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INNOVATIONS

SEPTEMBER 2017

A Gene Therapy Revolution?

New amfAR grants coincide with big step forward for gene therapy

Also Inside:

A Marker of Latently Infected Cells?

Forging Unlikely Collaborations

When Drugs Are the Price of Diamonds

SEPTEMBER 2017

The biannual newsletter of amfAR,
The Foundation for AIDS Research

120 Wall Street, 13th Floor
New York, NY 10005-3908
T: (212) 806-1600
F: (212) 806-1601

1100 Vermont Ave. NW
Suite 600
Washington, DC 20005
T: (202) 331-8600
F: (202) 331-8606

TREAT Asia
Exchange Tower
388 Sukhumvit Road
Suite 2104
Klongtoey, Bangkok 10110
Thailand
T: (+66) 2 663-7561
F: (+66) 2 663-7562

www.amfar.org

Innovations Staff:
Andrew McInnes, Editor
Megan Trusdell, Senior Staff Writer
Claudia Kaplan, Senior Staff Writer
Raoul Norman-Tenazas,
Creative Director
Yolande Hunter-Johnson,
Creative Coordinator



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New amfAR grants coincide with big step
forward for gene therapy

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A Virtuous Cycle

Photo: Getty Images

Six-year-old Emily Whitehead was close to death when she received an experimental treatment in a last-ditch effort to cure her aggressive leukemia. Mercifully, the treatment worked and today, six years on, Emily remains cancer-free.

This lifesaving therapy involved the use of designer immune cells – T cells taken from Emily’s blood, reengineered to make them able to zero in on cancer cells, and reinfused back into Emily’s bloodstream. In a major milestone, an FDA panel recently recommended that this experimental treatment be approved for use – the first ever gene therapy to be given the green light in the U.S.

So what does this have to do with HIV? Well, it’s increasingly clear that cancer research has a great deal in common with HIV cure research. For example, studies are underway in both areas to find ways of boosting the immune response, developing and refining gene-editing tools, and altering gene expression so that infected cells become visible to the immune system.

As you’ll read on pages 10-11, amfAR has just awarded an exciting new round of gene therapy grants, including two that involve strategies similar to the CAR (chimeric antigen receptor) cell therapy used to cure Emily

Whitehead. And it’s no coincidence that Dr. Carl June of the University of Pennsylvania, who pioneered the therapy, is a member of amfAR’s Cure Council.

All of this serves to remind us that HIV research has never existed in isolation. Since the beginning of the epidemic, it has been a testing ground for new concepts and technologies in drug development, diagnostics, and disease prevention. And many new treatments for diseases such as cancer, hepatitis, and heart disease have arisen from research on HIV/AIDS. So it’s a virtuous cycle.

At amfAR, we’ll continue to cast as wide a net as possible in our efforts to develop a cure for HIV and to collaborate with scientists from a range of fields and disciplines (see Forging Unlikely Collaborations, page 8). Innovation and collaboration are the principles that guide our research endeavors. And with your generous support, they will guide us to a cure for HIV.

With gratitude,

Making Sense of America's Opioid Crisis



Photo: © Syda Productions | Dreamstime

amfAR has launched a comprehensive online database to help communities, policymakers, and advocates effectively respond to the opioid epidemic.

The Opioid & Health Indicators Database—<http://opioid.amfar.org/>—provides local and national statistics on HIV and hepatitis C infections, opioid use, overdose death rates, and the availability of services such as drug treatment and syringe services programs. Users can browse data at the state and county levels and see the differential impact of the opioid, HIV, and hepatitis C epidemics in communities across America.

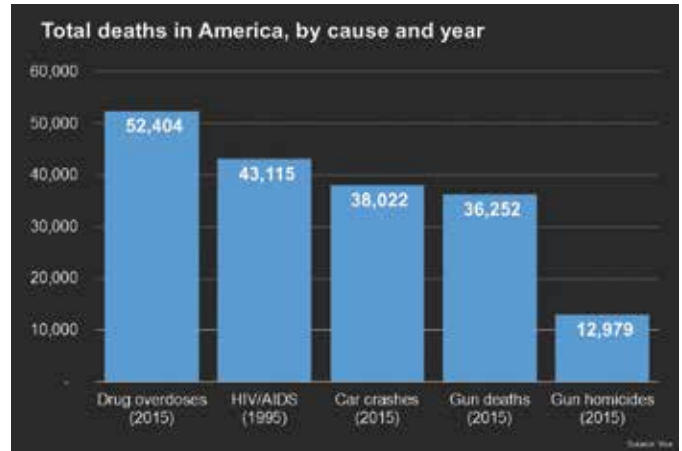
Injection drug users accounted for 10% of new HIV infections in 2015 and most cases of hepatitis C (HCV) are the result of drug use behaviors. More than 60% of people with HCV go on to develop chronic liver disease and 1–5% die from liver cancer or liver failure.

In spring 2015, rural Scott County, IN, experienced an unprecedented outbreak of

HIV and HCV largely attributed to injection drug use, prompting then-governor and current Vice President Mike Pence to declare a public health emergency.

“The first step in responding to a public health crisis of this magnitude is understanding where we need to be responding and what the barriers are to doing so,” said Alana Sharp, a policy associate at amfAR.

The database was unveiled at the amfAR Capitol Hill conference, “Making AIDS History: A Roadmap for Ending the Epidemic,” on June 14 (see story on opposite page).



A New Take on Harm Reduction

A novel effective approach to saving lives

Drug overdose fatalities have reached epidemic proportions in the U.S., largely because of opioids, particularly prescription painkillers and heroin. In addition, people who use drugs are at high risk for HIV infection, accounting for 11% of all men and 23% of all women living with HIV. Most hepatitis C (HCV) cases in the U.S. are also associated with injection drug use.

Many people who inject drugs lack access to sterile injection equipment and a safe, hygienic place to inject. This often drives them to share needles, spreading blood-borne infections such as HIV and HCV, and to inject in public spaces

including bathrooms in fast food restaurants, hospitals, libraries, and churches.

A new amfAR issue brief outlines the case for supervised consumption services (formerly, safe injection facilities), which provide a hygienic space for people to use illicit drugs under the supervision of trained staff. These facilities are designed to reduce the risk of HIV/HCV transmission, prevent overdose fatalities, and provide a bridge to treatment and other social services. Almost 100 such facilities are operating in Europe, Canada, and Australia.

Supervised consumption services have been shown to lower rates of syringe sharing, reduce public injecting, and promote safer and more hygienic drug use. Moreover, there is no evidence that they increase drug use or drug-related crimes, or initiate new users.

The issue brief concludes: “The evidence is clear that supervised consumption services are a remarkably effective and cost-effective approach to improving the lives of people who use drugs and the health and security of the communities in which they live.”

Read the issue brief at <http://bit.ly/2rVVCsy>.

Government, Health Leaders Urge Continued Investments in HIV/AIDS Programs

A substantial cut in federal funding for HIV/AIDS programs would jeopardize the progress made against the epidemic, according to government officials, scientists, and public health leaders who convened at the amfAR Capitol Hill conference, “Making AIDS History: A Roadmap for Ending the Epidemic,” on June 14.

The Trump Administration’s proposed fiscal year 2018 budget would slash \$800 million from global AIDS programs, resulting in tens of thousands more HIV infections and AIDS-related deaths.

“An 18% proposed cut for the National Institutes of Health (NIH) would also be a significant setback for the discovery of a cure and a vaccine, which are essential elements in our roadmap to end AIDS,” said Conference Chair Dr. Susan J. Blumenthal, amfAR’s senior policy and medical advisor and former United States Assistant Surgeon General.

Members of Congress, including Sens. Thad Cochran (R-MS) and Patrick Leahy (D-VT), chairman and ranking minority member of the Senate Appropriations Committee, House



Conference Chair Dr. Susan Blumenthal, amfAR senior policy and medical advisor (Photo: amfAR)



amfAR Chairman Kenneth Cole (Photo: Getty Images)



Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases (Photo: Getty Images)

Minority Leader Nancy Pelosi (D-CA), and Rep. Barbara Lee (D-CA), co-chair of the Congressional HIV/AIDS Caucus, voiced support for the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund, and vowed to protect U.S. investments in these transformative global health programs.

The conference included three panel discussions: “The Opioid Crisis, HIV/AIDS and Hepatitis C: Interconnected Epidemics

in America,” moderated by Joel Achenbach, author and staff writer at *The Washington Post*; “AIDS to Zika: National Security Implications of Epidemics,” moderated by *PBS NewsHour* Anchor Judy Woodruff; and “Aging with AIDS in America: The Health and Economic Impacts,” moderated by Regan Hofmann, UNAIDS Policy Advisor and an amfAR Trustee.

Other distinguished speakers included Ambassador Dr. Deborah Birx, U.S. Global AIDS Coordinator, UNAIDS Executive Director Michel Sidibé, amfAR Chairman Kenneth Cole, and veteran AIDS research leader Dr. Anthony Fauci, director of the NIH’s National Institute of Allergy and Infectious Diseases.

“If we make the right investments, and we’re smart about how we support the science, we will make AIDS history.”



Ambassador Dr. Deborah Birx, U.S. Global AIDS Coordinator (Photo: Getty Images)



Dr. David Smith, acting assistant secretary of defense for health affairs, and PBS NewsHour Anchor Judy Woodruff (Photo: Getty Images)

The afternoon ended with remarks from amfAR CEO Kevin Robert Frost, who provided an update on amfAR’s Countdown to a Cure initiative, which is aimed at developing the scientific basis of a cure by 2020.

“If we make the right investments, and we’re smart about how we support the science, we will make AIDS history,” he said.

To read more about the briefing, visit www.amfar.org/2017-amfAR-Capitol-Hill-Conference/.

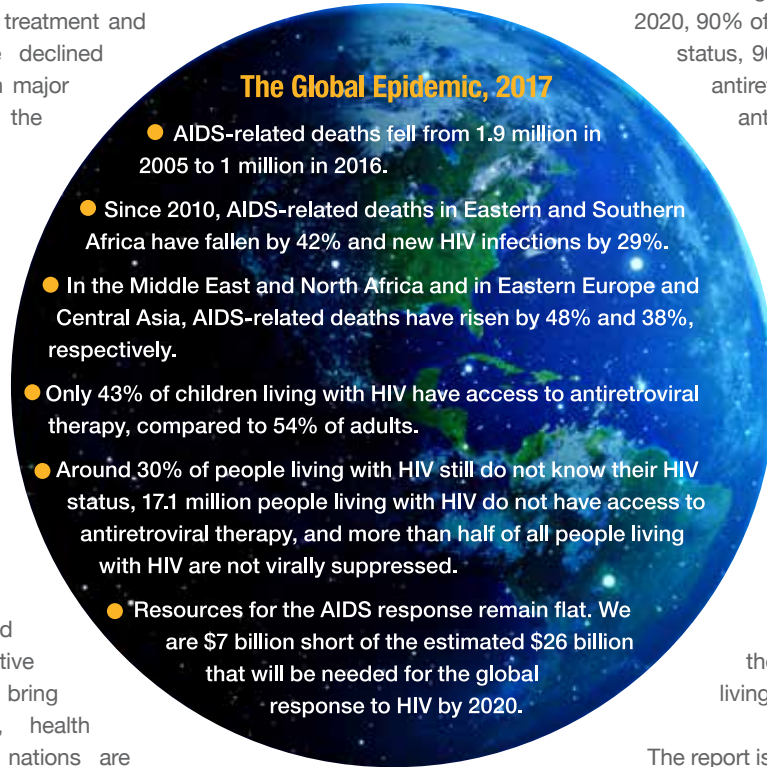
Record Number of People on Treatment

New report details progress toward 90-90-90 targets

In July, UNAIDS announced that more than half of all people living with HIV are on treatment and that AIDS-related deaths have declined by almost half since 2005—both major milestones in the fight against the epidemic.

In its report, “Ending AIDS—progress towards the 90-90-90 targets,” UNAIDS revealed that in 2016, 19.5 million of the estimated 36.7 million people living with HIV were taking antiretrovirals. If current trends continue, the target of 30 million people on treatment will be achieved by 2020.

“Communities and families are thriving as AIDS is being pushed back,” said UNAIDS Executive Director Michel Sidibé. “As we bring the epidemic under control, health outcomes are improving and nations are becoming stronger.”



The 90-90-90 targets were launched in 2014 so that, by 2020, 90% of all people living with HIV know their HIV status, 90% of those with diagnosed HIV are on antiretroviral therapy, and 90% of those on antiretroviral therapy are virally suppressed.

The UNAIDS report shows that the region showing the most progress is Eastern and Southern Africa, which accounts for half of all people living with HIV.

But progress has been poor in the Middle East and North Africa and in Eastern Europe and Central Asia.

Additionally, around 30% of people living with HIV still do not know their status, 17.1 million people living with HIV do not have access to antiretroviral therapy, and more than half of all people living with HIV are not virally suppressed.

The report is available at www.unaids.org.

Mexico City Policy Revived and Expanded

amfAR issue brief outlines potential impact on global AIDS funding

A U.S. policy that blocks federal funding for nongovernmental organizations (NGOs) performing or promoting abortion has been going back and forth since President Reagan introduced the measure in 1984. After being revoked by President Obama, the policy has been resuscitated and expanded by the Trump administration.

Under previous administrations, the so-called Mexico City Policy applied only to U.S. assistance for family planning programs. In fact, President Bush specifically exempted the President’s Emergency Plan for AIDS Relief (PEPFAR) when it was created in 2003.

However, Trump’s order extends the requirements to global health assistance furnished by all departments or agencies, including PEPFAR.

“All PEPFAR programs would end up being more expensive, less efficient, and less effective as a result.”

In a new issue brief, amfAR examines the potential impact of the policy and its effect on non-U.S. NGOs and non-U.S. partners. In a worst-case scenario based on 2016 data, the policy would affect \$703 million per year of PEPFAR funding and cause 14.9% of adults and children on antiretroviral therapy (ART)—including 24.7% of pregnant women—to experience treatment interruption or loss of services.

The revised Mexico City Policy could also dismantle long-established relationships the U.S. has with organizations implementing programs on the ground.

The issue brief concludes: “All PEPFAR programs would end up being more expensive, less efficient, and less effective as a result, and the lives of people living with HIV, including women and infants, would be put at risk.”

Read the issue brief at www.amfar.org/pepfar-mexico-city.

Researchers Report Rare Case of HIV Remission

Case is among highlights of international Conference on HIV Science

A 9-year-old South African child with HIV has been in remission for over eight years, scientists reported at the 9th IAS Conference on HIV Science in Paris in July. The child was born with HIV in 2007 and put on antiretroviral treatment at nine weeks of age. Treatment was interrupted at 40 weeks when the virus had been suppressed. The child has maintained an undetectable level of HIV.

There have been two other reported cases of a child in remission from HIV after early treatment. The Mississippi Baby, born with HIV in 2010, controlled the virus without drugs for 27 months before it reappeared in her blood. And in 2015, researchers reported that a French child, who was born with HIV in 1996 and treated for roughly six years, continued to control the virus more than 11 years later.

Commenting on the case of the South African child, amfAR Vice President and Director of Research Dr. Rowena Johnston said: “While we work toward our ultimate goal of a full cure for HIV, we can learn a great deal from cases of remission like this one,” such as understanding the HIV reservoir and various factors associated with post-treatment control of the virus.



“With that understanding, we could then devise ways to manipulate those factors in a manner that could be reliably replicated in more and more people living with HIV,” she said.

The presentation on the South African child was one of several highlights of the IAS Conference, which was attended by more than 8,000 researchers and advocates from over 140 countries. The conference was chaired by International AIDS Society (IAS) President Dr. Linda-Gail Bekker and organized in partnership with the ANRS (the French National Agency for Research on AIDS and Viral Hepatitis).

Forty-two amfAR-funded researchers delivered talks on their recent findings, and another 49, including seven TREAT Asia investigators, gave abstract or poster presentations.

“We’re at a critical juncture in HIV research,” said Bekker. “Despite the remarkable scientific progress made, there are many roadblocks

slowing its implementation. Now is the time for science to drive our progress forward.”

Other conference highlights included:

- **Treatment for HIV and coinfections are improving and becoming easier to take.** Monthly or bimonthly injections of ART could replace daily pills for people living with HIV, and long-acting injectable pre-exposure prophylaxis (PrEP) may be on the horizon.
- **Prevention efforts are gaining ground.** A large study, partially funded by amfAR, shows that gay HIV-positive men whose viral load is undetectable do not transmit the virus to their HIV-negative partners.

“We’re at a critical juncture in HIV research ... Now is the time for science to drive our progress forward.”

- **Links between treating HIV and cancer explored.** The conference was preceded by the IAS HIV Cure & Cancer Forum, the first major scientific gathering to address synergies in the treatment of HIV and cancer.
- **With enough will, prevention and treatment are achievable.** In Swaziland, the country with the highest HIV incidence in the world, expanded prevention and treatment has led to the incidence of HIV nearly halving in the past five years.

Also at the conference, amfAR Chairman Kenneth Cole, founder of the newly launched End AIDS Coalition (EAC), moderated a discussion with panelists including UNAIDS Executive Director Michel Sidibé, Marijke Wijnroks, the Global Fund’s interim executive director, and Ambassador Dr. Deborah Bix, U.S. Global AIDS Coordinator.

amfAR-Funded Researcher Honored



Dr. Maria Salgado of the IrsiCaixa AIDS Research Institute in Spain was honored with the Dominique Dormont Award during the 9th IAS Conference on HIV Science. The award recognizes young researchers working on chronic conditions, with a particular focus on the interface between HIV and other long-term illnesses.

Salgado is a member of the amfAR-created and funded IcsiStem, a consortium of European researchers that aims to replicate the case of Timothy Brown, the “Berlin patient” — the first and only person to be cured of HIV. Brown, who also had leukemia, received a stem cell transplant from a donor with a rare genetic mutation, CCR5-delta32, which confers resistance to HIV.

Forging Unlikely Collaborations

New cure research grants enlist help from bioengineers

amfAR is pairing HIV researchers with bioengineers to address the main barrier to a cure: persistent reservoirs of virus not cleared by antiretroviral therapy. A new round of Investment grants, totaling \$1.2 million, will support six such projects.

“Over the past couple of decades, stunning advances in bioengineering have led to the development of new technologies and therapeutics that will likely have a profound impact on treating and eradicating diseases,” said amfAR CEO Kevin Robert Frost. “Many of these exciting new technologies have yet to be evaluated in the realm of HIV cure research. We hope this new round of grants lays the groundwork for some innovative approaches to a cure.”

The Investment awards are milestone-based grants that provide up to \$1.5 million to each research team in three phases over four years.

Bioengineers with expertise in cutting-edge technologies, such as microfluidics, gene editing, and nanotechnology, will work closely with HIV cure scientists to tackle some of the most intractable challenges in HIV cure research.

One pair of researchers will apply magnetic levitation of single cells to identify and characterize HIV reservoirs (see sidebar). Another will use mass spectrometry to identify molecules on the surface of the cells that differentiate the latent reservoir from uninfected cells.

“This is a very exciting round of research grants that forges some unlikely but potentially groundbreaking scientific alliances,” said Dr. Rowena Johnston, amfAR vice president and director of research. “These highly innovative projects will undoubtedly move HIV cure research in some extraordinary new directions that, we hope, will get us closer to our goal.”

For more, go to www.amfar.org/bioengineers-grants



Outside the Box

amfAR researchers probe maglev technology

Magnetic levitation—maglev—is a technology typically associated with high-speed train travel. But Dr. Timothy Henrich, of the University of California, San Francisco, and the amfAR Institute for HIV Cure Research, and bioengineer Dr. Utkan Demirci from Stanford University, will use magnetic levitation of single cells to identify and characterize HIV reservoirs. amfAR spoke to Henrich about the role of bioengineering in HIV cure research and the details—and novelty—of their approach.



What role can bioengineering play in HIV cure research?

Engineering plays a huge role in HIV cure research. I often tell members in my laboratory that any scientific question can be answered provided we have the tools (and of course the wisdom to ask the right questions). No experiment is impossible. It just lacks the appropriate engineering to make it happen.

Can you explain in simple terms what you are hoping to achieve?

Basically, cells will levitate when placed within a very strong magnetic field (think of trying to put two magnets with the same pole together), and they will levitate at different heights depending on the magnetic density properties of the cell. Our idea is that infected cells may be physically different, perhaps only with a very small difference in density. If you apply a strong enough magnetic field to them in the right environment, then you can identify and separate these cells. The idea is a long shot, but some of our preliminary work is quite compelling.

How novel is the research you are conducting?

What we are doing is completely out of the normal box of HIV curative research. Rather than look for very specific markers on the surfaces of cells, or signals that the cells produce when latently infected, we have taken the opposite approach by looking at the entire cell in a non-specific nature. Normally, this is not how biological science is done, but this does not mean that it can't be useful.

A Marker of Latently Infected Cells?

Intriguing finding has scientific community abuzz

The difficulty in distinguishing immune cells that are latently infected with HIV—the viral reservoir—from uninfected cells remains one of the biggest obstacles to a cure for HIV.

In the March issue of the journal *Nature*, Dr. Monsef Benkirane of the University of Montpellier in France and colleagues at other

French research institutions announced they had discovered a protein that can differentiate latently infected cells.

The protein, called CD32a, is normally associated with immune cells of the innate immune system, and it is surprising to find this protein on the CD4 T cells that constitute the majority of the reservoir.

Researchers have long sought a specific marker of the reservoir. Its central importance to HIV cure research was underlined at amfAR's think tank in April in Palo Alto, CA, which brought together about a dozen scientists from around the world, including Benkirane, to discuss the latest advances

and future efforts to find such markers.

Further studies are needed to confirm and expand on Benkirane's findings.

But if his discovery holds up, CD32a could be used to scrutinize infected cells more closely and to help researchers design interventions to eliminate latently infected cells while leaving other cells untouched.

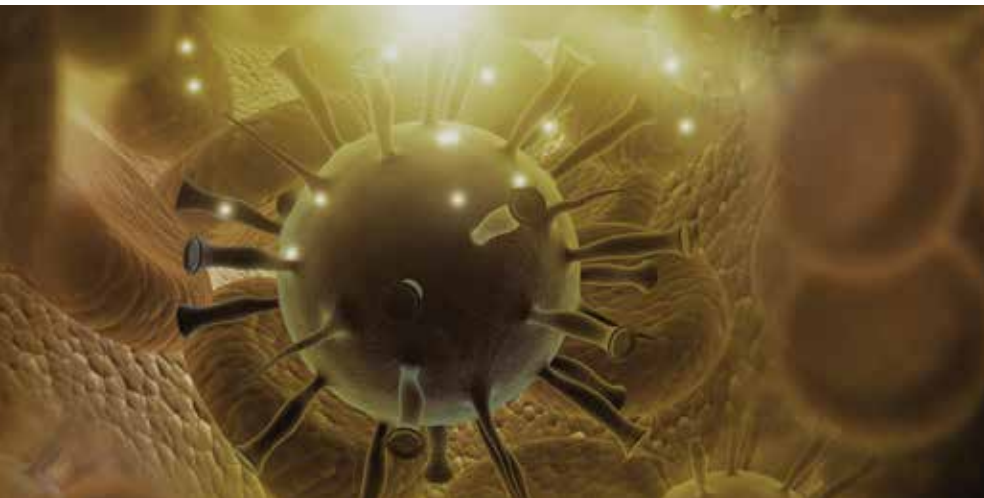
"Finding a definitive marker of latently infected cells would be a breakthrough for HIV cure research," said Dr. Rowena Johnston, amfAR vice president and director of research.



Dr. Monsef Benkirane
(Photo: Sarrauste de Menthère /CNRS IGH)

“Finding a definitive marker of latently infected cells would be a breakthrough for HIV cure research.”

New Grants Advance Innovative Approaches to HIV Cure



In July, amfAR announced a new round of Innovation grants totaling \$1.2 million to six researchers who will explore mechanisms of HIV persistence and the potential for eradicating the virus. Innovation grants are designed to test and advance pioneering ideas in the early stages of their development.

For instance, Dr. Andrew Badley, from the Mayo Clinic College of Medicine in Rochester, MN, will test whether ixazomib, a drug currently used to treat the blood cancer multiple myeloma, can reduce the HIV reservoir. Dr. Joshua Schiffer, from Fred Hutchinson Cancer Research Center in Seattle, will test a drug normally used to prevent organ transplant rejection for its potential to eliminate the reservoir.

continued on page 13

amfAR'S Research: Quantity and Quality

Since launching the Countdown to a Cure for AIDS initiative in 2014, **amfAR has awarded 58 Countdown grants totaling more than \$41 million to support research** conducted by **222 scientists working at 74 institutions in 10 countries.**

A review of recently published HIV cure research shows that **amfAR grantees consistently published their findings in journals with a higher impact factor** than researchers not funded by amfAR. A journal's impact factor reflects the influence and importance of the findings it publishes.

A Gene Therapy Revolution?

New amfAR grants coincide with big step forward for gene therapy

In July, amfAR awarded two research grants to explore the use of CAR (chimeric antigen receptor) cells to cure HIV. The announcement coincided with an FDA panel's recommendation to approve the first ever gene therapy-based treatment in the U.S. using a similar strategy for cancer.



Dr. Keith Jerome

The grants are part of a new round of seven awards totaling \$2.3 million in support of gene therapy-based approaches to curing HIV—modifying HIV or host cell DNA to permanently remove latent HIV reservoirs, the main barrier to a cure. They were awarded through the amfAR Research Consortium on HIV Eradication (ARCHE), a program that fosters collaboration among teams of scientists. The goal of the grants: to develop curative interventions that can be tested in clinical studies.

“Curing HIV is no longer a pipe dream, and the case of ‘the Berlin patient’ provides proof-of-principle that a cure is possible,” said amfAR CEO Kevin Robert Frost, referring to the only person known to have been cured of HIV with a procedure that points to the promise of gene therapy. “However, several complex scientific challenges remain, and these new grants reflect amfAR’s determination to pursue a range of strategies to overcome them.”

CAR Cells and Cure

CAR cells have shown promise in their ability to clear some cancers in patients. The treatment the FDA panel recommended for approval was first developed by Dr. Carl June of the University of Pennsylvania, a member of amfAR’s Cure Council, for children with B-cell acute lymphoblastic leukemia, the most common blood cancer in children. It requires removing a patient’s T cells and genetically engineering them with CAR cells that can recognize and kill tumors.

In the case of HIV, the goal is for CAR cells to recognize and kill the cells that harbor HIV.

For example, amfAR grantee Dr. Scott Kitchen, of the University of California, Los Angeles, hopes to improve the effectiveness of CAR cells by preventing them from being destroyed, either by becoming HIV

infected or by the usual processes of direct or indirect suppression of the immune system by the virus.

“We want the CAR cells to be protected from infection and allow them to persist and be as fully functional as they can be in an HIV-infected individual,” Kitchen said.

And amfAR grantee Dr. Richard Wyatt, of The Scripps Research Institute in La Jolla, CA, aims to generate CAR T cells that are able to not only recognize and kill reservoir cells, but also produce antibodies that can both direct the immune system to kill infected cells and neutralize any virus circulating in the body (see sidebar).

“That will restrict reinfection of any new cells in the absence of drugs,” he said.

Gene Therapy and HIV

In recent years, there has been an explosion in gene therapy research, in part because of CRISPR gene-editing and similar technologies, which allow scientists to replace defective genes with functional ones, said amfAR grantee Dr. Keith Jerome of the University of Washington in Seattle.

“We understand HIV, the way it persists in the body, and the ways the body fights back, better than we ever have before,” he said. “So gene therapy gives us a way to use all this new knowledge in the fight against HIV, and maybe even develop a cure.”

“Gene therapy gives us a way to use all this new knowledge in the fight against HIV, and maybe even develop a cure.”

Indeed, gene therapy offers the tantalizing possibility of targeting the viral DNA that makes up the HIV reservoir, altering the susceptibility of cells to HIV infection, or enhancing the ability of the immune system to attack or block the virus.

But it carries a number of risks and challenges. Scientists need to find ways to improve the efficiency of appropriately altering DNA, effectively target the gene therapy to the correct cells, and enable the therapy to safely persist long enough to have an effect.

Longtime HIV Researcher Turns to Gene Therapy

Dr. Richard Wyatt's career as an HIV researcher was jump-started with an amfAR fellowship in the mid-1990s. With a brother-in-law who was HIV positive, he had a personal connection to the illness. Wyatt is now the director of viral immunology at IAVI's Neutralizing Antibody Center at The Scripps Research Institute in La Jolla, CA. He was recently awarded an amfAR grant to support his work on a gene therapy approach to the cure of HIV.

amfAR awarded you your first grant. What did you study?

I was working to try and develop broadly neutralizing antibodies against the HIV envelope glycoprotein, which is the only protein on the surface of the virus that antibodies can bind to so that they can neutralize the virus. While I didn't solve it with that grant, it definitely jump-started my career.



How significant is the FDA panel's recent recommendation to approve the first gene therapy treatment for cancer?

It's huge. Gene therapy has really changed cancer outcomes, especially for liquid tumors [leukemia and lymphoma], where they're using CAR T technology. For what we're doing in infectious disease, it's a little newer, but I think it's quite exciting and could really have some important ramifications down the line.

You are proposing to use CAR T cells to cure HIV. Can you briefly describe your approach?

We would remove the infected person's T cells and reengineer them with broadly neutralizing antibodies that can bind to and recognize the HIV envelope glycoprotein [which enables HIV to gain entry into cells]. We would then reinfuse the modified T cells into the person. Presumably this would be a person on antiretroviral drugs who is already suppressing the virus very well. The idea would be to take those drugs away, then the CAR T cells would eliminate any cells starting to express the envelope glycoprotein. It's personalized medicine, and it has a lot of parallels to the immune-oncology approach.

What are the steps involved in testing this strategy?

We already have at least one CAR T cell with one broadly neutralizing antibody that can kill T cells in a test tube. Right now, we're working to make sure we can express the antibody against HIV. Then we can test this again in the test tube, and soon after use a mouse model. If that's successful, we could test it in monkeys infected with SIV [the monkey equivalent of HIV]. We would suppress the virus with drugs, take out their T cells, make our CAR T that can recognize the expressing cells and secrete antibodies to HIV, take the monkeys off the drugs, and see if their viral load is suppressed. If that happens, that would be very exciting and a good rationale for human clinical testing.

"All our gene therapy approaches have a big 'ask,' — they need to find their way to the right cells in the body, and they need to modify the DNA appropriately," said Jerome. "Today, we often do that by taking T cells or stem cells from the body, putting in our anti-HIV gene therapies, and giving them back. But it's a complicated process."

The other grantees are: Dr. Hildegard Büning of Hannover Medical School in Hannover, Germany; Dr. Hans-Peter Kiem of Fred Hutchinson Cancer Research Center in Seattle; Dr. Yasuhiro Takeuchi of University College London in the United Kingdom; and Dr. Drew Weismann of the University of Pennsylvania in Philadelphia.

They will pursue projects aimed at: designing and refining vectors that can accurately target the cells that make up the reservoir and regions such as the lymph nodes, where the reservoir cells tend to be concentrated; and exploring the potential of using viral and non-viral delivery mechanisms to deliver emerging types of genetic scissors that could, for example, cut the virus out of human DNA.

Biking the Distance for a Cure

South Florida woman pedaling 6,000 miles across North America for amfAR



Twenty years ago, Uli Shackmann pedaled 275 miles over three days with hundreds of other cyclists to raise money for a local HIV agency.

Now she's riding 6,000 miles solo over seven months for an HIV cure.

Shackmann, along with her 20-pound canine companion, Jackson, began her journey on May 8 in Anchorage, AK. She is riding—while

Shackmann, 58, of Fort Lauderdale, FL, participated in her first charity ride in 1996, mostly for the physical challenge. She was surprised that so many of the riders and crew were HIV positive.

"I really didn't know the impact of this disease," she said. "Over those three days, we built a really loving and supportive community."

"I share that same vision," she said. "I want to make a powerful statement that we need a cure."

For the ride, Bike America, a South Florida bicycle chain, gave her a Cannondale hybrid and supplies, including a trailer for Jackson. Bassist Chuck Panozzo of the rock band Styx donated an electric guitar to use as a fundraising tool.

So far, she has raised \$6,000. She hopes to complete her ride on November 19.

"Breakthroughs come from being committed to something, even if the path to achieve it is unclear," she said. "My path across the North American continent will demonstrate that, with belief and commitment, anything is possible."

To follow Shackmann's journey, visit www.ulisjourney.com.

"My path across the North American continent will demonstrate that, with belief and commitment, anything is possible."

Jackson runs beside her—50 miles a day south and then east to Key West, FL, with the goal of raising \$50,000 for amfAR.

"This journey will really represent the struggle of someone living with HIV/AIDS," Shackmann told amfAR prior to her departure. "There will be good days and days when things break down. It will be a constant reminder that you have to work through the struggles you're facing."

She has since done at least 18 rides to raise funds for HIV services, including the annual SMART Ride from Miami to Key West. Since 2003, the ride has raised more than \$8.5 million for AIDS organizations.

This year, Shackmann wanted to do something bold, "something out there," and she wanted to raise money for research. She was inspired by amfAR's goal of developing the scientific basis of a cure by 2020.

Remembering Wally Sheft



Longtime amfAR Trustee Wallace Sheft passed away peacefully in Florida on March 12. He was 87.

Mr. Sheft—or Wally, as he was affectionately known—joined the board of the National AIDS Research

Foundation (NARF) in September 1985. He became a founding director of amfAR a few weeks later, following the unification of the Los Angeles-based NARF and the New York-based AIDS Medical Foundation.

He served as amfAR's treasurer from March 1987 until his resignation from the Board in August 2015.

As business manager for the late Rock Hudson, Mr. Sheft was the executor of Hudson's estate after he died of AIDS-related causes in October 1985. Hudson donated \$250,000 to amfAR

in September 1985, making the first direct contribution to the nascent foundation.

Mr. Sheft retired from a certified public accounting firm that specialized in handling the business affairs of actors and others in the entertainment field.

"Wally was a reliable and dedicated supporter and caretaker for amfAR through many ups and downs in our earliest years," said amfAR Chairman Kenneth Cole. "We will always remember and be grateful for the knowledge, wisdom, and passion he brought to the organization and the cause."

2017 HIV CURE SUMMIT

TUESDAY, NOVEMBER 28
University of California, San Francisco

Join us at this free, half-day
community event where you'll
hear the latest from scientists at the
amfAR Institute for HIV Cure Research.

For more information, visit www.curecountdown.org.

continued from page 9

Additionally, Drs. Andrew Henderson, from Boston University School of Medicine in Boston, and Fabio Romerio, from the University of Maryland in Baltimore, will explore a cure strategy known as “block & lock,” which aims to silence HIV and prevent its re-emergence when antiretroviral therapy is stopped.

At the George Washington University in Washington, D.C., Dr. Brad Jones aims to develop a new class of broadly neutralizing antibodies that enables the immune system to recognize proteins not normally accessible to the body’s antibody-making machinery. The goal is to increase the number of people in whom broadly neutralizing antibodies are able to find and kill HIV-infected cells.

And to better understand how Timothy Brown, the “Berlin patient,” was cured of HIV, Dr. Benjamin Burwitz, from Oregon Health and Science University in Portland, will explore the precise mechanisms that led to his cure by generating a monkey model lacking the protein CCR5, the primary means by which most types of HIV infect cells.

For more, go to www.amfar.org/Innovation-Grants-July-2017



amfAR Promotes AIDS Research at NYC Pride March

More than 150 amfAR supporters and staff marched down Fifth Avenue alongside amfAR’s float in the New York City Pride March on June 25. Among those aboard the science-themed float with giant-sized test tubes were amfAR generationCURE Ambassador Kelly Osbourne, drag performer Ongina, actor Gbenga Akinnagbe, amfAR CEO Kevin Robert Frost, and amfAR Trustee Aileen Getty. (Photo: Getty Images)

Special thanks: AssistRx, Cadillac, and HBO

When Drugs Are the Price of Diamonds

Millions lack access to lifesaving treatment for hepatitis C

About 71 million people worldwide are infected with hepatitis C (HCV), according to the World Health Organization, and approximately 400,000 die each year as a result of the infection, primarily from liver cancer and cirrhosis.

Today's direct-acting antiviral drugs (DAAs) can cure more than 95% of infected people with a 12-week course of medicine.

So why are there so many deaths?

The uneven and inadequate access to lifesaving DAAs was a major theme of the International Liver Congress in Amsterdam, April 19-23, which was attended by 10,000 experts in liver research.

"There is wide variability throughout countries of the Asia-Pacific region in the availability, registration status, and price of generic and brand-name DAAs," said Giten Khwairakpam, TREAT Asia's project manager of community and policy, in a community summit presentation prior to the main congress. "Whether you can get specific DAAs, and how much you will have to pay for them, depends on where you live."



5 gm each of diamonds (left) and the active ingredient of daclatasvir (right). (Photo: Dr. Andrew Hill)

"It remains one of the greatest tragedies of modern times that these lifesaving drugs are not being deployed on a mass scale."

Dr. James Freeman of FixHepC in Hobart, Australia, agreed. "It remains one of the greatest tragedies of modern times that these lifesaving drugs are not being deployed on a mass scale," he said during his presentation at the conference.

He pointed out that 5 grams of the brand-name version of the DAA daclatasvir, which can be part of a 12-week treatment, costs \$50,000, the same as 5 grams of diamonds. But a similar supply of the generic can be made for under \$100.

Treatment Snapshot: Dolutegravir

Dolutegravir (DTG) belongs to a newer class of antiretroviral medicines known as integrase inhibitors. It is used for the treatment of HIV in combination with other antiretrovirals in adults, adolescents, and older children.

The World Health Organization (WHO) has recommended its use as an alternate first-line medicine, which could substantially change the landscape for ART scale-up and implementation. Because it is a highly durable drug and less susceptible to the emergence of resistance, access to DTG in countries that need it is an emerging issue in the global HIV/AIDS response.

amfAR's TREAT Asia program has prepared a fact sheet that summarizes key regulatory information, clinical research, and current pricing of DTG. It can be accessed at www.amfar.org/dtg/.



Tablet sizes of efavirenz 600 mg (top) and 200 mg (middle) compared to dolutegravir 50 mg (bottom). Markings on the tablet, color, and design may differ among manufacturers.

Freeman highlighted the REDEMPTION-1 study, which demonstrated the effectiveness of generic DAAs. So far, data have been collected on 1,160 patients receiving generic drugs in 88 countries.

However, "regulatory red tape" makes manufacturing and distributing generic versions difficult, said study co-author Dr. Andrew Hill of the University of Liverpool.

"With enough willpower, this epidemic could be over in 5–10 years," Hill said. "Otherwise, hepatitis C medications could be priced out of reach for all but the extremely rich."

PrEP in the Philippines

Project PrEP seeks to assess feasibility of HIV prevention drug among at-risk population

In July, enrollment began for a two-year pilot project that introduces pre-exposure prophylaxis (PrEP)—an oral antiretroviral drug—to men who have sex with men (MSM) and transgender women at risk of HIV infection in the Philippines.

The project, known as PrEP (PrEP Pilipinas), will evaluate community-based, peer-driven delivery of PrEP at two clinics in metro Manila. A total of 200 HIV-negative MSM and transgender women will be offered PrEP for free. The project will include routine HIV testing, PrEP education, treatment preparedness, and adherence and peer support. The Philippines is one of the first countries in Asia to introduce the HIV prevention intervention.

amfAR is among several organizations involved in Project PrEP, a multiagency collaboration with



Volunteers at a LoveYourself clinic in Manila

an international team of experts from government, academia, and multilateral and nongovernmental organizations. The World Health Organization (WHO) Regional Office for the Western Pacific, the Research Institute for Tropical Medicine (RITM),

and LoveYourself, an LGBT community organization in Manila, are also partners.

“Efforts to address the burgeoning HIV epidemic in the Philippines are inadequate, and there is now an urgent need to take more effective measures to reduce HIV transmission among vulnerable populations,” said amfAR CEO Kevin Robert Frost. “We’re excited to be a part of this unique partnership in deploying an important tool in our arsenal against HIV, especially among MSM.”

Over 9,200 HIV infections were reported in the Philippines in 2016, and 85% of new infections are among MSM.

“We’re excited to be a part of this unique partnership in deploying an important tool in our arsenal against HIV.”

amfAR Summit Shines Spotlight on HIV/AIDS in Brazil

In a recent community education initiative, amfAR hosted an HIV research summit at the University of São Paulo, Brazil, on March 29.

The conference, which drew 250 community members, medical students, healthcare professionals, and representatives from 10 São Paulo-based nongovernmental organizations, was held in conjunction with the Advanced Course on HIV Pathogenesis at the university’s School of Medicine.

The summit featured presentations by Dr. Esper Kallas, an infectious disease specialist and a professor at the University of São Paulo School of Medicine, Dr. Mario Stevenson, a professor of medicine at the University of Miami’s Miller School of Medicine and former chair of amfAR’s Scientific Advisory Committee, and amfAR Vice President and Director of Research Dr. Rowena Johnston.

“Historically, Brazil has shown robust leadership in combating HIV/AIDS,” said Johnston. “We’ve learned over the years that there is much to be gained from the exchanging of information and ideas with colleagues in Brazil and other countries that have mounted an effective response to HIV.”



amfAR’s Research, Cure, Community HIV/AIDS Summit at the University of São Paulo (Photo: Simon Plestenjak)



amfAR Gala Cannes

Supremes icon Diana Ross delivered a show-stopping performance of classic hits at the 24th annual amfAR Gala Cannes in Antibes, France, on May 25, during the Cannes Film Festival. The event, which raised more than \$20 million, featured a dazzling Golden Age of Hollywood Collection runway show curated by longtime amfAR supporter Carine Roitfeld. The collection was showcased by 30 of the world's top models and auctioned off in its entirety for more than \$3 million. Guests included Will Smith, Leonardo DiCaprio, Jessica Chastain, Dustin Hoffman, Nicole Kidman, Uma Thurman, Eva Longoria, and amfAR Chairman Kenneth Cole. In addition to Diana Ross, Nicki Minaj, Rita Ora, and DNCE brought the crowd to their feet with sensational performances.



Special thanks: Harry Winston, Bold Films, Moët Hennessy, Persol, Renault, and Delta Air Lines

1. Nicki Minaj took the stage with an explosive medley of some of her biggest songs, including "Swalla" and "Truffle Butter." **2.** Nicole Kidman and Dustin Hoffman opened the show. **3.** DNCE closed the evening with their Billboard Hot 100 debut single, "Cake by the Ocean." **4.** Diana Ross delivered an unforgettable performance of classic hits, including "I'm Coming Out," "Ain't No Mountain High Enough," and "I Will Survive." **5.** Rita Ora debuted "Your Song," the first single to be released from her forthcoming album. **6.** Bella Hadid and amfAR Chairman Kenneth Cole **7.** Carine Roitfeld with models wearing the Golden Age of Hollywood Collection **8.** Chris Tucker, Uma Thurman, Will Smith, Jessica Chastain, Tobey Maguire, and auctioneer Simon de Pury (Photos: Getty Images and Kevin Tachman)





amfAR Gala New York

Scarlett Johansson and Donatella Versace were honored for their outstanding contributions to the fight against AIDS at the 19th annual amfAR Gala New York on February 8, an event that raised nearly \$2 million. Mark Ruffalo presented the amfAR Award of Courage to Johansson while Naomi Campbell bestowed the award on Versace. Longtime amfAR supporter Iman opened the evening, which featured spectacular live performances by British pop star Ellie Goulding and Aluna Francis of the electronic music duo AlunaGeorge. Guests included amfAR Chairman Kenneth Cole, Heidi Klum, Naomi Campbell, Alan Cumming, Alessandra Ambrosio, Diane Kruger, Adriana Lima, and Jeremy Piven.

Special thanks: Harry Winston, Moët Hennessy, FIJI Water, Mandarin Oriental, New York, and Delta Air Lines



Proud to be supporting such an important cause in the fight against HIV/AIDS #amfARNewYork



@donatella_versace



1. Aluna Francis, of the electronic music duo AlunaGeorge, gave a soulful performance of their hit "Not Above Love." 2. Honoree Donatella Versace 3. Mark Ruffalo 4. amfAR CEO Kevin Robert Frost and honoree Scarlett Johansson 5. Alan Cumming 6. amfAR Chairman Kenneth Cole, Iman, and Zac Posen 7. Diane Kruger 8. British pop sensation Ellie Goulding ended the evening with an explosive set of her biggest songs, including "On My Mind," "Burn," and "Love Me Like You Do." 9. Honoree Donatella Versace, Naomi Campbell, Heidi Klum, Alessandra Ambrosio, and Zoe Kravitz (Photos: Getty Images, Kevin Tachman, amfAR)



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amfAR Gala Hong Kong

Charlize Theron, Naomi Campbell, Jackie Chan, and amfAR Chairman Kenneth Cole were among those present at the third annual amfAR Gala Hong Kong on March 25. Sir David Tang presented the amfAR Award of Courage to philanthropist and business leader Pansy Ho for her personal commitment to ending the global AIDS epidemic. The gala raised more than \$3.5 million, helped by a live auction that included a winning \$300,000 bid for an appearance with Chan in his upcoming film with Sylvester Stallone and attendance at the movie's premiere in Beijing. The evening culminated in a rousing performance by Grammy-nominated British pop sensation Charli XCX and an after-party featuring a DJ set by five-time Grammy Award-winning musician Mark Ronson.



3



4

Special thanks:

Harry Winston, AMTD, Audi, Moët Hennessy, The Upper House, and Delta Air Lines



5



amfAR Paris

Nearly 200 amfAR supporters gathered in Paris for an intimate benefit dinner and auction during Couture Week on July 2. Guests were treated to a special performance by singer/songwriter and former First Lady of France Carla Bruni. (Photo: Kevin Tachman)

Special thanks: Harry Winston, Moët Hennessy, and Renault



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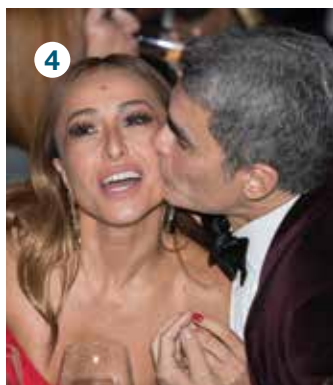
1. Charlize Theron 2. Naomi Campbell 3. Mark Ronson kicked off the after-party with a DJ set that kept guests dancing until the morning. 4. K-Pop superstar CL (Lee Chae-rin) took to the stage to perform her debut American singles. 5. amfAR CEO Kevin Robert Frost, Jackie Chan, honoree Pansy Ho, and amfAR Chairman Kenneth Cole 6. Achille Boroli (center) and guests 7. Charli XCX brought the crowd to their feet with a set of her top hits, including "Boom Clap," "Fancy," and "I Don't Care." (Photos: Getty Images, Ryan Emberley, amfAR)



amfAR Gala São Paulo

Brazilian artist Vik Muniz received the Award of Courage at the seventh annual amfAR Gala São Paulo on April 27 for his contributions of nearly \$400,000 to HIV research. Kate Moss, Dinho Diniz, and Felipe Diniz hosted the event at the São Paulo home of Dinho Diniz. Regina Casé, host of the 2016 Rio Olympics opening ceremony, presented the award to Muniz. Guests—including Katie Holmes, Sabrina Sato, Mert Alas, Barbara Fialho, and Julian Lennon—enjoyed musical performances by Brazilian singer Preta Gil and two-time Latin Grammy Award-nominated singer Anitta. The event raised more than \$1.3 million.

Special thanks: Harry Winston, Moët Hennessy, Iguatemi São Paulo, Karavelle, Mercedes-Benz, Tivoli Mofarrej - São Paulo, Vogue Brasil, and Delta Air Lines



generationCURE Ambassador Kelly Osbourne, Christian Siriano, and Jackie Cruz (Photo: Getty Images)

generationCURE Solstice

More than 250 young professionals joined amfAR Chairman Kenneth Cole, amfAR CEO Kevin Robert Frost, generationCURE Ambassador Kelly Osbourne, Victoria Justice, Christian Siriano, Jackie Cruz, Serayah, and others for the sixth annual generationCURE Solstice fundraiser on June 20 at New York City's Mr. Purple. The event, which raised \$70,000, was DJed by The Misshapes and Jilly Hendrix and featured live performances by Decora and Andrew Mancilla.

Special thanks: Cadillac, Gerber Group, Moët Hennessy, and The Roxy Hotel Tribeca

What an honor for me to perform at amfAR Brasil tonight. #amfARSaoPaulo

@anitta



1. Kate Moss 2. Sabrina Sato and Felipe Diniz 3. Dinho Diniz 4. Honoree Vik Muniz 5. Brazilian singer Preta Gil gave a meaningful performance of "Children of the Rainbow," an upcoming song to benefit amfAR. 6. Anitta delivered an explosive set of her biggest hits that kept guests dancing into the night. 7. Katie Holmes (Photos: Getty Images, Ryan Emberley, amfAR)

amfAR salutes Delta Air Lines for their high-flying generosity as our official airline partner since 2011.

Thank you for seven years of partnership and safe travel to all of our research and fundraising destinations.



 DELTA

Upcoming Events

- | | |
|------------|---|
| October 13 | amfAR Gala Los Angeles
Los Angeles |
| October 28 | TWO x TWO for AIDS and Art
Dallas |
| October 28 | The Fabulous Fund Fair
New York City |
| December | generationCURE Holiday Party
New York City |

amfAR, The Foundation for AIDS Research
120 Wall Street, 13th Floor, New York, NY 10005-3908
www.amfar.org