



ALLIANCE FOR MICROBICIDE DEVELOPMENT

09 February 2007, Volume 8, Number 5

The Alliance for Microbicide Development *News Digest* is an unedited compilation of:

- Media coverage of microbicides;
- Abstracts of articles on microbicides and relevant science in peer-reviewed journals;
- Material on other reproductive health and HIV prevention technologies, including HIV vaccines; and
- Matters of policy and politics with importance for microbicide research, development, and advocacy.

Its purpose is to:

- Raise awareness around the range of opinions and information about microbicides disseminated in the press and scientific journals; and
- Provide a neutral, objective basis for decision-making and evidence-based advocacy.

The *News Digest* is produced in a web-based format. Readers can view individual articles or complete issues at <http://www.microbicide.org/publications/> and may also search by keyword for articles included in issues of the *Digest* created after 27 January 2006, at <http://www.microbicide.org/publications/search.html>. Should you wish to be removed from the *Digest* distribution list, please advise us at digest@microbicide.org. We welcome comments, questions, and ideas about other microbicide-relevant topics we might cover, services we might provide, and better ways of providing them!

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1. MONTHLY MICROBICIDE PIPELINE UPDATE

February 2007

Each month, the *Digest* includes an update on overall progress in the field. Currently, there are 10 **microbicide** candidates in clinical development and over 30 in preclinical development. As a continued effort to maintain the most up-to-date information, we urge you to visit the Alliance website at www.microbicide.org or contact Carolyn Plescia, Alliance Writer/Research Associate, by email (cplescia@microbicide.org) or by phone (301-587-3302) with any updates, questions, or comments.

MICROBICIDES IN ONGOING AND PLANNED CLINICAL TRIALS
<i>Vaginal defense enhancers</i>
ACIDFORM [®] /Amphora [®] (Phase 1)
BufferGel [®] (Phase 2/2B)
<i>Entry/fusion inhibitors</i>

VivaGel [®] /SPL7013 (Phase 1)
Invisible Condom [®] (Phase 1/2)
Carraguard [®] (Phase 3)
PRO 2000 (Phase 3)
Replication inhibitors
UC-781 (Phase 1)
Dapivirine (TMC120) (Phase 1/2)
Tenofovir/PMPA gel (Phase 2)
Combinations
PC 815 (Carraguard [®] and MIV-150) (Phase 1)
<p>© Alliance for Microbicide Development</p> <p><i>Some candidates are in more than one phase of clinical testing. The phase listed in this table represents the most advanced clinical trial currently planned or underway for each candidate. This table does not include trials of contraceptive efficacy. For modifications, please contact Carolyn Plescia, email cplescia@microbicide.org, tel. 301-587-3302.</i></p>

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2. ALLIANCE UPDATES AND COMMUNITY NEWS

Continuing coverage of closure of cellulose sulfate trials

Last week, the Alliance published *News Alerts* compiling press releases and media coverage of the closure of the Phase 3 trials of cellulose sulfate conducted by CONRAD and Family Health International. Since there has been significant continued coverage of the closures over the past week, we have chosen to include in this week's issue of the *News Digest* a selection of statements and media coverage that is representative of the range of actions that have been undertaken in the past few days, opinions that have been expressed through a variety of media outlets, and regions in which media coverage has occurred:

- **"AIDS fight suffers setback"**

Los Angeles Times

<http://www.latimes.com/business/la-fi-aids3feb03,1,6909954.story>

- **"AIDS group urges restart for S.Africa gel trials"**

Reuters

[http://today.reuters.com/news/articlenews.aspx?type=healthNews&storyID=2007-02-](http://today.reuters.com/news/articlenews.aspx?type=healthNews&storyID=2007-02-07T135913Z_01_L07897753_RTRUKOC_0_US-SAFRICA-AIDS-TRIALS.xml&WTmodLoc=HealthNewsHome_C2_healthNews-5)

[07T135913Z_01_L07897753_RTRUKOC_0_US-SAFRICA-AIDS-](http://today.reuters.com/news/articlenews.aspx?type=healthNews&storyID=2007-02-07T135913Z_01_L07897753_RTRUKOC_0_US-SAFRICA-AIDS-TRIALS.xml&WTmodLoc=HealthNewsHome_C2_healthNews-5)

[TRIALS.xml&WTmodLoc=HealthNewsHome_C2_healthNews-5](http://today.reuters.com/news/articlenews.aspx?type=healthNews&storyID=2007-02-07T135913Z_01_L07897753_RTRUKOC_0_US-SAFRICA-AIDS-TRIALS.xml&WTmodLoc=HealthNewsHome_C2_healthNews-5)

- **"Anti-HIV specialists disappointed over calling off human trial"**

The Hindu

<http://www.hindu.com/thehindu/holnus/002200702041654.htm>

- **"Increased HIV infection stops microbicide trial"**

Bay Area Reporter

<http://www.ebar.com/news/article.php?sec=news&article=1548>

- **"Medical research trial guinea pigs contract HIV"**

City Press

http://www.news24.com/City_Press/News/0,7515,186-187_2064124,00.html

- **"S. Africa orders probe into botched HIV gel trials"**

Reuters

<http://www.sciam.com/article.cfm?chanID=sa001&articleID=88F64D69018AF616ABF977934EC8226C>

- **"Safety concerns halt trials of HIV microbicide"**

SciDev.net

<http://www.scidev.net/news/index.cfm?fuseaction=readnews&itemid=3393&language=1>

- **"Scientists fight on behalf of SA women"**

The Star

Not available online; please see text below

- **"South Africa: Clarity sought in microbicides furore"**

Kenya London News

http://www.kenyanetwork.com/artman/publish/article_2633.shtml

- **"South Africa: Minister orders relook at anti-HIV gel trials"**

Business Day

<http://allafrica.com/stories/200702070294.html>

- **"South Africa; Spotlight turns to microbicide trials"**

Health-e

<http://allafrica.com/stories/200702070700.html>

- **TAC comment on the termination of Ushercell microbicide trial**

Treatment Action Campaign Newsletter

<http://www.tac.org.za/nl20070207.html>

- **"The error of trials"**

Hindustan Times

http://www.hindustantimes.com/news/181_1919830,0012.htm?cid=1113201586&ei=7F3HRfXTD7TIHOuHnZo

H

- **"Twenty women HIV-positive after drug trial"**

South African Press Association

http://www.mg.co.za/articlePage.aspx?articleid=298397&area=/breaking_news/breaking_news__national/

- **"Uganda: 234 women join new HIV drug trials"**

New Vision

<http://allafrica.com/stories/200702050603.html>

"Scientists fight on behalf of SA women"

Author(s): Jillian Green

Date: 7 February 2007

Source: *The Star (South Africa)*

With each day that passes, researchers Sibongile Walaza and Jocelyn Moyes are one step closer to reaching their goal “ and if they achieve it, they could save the lives of millions of women. The two are among several scientists in South Africa and worldwide who are working to provide women with a way to protect themselves from HIV infection through **microbicides**, a gel-like substance that could prevent the virus from attaching or entering host cells in the body.

But their mission has been dealt a blow. Recently, two trials involving the testing of **microbicide** candidate Ushercell were stopped after it came to light that women who had volunteered to test the product may actually be increasing their risk of infection by using the product during sex. And while this is not the product the two are testing, the halting of those trials could have ramifications for their own.

Based at the Reproductive HIV Research Unit at the Chris Hani Baragwanath hospital complex, Walaza, Moyes and their teams are hoping to enlist 3 000 women from Orange Farm and Soweto into their trial to test PRO 2000/5. Already, the odourless, colourless gel known as the "invisible condom" has been shown in laboratory tests to block the entry of HIV in human cells and to protect animals against infection. In addition, it has also shown to be effective in the laboratory against other sexually transmitted pathogens like herpes and chlamydia. But the final hurdle in proving its ability to protect against HIV infection requires its use by human volunteers. "The ultimate test for any product is to determine whether it will work in the general population and not only in a controlled laboratory environment. Each person is different and will react differently to products," Moyes explained.

Showing that this **microbicide** protects against HIV would represent a tremendous breakthrough in the fight against the spread of HIV/ Aids. Over half of all people living with HIV in the developing world are women, with the majority of new adult infections acquired through heterosexual intercourse. According to a study by the London School of Hygiene and Tropical Medicine, the introduction of a **microbicide** “ which would reduce a person's risk of infection by 40% “ in 73 lower-income countries, at 30% coverage, would avert 6-million HIV infections over three years in men, women and children. This effect would reduce the healthcare costs by a staggering \$3,2-billion (about R23-billion).

PRO 2000/5 is a topical **microbicide**, which women volunteers insert into their vaginas an hour before sexual intercourse, by means of an applicator. The researchers hypothesise that the use of the gel will prevent the HI-virus from attaching to cells on the vaginal wall and thereby prevent infection. "We have had such an awesome response. Women are lining up at the clinic to join the trial. We would like to think that the halting of other trial will not affect us adversely," Moyes said.

Walaza explained that the recruitment process involved intensive counselling and education about the trial and the product. "Each prospective participant is told in detail about the benefits and known risks of taking part in the trial. Each is presented with a 16-page informed consent document in their language of choice, which also explains the trial process. And they are told that even once they have signed to take part, they can withdraw at any point without giving reasons," Walaza said.

Walaza said that it is still too early to determine whether their trial would suffer from the halting of the Ushercell trials. "The two products are different. We are not continuing a trial with the same product. This country has a rigorous trial-application process before a trial can go ahead. And even while it is ongoing, data is routinely collected and studied to

determine whether it is safe to continue," Moyes, adding that a community advisory group had been established to ensure the well-being of community participants.

Solomon Nzama, a member of the community advisory group in Orange Farm, said he hadn't received any complaints from the participants involved in the PRO 2000/5 trial. "They say they understand the information about the trial they are taking part in and they know this is a different product to the one which was halted (Ushercell)," he said. "But we will continue to monitor the process," he added.

Ushercell or Cellulose Sulfate phase III trials "which test the effectiveness of a product" were being conducted in SA, Benin, Uganda and India. Professor Gita Ramjee, of the Medical Research Council and a principal investigator in South Africa for Ushercell, explained that the trial was stopped after the data-monitoring committee found that a higher number of women using the gel containing cellulose sulphate had acquired HIV than those using a placebo gel. Cellulose Sulfate was one of four **microbicide** compounds being evaluated in large-scale studies. "Cellulose Sulfate is just one product. Data-monitoring committees of the other products have said that these other studies can go on and they must.

"If we give up on all **microbicide** candidates (because of cellulose sulphate) we are giving up on empowering all women in Africa and the developing world," Ramjee said.

Health Minister Manto Tshabalala-Msimang yesterday requested an investigation by the research ethics council into the **microbicide** trials.

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3. MEDIA COVERAGE OF MICROBICIDES

"New HIV developments, Pacific possibilities"

Date: 06 February 2007

Source: *PacNews (Pacific Island News Service)*

<http://www.scoop.co.nz/stories/WO0702/S00070.htm>

HIV and AIDS prevention has come along way from terrifying posters aimed to scare people away from AIDS. Now we know the benefits of using condoms, encouraging HIV testing, spreading HIV awareness and promoting safe behaviour. There is also increased access to antiretroviral treatment (ART), the life prolonging medicine used to slow the disease progression, and an estimated 360 HIV positive people have access to this medicine in the Pacific Islands.

New campaigns and new technologies are developing all the time. Scientists are doing everything they can to find a cure, and if not a cure then a remarkable solution to prevent HIV transmission. It is exciting and offers great hope. But then reality steps in. Most new technologies for HIV prevention are very out of reach for the Pacific Islands.

First, most new developments are three to ten years away from being accessible to the public. Second, while medical trials have started in some parts of the world, they will probably never reach the Pacific Islands because of the small

populations and low HIV prevalence. Third, when the technologies are available, they will likely be extremely expensive making access limited.

Hope remains. It may be out of reach at moment, but it is not lost. Five years ago, access to ART was seen as a hopeless dream to many in the Pacific Islands, in fact there are many who still do not have access to ART today. But at least now ART is becoming a reachable dream.

These new technologies are not so far out of reach. Even if it takes five or ten years.

Here is what is in the pipeline:

1. Male circumcision: Male circumcision is not a new idea, but in August 2006 at the International AIDS Conference there was a whole lot of excitement about this issue. New research suggests that men who are circumcised are up to 50 percent less likely to be infected with HIV. These facts are still being investigated. There are many factors to think about such as access to safe circumcision, cultural barriers, and of course it is NOT FOOL PROOF. The best known method of prevention is still a condom.
2. HSV-2 Suppression: What this actually means is 'the suppression of the herpes virus'. The aim is to provide medicine that will reduce or suppress genital herpes HSV-2 in order to prevent genital ulcers that increase the risk of HIV infection.
3. **Microbicides**: This is the term for a medical cream or gel inserted into a woman's vagina that would stop pregnancy and HIV infection. The benefits are huge, allowing women to control their own reproductive and sexual health. At present **microbicides** are not available. They are currently being researched and will take at least three more years to reach public access. At present, five different **microbicides** have reached Phase 2 or 3 of medical trails meaning that they are being tested on humans.
4. HIV vaccines: There are two types of vaccines being looked at: Preventative Vaccines and Therapeutic Vaccines. Preventative Vaccines aim to stop HIV infection whereas Therapeutic Vaccines aim to boost the viral response of people already living with HIV. Like **microbicides**, vaccines are still being researched. Results from current medical trials and tests are expected in 2010.

In the mean time, condoms and access to antiretroviral treatment (ART) are the best solutions.

"IPM receives grant from EC for microbicide development"

Date: 30 January 2007

Source: *Anti-Infective Drug News*

The **International Partnership for Microbicides Belgium (IPM)** has received a EUR 4.2 million grant from the European Commission to develop safe and effective **microbicides** that prevent HIV transmission in women. The grant will be provided over a three-year period from 2007 to 2009 and will fund the development of up to eight clinical trial sites in Kenya, Rwanda, South Africa and Zimbabwe. As part of the project, the Belgium-based Institute of Tropical Medicine will provide clinical laboratory training for the development of sites in Africa. IPM will provide additional funds, thus bringing the total project cost to EUR 5.25 million. In addition to clinical capacity development, the grant will seek to build community participation in clinical trials and work with national regulatory agencies to help lay the groundwork for future access to safe and effective **microbicides**.

"Many hands make great patchwork: Prominent Canadians sign in support of Kamloops' CanGo Grannies fundraiser"

Date: 30 January 2007

Source: *Kamloops Daily News (British Columbia)*

Author(s): Mike Youds

The CanGo Grannies of Kamloops have sewn together a quilting project as ambitious as Canada is wide. And The Great Canadian Quilt project -- with which they hope to raise an estimated \$500,000 -- got a helping hand Monday from Stephen Lewis, whose Thompson Rivers University speech on HIV/AIDS in Africa inspired the group's formation three years ago. One hundred and thirty-one other groups of Canadian grandmothers have followed suit since, helping in whatever way they can to bring relief to a continent in crisis through the Stephen Lewis Foundation (SLF).

Lewis, keynote speaker at a conference at Sun Peaks Resort on the weekend, was asked to meet with the CanGo Grannies in Kamloops to lend support to a local fundraiser with national appeal. He spoke for more than an hour with the 35-member group, mostly about the HIV/AIDS epidemic, but noting that the local group is twice distinguished in their efforts. "I hope you understand that you're not only the original group but also the most energetic and ambitious group I've encountered," said Lewis, former UN special envoy for HIV/AIDS in Africa.

The quilt's Maple Leaf is divided into 200 squares, most of which now contain the signatures of 194 well-known Canadians from Paul Anka to Moses Znaimer. Prime Minister Stephen Harper and all surviving former prime ministers signed on to the project, which has been quietly taking shape over the past 18 months. Local signatures include those of Nancy Greene Raine, Len Marchand and Lesra Martin.

Lewis offered to enlist the support of the foundation in obtaining the last few hard-to-get signatures before the quilt is ready to be auctioned at a gala dinner June 9 at Vancouver's Sheraton Wall Centre. Global TV's Pamela Martin will host the gala and Lewis promised Monday he will be sure to attend.

The GoGo Grannies of Johannesburg, 75 grandmothers who care for 800 AIDS orphans, are formidable as an inspiration, said Barbara Mowat. "The least we can do is be formidable in our end of the spectrum," she told Lewis.

The Great Canadian Quilt places on a national stage work that was previously done on a purely local, grassroots level. The CanGo Grannies started small, selling T-shirts and cookbooks to lend support to their South African counterparts. It was Sue Cooper, a member of the group and a local quilter, whose insomnia led to the undertaking. Wide-eyed at 3 a.m., she asked herself: "What skill do I know? The only thing I know how to do is quilt." From there the grannies used every conceivable contact, personal and professional, to solicit signatures of famous Canadians. They embraced a principle known as Six Degrees of Separation, which holds that anyone on Earth can be connected to anyone else with no more than five intermediaries. "All we're doing is using a network of people we know, of people we do business with over the year, in making that contact," Mowat said. "No one has said no." The SLF finances 170 projects in 47 countries, Lewis told the group.

Despite medical progress toward controlling the spread of HIV/AIDS, Africa remains the global epicentre for a number of economic and cultural reasons, he said. Twenty-eight million Africans, a population slightly less than that of Canada, are infected. Transient mine workers, transport drivers and military helped spread the virus in what he described as "a conflagration of elements, of vectors of transmission more prescient in Africa." A **microbicide** for

preventing its spread could be available in four or five years, however, the rate of infection has so far outstripped the ability to respond.

The recent emergence of new, drug-resistant forms of tuberculosis, the disease that ultimately kills most HIV/AIDS victims in Africa, is particularly worrisome, Lewis said. "Enough for this continent. This is just plague after plague after plague. You think you're making progress and then somehow, something else haunts you."

Prior to its journey to Vancouver for a highly publicized auction, the quilt will be publicly displayed in Kamloops.

SIGNED UP FOR THE QUILT: Paul Anka, Moses Znaimer, Wayne Gretzky, Joe Clark, Kim Campbell, Jean Chretien, Brian Mulroney, Paul Martin, Nancy Greene Raine, Len Marchand, Lesra Martin . . . and many, many more.

"Melinda Gates' public role in husband's high profile world"

Date: 27 January 2007

Source: *Associated Press*

Author(s): Edith M. Lederer

http://seattlepi.nwsourc.com/local/6420AP_World_Forum_Melinda_Gates.html

Melinda Gates has traveled the world with her husband, meeting with the rich and powerful and visiting its poorest in remote African villages. She and her husband share top-billing at the world's richest foundation, but Bill Gates always dominated the spotlight - until this year. Taking the stage at this week's World Economic Forum for the first time, Melinda addressed health, development and women's issues before a VIP audience. Sitting in a comfortable chair beside her husband Bill Gates for an informal conversation over breakfast Saturday, Melinda told about 200 invited guests that she chose a more public role so people would realize that the Bill & Melinda Gates Foundation is definitely a his and hers operation.

Melinda was managing several Microsoft units when she met the Microsoft founder and chairman at a press event in New York for the computer powerhouse in 1987. The Dallas native with an MBA from Duke and the Harvard dropout from Seattle married on New Year's Day 1994 when he was already the world's richest man, and quickly began a family. Melinda said she decided to keep a low profile because she wanted to be with her children who are still very young - Jennifer, 10, Rory, 7, and Phoebe, 4. "We're both very, very engaged parents," she said. After Phoebe celebrated her first birthday, Melinda said, "I felt like, OK, now's the time."

"I was seeing so much in the developing world. But what was happening because I wasn't out talking about what I was doing, or what we were doing, is people started naturally to think, well this is Bill's foundation. And that couldn't have been further from the truth," Melinda said. "And both of us felt that it was very important that people understood that this is a joint effort - the two of us are absolutely moving it forward as a couple. And so getting that out, and letting people know that we both cared about it is one reason," she said.

In 2005, she started speaking about the work of the foundation - which has a \$32 billion endowment including \$1.6 billion from billionaire U.S. investment wizard Warren Buffett - according to the foundation's Web site. Melinda said she was especially moved by the burden that falls on women in the developing world, who are called on to deal not only with the daily struggle of feeding their families but with sickness, death and other emergencies. "I felt like I was

seeing too much not to speak out ... to give voice to the voiceless," she said.

She said 60 percent of AIDS sufferers in Africa today are women, a shift in the past decade. The Gates foundation, which is funding research for an AIDS vaccine, is also working on pills and **microbicide** gels likely to available sooner that women could take without informing their sex partners so they have the power to prevent AIDS, she said.

In a speech Thursday, she said that despite many programs to fight poverty and disease in the developing world, "millions of children still die every year of diseases we can prevent easily and cheaply. And more than 1 billion people live on less than a dollar a day, suffer from chronic hunger, and don't have enough clean water to cook with or drink."

"By contrast, each of us in this room had the chance to grow up healthy, get a good education, and live our dreams," she said. "Bill and I started our foundation because we believe that people living in extreme poverty and dying of preventable diseases deserve the same chance we all had: the chance to make the most of their lives."

She stressed, however, that government leaders must recognize that the private sector cannot solve complex problems like poverty and disease without their support. Even though the Gates foundation is the world's largest, it still accounts for less than 1 percent of American giving, she said. And its \$32 billion would barely cover the gap between the need for health services in the developing world and the funds available for one year, she said. The 42-year-old said another reason for speaking out now was "to say to my daughters that I want them to be powerful, strong women going forward."

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4. PUBLISHED RESEARCH: MICROBICIDE-SPECIFIC

"A dual chamber model of female cervical mucosa for the study of HIV transmission and for the evaluation of candidate HIV microbicides"

Author(s): Van Herrewege Y, Michiels J, Waeytens A, et al

Reference: N/A Epub ahead of print.

Published Abstract: A dual chamber system was established to model heterosexual HIV transmission. Cell-associated, but not cell-free HIV, added to a confluent layer of cervical epithelial cells in the apical chamber, reproducibly infected monocyte-derived dendritic cells (MO-DC) and CD4(+) T cells in the basal compartment. Only minimal epithelial transmigration of HIV-infected mononuclear cells (HIV-PBMCs) was observed. Most evidence points to transepithelial migration of virus, released from HIV-PBMCs after their activation by epithelial cells. We used this model for evaluation of the therapeutic index of various potentially preventive antiviral compounds, including non-nucleoside reverse transcriptase inhibitors (NNRTIs, including UC781 and various diarylthiazines and diarylpyrimidines), poly-anionic entry inhibitors (including PRO2000, cellulose sulphate, dextrane sulphate 5000 and polystyrene sulphonate) and the fusion inhibitor T-20. The epithelium was pre-treated with compound and incubated with HIV-PBMCs for 24h. Afterwards the apical chamber was removed and MO-DC/CD4(+) T cell co-cultures were further cultured without compound. NNRTIs, including a TMC120 gel, blocked infection of the sub-epithelial targets at sub-micromolar concentrations. Polyanionic entry inhibitors (up to 100µg/ml) and T-20 (up to 449µg/ml) failed to inhibit transmission. Moreover, whereas the NNRTIs used interfered with epithelial integrity with cervical epithelium

only at very high concentrations, the evaluated entry inhibitors showed toxicity at concentrations that did not prevent infection.

"Evaluation of -2 RANTES vaginal microbicide formulations in a nonhuman primate simian/human immunodeficiency virus (SHIV) challenge model"

Author(s): Kish-Catalone T, Pal R, Parrish J, et al

Reference: N/A 23(1):33-42.

Published Abstract: A potential strategy to combat the worldwide AIDS epidemic is to develop a vaginal **microbicide** that prevents the sexual transmission of HIV-1. One approach for preventing vaginal HIV transmission is to block the viral coreceptor CCR5 with naturally occurring chemokine ligands. In this study, we used a cynomolgus macaque model to evaluate whether a variant of the CCR5 ligand RANTES (-2 RANTES), tested alone or in a nonphospholipid liposome carrier (Novasomes 7474), blocks vaginal challenge with a CCR5-tropic simian/human immunodeficiency virus (SHIV(162P3)). When tested *in vitro*, the synthetic chemokine potently inhibited SHIV(162P3) infection of cynomolgus macaque peripheral blood mononuclear cells (PBMC). Colposcopic examinations of treated animals and histological examination of cervicovaginal biopsies showed minimal signs of tissue inflammation following vaginal application of Novasomes 7474, -2 RANTES formulated in Novasomes 7474, or -2 RANTES alone. Following vaginal challenge with SHIV(162P3), complete protection was observed in four of six animals treated vaginally with -2 RANTES (0.13 mM) formulated in Novasomes 7474. However, the same proportion of animals was protected by treatment with Novasomes 7474 carrier alone. Two of five animals treated with 0.5 mM -2 RANTES in PBS were protected from infection. Further, all animals were infected when treated with lower chemokine concentrations. These findings indicate that natural CCR5 ligands may have limited efficacy in stringent nonhuman primate models for vaginal infection. In comparison, liposomal agents such as Novasomes 7474 provide comparatively robust protection against vaginal transmission.

"Hyperosmolar sexual lubricant causes epithelial damage in the distal colon: potential implication for HIV transmission"

Author(s): Fuchs EJ, Lee LA, Torbenson MS, et al

Reference: N/A 195(5):703-10.

Published Abstract: Background. Many sexual lubricants are hyperosmolar. Hyperosmolar enemas induce epithelial damage, and enema use has been associated with an increased risk of HIV infection. To inform the development of rectal **microbicide** formulation, we evaluated the effects of hyperosmolar gels on the rectal mucosa. Methods. Two commercial lubricants were compounded into iso-osmolar and hyperosmolar mixtures (283 and 3429 mOsm/kg, respectively). Each gel was radiolabeled with 500 μ Ci of (99m)Technetium-diethylene triaminepentaacetic acid, and 10 mL was given rectally to 10 subjects in random sequence. Sigmoidoscopy by an endoscopist blinded to treatment assignment was performed 90 min later to obtain luminal and mucosal samples. Urine radiolabel detection was used to assess mucosal permeability. Results. Epithelial denudation 10 cm from the anus occurred to a greater degree with the hyperosmolar gel than with the iso-osmolar formulation (median toxicity grade, 2.50 vs. 1.17 out of 3, respectively; $P=.009$). The hyperosmolar gel was also associated with lower isotope

luminal concentration at 10 cm, compared with the iso-osmolar gel (median, 8.9% vs. 54.6% of administered concentration, respectively). Mucosal permeability measured through 12 h was reduced with the hyperosmolar gel (P=.037). Conclusion. Rectally applied hyperosmolar gels induce greater epithelial denudation and luminal secretion than iso-osmolar gels. Because denudation plausibly increases the risk of HIV transmission, hyperosmolar gels make poor rectal **microbicide** formulations, and hyperosmolar sexual lubricants may increase susceptibility to HIV infection.

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5. PUBLISHED RESEARCH: RELEVANT BASIC AND TRANSLATIONAL SCIENCE

"Addition of a C-terminal cysteine improves the anti-herpes simplex virus activity of the TAT protein transduction domain peptide"

Author(s): Bultmann H, Teuton J, Brandt CR

Reference: N/A Epub ahead of print.

Published Abstract: Previous studies have shown that peptides containing the protein transduction domain (PTD) of the HIV tat protein (GRKKRRQRRR) inhibited HSV-1 entry (J. Biol. Chem. 277:36018-36023). We now show that the addition of a single cysteine residue to the C-terminus of the TAT-PTD (TAT-C peptide) improves the antiviral activity against HSV-1 and HSV-2. The principle effects of adding the cysteine were to add the capability to inactivate virions (EC50 approximately 100 microM) and to induce a state of cellular resistance to infection (EC50 approximately 5 microM). TAT-C acted extracellularly, blocking entry of adsorbed virus immediately without eluting virions. TAT-C also prevented VP16 translocation to the nucleus and syncytium formation indicating that TAT-C is a fusion inhibitor. The induction of cellular resistance was rapid, recovered with a t(1/2) of 5-6 hours, and could be rapidly re-induced by peptide treatment. TAT-C bound to cell surface heparan sulfate (HS) but was a poor competitor for adsorption suggesting that TAT-C and virions recognize different structural features of HS. The replacement of positively charged lysine or arginine residues with norleucine reduced the antiviral activity indicating net charge was critical. Peptides composed entirely of d-amino acids were equally effective as l-amino acid versions, thus chirality does not play a role. The free sulfhydryl group was not essential for antiviral activity but TAT-C dimers were more effective on a molar basis. The unique combination of antiviral activities and the low toxicity make TAT-C a strong candidate for further development as a drug to block HSV infection.

"Interaction of HIV-1 with dendritic cell-specific intercellular adhesion molecule-3-grabbing nonintegrin-expressing cells is influenced by gp120 envelope modifications associated with disease progression"

Author(s): Nabatov AA, van Montfort T, Geijtenbeek TB, et al

Reference: N/A 273(21):4944-58.

Published Abstract: Dendritic cells can enhance the replication of HIV-1 in CD4(+) lymphocytes through the interaction of the gp120 envelope protein with such molecules as dendritic cell-specific intercellular adhesion molecule-3-grabbing nonintegrin. The variable loops of gp120 have previously been shown to modulate the interaction of HIV-1 with its principal receptor CD4 and its various coreceptors, namely CCR5 and CXCR4. Here, we utilized a

panel of molecular cloned viruses to identify whether gp120 modifications can influence the virus interaction with immature dendritic cells or a cell line expressing dendritic cell-specific intercellular adhesion molecule-3-grabbing nonintegrin (Raji-DC-SIGN). The viruses encompass the R5, R5X4 and X4 phenotypes, and are based upon V1V2 and V3 sequences from a patient with disease progression. We found that dendritic cell-specific intercellular adhesion molecule-3-grabbing nonintegrin enhancement of virus replication can be modulated by the V1V2 length, the overall V3 charge and N-linked glycosylation patterns; similar results were observed with immature dendritic cells. Viruses with higher V3 charges are more readily transferred to CD4(+) lymphocytes when the V1V2 region is longer and contains an additional N-linked glycosylation site, whereas transfer of viruses with lower V3 charges is greater when the V1V2 region is shorter. Viruses differing in the V1V2 and V3 regions also demonstrated differential capture by Raji-DC-SIGN cells in the presence of mannan. These results indicate that the interaction between HIV-1 and immature dendritic cells via such molecules as dendritic cell-specific intercellular adhesion molecule-3-grabbing nonintegrin may have a role in selecting viruses undergoing transmission and evolution during disease progression.

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6. HIV/AIDS VACCINES

"Kenya: Major setback as top AIDS scientist is gunned down"

Date: 06 February 2007

Source: *The Nation*

Author(s): Arthur Okwemba

<http://allafrica.com/stories/200702060045.html>

A gangster's gun has abruptly ended the career of one of Kenya's leading Aids researchers. Prof Job Bwayo, a key researcher in the ongoing Kenya Aids Vaccine Initiative (KAVI) trials at the University of Nairobi, was gunned down on the Isinya-Kiserian road on Sunday night. His wife and an American friend, who were driving in the same car with him at the time of the shooting, are in critical condition at the Nairobi Hospital's intensive care unit, after sustaining serious bullet wounds. An Australian friend, who was also in the car, is said to be out of danger.

Prof Bwayo was killed by the very people who his work was probably going to benefit, either directly or indirectly. The promising HIV vaccine research was going into crucial stages in the next few months, at time when his services were going to be critical.

An eminent scientist

The vaccine is expected to protect people from HIV infection and replication of the virus among those infected, if proven safe and effective.

The director of the Kenya Medical Research Institute, Dr Davy Koech, described Prof Job Bwayo as "one of Africa's most distinguished and accomplished career scientist of his time".

"The Kemri family learnt with great sorrow and disbelief of the untimely demise of Prof Bwayo, an eminent scientist and scholar, whose vision and wisdom had contributed immensely to the KAVI," said Kemri in its tribute to Prof

Bwayo.

Described by his colleagues as a friendly man, his death has also left several undergraduate, postgraduate degree students, who were under his supervision in confusion. He was one of the celebrated lecturers in the immunology department.

Kenyans, who were eagerly looking up at the ongoing HIV vaccine trials, have lost as well.

Likewise, the media have lost a scientist who knew when information around his research work was to remain a guarded secret, and when it was prudent to release it for the public consumption.

When we visited his former Kenya Aids Vaccine Initiative department, his colleagues were both confused and scared to narrate what happened. They could be seen discussing in small groups, having lost somebody they looked up to, not only as a fellow scientist, but as father as well. His family was distraught to talk to the Press, saying they were still coming to terms with what happened.

Doctors from other departments at the university, who had interacted with him, were too mourning a fallen colleague. "We have lost a scientist who the country will take many years to replace. I think the thugs should be inquiring about your station in life before they shoot you," one of the doctors commented.

Prof Bwayo will be remembered as one of the scientists who were at the forefront of testing the first HIV vaccine in Africa, known as the DNA HIV vaccine, in collaboration with Oxford University. As the chairman of Medical Microbiology department, he guided the delicate discussions around how the vaccine was to be conducted in Kenya. This initiative saw the first ever state-of-the-art HIV vaccine laboratory in East and Central Africa built at Kenyatta National Hospital. It also resulted in the formulation of a memorandum of understanding that is used as model to guide other research collaborations across Africa. In the past two years, Prof Bwayo played a critical role in convincing the American vaccine gurus that Kenya was capable of conducting another Aids vaccine trial.

Commercial sex

This ended-up in the collaboration between the National Institute of Health of America, and the University of Nairobi on a vaccine that is currently under trial.

Prof Bwayo's career as a researcher spanned over two and half decades, concentrating on research around HIV and sexually transmitted infections. Much of his work with fellow researchers has been around commercial sex workers in Nairobi's Majengo slums. This had seen him publish widely on these diseases, with the findings benefiting the Government in the formulation of policies and pharmaceutical companies in research and development of drugs. Such contribution prompted the University of Nairobi to award him with professorship. Fellow doctors say he had given major guidance and contribution in the study of sexually transmitted infections, particularly when he was the chairman of Microbiology department. They said the country has lost a hard worker who believed in people beating the deadline to help ease the pain of mankind.

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7. OTHER PREVENTION APPROACHES

"Circumcision fever begins to sweep Swaziland"

Date: 02 February 2007

Source: *Mail & Guardian*

Author(s): Fran Blandy

http://www.mg.co.za/articlePage.aspx?articleid=297770&area=/breaking_news/breaking_news__africa/

Male nurse Moshoeshoe Makhubu has helped in many circumcisions but is visibly nervous as he prepares to undergo the snip himself, a procedure he grudgingly admits may boost chances of remaining HIV-free. In Swaziland, staying clear of the virus is hard as close to 40% of adults are living with HIV/Aids, the highest infection rate anywhere in the world according to the United Nations Children's Fund (Unicef). Trials in Kenya and Uganda have shown that circumcision, while not providing complete protection for the man, dramatically reduced the number of new infections. Thirty-year-old Makhubu, who works at the government hospital in the Swazi capital Mbabane, says he is aware he should "still use other preventative measures" if he wants to remain healthy.

Swaziland's only expert in the field, urologist Adam Groenevald of Holland, says the Kenyan and Ugandan trials -- which showed 53% and 48% reductions in new infections respectively --- have got Swazis thinking. "There are voices against it, but the momentum of the whole thing cannot be stopped," he says.

Many nurses are bringing in their husbands and sons for the snip as circumcision fever begins to sweep the country. Swaziland's health ministry is eager to roll out a mass programme but is awaiting advice first from the World Health Organisation. "If there was a vaccine with 65% efficacy, the whole world would have jumped on it, but an operation on the penis will not be that popular," Groenevald fears. His office, a room in an abandoned ward, bears mute testimony to the crippling shortage of nurses and doctors that will make the fulfilment of such a programme in Swaziland even more difficult. Only 100 or so doctors serve the population of more than one million in this south-east African mountain kingdom where two-thirds of people live in poverty. "We have to make the medical establishment and policymakers ready for the go ahead," says Groenevald. "If we are not ready and the go ahead comes there will be chaos. A number of unqualified people will start offering circumcisions and we need to avoid that at all costs."

To try and satisfy soaring demand for operations, doctors are being trained and are asked to help out on special "circumcision days" when the procedure is offered free of charge. These occasions typically see about 40 men operated upon, but up to 100 others are routinely turned away because there are not enough professional medical staff to carry out the circumcisions. Groenevald highlights the need for more doctors, saying if 200 000 men wanted to get circumcised -- a figure he deemed conservative -- it will require 40 000 operations to be performed annually for the next five years.

Faith Dlamini from the state-run National Emergency Response Council on HIV/Aids says the government would first focus on circumcising the 15 to 30 age group as it ran the highest risk of infection. According to the Unicef website, HIV prevalence among 20 to 30-year-olds is already nearing 50%, higher than the national adult average.

Apart from the sheer logistical problem of finding the doctors, mass circumcision faces deeper-rooted and more cultural barriers in Swaziland. Swazi boys are not circumcised traditionally as is the case in other parts of Southern

Africa. A 19th-century king banned the procedure, arguing that the lengthy healing process interfered with boys' war-readiness.

Thoko Tsabedze, an HIV-positive mother from Macatjeni district south-east of the capital, explains a common problem. "It is difficult even when you try to talk to your son about circumcision. He says, 'How am I going to take a bath publicly with my friends, I will be ridiculed'." Vusi Dlamini from the Family Life Association of Swaziland, the country's leading non-governmental organisation tackling HIV/Aids, believes this thinking can be overcome as people are very interested in circumcision and few view it as "un-Swazi".

The most popular theory behind circumcision's protective effect is that the foreskin has a very thin epithelium, or lining, and easily suffers minor abrasions during intercourse. These microscopic cuts make it easier for the Aids virus to enter the man's bloodstream.

Until now, the only prevention strategies have depended on condoms and sexual abstinence, both of which are of only limited effect. Campaigners caution that circumcision -- while low-cost, one-off and effective -- is no silver bullet and will not provide complete protection. "We want people to be aware it is not the answer, but an intervention within a package," says Faith Dlamini.

"Violence against women fueling spread of HIV worldwide, undermining prevention efforts, advocates say"

Date: 26 January 2007

Source: *Kaiser Daily HIV/AIDS Report*

http://www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=42502

Violence against women worldwide is fueling the spread of HIV in the population, and unwillingness among some governments to acknowledge the issue will continue to undermine prevention and education efforts, advocates said this week at the World Social Forum in Nairobi, Kenya, Inter Press Service reports. "Violence is largely a cause of HIV infection among many women; violence in the homes and in the streets, violence everywhere," Ludfine Anyango, the national HIV/AIDS coordinator at Action Kenya-International, said. Anyango also discussed women's inability to negotiate condom use with their partners, which puts them at an increased risk of HIV transmission. "Many cannot ask their husbands to use a condom because, in addition to being thought as unfaithful, they fear being beaten," Anyango said, adding, "The woman then has no choice but to continue having unprotected sex with her spouse." Violence against commercial sex workers also is an issue, according to Ros Sokunthy of the Cambodia-based Womyn's Agenda for Change, which promotes the rights of women and female sex workers. "A sex worker negotiates with one man," Sokunthy said, adding, "When she gets to the venue she finds more than one man, and they all want to have sex with her. When she refuses, she is beaten or raped." In addition, WSF participants discussed how some husbands beat their wives if they discover that they visited HIV/AIDS voluntary testing and counseling centers. "This fear discourages many women from knowing their HIV status and thus continue having unprotected sex with their spouses," Mary Watiti -- a counselor at a testing clinic in Kibera, Kenya -- said. According to Inter Press Service, these issues have renewed calls for laws to address all forms of violence against women, as well as implementation of laws in countries where such legislation exists. Male involvement in the fight against HIV/AIDS also is important, advocates said. According to experts, men seem to fear HIV/AIDS stigma more than women do and, as a result, avoid HIV

testing clinics. "As long as our men are not part of the war, then we should forget about ending HIV/AIDS infection and the violence that comes with it," Lilian Musang'u, a WSF participant from Malawi, said (Mulama, Inter Press Service, 1/24).

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8. POLITICS AND POLICY

"Choice is empowering: Getting strategic about preventing HIV infection in women"

Author(s): Gollub EL

Reference: N/A 32(4):209-12.

Published Abstract: Since the late 1980s and early 1990s, we have come a considerable distance in recognizing that successful HIV prevention work among women means the adoption of a woman-centered paradigm, one that is grounded in women's realities and acknowledges gender roles and gender-based power differentials as critical factors in women's ability to make and effect decisions regarding their health and welfare. We have learned that most women around the world cannot control male condom use, and we have begun to understand that women's attitudes toward and use of protective methods are based on personal, relational, sociocultural and structural factors, with a different mix for each woman. HIV prevention has required us to work on two levels: to achieve long-term, structural change in women's status, and to provide women with tools for protection over the short term.

"Seven habits of highly effective global public-private health partnerships: practice and potential"

Author(s): Buse K, Harmer AM

Reference: N/A 64(2):259-71.

Published Abstract: Global public-private health partnerships (GHPs) have become an established mechanism of global health governance. Sufficient evaluations have now been conducted to justify an assessment of their strengths and weaknesses. This paper outlines seven contributions made by GHPs to tackling diseases of poverty. It then identifies seven habits many GHPs practice that result in sub-optimal performance and negative externalities. These are skewing national priorities by imposing external ones; depriving specific stakeholders a voice in decision-making; inadequate governance practices; misguided assumptions of the efficiency of the public and private sectors; insufficient resources to implement partnership activities and pay for alliance costs; wasting resources through inadequate use of recipient country systems and poor harmonisation; and inappropriate incentives for staff engaging in partnerships. The analysis highlights areas where reforms are desirable and concludes by presenting seven actions that would assist GHPs to adopt better habits which, it is hoped, would make them highly effective and bring about better health in the developing world.

EDITORS' NOTE: Please see also a new publication from the Overseas Development Institute, "Global health: Making partnerships work," available at

<http://topics.developmentgateway.org/hiv/rc/ItemDetail.do~1089588?itemId=1089588>

9. ANNOUNCEMENTS

2007 American Public Health Association Annual Meeting: Call for Abstracts

<http://www.apha.org/meetings>

The American Public Health Association is announcing the Call for Abstracts for the 2007 Annual Meeting to be held November 3-7, in Washington, DC. The theme of the meeting is "Politics, Policy & Public Health." We encourage abstracts in all areas of public health and are also interested in abstracts that focus on the Annual Meeting theme. Abstracts should be no more than 250 words and must include learning objectives. All abstracts must be submitted online. An easy to use online form will walk you through the process step-by-step. The site is now opened so you may link directly to the abstract submission form through the APHA website at <http://www.apha.org/meetings> or <http://apha.confex.com/apha/135am/oasys.epl> Authors must provide complete and accurate contact information in order to be notified of abstract status. You do not have to be a member of APHA to submit an abstract, however, if your abstract is accepted, presenting authors must become an Individual member as well as register for the Annual Meeting. The deadline for submission of abstracts range from February 5 to February 9, 2007 depending on the Section, SPIG or Caucus to which you wish to submit. All submissions will end at 11:59 pm (Pacific Standard Time) on the due date listed on the Call for Abstracts.

NIAID RFA: HIV Interdisciplinary Network for Pathogenesis Research in Women (U19)

The National Institute of Allergy and Infectious Diseases (NIAID) invites applications from single institutions and consortia of institutions to participate in the HIV Interdisciplinary Network for Pathogenesis Research in Women program. The purpose of this new RFA is to support research that will expand knowledge of the pathogenesis of HIV infection in women through investigations of female-specific biologic mechanisms that impact HIV transmission and HIV disease acquisition, manifestations and progression in women. NIAID anticipates awarding a total of \$6 million in FY 2008 to support the Program. Additional information is available at <http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-07-009.html>

Key Dates

- Release Date: January 31, 2007
- Letters of Intent Receipt Date(s): May 14, 2007
- Application Receipt Date(s): June 25, 2007
- Peer Review Date(s): October, 2007
- Council Review Date(s): January, 2008
- Earliest Anticipated Start Date(s): March, 2008

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