Introduction to Immunology, Vaccinology, and COVID-19 Trials

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Director of External Relations, HVTN/CoVPN
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October 28, 2020

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Association of Nurses in AIDS Care

Housekeeping

- Participant lines muted during the webinar
- Type questions in the “Question” pane of your Dashboard
- Q & A session at the end of the webinar.

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Continuing Nursing Education

Upon full participation in this webinar & completion of an evaluation, participants will be awarded 1.0 contact hours.

The Association of Nurses in AIDS Care (ANAC) is accredited as a provider of nursing continuing professional development by the American Nurses Credentialing Center's Commission on Accreditation.

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Disclosures

The speaker has no relevant conflict of interest to disclose.

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Learning Objectives

At the conclusion of today's activity, participants will be able to:

- *Describe the basics of Immunology*
- *Discuss how a vaccine is developed*
- *Identify the different types and mechanisms of the COVID-19 vaccines currently under clinical trial*

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Agenda

1. Introductions
2. Speaker presentation
3. Question & Answer

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HIV VACCINE
TRIALS NETWORK

Introduction to Immunology

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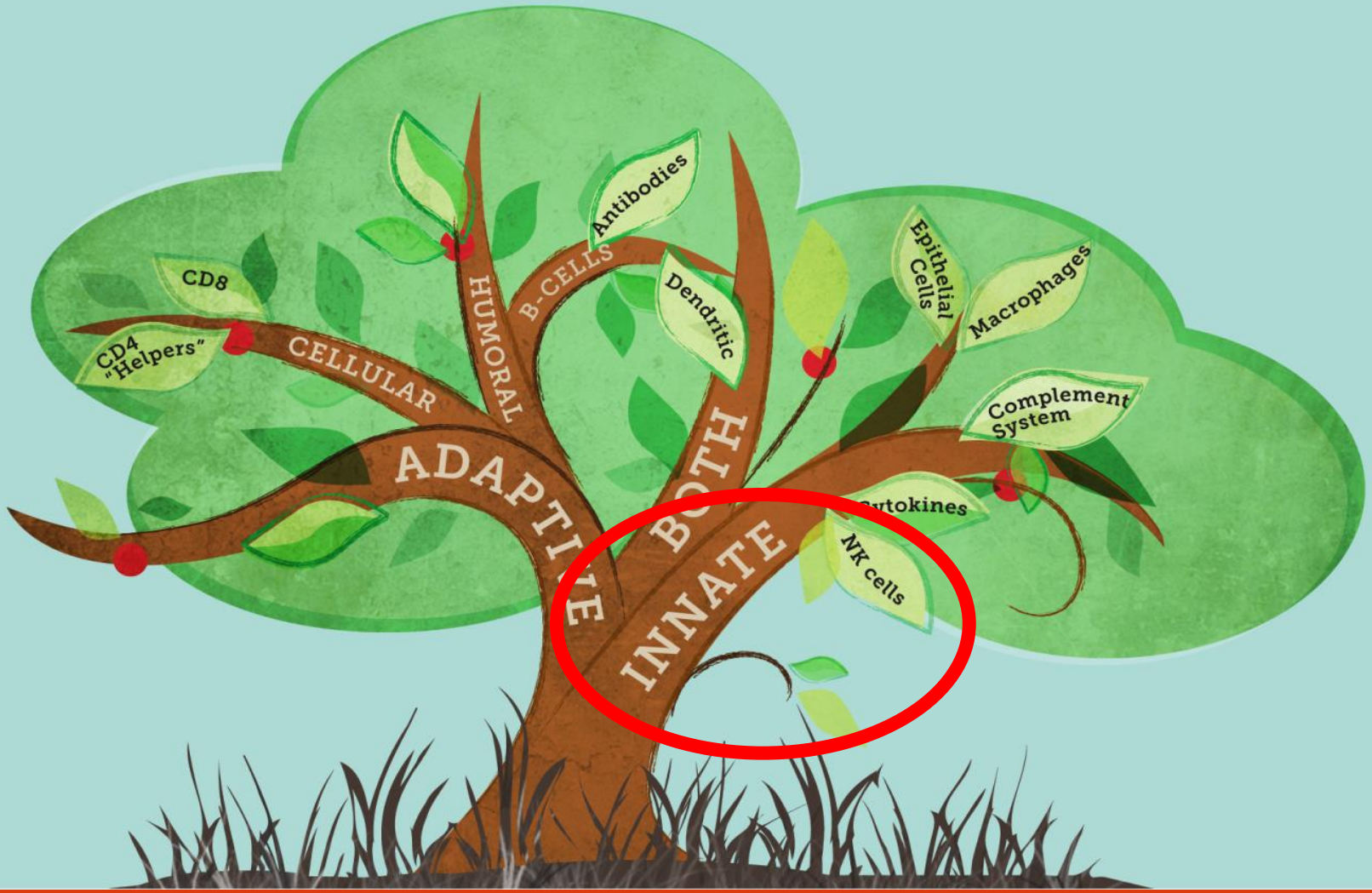
CD8
CD4
"Helpers"
CELLULAR
HUMORAL
B-CELLS
Antibodies
Dendritic
ADAPTIVE
BOTH
INNATE
Epithelial Cells
Macrophages
Complement System
Cytokines
NK cells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Innate Response

- First line of defense
- Prevents infection? No!
- NK cells activated when cells are infected
- Activation of innate response is required before the adaptive response can happen
- No immunological memory
- We don't think vaccination will help with immunological memory
- NK cells work by causing infected cells to burst, like a dart bursting a water balloon


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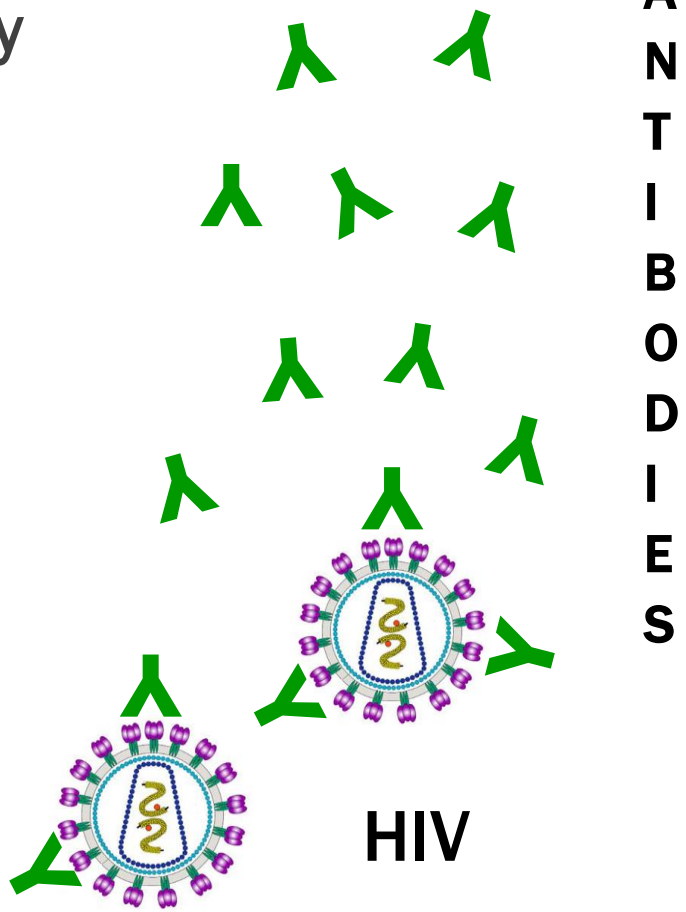
Adaptive = Acquired

- Antigen-specific defense mechanism
- Takes several days to become protective
- Develops throughout life

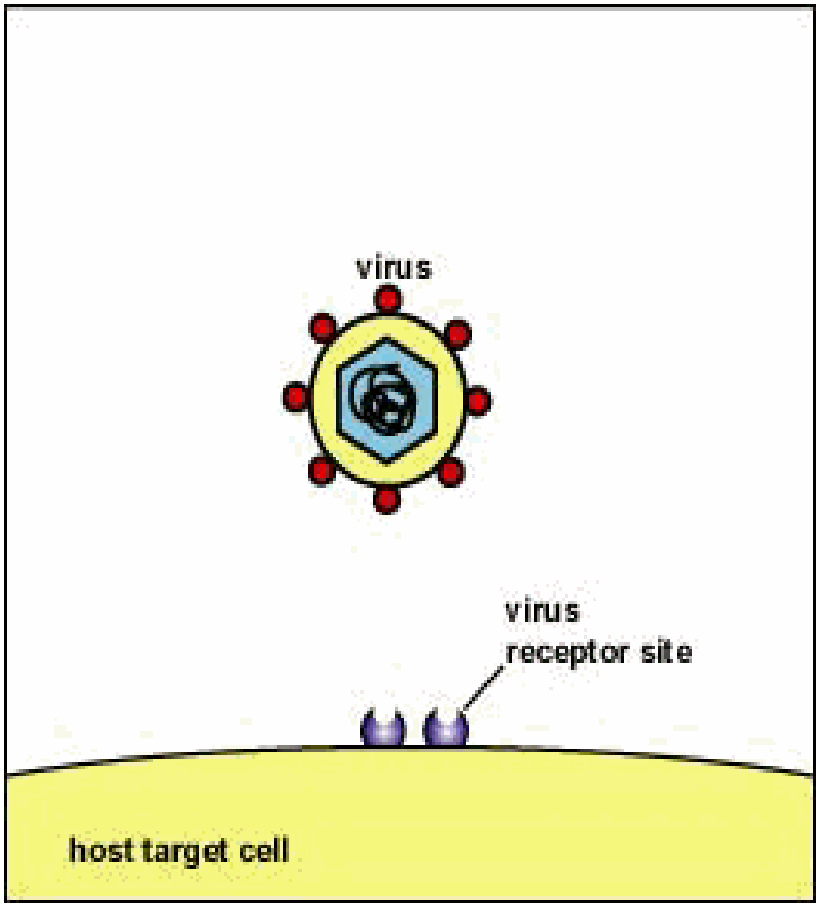
Adaptive – Part 1
(also known as humoral or antibodies)

- Antibodies are made by B cells in the first 2 days after infection, but usually takes 2 weeks for full effect
- Antibodies have three simultaneous functions:
  - neutralize or stop the virus
  - eliminate the virus through opsonization
  - sensitize the immune system to engage other functions
- Antibodies can prevent infection
- Antibodies have immunological memory



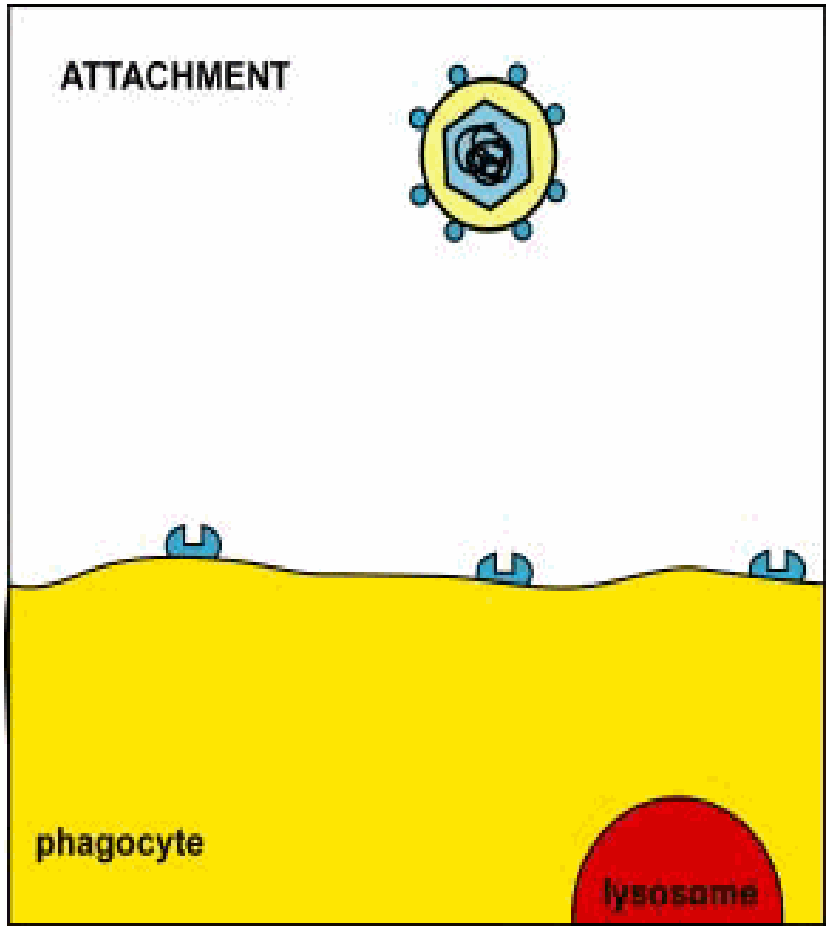
How Do Antibodies Prevent Infection?

1st way: Neutralization



How Do Antibodies Prevent Infection?

2nd way: Eliminate the virus



Opsonization uses other cells of the immune system to destroy HIV

Binding antibodies sensitize the immune system

Antibody **D**ependent **C**ellular **C**ytotoxicity (ADCC)

- NK cells may also be able to act like a CD8 killer T cell (“a hitman”)
- They need a binding antibody attached to the HIV to act like a “lookout”
- With the lookout in place, the NK cell can identify HIV and kill it

Humoral Response – Summary

- Antibodies attach to the virus at sites that are used by the virus for entry into cells.
- Neutralizing antibodies can work alone to block a virus from entering cells.
- Vaccines designed to elicit neutralizing antibodies against HIV have not worked very well in trials so far.
- Recent discoveries of several broadly neutralizing antibodies are very exciting, and designing a vaccine to produce these antibodies is underway!
- Binding antibodies can attach to HIV and call other parts of the immune system into action to help destroy it.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Adaptive Part Two - Cellular

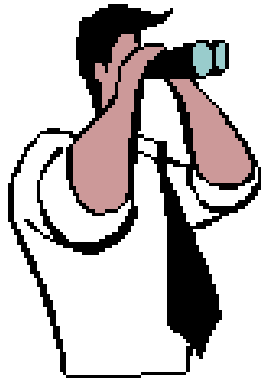
- Cellular response involves two types of cells:
  1) Helper T lymphocytes ($CD4^+$)
  2) Cytotoxic T lymphocytes (CTL or $CD8^+$)
- Have memory!
- Activated once infection occurs

The Two Types of Cells

- $CD4^+$ cells recognize HIV and help cells communicate with each other, calling the killers into action

- $CD8^+$ cells are the killers

How Does the Adaptive Response Work?



- T-cell function: immunosurveillance
- Checks other cells of the body (are they infected or abnormal?)
- Destroys infected or abnormal cells

CD8 Cells May Need Binding Antibodies – More sensitization!

Antibody **D**ependent **C**ell-mediated **V**iral **I**nhibition

- CD8 cells may also be able to do a better job of killing if they have an antibody acting as the “lookout”
- Their role is already to kill infected cells, but having the antibody in place amplifies their success

Adaptive Response – Summary

Cellular = Cytotoxic T lymphocytes (CTL or CD8+) and helper T lymphocytes (CD4+)

- Cannot prevent infection
- T cells are activated when cells become infected
- T cells can eradicate an established infection
- T cells have immunological memory
- T cells can be primed by vaccination

Questions?

Introduction to Vaccinology

History of Preventive Vaccines

- Used for decades around the world, most commonly in children
- Safe when manufactured and used properly
- Cost-effective compared to treatment
- Eliminated smallpox worldwide
- 2008: 1st vaccine for girls and young women against a cancer-causing virus, human papilloma virus (HPV), and 2009-10 approval for boys and young men

Vaccine Research in Perspective

VACCINE	DISCOVERY OF VIRUS	VACCINE DEVELOPED FOR HUMAN USE	YEARS TO VACCINE
H. Influenzae-B	1892	1985	93
Herpes (HSV-1)	1919	Not available	>90
Pertussis	1906	1926	20
Polio	1909	1954	47
Yellow Fever	1900	1935	35
Influenza	1933	1945	12
Measles	1911	1957	46
Hepatitis A	1973	1995	22
Hepatitis B	1967	1984	17
HPV	1974	2007	33
HIV	1983	Not available	>30

The Impact of Vaccines in the United States

DISEASE	BASELINE 20TH CENTURY PRE-VACCINE ANNUAL CASES	2008 CASES*	PERCENT DECREASE
Measles	503,282	140	99.9%
Diphtheria	175,885	0	100.0%
Mumps	152,209	454	99.7%
Pertussis	147,271	10,735	92.7%
Smallpox	48,164	0	100.0%
Rubella	47,745	16	99.9%
Haemophilus influenzae type b, invasive <5 yrs.)	20,000	30	99.9%
Polio, paralytic	16,316	0	100%
Tetanus	1,314	19	98.6%

***Provisional**

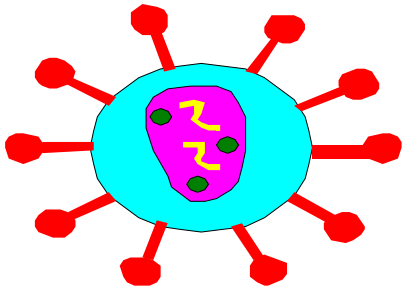
Source: *MMWR* 4/2/99, 12/25/09, 3/12/2010

What are Vaccines?

Vaccines teach your body to recognize and fight invaders.

How Does a Vaccine Work?

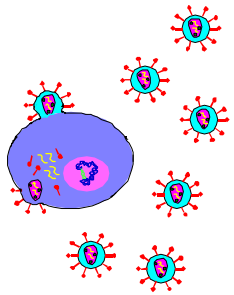
By teaching the body to recognize and fight invaders.



Body recognizes HIV virus

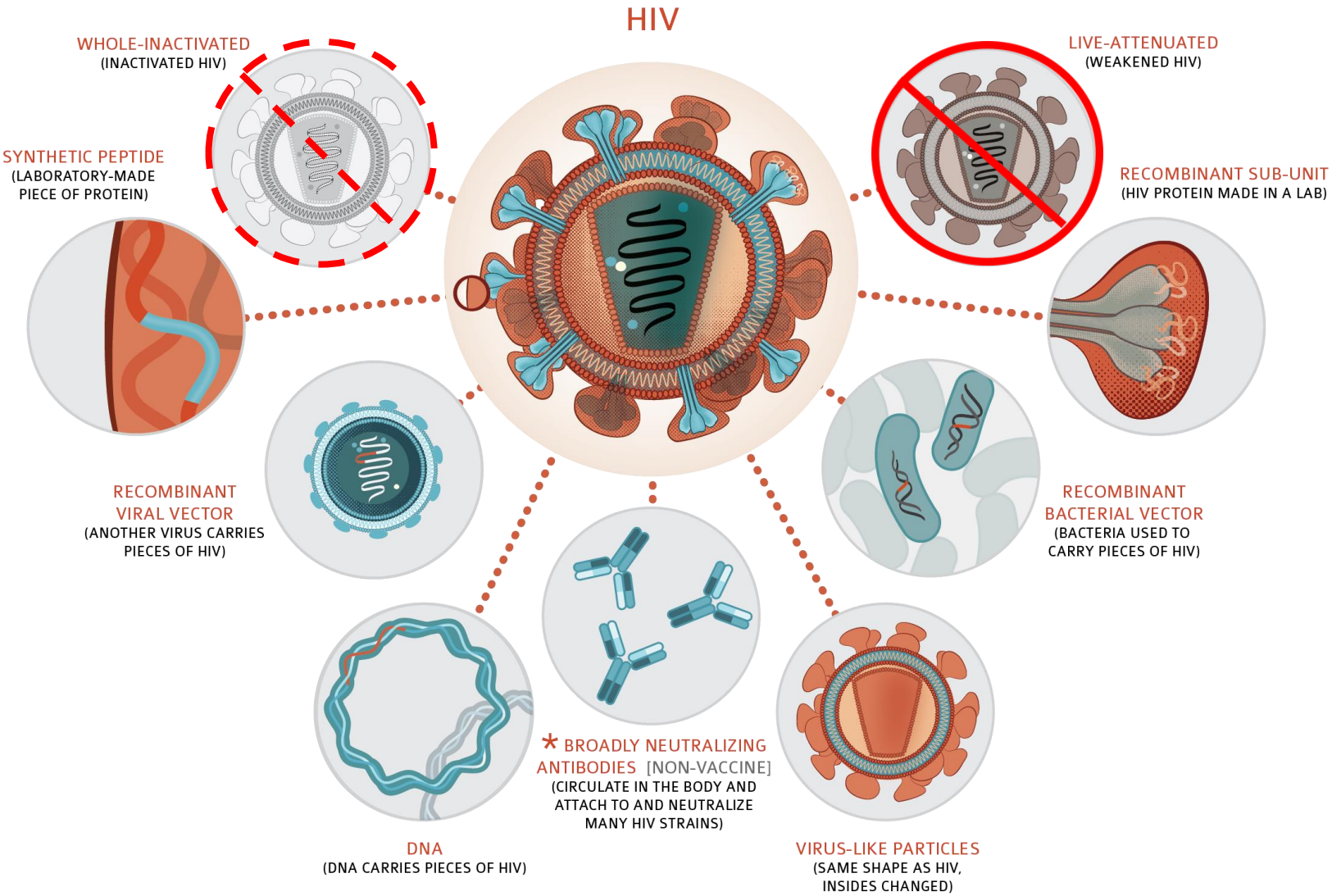
Body – Sounds Alarm

Fighter cells and proteins go into action



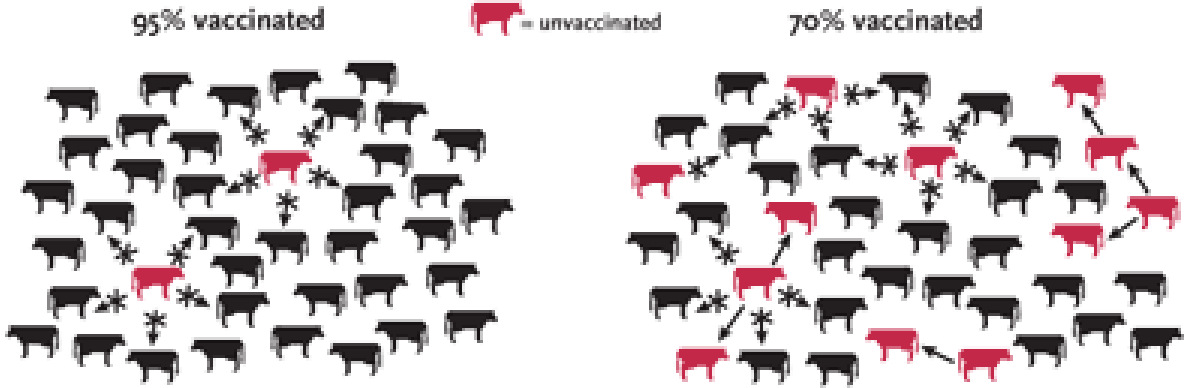
GOAL - HIV is controlled or killed

Vaccine and Related* Designs



HOW AN HIV VACCINE MIGHT WORK

What Might a Preventive HIV Vaccine Do?



Benefits for the person who gets the vaccine:

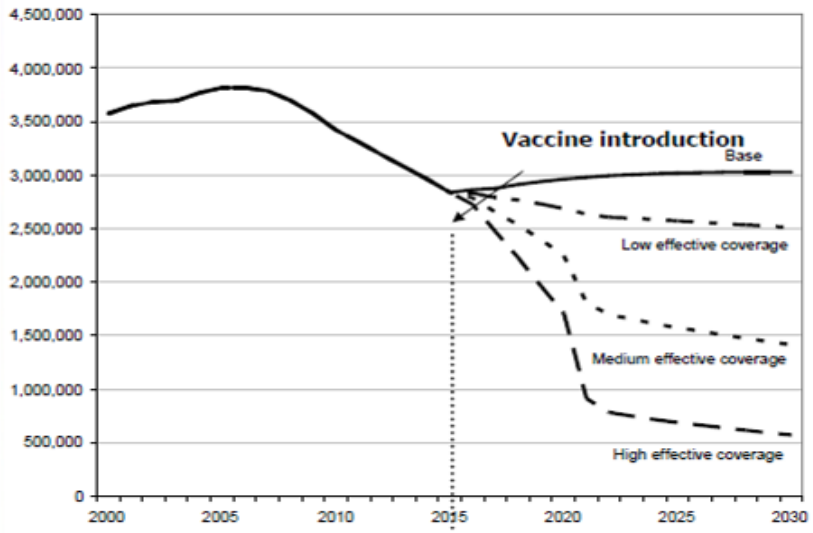
- ☑ Prevent infection
- ☑ Prevent disease
- ☑ Delay disease progression

Benefits for the entire community:

- ☑ Prevent further transmission
- ☑ Create “herd immunity”

Potential Impact of a Vaccine

New Adult Infections in Low- and Middle- Income Countries by Year and Vaccine Scenario



Total new infections averted by an AIDS vaccine between 2015-2030

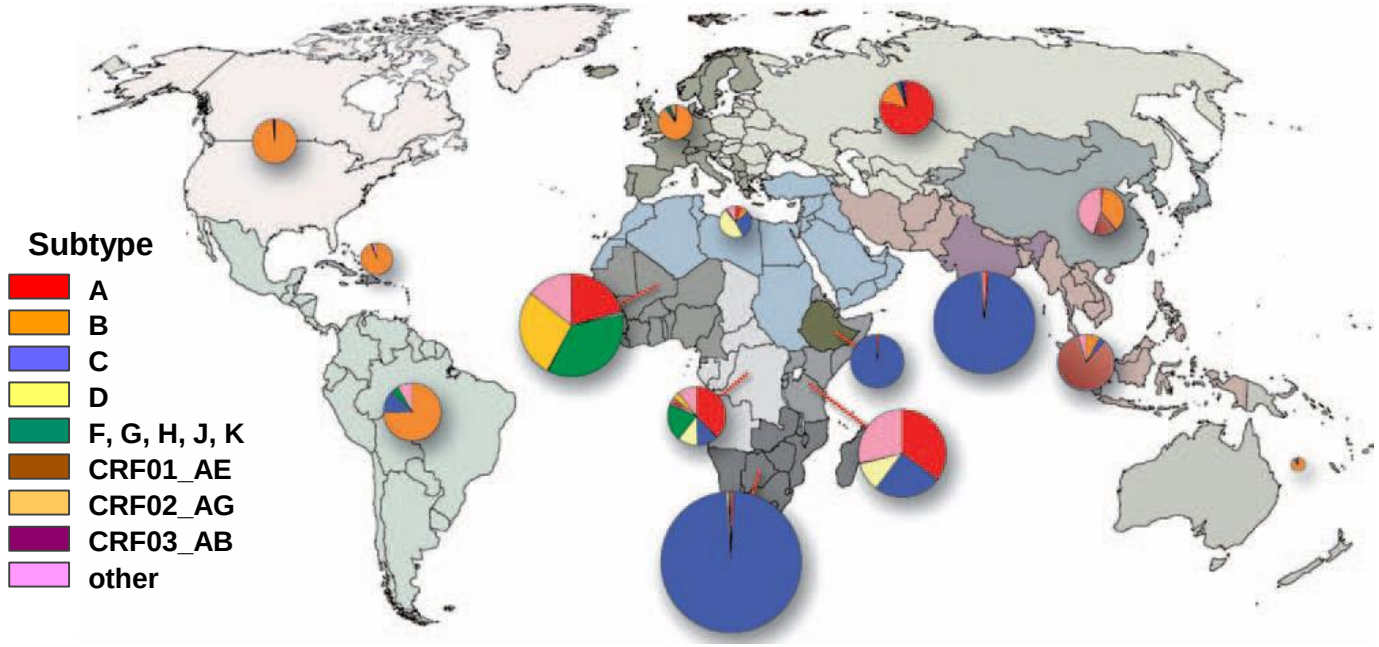
30% efficacy, 20% coverage	5.5 million
50% efficacy, 30% coverage	17 million
70% efficacy, 40% coverage	28 million

Even a vaccine with low efficacy and limited coverage can impact the epidemic and play a role in preventing future infections

Stover J, et al. The impact of an AIDS Vaccine in Developing Countries: A New Model and Initial Results. Health Affairs 26(4):1147-1158 (2007)

HIV-1 Diversity Worldwide

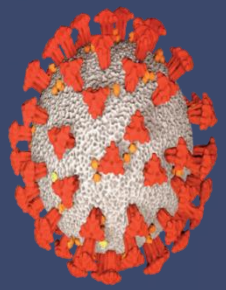
HIV-1 group M: 9 subtypes & several circulating recombinant forms



HIV genomes differ by 10-30%

Human genomes differ by about 0.1%

Hemelaar et al. 2004. WHO/UNAIDS.



COVID-19
Prevention Network

CoVPN Overview

Stephaun E. Wallace, PhD, MS

Director of External Relations, COVID-19 Prevention Network

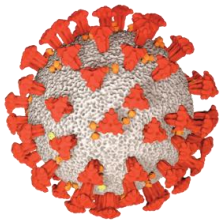
Staff Scientist, Vaccine and Infectious Disease Division, Fred Hutch

Clinical Assistant Professor, Dept of Global Health, UW

What is the COVID-19 PREVENTION NETWORK?

The HVTN was formed 2 decades ago by Dr. Anthony Fauci of the **National Institute of Allergy and Infectious Diseases**, part of the **National Institutes of Health**, to address HIV and other global vaccine needs. The network quickly pivoted to COVID-19 and studies to ensure a safe and effective COVID-19 vaccine. Comprised of the foremost infectious disease and vaccine experts in the country, the research network and its global partners are working hand in hand to address this urgent need in our fight against the pandemic.

Dr. Anthony Fauci, *Director of the National Institute of Allergy and Infectious Diseases*



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Conceptual Framework for COVID-19 Vaccine Development

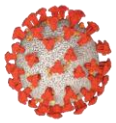
We need to develop multiple vaccine platforms.

No single vaccine platform can be manufactured at enough scale to immunize the 4.4 billion adult population on the planet and 3 billion children, 220 million adults in US alone

Use known platforms to cover the field scientifically. Manufacturing scalability is a key factor.

Coordinated USG effort to involve global vaccine manufacturing companies.

There must be an unprecedented coordinated approach to test, manufacture the vaccine at scale, and deliver the vaccine into peoples' arms throughout the world.



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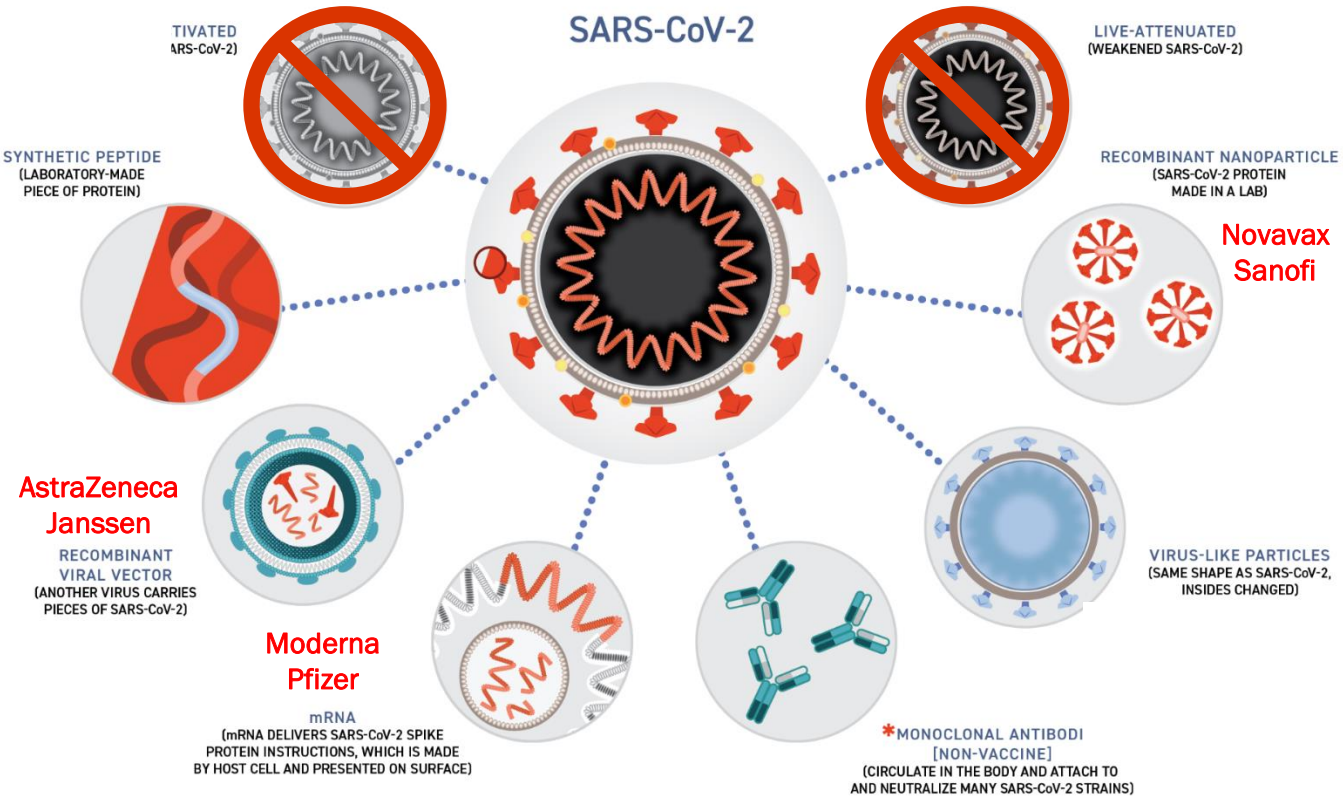
CoVPN Operations Center

- Built around structure of the HIV Vaccine Trials Network founded in 1999 at Fred Hutchinson Cancer Research Center
- Extensive clinical trials network: in early 2020, 52 sites in US and Latin America, and another 56 sites in sub-Saharan Africa. Now over 220 sites.
- Academically based CRO with Operations Center (Corey and Kublin), Statistical Data Management Center (Peter Gilbert PI) and centralized world class immunology and virology labs (Julie McElrath PI)
  - McElrath T cell Lab; Montefiori Pseudovirus Lab; Tomaras Binding Antibody Lab; and UW Virology/Jerome Lab are all HVTN Laboratories ; all validated in the HIV assays they perform and are now involved in OWS

Vaccine Designs

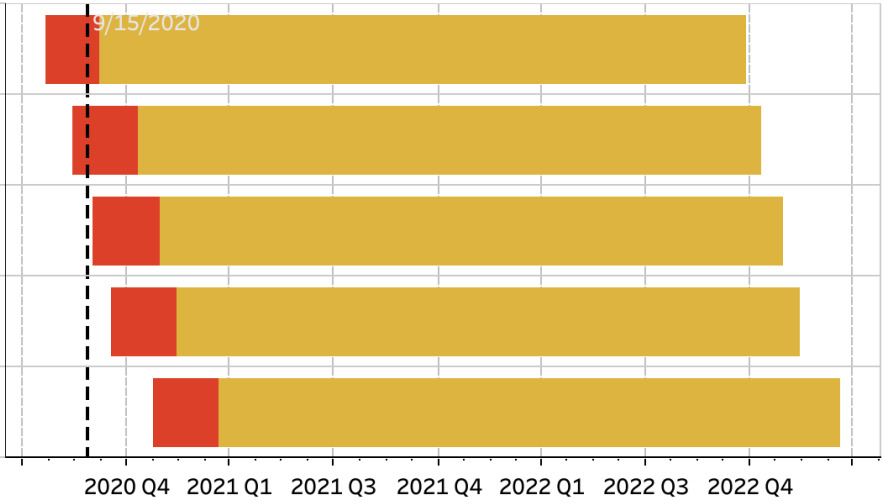


Protocol pipeline: COVID-19 studies

Date data refreshed

September 15, 2020 9:02 AM

Protocol Name	Concept Name	Study N	Protocol Open
Moderna phase 3	Moderna phase 3	30000	7/27/2020
AstraZeneca phase 3	AstraZeneca phase 3	30000	8/29/2020
Janssen phase 3	Janssen phase 3	60000	9/21/2020
Novavax phase 3	Novavax phase 3	30000	10/12/2020
Sanofi phase 3	Sanofi phase 3	30000	12/1/2020



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Interested in volunteering for a COVID-19 Prevention Clinical Study?

Thank you for your interest in our studies. Science can't move forward without your help!

Selecting the button below will take you to the CoVPN Volunteer Screening Registry.

The purpose of this screening registry is to create a list of potential volunteers who want to take part in current or future COVID-19 prevention clinical trials. You must be 18 years or older to participate. Participation involves completing a short online survey that includes some personal questions. Your participation is voluntary.

Volunteer Now!

Our studies enroll adults aged 18 and older, of all races and ethnicities, and of all gender identities.

Credit: iStock

www.preventcovid.org
www.coronavirusprevention network.org

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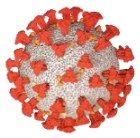
Community & Stakeholder Engagement Strategic Plan

Engagement and Participation Foci with Priority Populations

PRIORITY POPULATIONS

- **Native/Indigenous**
- **African American/Black**
- **Latinx**
- **Occupational Engagement**
- **People with pre-existing health conditions**
- **Communities experiencing health disparities**
- **Older Adults/Veterans Administration**
  - Nursing Home (mAb trials)
  - Assisted Living Facility residents (vaccine trials)

- **All activities are tailored for each of these vital priority populations**
- **Priority populations require varying:**
  - Outreach
  - Engagement
  - Recruitment approaches
- **Building and maintaining relationships with experts working with these groups**



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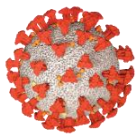
Community Engagement Activities

I. Materials for participants/potential participants *(English & Spanish)*

A. Community-based presentation of trial specific principles
B. CoVPN public website w/ registry – [www.PreventCOVID.org]

II. Materials for sites *(English & Spanish)*

A. Standardized informational tools for site staff involved in community engagement
B. Great ideas for community engagement
C. FAQs – ***incorporated in website***
D. COVID inequities slide set
E. General recruitment materials for use across vaccine studies: poster, flyer, postcard, palm cards
F. Site training/Preparation/Q&A calls in advance of each study
G. Educational Videos
H. National Heart, Lung, and Blood Institute Partnership w/ site specific support



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Community Engagement Activities

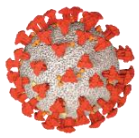
III. Priority Population Expert Panels

A. Scientists from and working with priority populations
   - Modeled after NIH review committees
   - Convene and discuss each protocol and related materials
   - Generate reports on significance, impact, ethics, etc. for larger priority population community

B. Native/Indigenous
C. African American/Black
D. Latinx
E. Older Adults/Veterans Administration

IV. Convening Community Working Groups with research familiarity for discussion

A. Utilizing Community Advisory Board and Community Action Board Models
B. Community Working Group convened and meeting regularly



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V. Stakeholder Engagement and Building Trust

A. Convening Community Listening Sessions (ongoing and iterative)
   - Opportunities for community to hear research updates

B. Virtual Town Halls/Webinars
   - Education sessions presenting and discussing community-level considerations for research engagement

C. Trade Unions
   - Meat/Poultry Industry, Restaurants, Factories

D. Grass Roots Organizations working on COVID and Social Justice
   - ThriveSS, BYP100, Urban Indian Health Institute

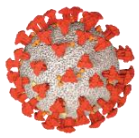
E. National Organizations
   - AARP, ANAC, NAACP, National Urban League, YWCA/YMCA, UnidosUS

F. Political Entities
   - Black Caucus, Hispanic Caucus, Progressive Caucus

G. CoVPN Faith Initiative - faith-based engagement

H. National Magazines

I. National Scientific Panels highlighting scientists of color



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CoVPN Virtual Town Halls/Webinars

Date	Title	Organizations
6/30/2020	The Blacker the Plan: Our People, Our Problem, Our Solution: Facts Only: How to Survive and Thrive During a Time of Pandemics	Black AIDS Institute, American Medical Association, CoVPN/HVTN
7/1/2020	COVID-19 Community Conversation Webinar	HANC CP, AVAC, TAG, CoVPN
7/2/2020	COVID-19 Pipeline Town Hall with CWG-NY and the CoVPN	COVID-19 Working Group-New York, CoVPN
7/8/2020	Fred Hutch Town Hall	Fred Hutch including HVTN and CoVPN
7/16/2020	NMAC Webinar	NMAC, CoVPN
7/16/2020	A 'We the People' Research Discussion on Medical Mistrust	BAI, CoVPN, HVTN, TAG
7/21/2020	Introduction to Vaccinology/Immunology	BAI, CoVPN, HVTN
7/23/2020	A 'We the People' Research Discussion on Vaccine Clinical Research	BAI, CoVPN, HVTN, Emory, Vanderbilt, HANC
8/19/2020	Community-Campus Partnerships for Health	CCPH, CoVPN
9/24/2020	COVID in Black: Honest Conversations about COVID-19 in Black Communities (Ep.1)	CoVPN
10/6/2020	COVID in Black: Black Women on COVID-19 (Ep.2)	CoVPN
10/6/2020	The Impact of COVID-19 on HIV Protection and Infection	National Minority Quality Forum, CoVPN, Latino Commission on AIDS, Merck, Gilead
10/14/2020	Intersections: How Do We Grapple With The Disproportionate Impact On Communities Of Color With COVID-19 In The Midst Of The Battle To End HIV By 2030?	Indiana University, Black AIDS Institute, CoVPN, TruEvolution
10/27/2020	CoVPN Overview and Introduction to Immunology/Vaccinology	Association of Nurses in AIDS Care, CoVPN

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CoVPN Faith Initiative

- **Faith Ambassadors & Clergy/Faith Leaders**
  - Geographically distributed across the US
  - Speaking to the intersection between faith and science
  - Establishing and enhancing networks of faith leaders to conduct COVID & CoVPN educational activities

- **Establish and Maintain a faith-based advisory council**
  - Provide guidance and direction for CE activities

- **Implementation of National faith-focused COVID & CoVPN Education program**
  - Educators will represent diverse faith, racial and ethnic identities
  - Program will integrate anti-racist, anti-xenophobic, anti-homophobic and Good Participatory Practice principles

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Community Engagement Activities

VI. Communications Creatives & Community Influencers

I. Lift up voices of people with lived experiences
II. Celebrity Champions
III. Marketing Campaign launched September 2020

VII. Sponsor CE Advisory Committees

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Thank You

COVPN Executive Committee

Larry Corey and Kathy Neuzil

David Stephens and Myron Cohen

Study Chairs

NIH Executive Team

- Mary Marovich
- Emily Erbelding
- Carl Dieffenbach
- Hilary Marston
- Cliff Lane

VRC

- John Mascola
- Barney Graham
- Julie Ledgerwood
- Sandra Sitar

Merlin Robb

NIH

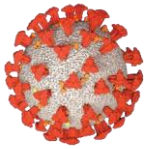
- Tony Fauci
- Francis Collins
- Doug Lowy

CoVPN Staff

HHS

Oracle

Fred Hutch



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Resources

- Stover J, et al. The impact of an AIDS Vaccine in Developing Countries: A New Model and Initial Results. Health Affairs 26(4):1147-1158 (2007)
- Hemelaar, J., Gouws, E., Ghys, P. D., & Osmanov, S. (2006). Global and regional distribution of HIV-1 genetic subtypes and recombinants in 2004. *Aids*, *20*(16), W13-W23.
- Centers for Disease Control and Prevention. (2010). Morbidity and Mortality Weekly Report. MMWR, 59(9), 253-288. https://www.cdc.gov/mmwr/index2010.html

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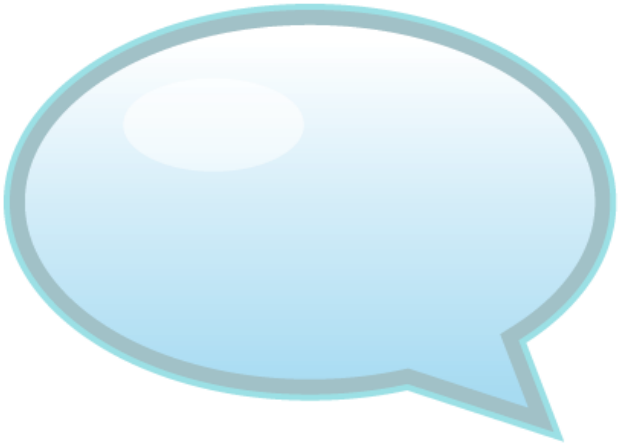
Q & A Discussion



Additional questions?
Email Erin at erin@anacnet.org

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To be awarded contact hours for this webinar, complete the evaluation found at

https://www.classmarker.com/online-test/start/?quiz=h6f5f7f385f49cc2

You will also receive an email with this link after the webinar

Additional questions?

Email Erin at erin@anacnet.org

The Association of Nurses in AIDS Care (ANAC) is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

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