New York Patient: ART interruption was initiated in 2020 and there is no evidence of viral rebound or detectable intact virus. HIV-specific antibodies have waned.

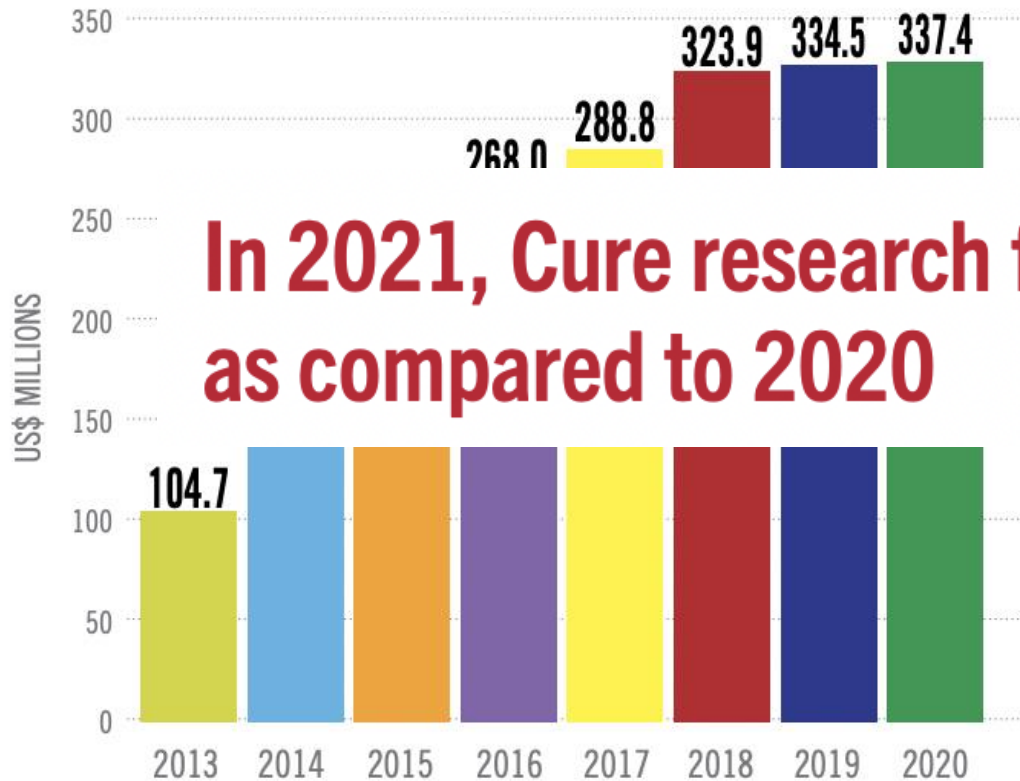
Paul Edmonds: ("City of Hope Patient"): ART interruption was initiated in 2021. Viral load remains undetectable and there is no evidence of viral rebound. HIV-specific cellular immune responses have waned.

A small group of elite controllers, known as "exceptional elites", may be considered "cured". These individuals have sero-reverted without intervention and replication-competent virus cannot be detected using the most advanced assays. There is no consensus on terminology for these individuals.

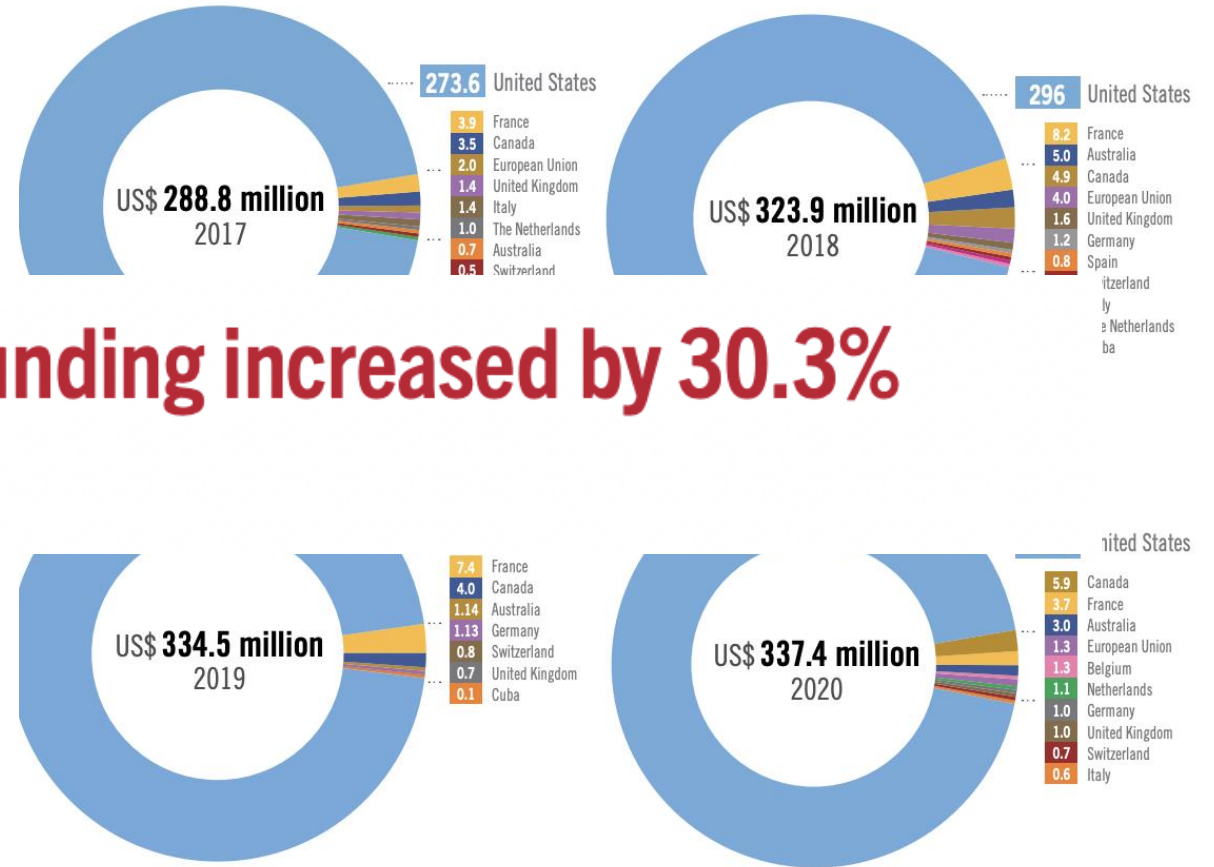
Investments in HIV Cure

Investments in HIV Cure Research by Country, 2017–2020 (US\$ millions)

Current Research Investment, 2013–2020 (US\$ millions)



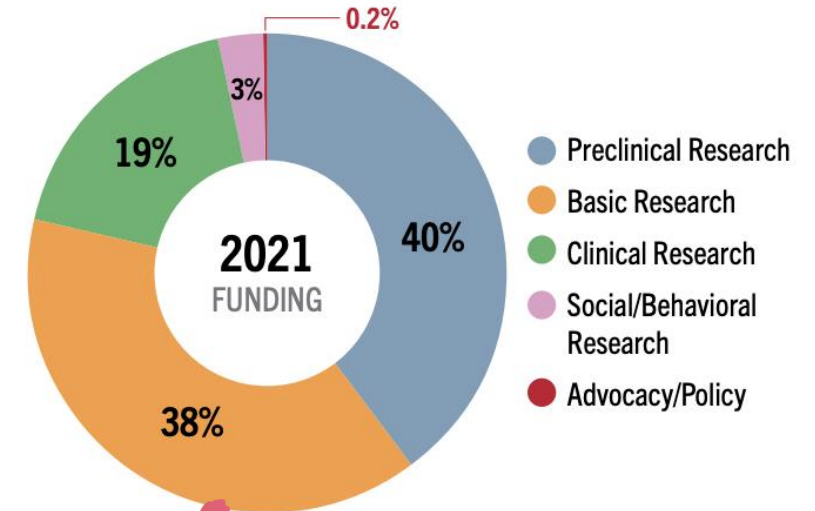
In 2021, Cure research funding increased by 30.3% as compared to 2020



Investments in HIV Cure

- Movement of the research from the bench to early phase clinical trials
- Increase in NIH-funded Martin Delaney Collaboratories including first pediatric collaboratory

HIV Cure Investment by Research Stage



PAVE Pediatric Adolescent
Virus Elimination

A Martin Delaney Collaboratory

IMPAACT
International Maternal Pediatric Adolescent
AIDS Clinical Trials Network

Pushing for Greater Diversity

Notice of Special Interest (NOSI): HIV Cure-Related Research in Diverse Populations

Notice Number:

NOT-AI-23-046

Key Dates

Release Date:

June 23, 2023



Notice of Special Interest (NOSI): Opportunities for HIV Cure Interventions at the Time of ART Initiation

Notice Number:

NOT-AI-22-072

Research | [Open access](#) | Published: 19 October 2020

Mycobacterium tuberculosis co-infection is associated with increased surrogate marker of the HIV reservoir

Jingna Xun, Tangkai Qi, Lei Zou, Qi Tang, Yinzhong Shen, Junyang Yang, Luman Xie, Yongjia Ji, Renfang Zhang, Li Liu, Jiangrong Wang, Corky Steinhart, Zhenyan Wang, Yang Tang, Wei Song, Jianjun Sun, Juan Cheng, Xiaoqin Le, Huanmei Wu, Xiaoqing He, Rong Chen, Jun Chen [✉](#) & Hongzhou Lu [✉](#)

AIDS Research and Therapy **17**, Article number: 63 (2020) | [Cite this article](#)

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DOI: 10.1089/aid.2021.0023

SOCIO-BEHAVIORAL

Considerations for Increasing Racial, Ethnic, Gender, and Sexual Diversity in HIV Cure-Related Research with Analytical Treatment Interruptions: A Qualitative Inquiry

Karine Dubé^{1,i} John Kanazawa^{1,ii} Chadwick Campbell^{2,3,iii} Cheriko A. Boone⁴ Allysha C. Maragh-Bass⁵ Danielle M. Campbell⁶ Moisés Agosto-Rosario⁷ Jamila K. Stockman⁸ Dázon Dixon Diallo⁹ Tonia Poteat^{10,iv} Mallory Johnson² Parya Saberi² and John A. Saucedo²



THANKS!

Any questions?

You can find me at

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