

LEC 27 HIV UPDATES

00:00:09:30
DAYS HOURS MINUTES SECONDS

Every 9½ minutes, someone in the U.S. is infected with HIV

ABOUT 1 IN 4 NEW
HIV INFECTIONS IS AMONG
YOUTH AGES 13-24



MOST OF THEM DO NOT KNOW THEY ARE
INFECTED, ARE NOT GETTING TREATED, AND CAN
UNKNOWINGLY PASS THE VIRUS ON TO OTHERS



CORRESPONDENCE

More on Shift of HIV Tropism in Stem-Cell Transplantation with *CCR5* Delta32/Delta32 Mutation

N Engl J Med 2014; 371:2437-2438 | December 18, 2014 | DOI: 10.1056/NEJMc1412279

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To the Editor:

In 2009, my colleagues and I reported the successful transplantation of stem cells with a 32-bp deletion in the chemokine (C-C motif) receptor 5 (*CCR5*) allele (*CCR5* delta32/delta32) in a patient who was infected with the human immunodeficiency virus type 1 (HIV-1). This finding has led to further research to find a cure for HIV-1 infection.¹ Repetition of this unique approach to provide a proof of principle was awaited. Kordelas et al. (Aug. 28 issue)² describe another patient in whom the same approach failed.

In fact, since 2007, when our patient underwent successful transplantation in Berlin, at least another six patients have received a graft from a donor who had been screened for homozygosity for the *CCR5* delta32/delta32 mutation (Table 1). Unfortunately, none of the six recipients survived for longer than 1 year, and in the case reported by Kordelas et al., a chemokine (C-X-C motif) receptor 4 (CXCR4)-tropic HIV-1 variant rebounded rapidly after transplantation. These unexpected results can be explained in part because the grafts were associated with a higher rate of early death among four of the six patients.

A lesson to be taken from the case described by Kordelas et al. may be to continue the administration of antiretroviral therapy during transplantation until a stable donor chimerism is achieved. In addition, finding appropriate unrelated donors for transplantation and selecting an HLA match as well as an adult donor who is homozygous for the *CCR5* delta32/delta32 mutation is worth careful consideration.⁴

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Dr. Hütter reports being employed by Cellex. No other potential conflict of interest relevant to this letter was reported.

TABLE 1

Men with Human Immunodeficiency Virus Type 1 (HIV-1) Infection Who Received an Allogeneic Transplant from a Stem-Cell Donor Who Was Homozygous for the *CCR5* delta32/delta32 Mutation.

nan Immunodeficiency Virus Type 1 (HIV-1) Infection Who Received an Allogeneic Transplant from a Stem-Cell ozygous for the *CCR5* delta32/delta32 Mutation.*

Age of Patient yr	Type of Cancer	Type of Graft	Outcome after Transplantation
40	Acute myeloid leukemia	HLA-matched unrelated	Alive after 7 yr, no viral rebound, no ART
53	Myelodysplastic syndrome	Combined haploidentical bridge with umbilical-cord blood	Died from relapse of the myelodysplastic syndrome and pneumonia after 2 mo
51	Non-Hodgkin's lymphoma	HLA-mismatched unrelated	Died from infection after 4 mo
30	Non-Hodgkin's lymphoma	HLA-matched unrelated	CXCR4-tropic HIV-1 rebound, died from relapse of non-Hodgkin's lymphoma after 12 mo
12	Acute lymphoblastic leukemia	Umbilical-cord blood	Died from GVHD after 3 mo
46	Non-Hodgkin's lymphoma	HLA-matched related	Died from pneumonia shortly afterward
37	Non-Hodgkin's lymphoma	Combined haploidentical bridge with umbilical-cord blood	Died from relapse of non-Hodgkin's lymphoma after 3 mo

viral therapy, and GVHD graft-versus-host disease.
et al.¹
t al.⁵
nal communication with the transplantation center.
s et al.²

Sangamo presents immunological data from SB-728-T HIV clinical study at CROI 2016

Published on February 25, 2016 at 1:09 AM · No Comments

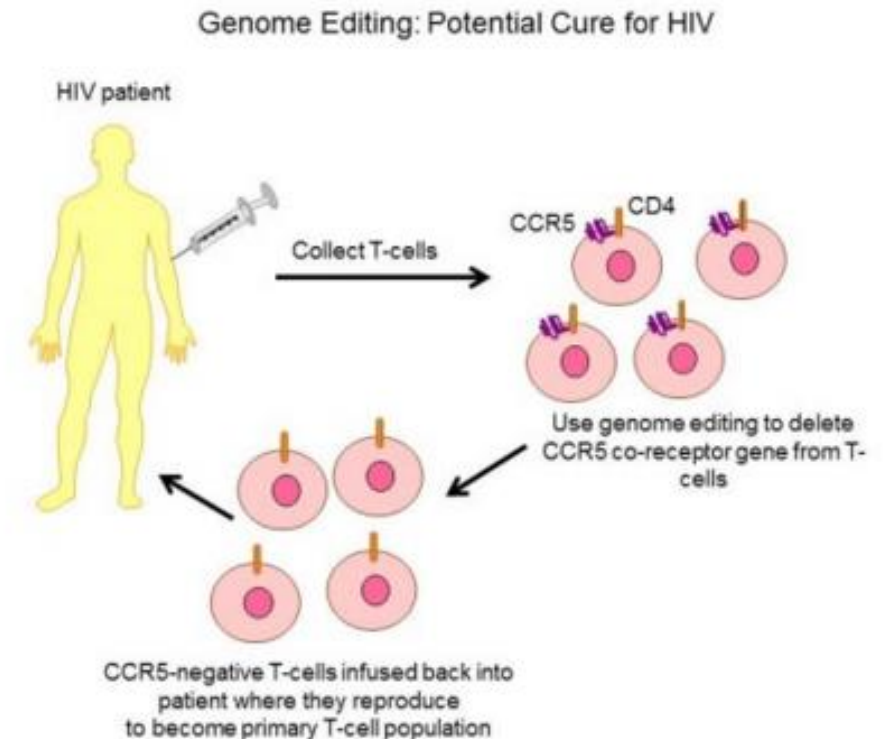


Sangamo BioSciences, Inc. (Nasdaq: SGMO), the leader in therapeutic genome editing, announced the presentation of immunological data from the Company's clinical trials of SB-728-T, a ZFP Therapeutic® designed to provide functional control of HIV. Analysis of data from Sangamo's most recent SB-728-1101 study suggests key, potentially interrelated mechanisms for viral load (VL) control in treated subjects during a treatment interruption (TI) from their antiretroviral therapy (ART). The analysis was presented by Sangamo's collaborator, Rafick-Pierre Sékaly, Ph.D., Richard Fasenmeyer Chair in Immunopathogenesis, Case Western Reserve University, at the 2016 Annual Conference on Retroviral and Opportunistic Infections (CROI 2016). The meeting is being held in Boston from February 22-26, 2016.

"A significant number of subjects treated with SB-728-T have experienced a striking control of their viral load for a sustained period in the absence of ART," stated Dr. Sékaly. "This is particularly notable in cohorts treated with optimal doses of Cytosine® in the SB-728-1101 study. Immunological and HIV reservoir analyses suggest that the best predictors for post-treatment viral control are higher levels of SB-728-T engraftment, specifically long-lived memory T-cells, evidence of polyfunctional antiviral CD8 responses during TI and lower HIV reservoir levels prior to TI. This may provide a model mechanism of action for SB-728-T and help identify HIV-infected individuals who will benefit most from this novel immune-based therapy."

- Lower viral loads, more antiviral CD8
- Modified cells multiply and last
- One delta 32 hetero has undetectable VL for 1 Yr without ART

Somatic gene therapy : infusion of T cells lacking CCR5



CROI Boston '16 2 yrs on Prep multidrug resistance breakout virus



First Man to Become **HIV**-Positive While on PrEP Is Rare E...

Advocate.com - Feb 26, 2016

... the U.S. (The other part is treatment as prevention—**TasP** — in which people who are **HIV**-positive take medication to reach viral suppression ...

169aLB HIV-1 Infection With Multiclass Resistance Despite Preexposure Prophylaxis (PrEP)

David C. Knox¹; Darrell H. Tan²; P. Richard Harrigan³; Peter L. Anderson⁴

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Background: PrEP is reported to have nearly 100% prevention efficacy in men who have sex with men (MSM) when adherence is high. We report a 43 year old MSM who seroconverted to multi-class resistant HIV-1 (day 0; 4th generation Ag/Ab combo screen positive, p24 positive, Western Blot negative) after 24 months of successful PrEP, despite clinical and pharmacokinetic data suggesting long-term adherence to FTC/TDF.

PrEP effective: STIs increasing

Sexually transmitted infections and pre-exposure prophylaxis: challenges and opportunities among men who have sex with men in the US

[Hyman M. Scott](#) and [Jeffrey D. Klausner](#)

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Abstract

Go to: 

Pre-Exposure Prophylaxis (PrEP) has shown high efficacy in preventing human immunodeficiency virus (HIV) infection among men who have sex with men (MSM) in several large clinical trials, and more recently in “real world” reports of clinical implementation and a PrEP demonstration project. Those studies also demonstrated high bacterial sexually transmitted infection (STI) incidence and raised the discussion of how PrEP may impact STI control efforts, especially in the setting of increasing *Neisseria gonorrhoeae* antimicrobial resistance and the increase in syphilis cases among MSM. Here, we discuss STIs as a driver of HIV transmission risk among MSM, and the potential opportunities and challenges for STI control afforded by expanded PrEP implementation among high-risk MSM.

Uganda's ABC Program UPDATE 2012

AFRICA

In Uganda, an AIDS Success Story Comes Undone

The New York Times

By JOSH KRON AUG. 2, 2012

On one hand, 90 percent of Ugandans today acknowledge sexual fidelity in a relationship as a health imperative, according to the survey results; on the other hand, roughly 25 percent of married men said they had multiple sexual partners.

The survey found that 75 percent of Ugandans were knowledgeable about condoms in sexual health but that fewer than 8 percent of married men who were having sex outside their marriage were using condoms.

Uganda's hard-line approach toward homosexuality, which is outlawed here, also fuels the spread of AIDS, experts say. [One report](#) indicated that one-third of the male respondents who had sex with other men said they had previously been married to women and fathered children. Fewer than half use condoms.

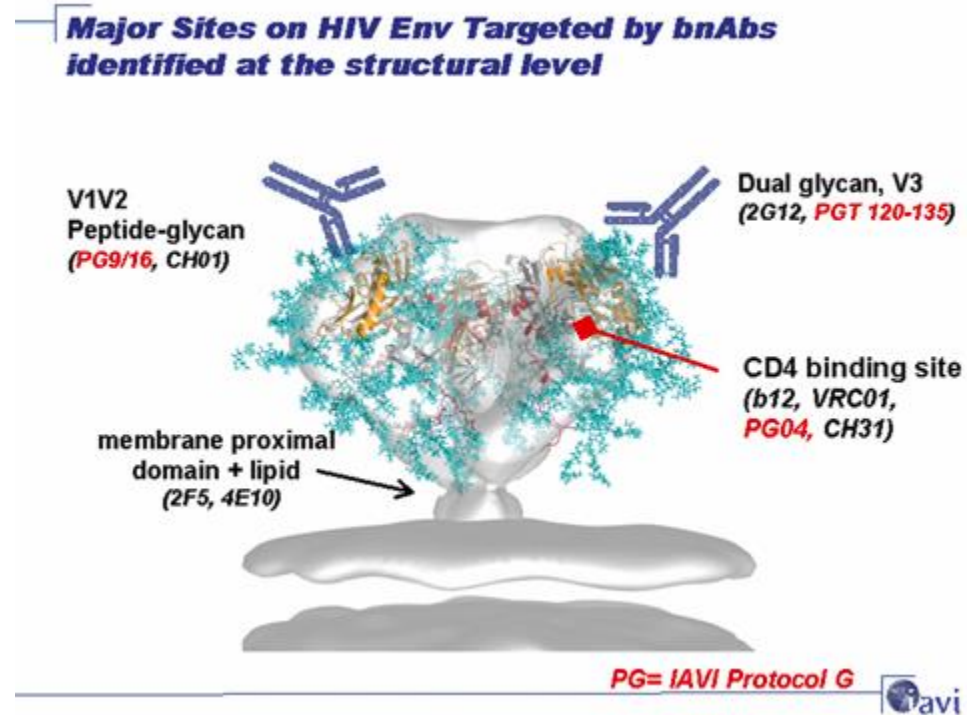


‘57% drop in HIV cases but illiteracy, unprotected sex still biggest hurdles’

Sumitra Deb Roy, TNN | Dec 2, 2013, 04:43 AM IST

The survey report underlines how the uneducated population contributes to 44% of the deaths, even though the rate of infection among them is only about 27%. Education, say experts, clearly has a defining role to play in HIV care but how and why is subject to further exploration. The report says the average time lost before a patient approaches a free anti-retroviral centre is about 7.4 months. "A delay in starting treatment could lead to faster deterioration of a patients' health and s/he may also fall prey to opportunistic infections, like TB," said a volunteer with one of the city's 69 Integrated Testing and Counselling Centres.

bnAbs: broadly neutralizing antibodies



- Attempts to treat with hyperimmune sera around since 1982
- Most HIV+ make bnabs
- VRCO1 isolated from EC with Undetected infection for 15yrs*
- Crystal structure Ab/gp120 to be published 4/26/2016
- Currently in Trials

140 1970s HIV-1 Genomes Reveal the Early History of the North American HIV/AIDS Epidemic

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Background: The precise origins of the western hemispheric HIV/AIDS pandemic remain contentious. Phylogenetic studies based upon HIV-1 sequences sampled after (in most cases long after) the recognition of AIDS in 1981 have suggested a lengthy cryptic period of circulation in the U.S. and Canada throughout the 1970s, and an even older presence in the Caribbean. However, no comprehensive evolutionary genomic analysis of HIV-1 in North America closer to the putative emergence of the virus in the 1970s has been possible since no non-African HIV-1 complete genomes from that era have been sequenced to date.

Methods: Here, we combine approaches from molecular biology, phylogenetics, and historical analysis to investigate the timing and geography of the emergence of HIV-1 group M subtype B in the U.S. We designed an approach to overcome the challenge of recovering HIV-1 genetic material from older serum specimens in which viral RNA template material is highly fragmented and at low concentration. We recovered near-full length HIV-1 genome sequences from eight U.S. patient serum samples from 1978-79 (comprising eight of the nine earliest HIV-1 group M genomes sequenced worldwide to date) and also from the individual known as 'Patient 0'. We then used maximum likelihood and Bayesian 'relaxed molecular clock' phylogenetic and phylogenomic methods to infer timing and geography.

Results: This early genomic 'snapshot' of HIV-1 reveals that by 1978-79 the HIV-1 epidemic in the U.S. already exhibited extensive genetic diversity – particularly in New York City (NYC) – having emerged around 1970 from a founder virus drawn from an older and more diverse subtype B epidemic in the Caribbean. Moreover, there is neither biological nor historical evidence that Patient 0 was the primary case in the U.S. or for subtype B as a whole.

Conclusions: Our findings reveal a series of key founder events in the genesis of the subtype B epidemic, with a single virus moving from the African epicenter of HIV-1 group M to the Caribbean by 1967 [1964-1970], a single virus moving from the Caribbean to establish an epidemic in NYC by 1971 [1969-73], and yet another single virus moving from there to San Francisco by ~1975 (but with extensive geographical mixing in the U.S. and beyond shortly thereafter). We discuss, in the context of these insights into the early spread of HIV/AIDS in North America, the genesis and persistence of beliefs about 'Patient 0' that are unsupported by scientific data.



CDC: Half of black gay men will be diagnosed with HIV

About a quarter of gay Hispanic men are also estimated to be diagnosed with the disease at some point in their lifetime.

By Stephen Feller | Feb. 24, 2016 at 11:41 AM [Follow @upi](#)

Based on current rates of infection, the agency found 1 in 6 men who have sex with other men will be diagnosed with HIV at some point during their lifetime, which represents a 79 times greater chance of diagnosis than heterosexual men. The risk varies by race and ethnicity, researchers found, as gay and bisexual black men have a 1 in 2 risk of diagnosis, while Hispanic men have a 1 in 4 risk and white men have a 1 in 11 risk.

HIV progress lags for gay, bisexual minorities, Southern states

December 7, 2015

 READ/SUBMIT COMMENTS  EMAIL  PRINT  SAVE    

ATLANTA — New cases of HIV infection in the United States dropped 19% from 2005 to 2014 due to continuing declines among several populations, according to data presented at the CDC's National HIV Prevention Conference. However, the data suggested that gay and bisexual minorities and people residing in the South are disproportionately affected by HIV.

See Also

[CDC recognizes National Black HIV/AIDS Awareness Day ...](#)

[Health ads on social media reach Rhode Island MSM](#)

[HIV testing rates low for gay male adolescents](#)

According to the CDC, 1.2 million people in the U.S. have HIV, and 40,000 new infections are diagnosed each year.

HIV trends vary by race, ethnicity

While new infections in white gay and bisexual men decreased by 18%, diagnoses among Hispanic gay and bisexual men steadily increased up to 24% even though HIV testing remained stable in recent years (2010-2014). In addition, new diagnoses increased by 22% in black gay and bisexual men before leveling off in 2010. Further increases were observed in younger black gay and bisexual men aged 13 to 24 years, with an 87% increase between 2005 and 2014. The trend, however, showed a 2% decline since 2010, according to the data.

Featured



- Highest HIV infection rate
- # 1 Miami
- # 10 Orlando
- # 15 Jacksonville

**Irene Monroe**

♥ Become a fan

Nationally renowned African-American lesbian activist,
scholar, public theologian and writer

On World AIDS Day report on black community still grim

Posted: 12/02/2015 11:52 am EST | Updated: 12/02/2015 11:59 am EST

According to **HIV/AIDS data** in my state there are 26,000 - 27,000 individuals currently living with HIV/AIDS throughout the Commonwealth of Massachusetts with urban areas the hardest hit. Although African American and Latinos comprise of 6 percent and 10 percent, respectively, of the total Massachusetts population, shockingly African American and Latino populations are diagnosed with HIV infection at levels 10 and 6 times that of the white population, respectively. And, infections among MSM increased from 32 percent in 2004 to 46 percent in 2013.

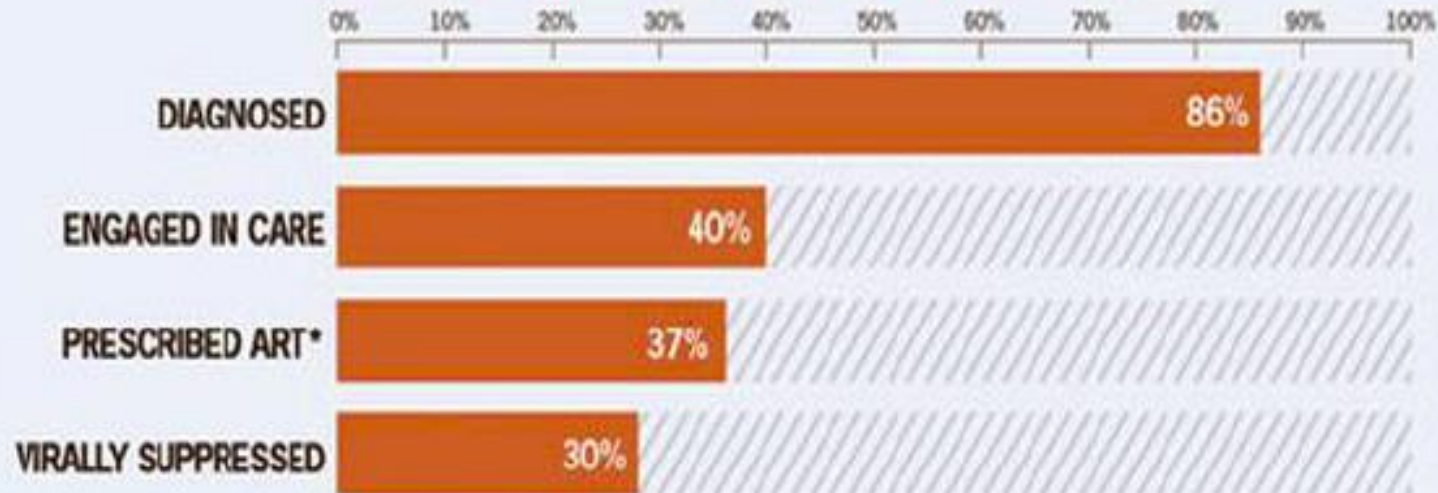
WHY is HIV transmission hetero vaginal in resource poor parts of the world

- co-infection with other sexually transmitted diseases, circumcision practices, poor acceptance of condoms,
- patterns of sexual partner selection*,
- locally circulating viral subtypes,
- high viral loads among those who are infected
- Access to health care
- * segregating factors

30 years... 35 Million dead... 30% treated

HIV Care Continuum Shows Where Improvements are Needed

In the US, 1.2 million people are living with HIV. Of those:



SOURCES: CDC National HIV Surveillance System and Medical Monitoring Project, 2011.

*Antiretroviral therapy

- **> 70 Million infections, 39M currently infected**