AIDS Vaccine Program at the XVII International AIDS Conference, August 3-8, 2008 Mexico City

This special issue provides a guide to the AIDS vaccine-related sessions at the XVII International AIDS Conference in Mexico City. For additional information on these sessions, visit www.aids2008.org to search by abstract number, author, or keyword. The August issue of *VAX* will feature coverage of the key findings from the meeting related to AIDS vaccine research, as well as other HIV prevention technologies.

Session/Venue (Format)	Time	Code	Title	Speaker (Country)
Sunday, August 3				
Coordinating HIV Vaccine Research and Development Efforts to Contribute to the Goals of the Global HIV Vaccine Enterprise *Skills Building Room 7*	11:15	SUSAT1801	Update on the Global HIV Vaccine Enterprise	A. Bernstein (Canada)
	11:30	SUSAT1802	Global tracking of HIV vaccine investments	M. Warren (US)
	11:45	SUSAT1803	Canadian HIV Vaccine Initiative	F. Plummer (Canada)
	12:00	SUSAT1804	Overview of low- and middle-income countries and European networks	H. Wong (US)
	12:15	SUSAT1805	African perspective	C. Toure (Senegal)
New Minds, New Ideas: Attracting the Next Generation of Investigators and Technologies to HIV Vaccine Research (NCS) *Skills Building Room 8*	15:45-17:45	SUSAT55	The Global HIV Vaccine Enterprise will hold a discussion with leaders in HIV vaccine research	A. Bernstein (Canada), P. Johnston (US), D. Barouch (US), J. Esparza (US), T. Ndung'u (S. Africa), G. Pantaleo (Switzerland)
Monday, August 4				
Animal & Cellular Models of HIV Pathogenesis (OAS) *Session Room 5*	11:00	MOAA0101	Humoral responses have little effect controlling viremia in green monkeys	T. Gaufin (US)
	11:15	MOAA0102	Humanized mice model for HIV-1 antibody responses	K. Sango (US)
	11:45	MOAA0104	Development of cervicovaginal murine model for study of HIV-1 transmission	T. Kish-Catalone (US)
Vaccines and Microbicides: Where Do We Go From Here? (SY) *Session Room 1*	11:00	MOSY0101	Overview of current challenges	T. Yamada (Japan)
	11:15	MOSY0102	An HIV vaccine: Where do we go from here?	A. Bernstein (Canada)
	11:25	MOSY0103	STEP vaccine trial lessons learned	S. Buchbinder (US)
	11:35	MOSY0104	New priorities for IAVI	S. Berkley (US)
	12:15	MOSY0108	Vaccine advocacy and community leadership in the south	P. Goicochea (Peru)
New Insights into HIV Transmission and Pathogenesis (SY) *Session Room 3*	14:30	MOSY0601	Determinants of HIV transmission	E. Hunter (US)
	14:45	MOSY0602	Novel animal models for HIV transmission and pathogenesis	V. Garcia Martinez (US)
	15:00	MOSY0603	Host restrictions in T cells and macrophages	M. Stevenson (US)
	15:15	MOSY0604	Immune basis of HIV pathogenesis	G. Silvestri (US)
Viral & Molecular Determinants of Transmission and Pathogenesis of HIV (OAS) *Session Room 6*	16:30	MOAA0301	Mechanism of sexual transmission of HIV-1 via foreskin epithelium	Y. Ganor (France)
	16:45	MOAA0302	HIV in genital fluids during sexual transmission	D. Boeras (US)
	17:00	MOAA0303	Role of neutralizing antibodies in bottleneck of vertical transmission	E. Russel (US)
	17:15	MOAA0304	Recombination rates higher in tissues with significant macrophage infiltration	M. McGrath (US)
HIV Vaccine Research: Cross-Cutting Issues (OAS) *Session Room 3*	16:30	MOAX0301	Introduction	C. Beyrer (US)
	16:35	MOAX0302	HIV vaccines, mucosal immunity, and circumcision: What are the connections?	S. Buchbinder (US)
	17:20	MOAX0305	Using the internet to attract MSM to HIV vaccine trials	S. Im (US)
	17:35	MOAX0306	Inter-epitope interference modulate HIV-1-specific CD8$^+$ T cell immuno-dominance patterns in primary infection	H. Streeck (US)
No Simple Solution: Investing in HIV Prevention Research for Women (NCS) *Session Room 6*	18:30-20:30	MOSAT13	Panelists will address microbicides, vaccines, and PrEP as potential future female-initiated or controlled HIV prevention options	S. Lewis (US)
Tuesday, August 5				
Prevention Strategies, Substance Abuse and Harm Reduction, MSM (PL) *Session Room 1*	9:00	TUPL0101	Prevention of sexual transmission of HIV-1: A view from early in the 21st century	M. Cohen (US)
Show Me the Money: Accountability, Transparency and Resources (OAS) *Session Room 10*	11:00	TUAE0101	Building a comprehensive response: funding for HIV vaccines, microbicides and other new prevention tools: 2000 to 2007	K. Fisher (US)
The Lancet Series on HIV Prevention (SS) *Session Room 9*	12:45	TUSS0201	The history and challenge of HIV prevention	J. O'Malley (US)
	13:00	TUSS0202	Biomedical interventions to prevent HIV: Evidence, challenges, and the way forward	N. Padian (US)
	13:15	TUSS0203	Behavioral strategies to reduce HIV transmission: How to make them work better	T. Coates (US)
	14:00	TUSS0206	Coming to terms with complexity: A call to action for HIV prevention	P. Piot (Belgium)
New Frontiers in HIV Prevention Sciences (SY) *Session Room 1*	16:30	TUSY0801	Addressing structural determinants of HIV and measuring change	J. Kim (South Africa)
	16:40	TUSY0802	Lessons learned from working with communities in HIV prevention research	J. O'Malley (US)
	16:50	TUSY0803	Assessing HIV prevention approaches: Beyond randomized trials	T. Coates (US)

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Session/Venue (Format)	Time	Code	Title	Speaker (Country)
Wednesday, August 6				
Looking to the Future: The Epidemic in 2031 and New Directions in AIDS Research (SS) *Session Room 1*	12:45	WESS0101	The future of AIDS research	A. Fauci (US)
	13:05	WESS0102	2031 Initiative: Where will we be in terms of epidemic and response?	P. Piot (Belgium)
	13:25	WESS0103	The future of AIDS advocacy	M. Harrington (US), V. Dubula (South Africa), F. Chia Iskander (Indonesia)
Preclinical Development of HIV Vaccines (PD) *Skills Building Room 2*	13:00	WEPDA201	Long lasting CD8 cellular immune responses can suppress viral replication and protect macaques from AIDS-like symptoms	J. Boyer (US)
	13:05	WEPDA202	SIV Nef-mediated MHC class I down-regulation protects SIV-infected rhesus macaque CD4$^+$ T-cell clones from SIV Gag-specific CD8$^+$ T cell-mediated suppression of virus replication *in vitro*	C. Ohlen (US)
	13:10	WEPDA203	Propagation enhancement of a VEE/SHIV live-attenuated virus vaccine	K. Young (US)
	13:15	WEPDA204	Characterization of vaccine-vectors expressing Nef of the BF recombinant HIV-1 circulating form and evaluation of the immune response induced in mice	A.M. Rodriguez (Argentina)
	13:20	WEPDA205	Candidate vaccine capable of eliciting broadly reacting antibody response to structurally conserved areas on the V3 region	A. Maksyutov (Russian Fed.)
	13:25	WEPDA206	Design of HIV-1 envelope gp140 immunogens by selective addition or removal of N-glycosylation sites	N. Willkomm (France)
Innate and Adaptive Immunity (OAS) *Session Room 5*	14:30	WEAA0201	Mapping specificities of antibodies in broadly cross-reactive plasma from HIV-1 subtype C blood donors	E. Gray (South Africa)
	14:45	WEAA0202	Selection of CTL escape mutations determined by both ability to avoid CTL recognition and minimizing impact on viral replicative capacity	A. Schneidewind (US)
	15:00	WEAA0203	Expression of activating & inhibitory receptors on NK cells in HIV-1 and HIV-2	S. Nuvor (Kenya)
	15:15	WEAA0204	Ectocervical expression of C-type lectin receptors in exposed seronegative women	T. Kaldensjo (Sweden)
	15:30	WEAA0205	Variations in antimicrobial components in relation to STIs and HIV neutralization in vaginal fluid of HIV-uninfected Kenyan sex workers	P. Levinson (Sweden)
Preclinical Development and Animal Models for HIV Vaccines (OAS) *Session Room 7*	16:30	WEAA0301	Preclinical development	M. Morgado (Brazil)
	16:45	WEAA0302	Animal models	G. Vyas (US)
	17:00	WEAA0303	Electroporation of optimized DNA vaccines leads to greatly enhanced responses in blood and mucosal surfaces	A. Valentin (US)
	17:15	WEAA0304	Immune analysis of SIV-specific responses induced by co-vaccination of SIV + IL-12 plasmid by electroporation in non-human primates	L. Hirao (US)
	17:30	WEAA0305	A novel epitope model presented by 7mer constrained peptide indicates the minimal gp41 sequence required for highly specific recognition by broadly neutralizing anti-HIV-1 mAb 2F5	Y. Palacios-Rodriguez (Mexico)
"AIDS Vaccines – 2010 and Beyond": Charting a Course for the Future of AIDS Vaccine Research (NCS) *Session Room 9*	18:30-20:30	WESAT16	A session with experts engaged in AIDS vaccine research on current priorities for research and pointers on new directions for the field based on the 2008 IAVI Vaccine Blueprint	S. Berkley (US), A. Bernstein (Canada), A. Binagwaho (Rwanda), S.A. Karim (S. Africa), C. McClure (Switzerland), M. Schechter (Brazil)
Making HIV Trials Work for Women and Adolescent Girls (NCS) *Skills Building Room 2*	18:30	WESAT1901	Women and clinical trials: Where have we been and where are we going?	C. Hankins (Canada)
	18:40	WESAT1902	Women and trials in low- and middle-income settings	TBD (Denmark)
	18:50	WESAT1903	She shoots but does she score: Women's participation in clinical trials – are they on the scoreboard?	S. Walmsley (Canada)
	19:00	WESAT1904	The clinical investigator's perspective	J. Currier (US)
Thursday, August 7				
HIV Viral Entry and Tropism (OAS) *Session Room 6*	11:00	THAA0101	HIV-1 and intestinal epithelial cells: Mechanisms of entry and infection	S. Gauthier (Canada)
	11:45	THAA0104	Mutations in the C-terminal BBXB domains of CXCL12γ restore chemotactic activity and enhance anti-HIV effects	J. Altenburg (US)
Elite Controllers and Long-Term Nonprogressors (OAS) *Session Room 6*	14:30	THAA0201	Expression pattern of talomere genes maintenance and shelterin genes in HIV-1 CD8$^+$ T cells from HIV-1 elite controllers	M. Lichterfeld (US)
	14:45	THAA0202	Reduced *in vitro* replication capacity by chimeric NL 4-3 viruses encoding gag-protease from HIV-1 elite controllers	T. Miura (US)
	15:00	THAA0203	Evolution of the functional profile of HIV-1 specific CD8$^+$ T cells in LTNP	J. Benito (Spain)
	15:15	THAA0204	Host genetic expression patterns in HIV-infected individuals with divergent disease progression	M. Salgado (Spain)
	15:30	THAA0205	IL-15 is highly expressed by monocytes of HIV-infected LTNPs and is responsive to IFN-γ stimulation	M. Terkowski (Italy)
Understanding and Communicating Results from Recent AIDS Vaccine Efficacy Trials *Skills Building Room 9*	14:30-16:00	THSB19	A workshop focusing on recent trial results, best practices for communicating results, and the role of communities in AIDS vaccine research	Facilitator: D. Grant (US)

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AIDS 2008: A changing landscape for vaccine research

AIDS vaccine researchers were unexpectedly pushed in new directions 11 months ago, following the suspension of immunizations in the STEP trial involving 3,000 volunteers. The vaccine candidate known as MRKAd5, made by genetically altering a common cold virus to include fragments of HIV, showed no efficacy in preventing HIV infection or in reducing the amount of virus in the blood of individuals who subsequently became HIV infected through natural exposure to the virus. Later, researchers observed a trend toward increased susceptibility to HIV infection among certain sub-groups of trial volunteers—uncircumcised men who have sex with men (MSM) who had pre-existing immunity to the modified cold virus that was used as a vector because of being naturally exposed to the same type of cold virus before.

Following MRKAd5's disappointing performance, at least one large vaccine trial was curtailed and others were put in limbo. Researchers, meanwhile, are returning to the laboratory to re-evaluate current approaches to AIDS vaccine development, with a focus on basic discovery research. Major funders of AIDS vaccine research, such as the US National Institute of Allergy and Infectious Diseases (NIAID), are trying to attract new investigators and spark novel ideas about how to induce broadly neutralizing antibodies against HIV and determine the precise role of mucosal immunity in HIV prevention.

This shift in priorities is now expected to dominate much of the discussions at the sprawling XVII International AIDS Conference in Mexico City, August 3-8. This biannual AIDS conference is expected to attract about 25,000 participants and is generally seen as a venue for activists, advocates, and policymakers, rather than an arena for breakthrough AIDS research.

"My experience attending these meetings is you just never know the issues that will attract the most attention," says Anthony Fauci, director of NIAID. "But superimposed over all the discussions in Mexico City will be a topic that will be huge: Where do we go in the direction of AIDS vaccine research?"

Fauci will decide this month whether to move forward with a scaled-down version of PAVE 100, a trial testing a combination of vaccine candidates, one of which is similar to MRKAd5 (see *VAX* June 2008 *Spotlight on Nearing a Decision on PAVE*). Fauci is already gearing up to answer questions about this highly anticipated announcement during a special satellite session he will participate in: "Looking to the Future: The Epidemic in 2031 and New Directions in AIDS" (see *AIDS Vaccine Program*, this issue).

Pedro Goicochea, an AIDS researcher with Investigaciones Médicas en Salud in Lima, Peru, who is participating in another symposium on the future direction of vaccines and microbicides, says this AIDS conference will be an opportunity to clarify lingering questions about the STEP trial results and vaccine efficacy trials in general. "The explanations were so technical," says Goichochea. "It is still a work in progress trying to find out what happened and the community doesn't have the message clear."

Goichochea said that three pre-exposure prophylaxis (PrEP) trials, which are testing oral antiviral drugs as preventive measures against HIV, will likely be a major topic at the conference as well.

Myron Cohen, an immunologist with the Center for HIV/AIDS Vaccine Immunology who is delivering one of the conference's plenary talks, said the devastation caused by the 27-year-old epidemic makes the long-term goal clear. "We have to continue to extend every [available] strategy for prevention," he says. "We have no choice but to [also] try and make a vaccine. We have to keep trying to identify how we modify immune responses in such a way to prevent HIV." Cohen says the AIDS vaccine community also has to let go of the notion that scientists will find the equivalent of a home run.

Pedro Cahn, president of the International AIDS Society, the organization that sponsors the conference, says universal access to treatment and prevention will also be major themes at this conference. "Some voices are being raised regarding too much money being spent on AIDS and that this could be seen as detrimental for other healthcare services," says Cahn. "We think it's exactly the opposite. Really, the provision of AIDS services has helped strengthen healthcare services." – *Regina McEnery*

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IAVI is a global not-for-profit organization working to speed the search for a vaccine to prevent HIV infection and AIDS. Founded in 1996 and operational in 24 countries, IAVI and its network of partners research and develop vaccine candidates. IAVI also advocates for a vaccine to be a global priority and works to assure that a future vaccine will be accessible to all who need it. For more information, go to www.iavi.org.

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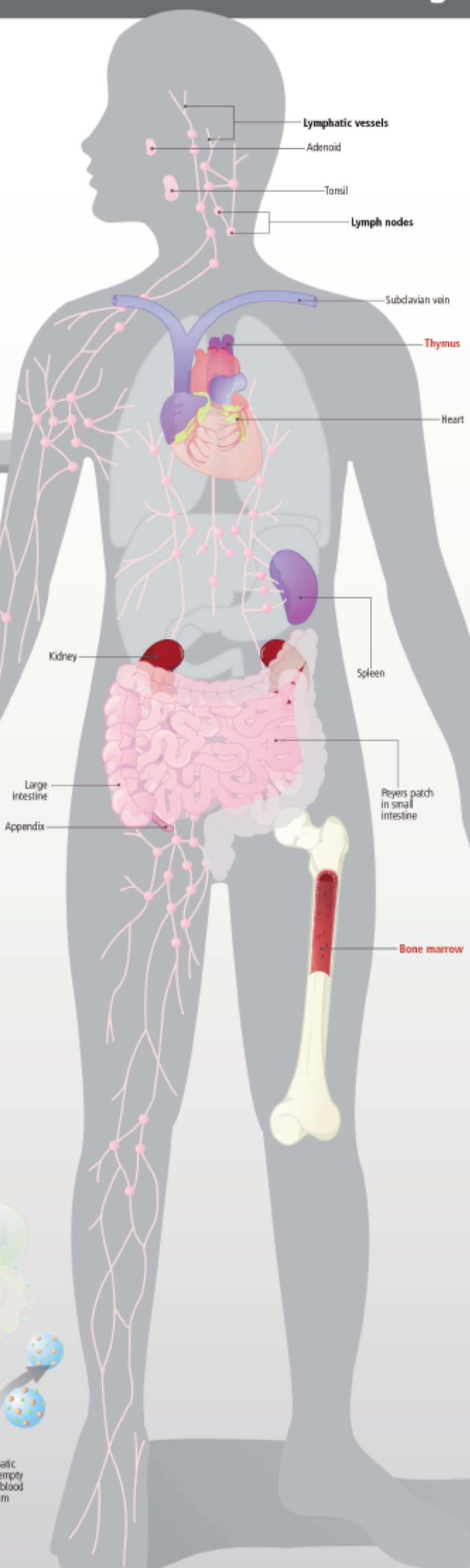
[*The publication on international AIDS vaccine research*]

Understanding the Immune System and AIDS Vaccine Strategies

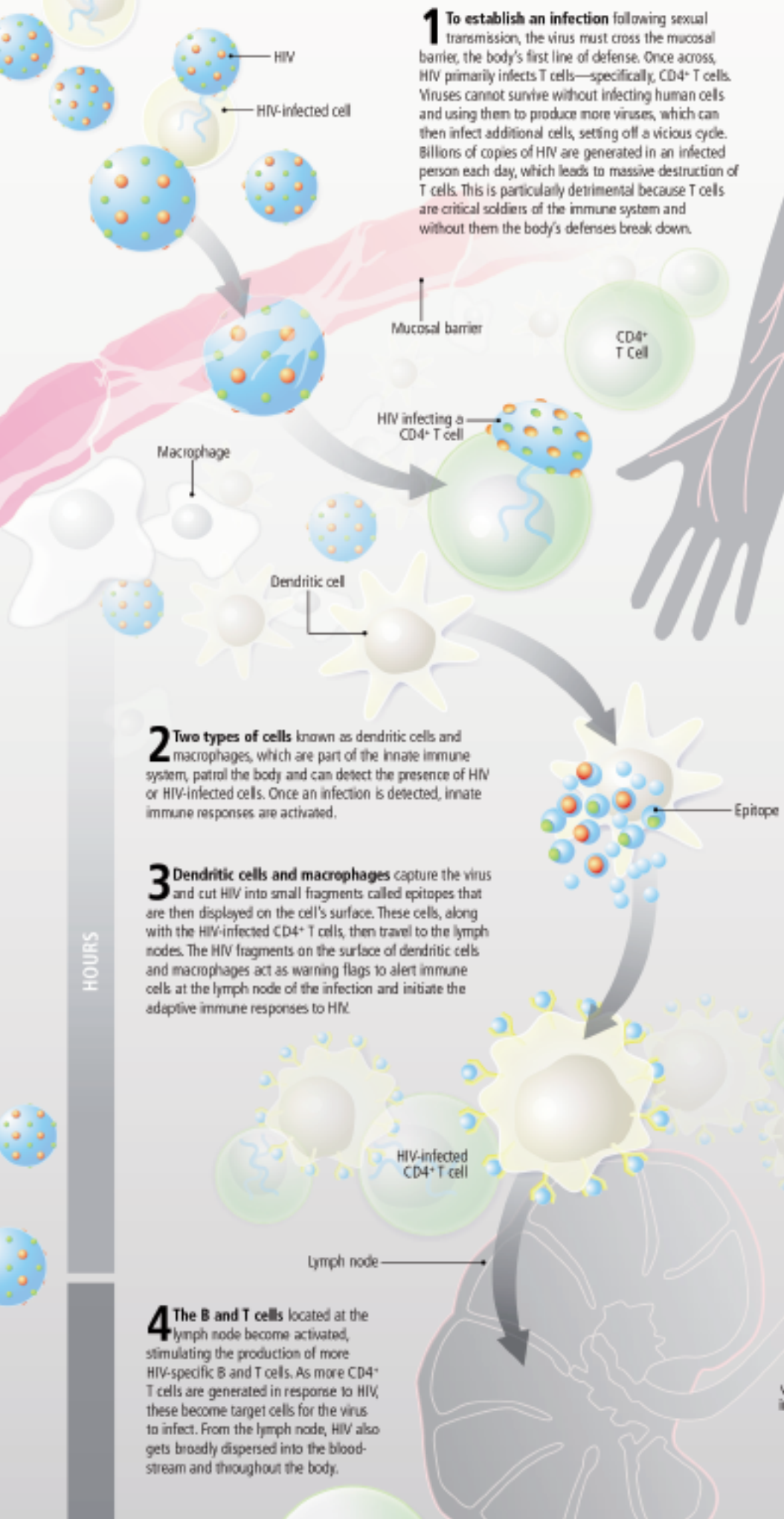
HUMANS ARE REPEATEDLY EXPOSED to various disease-causing organisms known as pathogens, including viruses and bacteria, which pose a threat to their health. The body defends itself against these foreign invaders using an incredibly complex network of cells, molecules, tissues, and organs, which together make up the immune system.

There are two categories of defenses the immune system uses to combat pathogens: innate and adaptive. The innate immune responses are the first responders against an invading virus, acting within hours. These responses are not specific, so whether the pathogen is a cold virus or HIV, the response will be very similar. Innate immune responses don't always clear an infection. Instead they help control the virus until the adaptive immune responses are ready to kick in. The adaptive immune responses take days to weeks to activate, partly because they are produced in response to a specific pathogen. Adaptive responses are further divided into two types: cellular and antibody responses.

The adaptive immune responses are orchestrated by two main classes of cells: B cells, which produce antibodies, and T cells, which conduct cellular immune responses. B and T cells are generated in the bone marrow and thymus (*shown in red*) and from there migrate throughout the body. They mature in the lymph nodes, spleen, and the mucosal tissues that line the intestine, nasal, respiratory, and genital tracts. B and T cells travel between tissues and organs using a network of vessels known as the lymphatic system. Lymph nodes occur where lymphatic vessels converge and are the communication hubs where different cells of the immune system meet and greet.



HOW HIV INTERACTS WITH THE IMMUNE SYSTEM

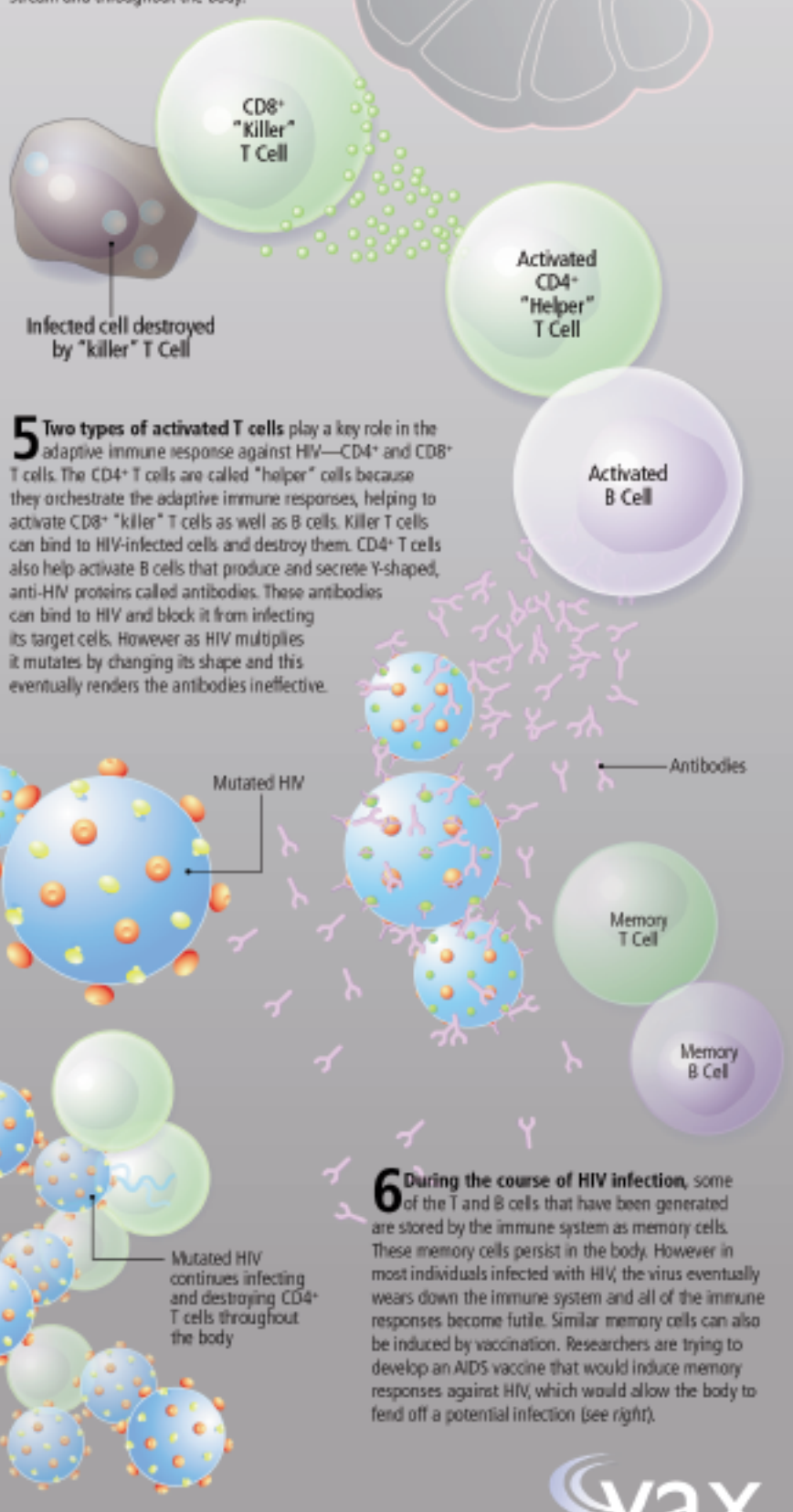


1 To establish an infection following sexual transmission, the virus must cross the mucosal barrier, the body's first line of defense. Once across, HIV primarily infects T cells—specifically, CD4+ T cells. Viruses cannot survive without infecting human cells and using them to produce more viruses, which can then infect additional cells, setting off a vicious cycle. Billions of copies of HIV are generated in an infected person each day, which leads to massive destruction of T cells. This is particularly detrimental because T cells are critical soldiers of the immune system and without them the body's defenses break down.

2 Two types of cells known as dendritic cells and macrophages, which are part of the innate immune system, patrol the body and can detect the presence of HIV or HIV-infected cells. Once an infection is detected, innate immune responses are activated.

3 Dendritic cells and macrophages capture the virus and cut HIV into small fragments called epitopes that are then displayed on the cell's surface. These cells, along with the HIV-infected CD4+ T cells, then travel to the lymph nodes. The HIV fragments on the surface of dendritic cells and macrophages act as warning flags to alert immune cells at the lymph node of the infection and initiate the adaptive immune responses to HIV.

4 The B and T cells located at the lymph node become activated, stimulating the production of more HIV-specific B and T cells. As more CD4+ T cells are generated in response to HIV, these become target cells for the virus to infect. From the lymph node, HIV also gets broadly dispersed into the blood-stream and throughout the body.

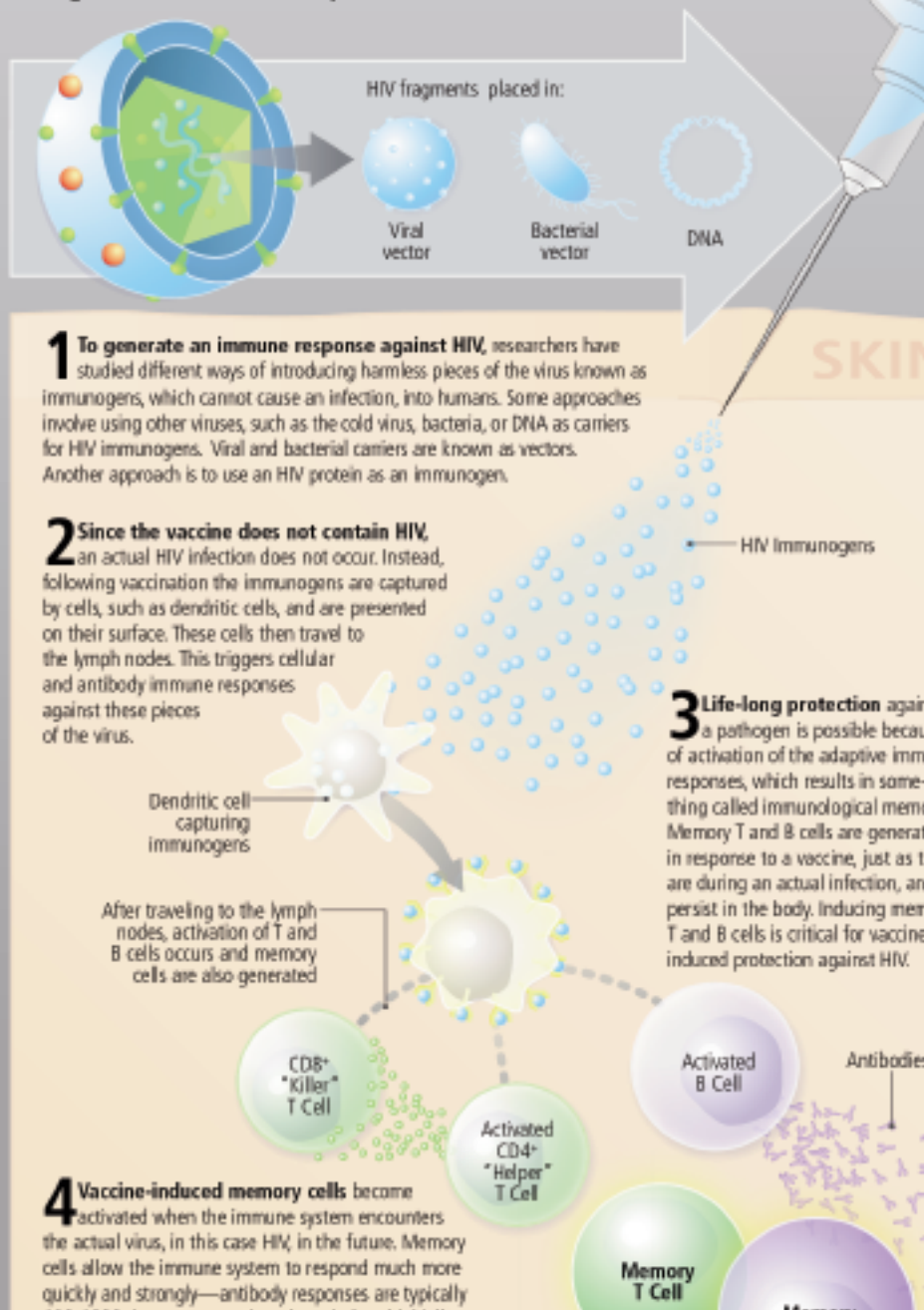


5 Two types of activated T cells play a key role in the adaptive immune response against HIV—CD4+ and CD8+ T cells. The CD4+ T cells are called "helper" cells because they orchestrate the adaptive immune responses, helping to activate CD8+ "killer" T cells as well as B cells. Killer T cells can bind to HIV-infected cells and destroy them. CD4+ T cells also help activate B cells that produce and secrete Y-shaped, anti-HIV proteins called antibodies. These antibodies can bind to HIV and block it from infecting its target cells. However as HIV multiplies it mutates by changing its shape and this eventually renders the antibodies ineffective.

6 During the course of HIV infection, some of the T and B cells that have been generated are stored by the immune system as memory cells. These memory cells persist in the body. However in most individuals infected with HIV, the virus eventually wears down the immune system and all of the immune responses become futile. Similar memory cells can also be induced by vaccination. Researchers are trying to develop an AIDS vaccine that would induce memory responses against HIV, which would allow the body to fend off a potential infection (see right).

CURRENT STRATEGIES IN AIDS VACCINE RESEARCH

Vaccines are a highly effective way to train the immune system to combat pathogens. Scientists only began studying the immune system after the concept of vaccination was discovered. Researchers are currently exploring multiple strategies in an effort to develop an effective AIDS vaccine.



1 To generate an immune response against HIV, researchers have studied different ways of introducing harmless pieces of the virus known as immunogens, which cannot cause an infection, into humans. Some approaches involve using other viruses, such as the cold virus, bacteria, or DNA as carriers for HIV immunogens. Viral and bacterial carriers are known as vectors. Another approach is to use an HIV protein as an immunogen.

2 Since the vaccine does not contain HIV, an actual HIV infection does not occur. Instead, following vaccination the immunogens are captured by cells, such as dendritic cells, and are presented on their surface. These cells then travel to the lymph nodes. This triggers cellular and antibody immune responses against these pieces of the virus.

3 Life-long protection against a pathogen is possible because of activation of the adaptive immune responses, which results in some-thing called immunological memory. Memory T and B cells are generated in response to a vaccine, just as they are during an actual infection, and persist in the body. Inducing memory T and B cells is critical for vaccine-induced protection against HIV.

4 Vaccine-induced memory cells become activated when the immune system encounters the actual virus, in this case HIV, in the future. Memory cells allow the immune system to respond much more quickly and strongly—antibody responses are typically 100-1000 times stronger than those induced initially —and can block an infection from occuring.

Illustration by Lucy Reading-Ikkanda

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