Therapeutic approaches for a sustainable remission and cure for HIV

Steven Deeks, MD
Professor of Medicine
Division of HIV, Infectious Diseases and Global Medicine
University of California, San Francisco

This activity is jointly provided by Physicians' Research Network and the Medical Society of the State of New York.

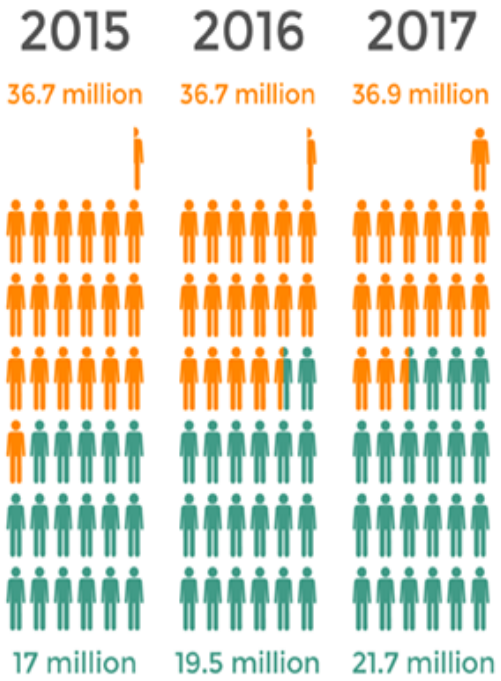
Therapeutic approaches for a sustainable remission and cure

Steven Deeks, MD
Professor of Medicine
Division of HIV, Infectious Diseases, and Global Medicine
Zuckerberg San Francisco General
University of California, San Francisco

UCSF University of California San Francisco
ZUCKERBERG SAN FRANCISCO GENERAL Hospital and Trauma Center
BILL & MELINDA GATES foundation
ACTG AIDS CLINICAL TRIALS GROUP
Delaney AIDS Research Enterprise DARE to find a cure
amfAR Institute FOR HIV CURE RESEARCH

Why do we need a cure in an era of effective ART?

- Human costs
  - Stigma/discrimination
  - Long-term health: Obesity, co-morbidities, polypharmacy



- Public health costs
  - ART is lifelong and expensive: Total spent on HIV/AIDS: ~ $50 billion/year
  - Social disruptions affect access (COVID)
  - Despite massive global investments, many (~50%) not

What will a cure need to do?

Optimal (aspirational) target product profile

From a public health perspective, the ideal curative intervention will be readily scalable, safe, effective in everyone – including those not on ART – and protect against re-infection

What will a cure need to do?

Optimal (aspirational) target product profile

A cure is not needed for those who are doing well on ART and can access these drugs indefinitely but for everyone else, including those who are untreated

Why does HIV persist indefinitely?

The Problem: Latent Reservoir

- HIV persists as fully integrated genome in largely tissue-based memory T cell population
- Only ~1% of genomes are fully intact and only a subset of these proviruses are “rebound-competent”, making reservoir hard to measure

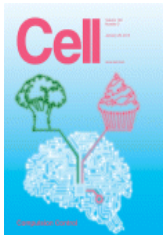
T cell proliferation is the main cause of persistence

Specific HIV integration sites are linked to clonal expansion and persistence of infected cells

F. Maldarelli,[1]* X. Wu,[2]* L. Su,[2] F. R. Simonetti,[1,3] W. Shao,[2] S. Hill,[1] J. Spindler,[1] A. L. Ferris,[1] J. W. Mellors,[4] M. F. Kearney,[1] J. M. Coffin,[5] S. H. Hughes[1]†

Proliferation of cells with HIV integrated into cancer genes contributes to persistent infection

Thor A. Wagner,[1,2]* Sherry McLaughlin,[1,2]* Kavita Garg,[3] Charles Y. K. Cheung,[3] Brendan B. Larsen,[2] Sheila Styrchak,[1] Hannah C. Huang,[1] Paul T. Edlefsen,[2,3] James I. Mullins,[2]* Lisa M. Frenkel[1,2]*†



HIV-1 Integration Landscape during Latent and Active Infection

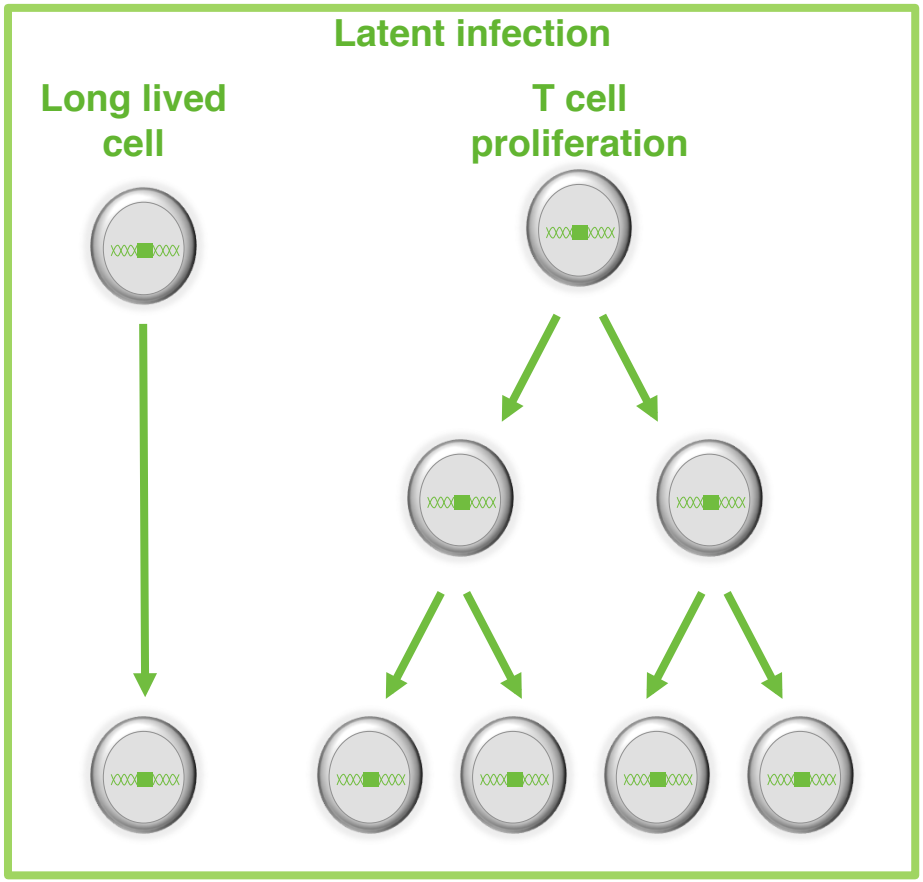
Lillian B. Cohn,[1] Israel T. Silva,[1,2] Thiago Y. Oliveira,[1] Rafael A. Rosales,[3] Erica H. Parrish,[4] Gerald H. Learn,[4] Beatrice H. Hahn,[4] Julie L. Czartoski,[5] M. Juliana McElrath,[5] Clara Lehmann,[6,7] Florian Klein,[1] Marina Caskey,[1] Bruce D. Walker,[8,9] Janet D. Siliciano,[10] Robert F. Siliciano,[9,10] Mila Jankovic,[1] and Michel C. Nussenzweig[1,9,*]

Longitudinal Genetic Characterization Reveals That Cell Proliferation Maintains a Persistent HIV Type 1 DNA Pool During Effective HIV Therapy

Susanne von Stockenstrom,[1,2] Lina Odevall,[1] Eunok Lee,[3,4] Elizabeth Sinclair,[5] Peter Bacchetti,[6] Maudi Killian,[5] Lorrie Epling,[5] Wei Shao,[7] Rebecca Hoh,[5] Terence Ho,[5] Nuno R. Faria,[9] Philippe Lemey,[9] Jan Albert,[1,2] Peter Hunt,[5] Lisa Loeb,[5] Christopher Pilcher,[5] Lauren Poole,[5] Hiroyu Hatano,[5] Ma Somsouk,[5] Daniel Douek,[8] Eli Boritz,[8] Steven G. Deeks,[5] Frederick M. Hecht,[5a] and Sarah Palmer[1,3,4,a]

Cells maintained by homeostatic proliferation; designed to persist indefinitely

Proliferation: latently infected cells clonally expand



- Clonally expanded cells make up most of the reservoir
- Expanded cells can produce virus resulting in low level viremia and/or viral rebound
- Drivers for proliferation
  - Antigen specific expansion
  - Homeostatic proliferation
  - Site of integration

\Wang Z, et al. *Proc Natl Acad Sci USA* 2018; Lorenzo G, et al. *Proc Natl Acad Sci USA* 2016; Huang *J Exp Med* 2017; Bui *Plos Path* 2017; McManue J Clin Inv 2019; De Scheerder et al., Cell Host Microbe 2019

Slide: Nicolas Chomont

How will it be defined and measured?

Goal of therapy: Cure (eradication)

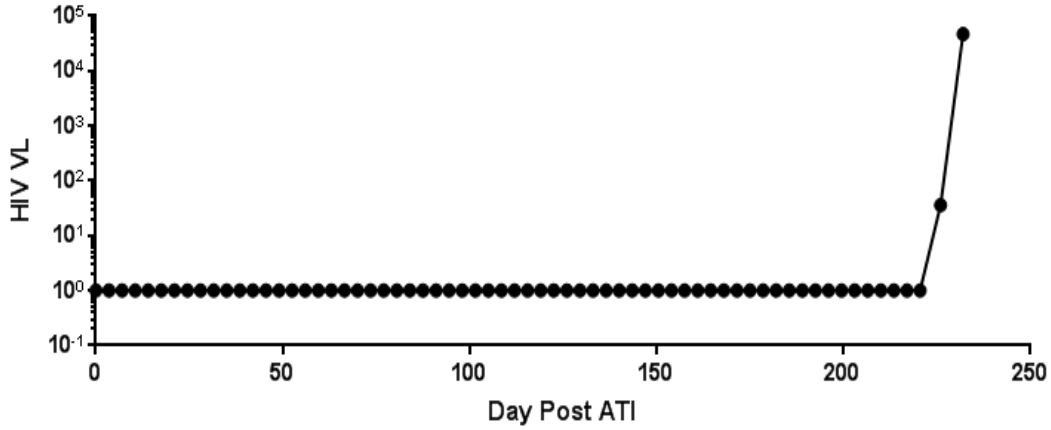
- Complete removal of all replication-competent HIV
- No residual stigma (key outcome in surveys)
- May have been achieved with Berlin Patient but impossible to prove
  - People may never really know if they are cured
- Will likely require gene modifications therapies

Goal of therapy: Remission (control)

- Durable control of a residual population
  - Elite/exceptional control
  - Post-treatment controllers
  - Long-term ART (depot formulations)
- Antibody positive, persistent inflammation, possible risk of rebound
- Readily achieved in monkey models with various combination approaches (immunotherapy)

HIV-1 persistence following extremely early initiation of antiretroviral therapy (ART) during acute HIV-1 infection: An observational study

Timothy J. Henrich[1]*, Hiroyu Hatano[2], Oliver Bacon[2,3], Louise E. Hogan[1], Rachel Rutishauser[1,2], Alison Hill[4], Mary F. Kearney[5], Elizabeth M. Anderson[5], Susan P. Buchbinder[2,3], Stephanie E. Cohen[2,3], Mohamed Abdel-Mohsen[2,6], Christopher W. Pohlmeyer[7], Remi Fromentin[8], Rebecca Hoh[2], Albert Y. Liu[2,3], Joseph M. McCune[1], Jonathan Spindler[5], Kelly Metcalf-Pate[7], Kristen S. Hobbs[1], Cassandra Thanh[1], Erica A. Gibson[1], Daniel R. Kuritzkes[9,10], Robert F. Siliciano[11,12], Richard W. Price[13], Douglas D. Richman[14,15], Nicolas Chomont[8], Janet D. Siliciano[10], John W. Mellors[16], Steven A. Yukl[17,18], Joel N. Blankson[7], Teri Liegler[2], Steven G. Deeks[2]



Initation of ART as PrEP ("Fiebig 0") resulted in multi-log reduction in reservoir, but at least one virus had established latency

Delaney AIDS Research Enterprise DARE to find a cure

amfAR Institute FOR HIV CURE RESEARCH

THE LANCET
HIV

Recommendations for analytical antiretroviral treatment interruptions in HIV research trials—report of a consensus meeting

Boris Julg, Lynda Dee, Jintanat Ananworanich, Dan H Barouch, Katharine Bar, Marina Caskey, Donn J Colby, Liza Dawson, Krista L Dong, Karine Dubé, Joseph Eron, John Frater, Rajesh T Gandhi, Romas Geleziunas, Philip Goulder, George J Hanna, Richard Jefferys, Rowena Johnston, Daniel Kuritzkes, Jonathan Z Li, Udom Likhitwonnawut, Jan van Lunzen, Javier Martinez-Picado, Veronica Miller, Luis J Montaner, Douglas F Nixon, David Palm, Giuseppe Pantaleo, Holly Peay, Deborah Persaud, Jessica Salzwedel, Karl Salzwedel, Timothy Schacker, Virginia Sheikh, Ole S. Søgaard, Serena Spudich, Kathryn Stephenson, Jeremy Sugarman, Jeff Taylor, Pablo Tebas, Caroline T Tiemessen, Randall Tressler, Carol D Weiss, Lu Zheng, Merlin L Robb, Nelson L Michael, John W Mellors, Steven G Deeks, Bruce D Walker

- Carefully performed treatment interruptions often the only interpretable way to answer the question
  - No validated biomarker of the systemic rebound-competent reservoir
  - No validated immunologic correlates of post-ART control
- Can it be done safely?
  - Exclude those with low nadir, history of cancer/CAD
  - High baseline CD4+ T cell count
  - Age limits
  - Partner engagement (PrEP)
  - Conservative restart criteria: Symptoms, CD4+ T cell decline, sustained viremia

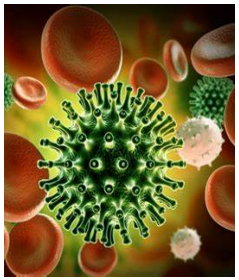
How will HIV be cured?

HIV cure strategies

Most approaches involve combination of reservoir reduction and immune enhancement ("reduce and control"), with growing interest in gene therapy and eventually "one shot" cures

Early ART

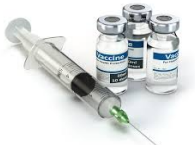
Latency reversal
Latency silencing

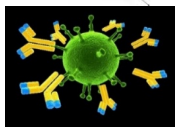


Gene therapy

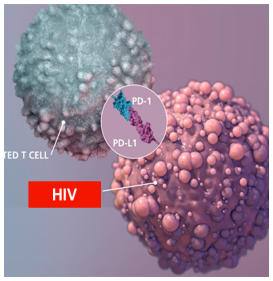
Reservoir reduction and elimination

Vaccines
Antibodies





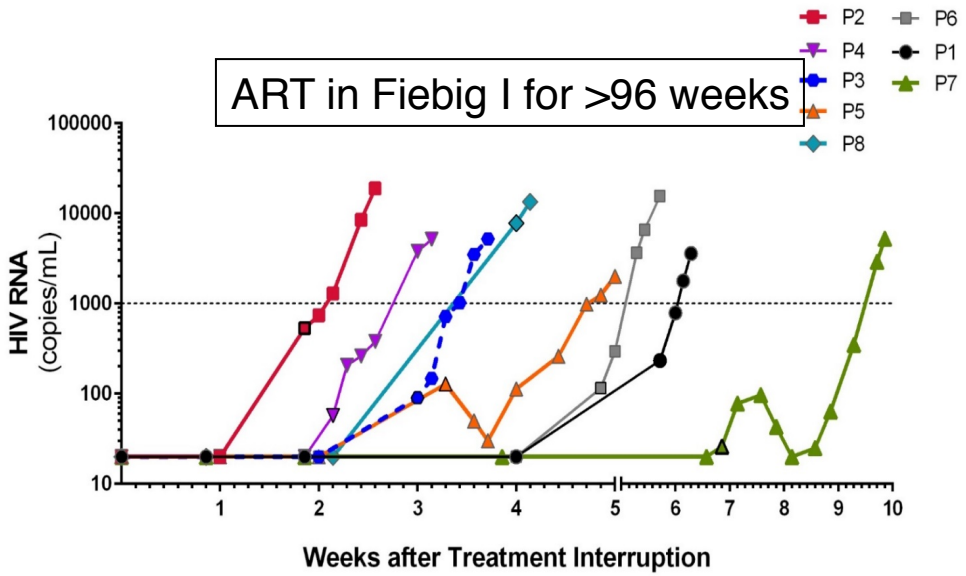
Immunotherapy



Immune enhancement

Early ART

Very early ART is not curative

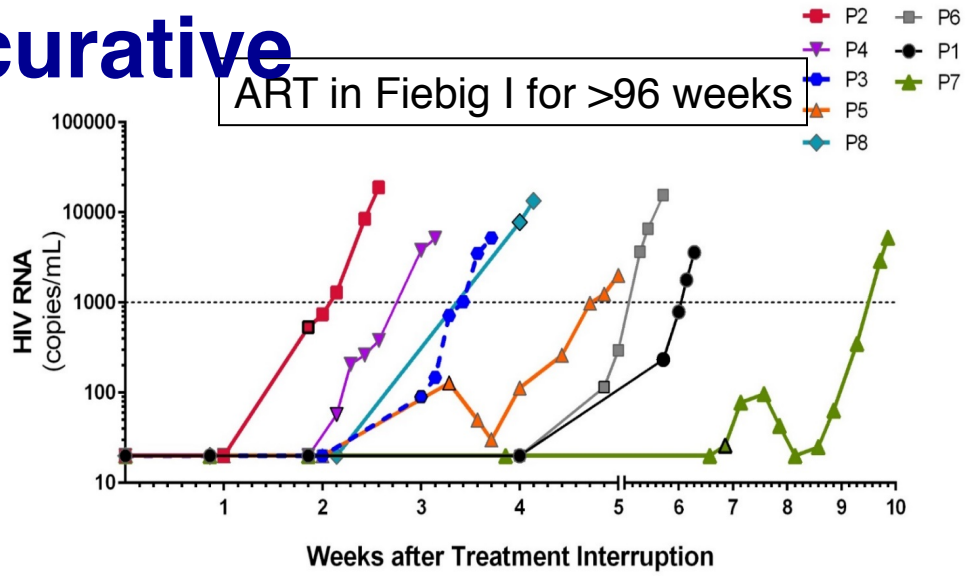


nature medicine

Rapid HIV RNA rebound after antiretroviral treatment interruption in persons durably suppressed in Fiebig I acute HIV infection

Donn J. Colby[1], Lydie Trautmann[2,3], Suteeraporn Pinyakorn[2,3], Louise Leyre[4], Amélie Pagliuzza[4], Eugène Kroon[1], Morgane Rolland[2,3], Hiroshi Takata[2,3], Supranee Buranapraditkun[2,3,5,6], Jintana Intasan[1], Nitiya Chomchey[1], Roshell Muir[7], Elias K. Haddad[7], Sodsai Tovanabutra[2,3], Sasiwimol Ubolyam[8], Diane L. Bolton[2,3], Brandie A. Fullmer[9], Robert J. Gorelick[9], Lawrence Fox[10], Trevor A. Crowell[2,3], Rapee Trichavaroj[11], Robert O'Connell[11], Nicolas Chomont[4], Jerome H. Kim[2,13], Nelson L. Michael[2], Merlin L. Robb[2,3], Nittaya Phanuphak[1], Jintanat Ananworanich[1,2,3,12*] and The RV411 study group

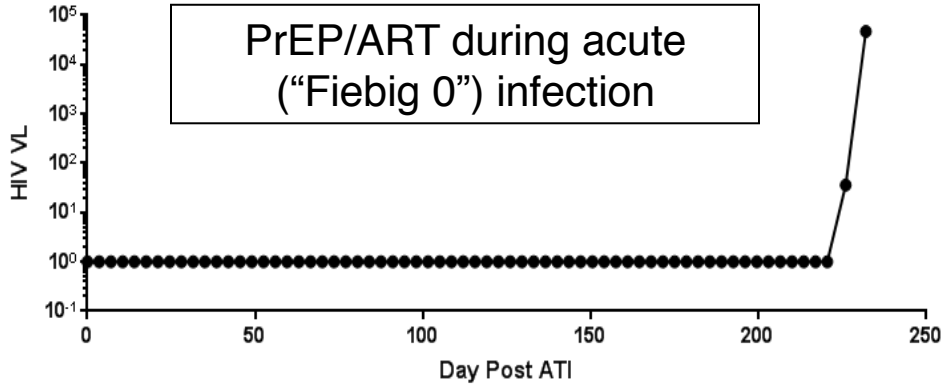
Very early ART (including “Fiebig 0”) is not curative



nature medicine

Rapid HIV RNA rebound after antiretroviral treatment interruption in persons durably suppressed in Fiebig I acute HIV infection

Donn J. Colby[1], Lydie Trautmann[2,3], Suteeraporn Pinyakorn[2,3], Louise Leyre[4], Amélie Pagliuzza[4], Eugène Kroon[1], Morgane Rolland[2,3], Hiroshi Takata[2,3], Supranee Buranapraditkun[2,3,5,6], Jintana Intasan[1], Nitiya Chomchey[1], Roshell Muir[7], Elias K. Haddad[7], Sodsai Tovanabutra[2,3], Sasiwimol Ubolyam[8], Diane L. Bolton[2,3], Brandie A. Fullmer[9], Robert J. Gorelick[9], Lawrence Fox[10], Trevor A. Crowell[2,3], Rapee Trichavaroj[11], Robert O'Connell[11], Nicolas Chomont[4], Jerome H. Kim[2,13], Nelson L. Michael[2], Merlin L. Robb[2,3], Nittaya Phanuphak[1], Jintanat Ananworanich[1,2,3,12]*
and The RV411 study group



PLOS MEDICINE

HIV-1 persistence following extremely early initiation of antiretroviral therapy (ART) during acute HIV-1 infection: An observational study

Timothy J. Henrich[1]*, Hiroyu Hatano[2], Oliver Bacon[2,3], Louise E. Hogan[1], Rachel Rutishauser[1,2], Alison Hill[4], Mary F. Kearney[5], Elizabeth M. Anderson[5], Susan P. Buchbinder[2,3], Stephanie E. Cohen[2,3], Mohamed Abdel-Mohsen[2,6], Christopher W. Pohlmeyer[7], Remi Fromentin[8], Rebecca Hoh[2], Albert Y. Liu[2,3], Joseph M. McCune[1], Jonathan Spindler[5], Kelly Metcalf-Pate[7], Kristen S. Hobbs[1], Cassandra Thanh[1], Erica A. Gibson[1], Daniel R. Kuritzkes[9,10], Robert F. Siliciano[11,12], Richard W. Price[13], Douglas D. Richman[14,15], Nicolas Chomont[8], Janet D. Siliciano[10], John W. Mellors[16], Steven A. Yukl[17,18], Joel N. Blankson[7], Teri Liegler[2], Steven G. Deeks[2]

The Journal of Infectious Diseases

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

Golnaz Namazi,[1,a] Jesse M. Fajnzylber,[1,a] 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,[16] Keith Henry,[16] Pablo Tebas,[17] Steven G. Deeks,[4] Tae-Wook Chun,[3] Ann C. Collier,[18] Jean-Pierre Routy,[13] Frederick M. Hecht,[4] Bruce D. Walker,[19] and Jonathan Z. Li[1]

PLOS | PATHOGENS

Post-Treatment HIV-1 Controllers with a Long-Term Virological Remission after the Interruption of Early Initiated Antiretroviral Therapy ANRS VISCONTI Study

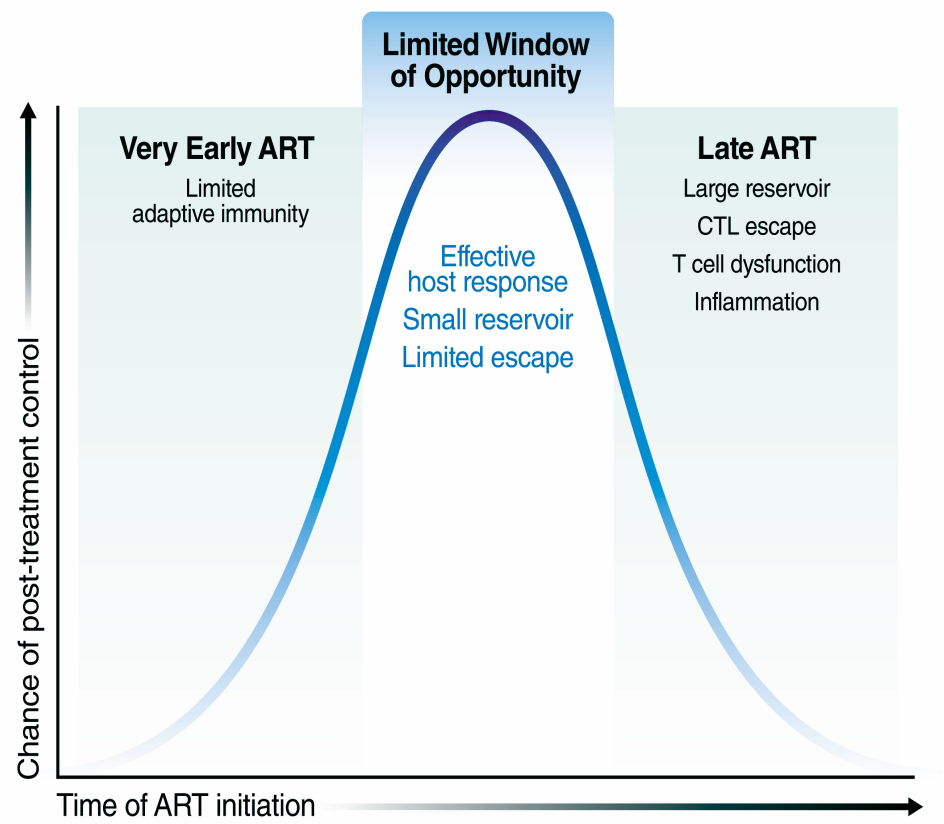
Asier Sáez-Cirión[1]*, Charline Bacchus[2], Laurent Hocqueloux[3], Véronique Avettand-Fenoel[4,5], Isabelle Girault[6], Camille Lecuroux[6], Valerie Potard[7,8], Pierre Versmisse[1], Adeline Melard[4], Thierry Prazuck[3], Benjamin Descours[2], Julien Guergnon[2], Jean-Paul Viard[5,9], Faroudy Boufassa[10], Olivier Lambotte[6,11], Cécile Goujard[10,11], Laurence Meyer[10,12], Dominique Costagliola[7,8,13], Alain Venet[6], Gianfranco Pancino[1], Brigitte Autran[2], Christine Rouzioux[4,5]*, the ANRS VISCONTI Study Group*

- Some (~10%) of people who start therapy early (but not too early) and remain on therapy for years exhibit at least partial control after ART is interrupted
  - May occur in chronic infection (rare)
- No biomarker available
- Mechanism unknown
  - Elite controllers: Adaptive immunity (CD8+ T cells)
  - PTCs: Innate immunity (NK cells)

PLOS | PATHOGENS

HIV control: Is getting there the same as staying there?

Philip Goulder[1,2]*, Steven G. Deeks[3]

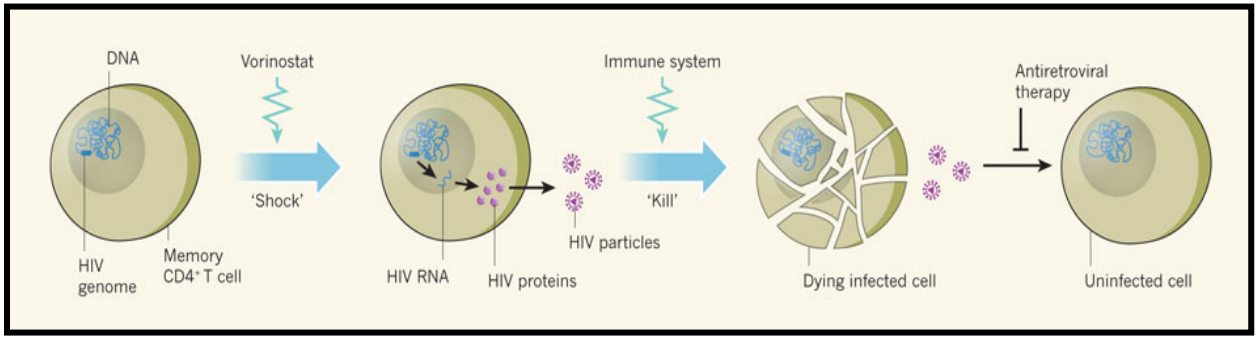


Most PTCs started ART early, but not too early

Some host response likely needs to be primed (but not overwhelmed) during acute infection to set the stage for post-treatment control

Latency reversal (shock and kill)

Shock and kill



- Multiple latency reversing agents (LRAs) tested: effect in humans is modest at best and inconsistent, and has rarely associated with reservoir reduction
- Basic discovery aimed at identifying novel pathways or combinations

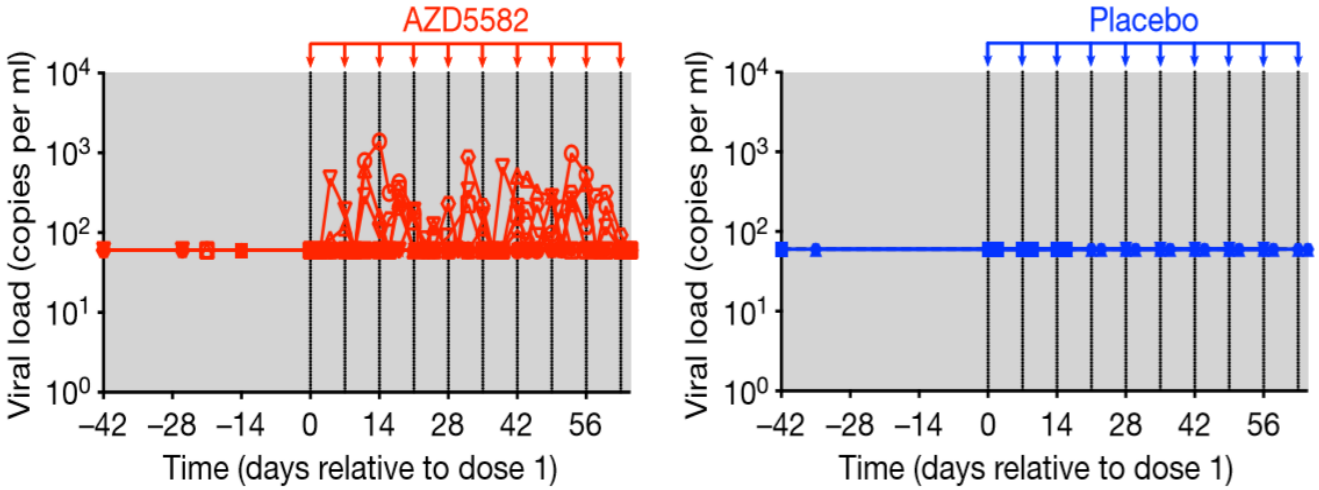
SMAC-mimetics routinely induce latency reversal in animal models

nature

Systemic HIV and SIV latency reversal via non-canonical NF-κB signalling in vivo

https://doi.org/10.1038/s41586-020-1951-3
Received: 12 April 2019
Accepted: 16 December 2019
Published online: 22 January 2020

Christopher C. Nixon[1,2,3,20], Maud Mavigner[4,20], Gavin C. Sampey[2,3,5,6], Alyssa D. Brooks[4], Rae Ann Spagnuolo[1,2,3], David M. Irlbeck[6,7], Cameron Mattingly[4], Phong T. Ho[1,2,3], Nils Schoof[4], Corinne G. Cammon[1,2,3], Greg K. Tharp[3], Matthew Kanke[8,9], Zhang Wang[10], Rachel A. Cleary[1,2,3], Amit A. Upadhyay[4], Chandrav De[1,2,3], Saintedym R. Wills[2,3,5,6], Shane D. Falcinelli[2,3,5,12], Cristin Galardi[6,7], Hasse Walum[3], Nathaniel J. Schramm[1,2,3], Jennifer Deutsch[11], Jeffrey D. Lifson[11], Christine M. Fennessey[11], Brandon F. Keele[11], Sherrie Jean[3], Sean Maguire[11], Baolin Liao[1,2,3,14], Edward P. Browne[2,3,5], Robert G. Ferris[6,7], Jessica H. Brehm[6,7], David Favre[6,19], Thomas H. Vanderford[6], Steven E. Bosinger[8,15], Corbin D. Jones[8,16], Jean-Pierre Routy[16,17], Nancie M. Archin[2,3,5], David M. Margolis[2,3,5,6,12,18], Angela Wahl[1,2,3], Richard M. Dunham[2,3,5,6,21*], Guido Silvestri[4,15], Ann Chahroudi[4,6,18,21*] & J. Victor Garcia[1,2,3,21*]



- No change in reservoir or delay in rebound
  - Why do productive, virus-producing cells persist?
- Toxicity may prevent rapid clinical development

Latency silencing (block and lock)

Natural cures and exceptional control

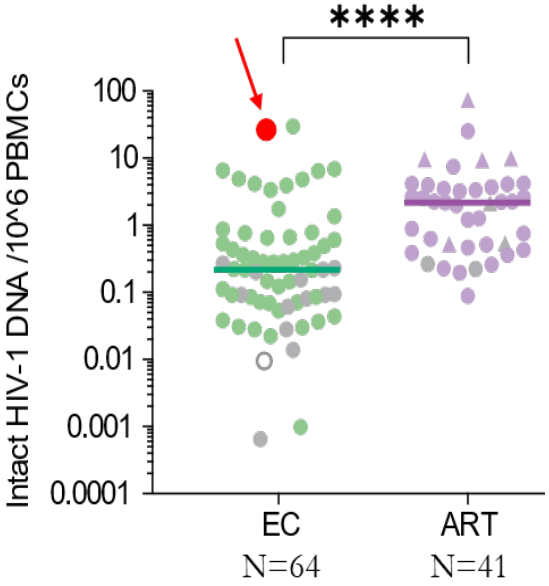
Intact proviral genomes accumulate in “gene deserts”, which is associated with deep and possibly irreversible latency

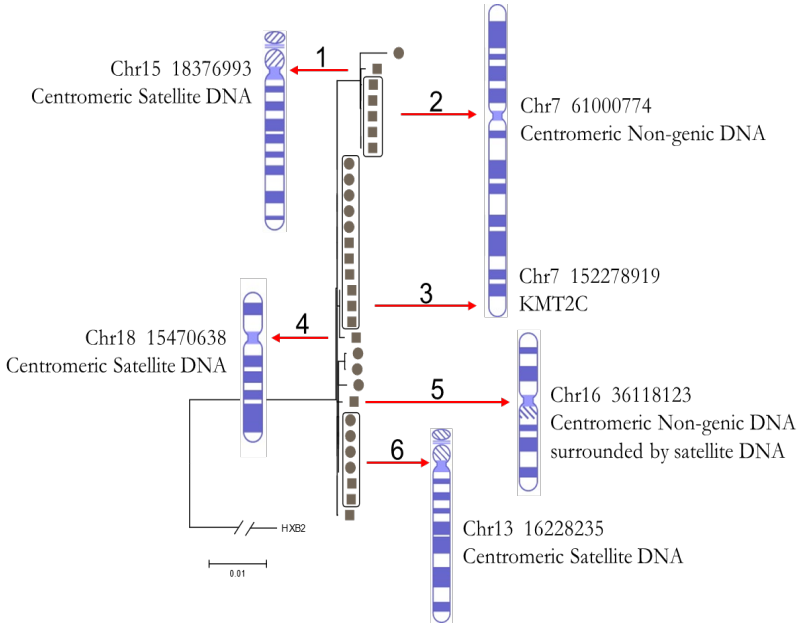
nature

Distinct viral reservoirs in individuals with spontaneous control of HIV-1

/doi.org/10.1038/s41586-020-2651-8
ed: 2 October 2019
ted: 15 July 2020
ed online: 26 August 2020
eck for updates

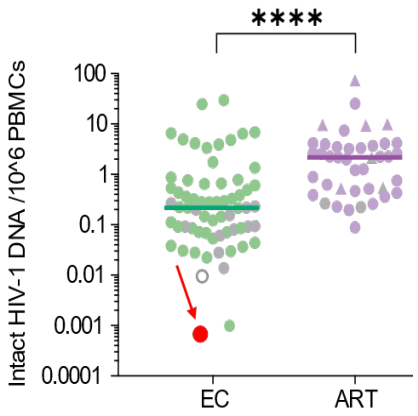
Chenyang Jiang[1,2,15], Xiaodong Lian[1,2,15], Ce Gao[1,15], Xiaoming Sun[1], Kevin B. Einkauf[1,2], Joshua M. Chevalier[1,2], Samantha M. Y. Chen[1], Stephane Hua[1], Ben Rhee[1,2], Kaylee Chang[1], Jane E. Blackmer[1], Matthew Osborn[1], Michael J. Peluso[3], Rebecca Hoh[3], Ma Somsouk[3], Jeffrey Milush[3], Lynn N. Bertagnolli[4], Sarah E. Sweet[4], Joseph A. Varriale[4], Peter D. Burbelo[5], Tae-Wook Chun[6], Gregory M. Laird[7], Erik Serrao[8,9], Alan N. Engelman[8,9], Mary Carrington[1,10], Robert F. Siliciano[4,11], Janet M. Siliciano[4,11], Steven G. Deeks[3], Bruce D. Walker[1,11,12,13], Mathias Lichterfeld[1,2,14] & Xu G. Yu[1,2]✉





Natural Cure

HIV diagnosed in 1992, no ART, undetectable virus 24 years (39 viral loads; one blip), no intact HIV DNA, low and declining HIV antibody levels; lowest level of HIV ever recorded



Test	Cell number	Cell type
Sequencing	>1.5b	PBMC
Intact DNA (PCR)	14m	Resting CD4
Viral outgrowth	340m	Resting CD4

Exceptional Controllers and “Block and Lock”

- Rare clinical phenotype
- Mechanism unknown
- Are we treating too many elite controllers?
- Can we recapitulate this phenotype therapeutically?
  - Lock-and-block strategies: mTOR inhibitors
  - Long-term ART

JCI The Journal of Clinical Investigation

Intact HIV-1 proviruses accumulate at distinct chromosomal positions during prolonged antiretroviral therapy

Kevin B. Einkauf,[1,2] Guinevere Q. Lee,[1,2] Ce Gao,[2] Radwa Sharaf,[1] Xiaoming Sun,[2] Stephane Hua,[2] Samantha M.Y. Chen,[2] Chenyang Jiang,[1,2] Xiaodong Lian,[1,2] Fatema Z. Chowdhury,[2] Eric S. Rosenberg,[3] Tae-Wook Chun,[4] Jonathan Z. Li,[1] Xu G. Yu,[1,2,5] and Mathias Lichterfeld[1,2,5]

Gene therapy

Gene editing for an HIV Cure: Proof of Concept

"It's great that I finally have someone added to my family. It's been too long"
Timothy Brown, Science March 2019

The NEW ENGLAND JOURNAL of MEDICINE

Long-Term Control of HIV by *CCR5* Delta32/ Delta32 Stem-Cell Transplantation

Gero Hütter, M.D., Daniel Nowak, M.D., Maximilian Mossner, B.S., Susanne Ganepola, M.D., Arne Müßig, M.D., Kristina Allers, Ph.D., Thomas Schneider, M.D., Ph.D., Jörg Hofmann, Ph.D., Claudia Kücherer, M.D., Olga Blau, M.D., Igor W. Blau, M.D., Wolf K. Hofmann, M.D., and Eckhard Thiel, M.D.

nature

HIV-1 remission following CCR5Δ32/Δ32 haematopoietic stem-cell transplantation

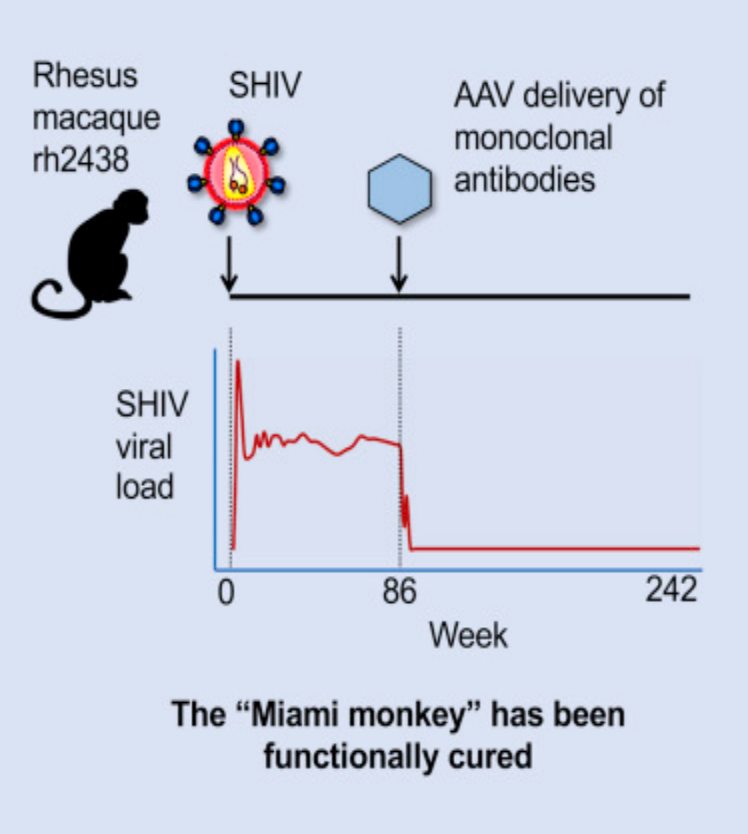
Ravindra K. Gupta[1,2,3,4,5]*, Sultan Abdul-Jawad[1], Laura E. McCoy[1], Hoi Ping Mok[4], Dimitra Peppa[3,6], Maria Salgado[7], Javier Martinez-Picado[7,8,9], Monique Nijhuis[10], Annemarie M. J. Wensing[10], Helen Lee[11], Paul Grant[12], Eleni Nastouli[12], Jonathan Lambert[13], Matthew Pace[6], Fanny Salasc[4], Christopher Monit[1], Andrew J. Innes[14,15], Luke Muir[1], Laura Waters[3], John Frater[6,16], Andrew M. L. Lever[4,17], Simon G. Edwards[3], Ian H. Gabriel[14,15,18,19] & Eduardo Olavarria[14,15,19]

Gene Therapy: Targets and Strategies

- **Protect:** engineer uninfected cells to be resistant to HIV
  - Proof-of-concept: Berlin, London and Dusseldorf cases
- **Kill:** enhance anti-HIV immune responses (CAR-T cells)
  - Proof-of-concept in people pending
- **Control:** Induce life-long production of antiviral antibodies
  - POC established in monkeys (Miami monkey)
  - POC in people pending (VRC07, CROI LB)
- **Purge:** Selectively disrupt and deactivate provirus
  - POC established in mice

Paula Cannon

One-shot cure approaches



nature COMMUNICATIONS

Sequential LASER ART and CRISPR Treatments Eliminate HIV-1 in a Subset of Infected Humanized Mice

Prasanta K. Dash[1,4], Rafal Kaminski[2,4], Ramona Bella[2,4], Hang Su[1], Saumi Mathews[1], Taha M. Ahooyi[2], Chen Chen[2], Pietro Mancuso[2], Rahsan Sariyer[2], Pasquale Ferrante[2], Martina Donadoni[2], Jake A. Robinson[2], Brady Sillman[1], Zhiyi Lin[1], James R. Hilaire[1], Mary Banoub[1], Monalisha Elango[1], Nagsen Gautam[3], R. Lee Mosley[1], Larisa Y. Poluektova[1], JoEllyn McMillan[1], Aditya N. Bade[1], Santhi Gorantla[1], Ilker K. Sariyer[2], Tricia H. Burdo[2], Won-Bin Young[2], Shohreh Amini[2], Jennifer Gordon[2], Jeffrey M. Jacobson[2], Benson Edagwa[1], Kamel Khalili[2] & Howard E. Gendelman[1]

Immunity

Adeno-Associated Virus Delivery of Anti-HIV Monoclonal Antibodies Can Drive Long-Term Virologic Suppression

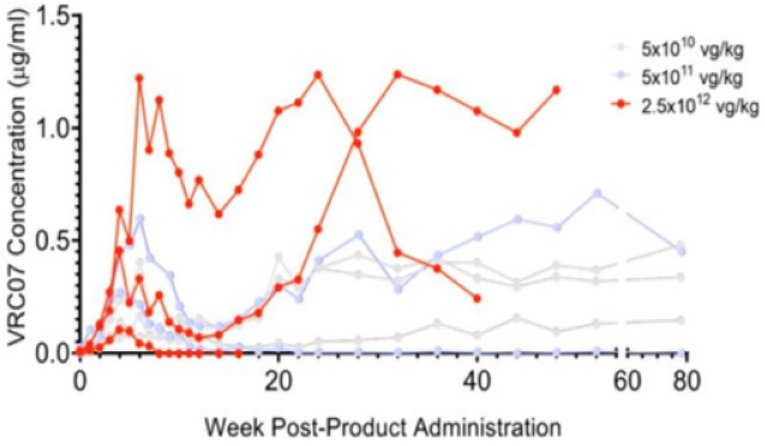
José M. Martinez-Navio,[1,5] Sebastian P. Fuchs,[1,5] Shara N. Pantry,[1] William A. Lauer,[1] Natasha N. Duggan,[1] Brandon F. Keele,[2] Eva G. Rakasz,[3] Guangping Gao,[4] Jeffrey D. Lifson,[2] and Ronald C. Desrosiers[1,6,7,*]

Gene delivery of long-acting antiviral (bANb) or direct *in vivo* gene editing (HIV, CCR5) might eventually lead to durable cure for treated and even untreated people

Aspirational, but theoretically possible

Gene editing for an HIV Cure

Can cells be made into antibody factories that persist indefinitely?



- Miami Monkey: Cured by with a vector (AAV) that introduced bNAb genes into tissues
- VRC 603: 8 people received AAV (three doses); 2/3 at high dose had sustained production of VRC-07

Immunity

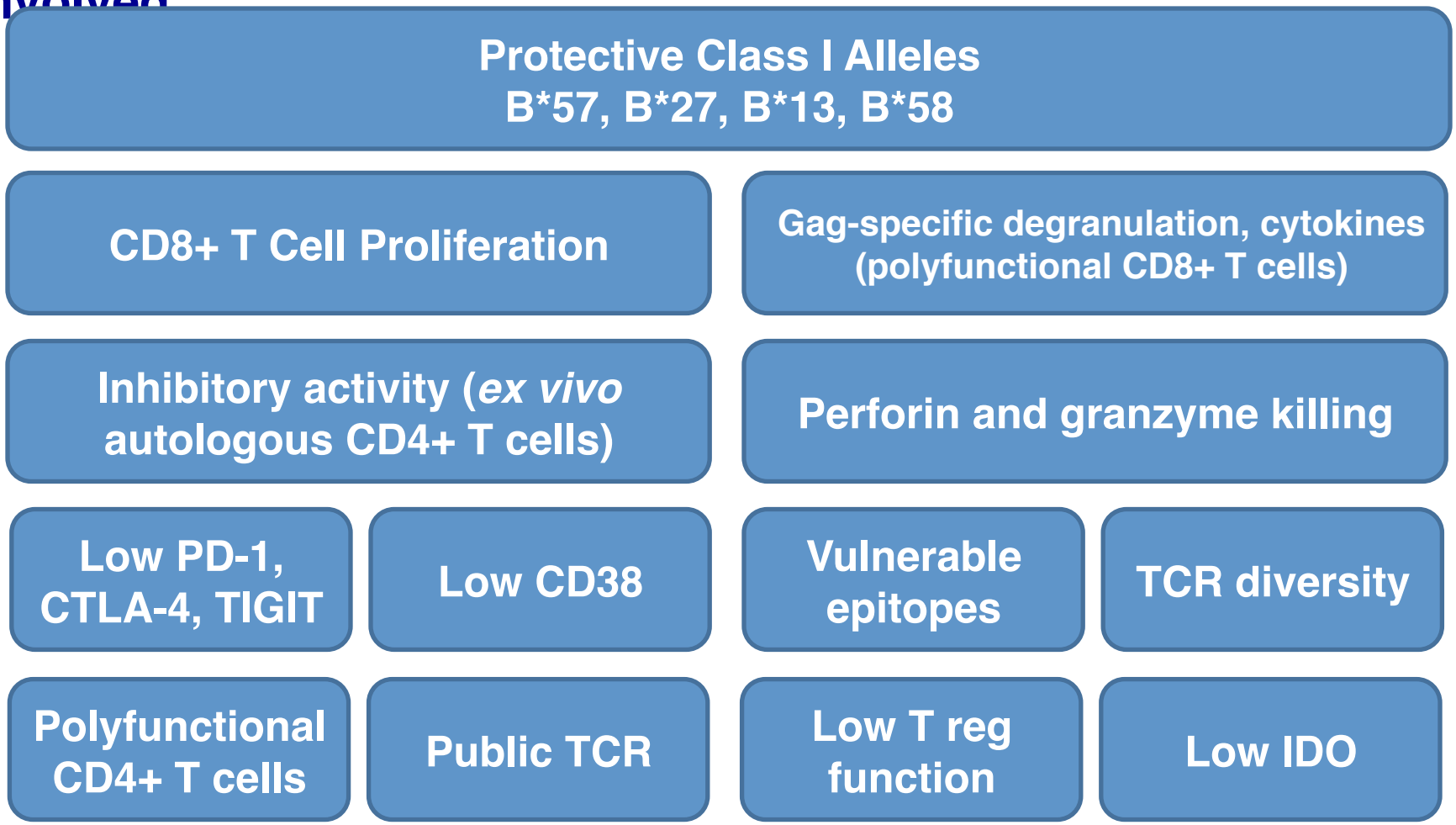
Adeno-Associated Virus Delivery of Anti-HIV Monoclonal Antibodies Can Drive Long-Term Virologic Suppression

José M. Martinez-Navio,[1,5] Sebastian P. Fuchs,[1,5] Shara N. Pantry,[1] William A. Lauer,[1] Natasha N. Duggan,[1] Brandon F. Keele,[2] Eva G. Rakasz,[3] Guangping Gao,[4] Jeffrey D. Lifson,[2] and Ronald C. Desrosiers[1,6,7,*]

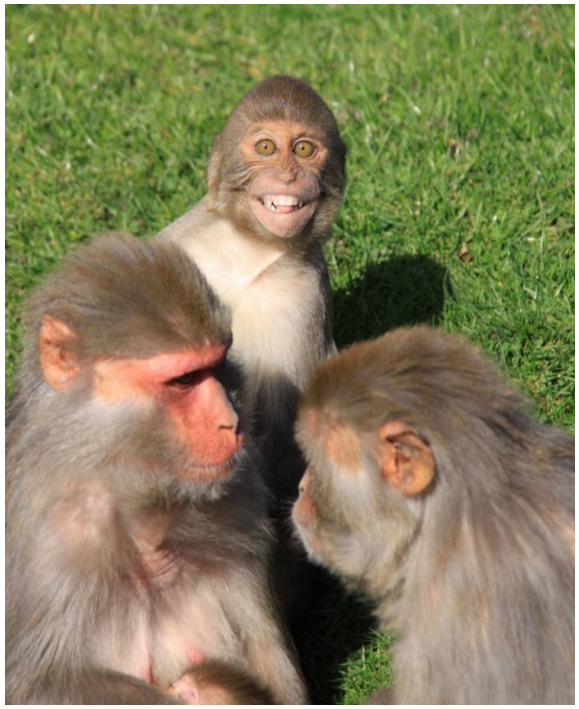
Casazza et al., CROI 2020 (LB 41)

Immunotherapy: Vaccines, broadly neutralizing antibodies, adjuvants, cytokines, and immune checkpoint blockers

"Elite" control is most consistently associated with HIV-specific CD8+ T cell responses, although other pathways are likely involved



Combination Immunotherapy: Proof-of-concept in monkeys



nature

Immune clearance of highly pathogenic SIV infection

Scott G. Hansen[1]*, Michael Piatak Jr[2]*, Abigail B. Ventura[1], Colette M. Hughes[1], Roxanne M. Gilbride[1], Julia C. Ford[1], Kelli Oswald[2], Rebecca Shoemaker[2], Yuan Li[2], Matthew S. Lewis[1], Awbrey N. Gilliam[1], Guangwu Xu[1], Nathan Whizin[1], Benjamin J. Burwitz[1], Shannon L. Planer[1], John M. Turner[1], Alfred W. Legasse[1], Michael K. Axthelm[1], Jay A. Nelson[1], Klaus Früh[1], Jonah B. Sacha[1], Jacob D. Estes[2], Brandon F. Keele[2], Paul T. Edlefsen[3], Jeffrey D. Lifson[2] & Louis J. Picker[1]

nature

Ad26/MVA therapeutic vaccination with TLR7 stimulation in SIV-infected rhesus monkeys

Erica N. Borducchi[1], Crystal Cabral[1], Kathryn E. Stephenson[1], Jinyan Liu[1], Peter Abbink[1], David Ng'ang'a[1], Joseph P. Nkolola[1], Amanda L. Brinkman[1], Lauren Peter[1], Benjamin C. Lee[1], Jessica Jimenez[1], David Jetton[1], Jade Mondesir[1], Shanell Mojta[1], Abishek Chandrashekar[1], Katherine Molloy[1], Galit Alter[2], Jeffrey M. Gerold[3], Alison L. Hill[3], Mark G. Lewis[4], Maria G. Pau[5], Hanneke Schuitemaker[5], Joseph Hesselgesser[6], Romas Geleziunas[6], Jerome H. Kim[7]†, Merlin L. Robb[7], Nelson L. Michael[7] & Dan H. Barouch[1,2]

nature

Early antibody therapy can induce long-lasting immunity to SHIV

Yoshiaki Nishimura[1], Rajeev Gautam[1], Tae-Wook Chun[2], Reza Sadjadpour[1], Kathryn E. Foulds[3], Masashi Shingai[1], Florian Klein[4,5], Anna Gazumyan[6], Jovana Golijanin[6], Mitzi Donaldson[3], Olivia K. Donau[1], Ronald J. Plishka[1], Alicia Buckler-White[1], Michael S. Seaman[7], Jeffrey D. Lifson[8], Richard A. Koup[3], Anthony S. Fauci[2], Michel C. Nussenzweig[6,9] & Malcolm A. Martin[1]

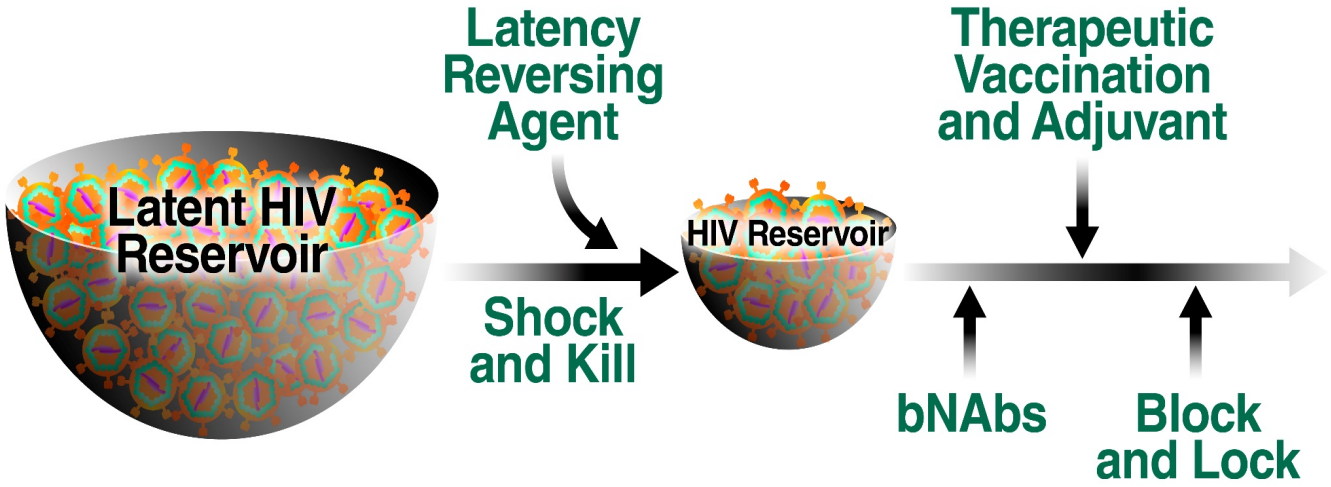
nature

Antibody and TLR7 agonist delay viral rebound in SHIV-infected monkeys

Erica N. Borducchi[1,6], Jinyan Liu[1,6], Joseph P. Nkolola[1,6], Anthony M. Cadena[1,6], Wen-Han Yu[2], Stephanie Fischinger[2], Thomas Broge[2], Peter Abbink[1], Noe B. Mercado[1], Abishek Chandrashekar[1], David Jetton[1], Lauren Peter[1], Katherine McMahan[1], Edward T. Moseley[1], Elena Bekerman[3], Joseph Hesselgesser[3], Wenjun Li[4], Mark G. Lewis[5], Galit Alter[2], Romas Geleziunas[3] & Dan H. Barouch[1,2]*

Reduce and Control

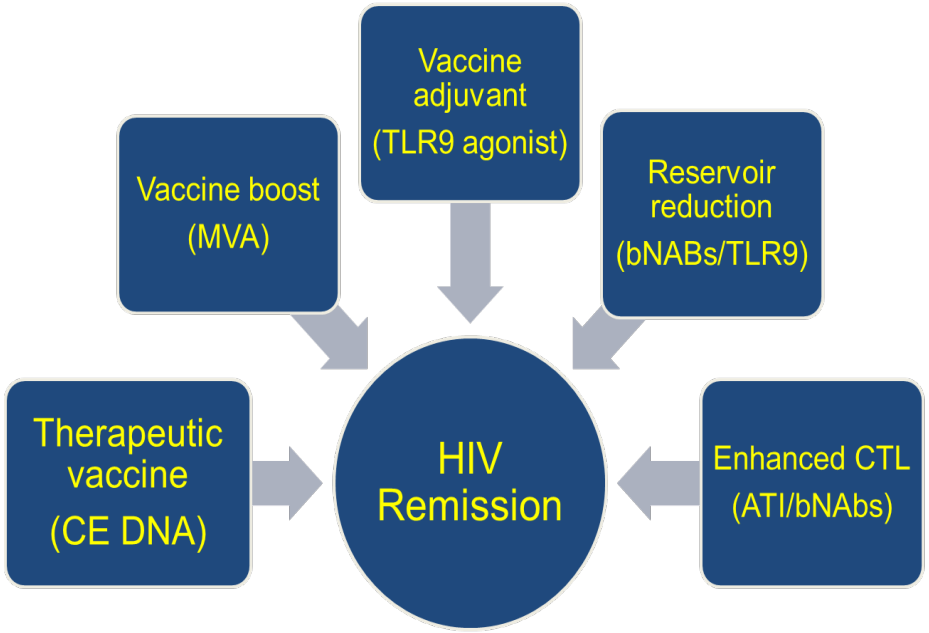
Combining Multiple Modalities To Achieve a Sustained Viral Remission in the Absence of ART



Courtesy of Warner Greene

17040B

Combinatorial therapy with a therapeutic conserved element DNA/MVA vaccine strategy, a TLR9 agonist and broadly neutralizing antibodies: A pilot study aimed at inducing an HIV remission (IND 18488)



amfAR Institute
FOR HIV CURE RESEARCH

GILEAD

The Rockefeller University 1901

ichor medical systems

GeoVax

PROFECTUS BIOSCIENCES

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

MOLOGEN AG
THE POWER OF IMMUNOTHERAPIES

Dale and Betty Bumpers
VACCINE RESEARCH CENTER
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Department of Health and Human Services

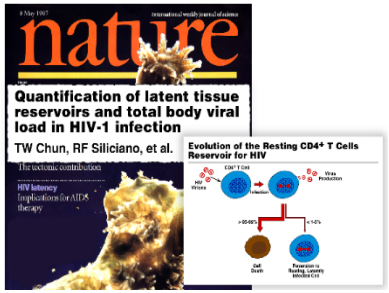
NIH National Institute of Allergy and Infectious Diseases

iavi
International AIDS Vaccine Initiative

NIH NATIONAL CANCER INSTITUTE

A short history of HIV cure research: from cure to remission to cure again

1997
HIV latency identified



2009
The Berlin patient

2010
Post treatment control (remission)

2014-now
Case reports of remission

2019
The London patient

VISCONTI
SPARTAC
CHAMP

Conclusions

- Progress continues to be made, primarily in animal models
- Multiple approaches are being tested
  - All are likely to initially be less effective than optimally delivered ART
  - Iterative process expected with multiple “shots on goal” and ultimate optimization for addressing the needs of the global pandemic
- Massive synergies exist with HIV prevention (vaccines, bNAbs) and non-HIV immunotherapies (cancer, transplant, autoimmunity)


Thank You for Your Attendance!
Please visit us at:
www.prn.org