Advancing Science in HSV:

2023 NIH Strategic Plan for Herpes Simplex Virus Research

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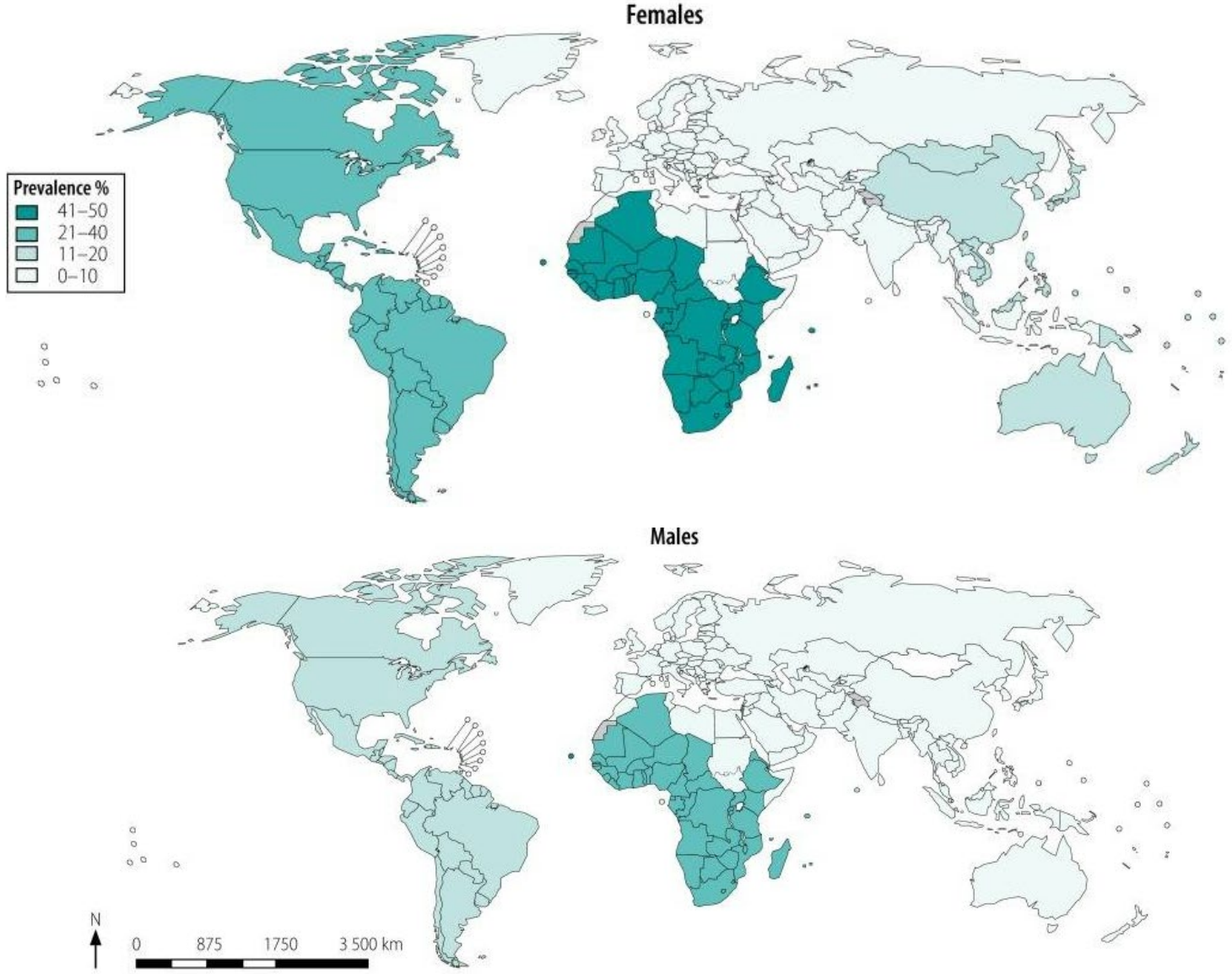
NINDS

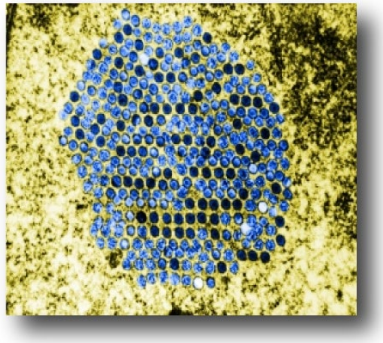
HSV-2 prevalence estimates: 491.1 million infections globally in 2016



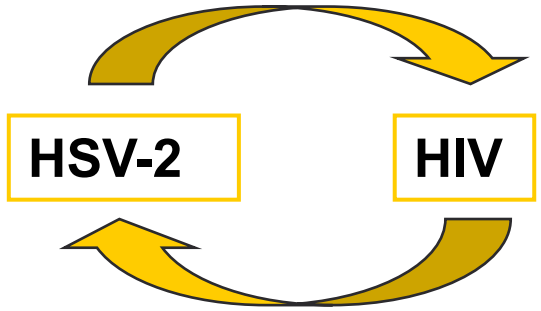
Bull World Health Organ. 2020 May 1; 98(5): 315–329. Published online 2020 Mar 25. doi: 10.2471/BLT.19.237149

Herpes simplex virus

Leading cause of genital ulcer disease (GUD) worldwide



HIV-1 acquisition and transmission



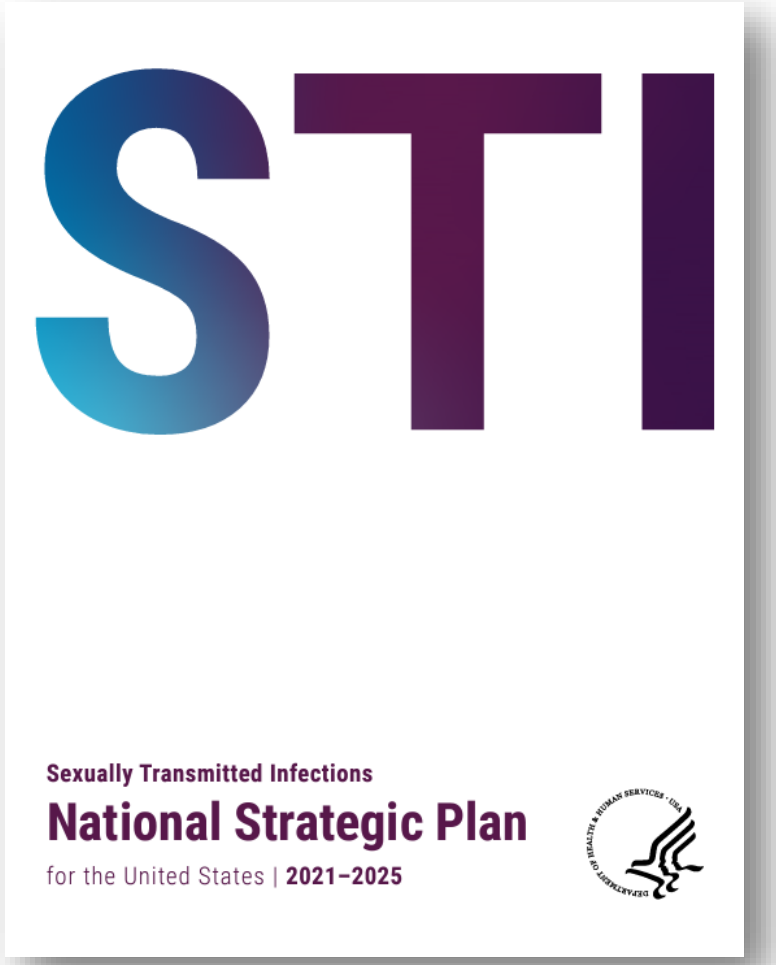
Impact on sexual and reproductive health (SRH)

Neonatal herpes

- Incurable infection with substantial stigma and psychosocial impact
- Estimated **187 million people** with at least one episode of HSV genital ulcer disease (GUD) in 2016
- Prevalent HSV-2 infection increases HIV risk by **3-fold**
- Available interventions unlikely to have population impact

Source: Looker et al, BMJ Glob Health 2020; Looker et al, Lancet Inf Dis 2020.

Sexually Transmitted Infections: National Strategic Plan 2021-2025



- In 2020, the USG coordinated development of inaugural National STI Strategic Plan.
- Sets national goals, objectives, strategies to respond to upward trends in STI rates
- Plan focused on HPV, *Neisseria gonorrhea, Chlamydia trachomatis, and Treponema pallidum*
- HSV-1 and -2 infection not included

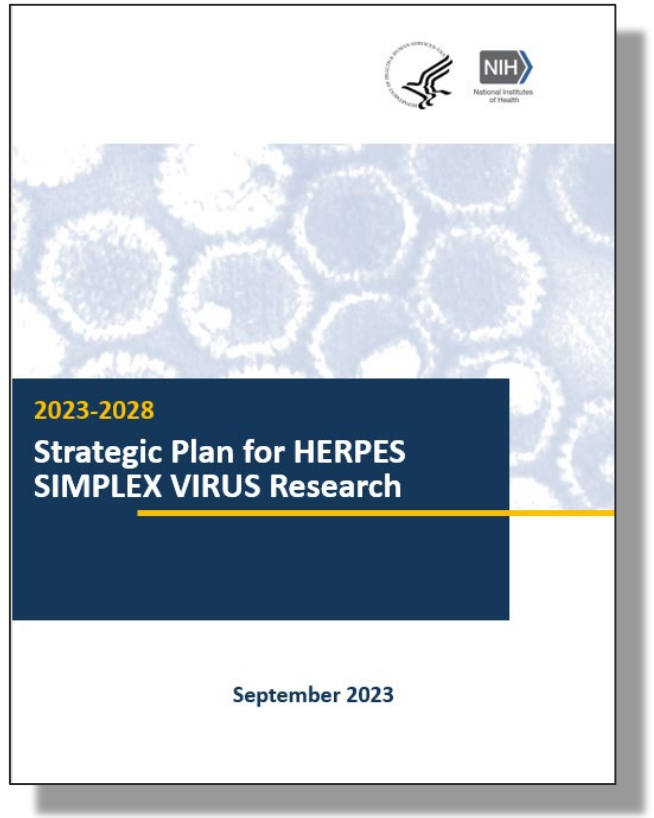
Response to Congressional Request on HSV 1 and 2

- NIAID led establishment of trans-NIH WG to develop HSV strategic plan
  - NINDS, NIA – neurodegenerative impacts
  - NIMH – mental health
  - NEI – ocular keratitis
  - NICHD – neonatal health
  - NIMHD – health disparities

BREADTH OF HSV IMPACT ON HEALTH

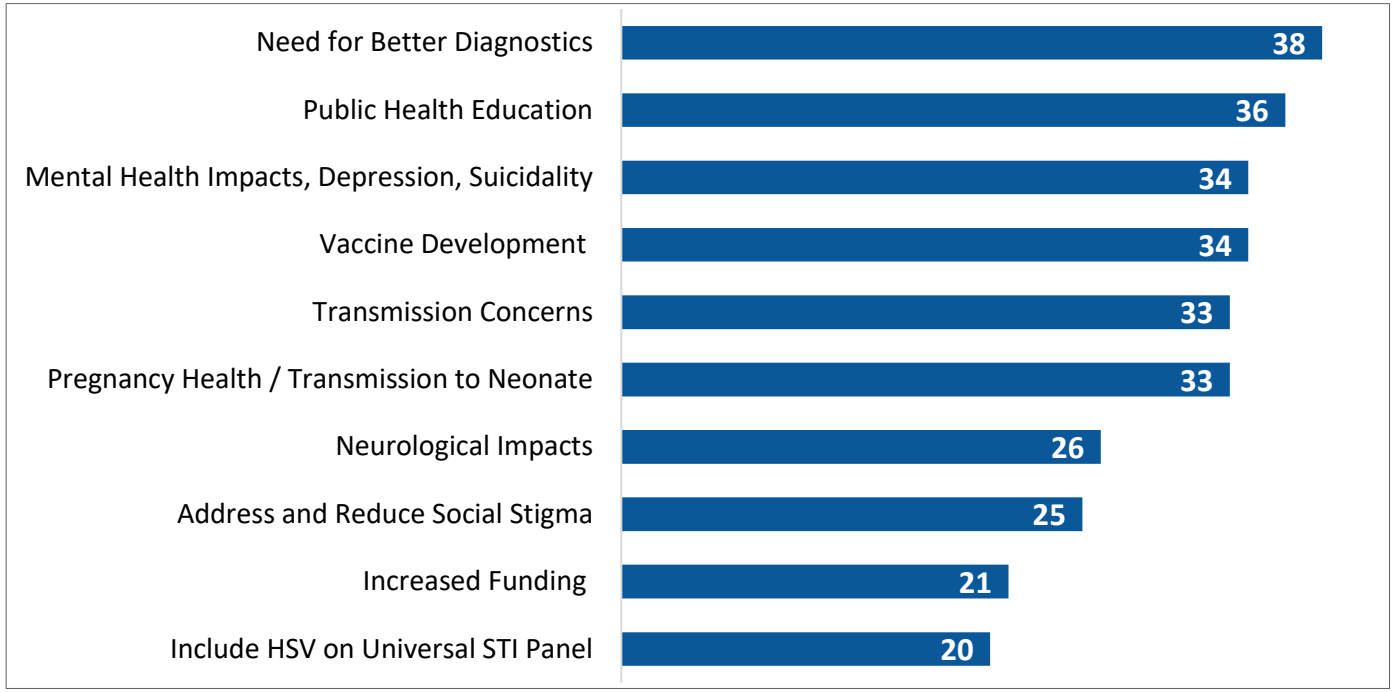
Public Input in the HSV Strategic Planning Process

- Request for Information (RFI) published for public input - April 21, 2023, to June 21, 2023



HSV Strategic Plan Request for Information (RFI)

Most frequently mentioned topics of interest from RFI responses

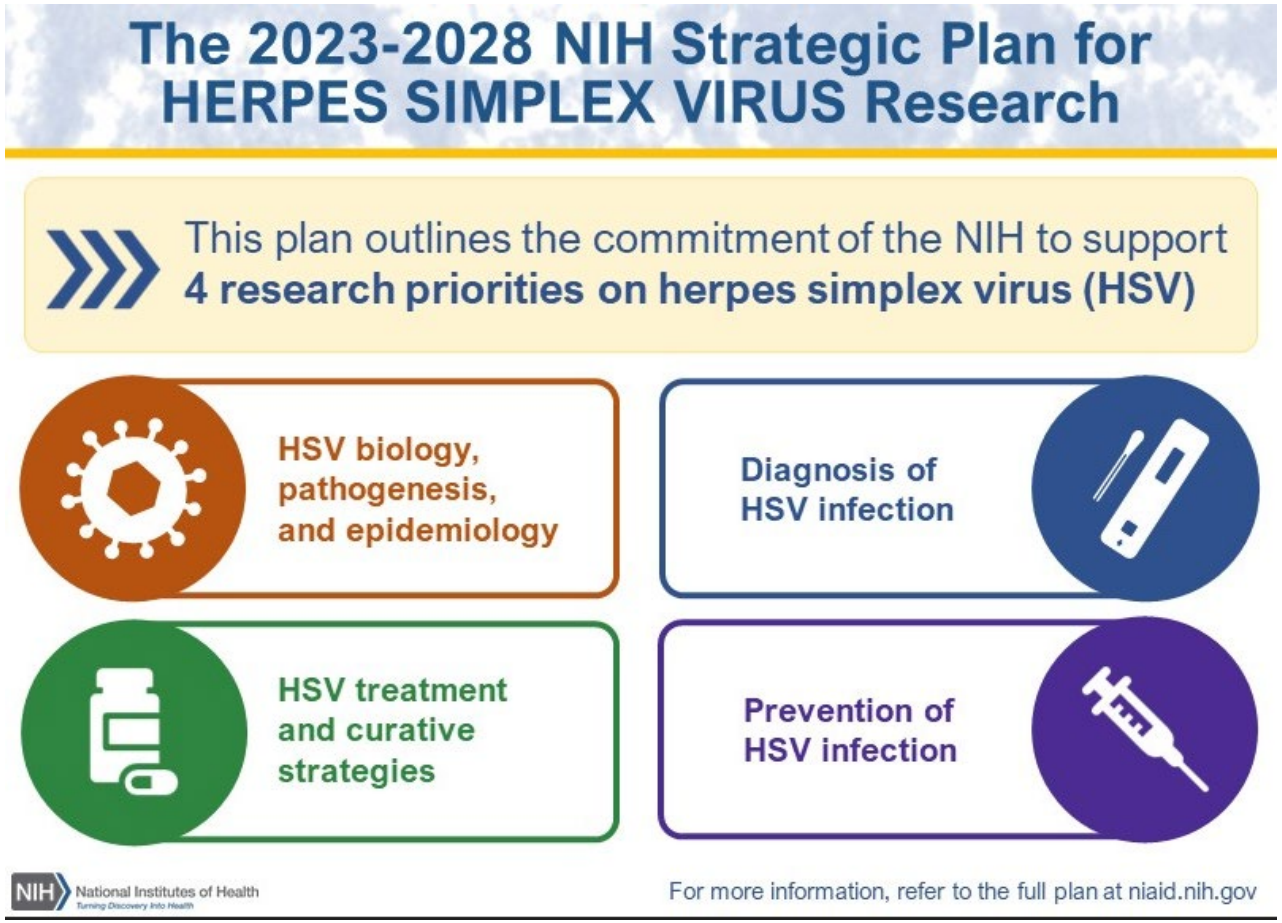


NIH received **105** responses to RFI

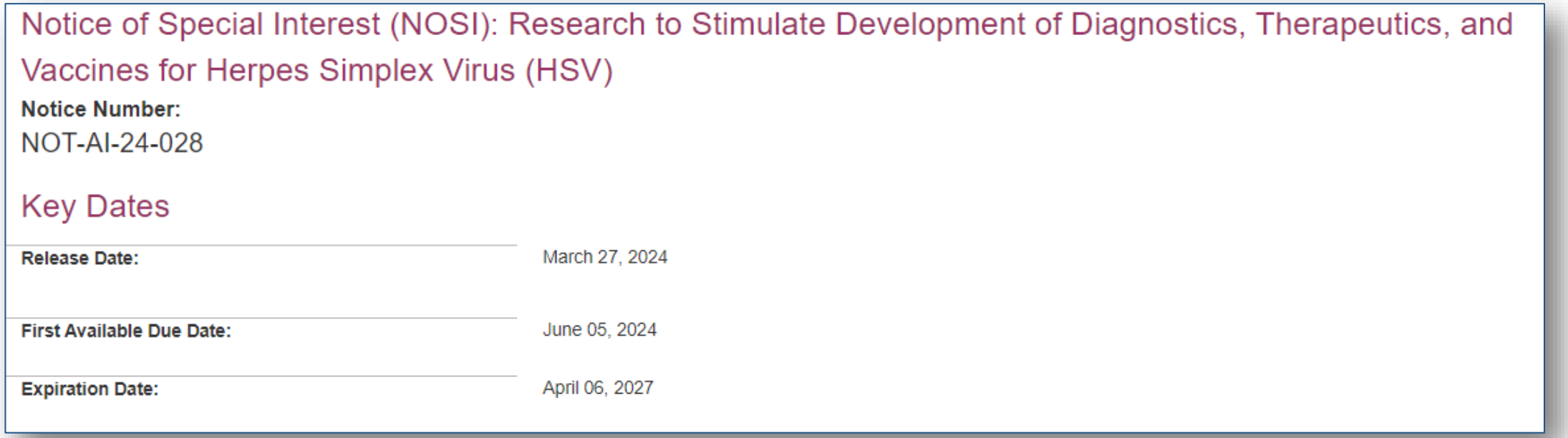
- Full summary of RFI responses were included as appendix in the final plan

NIH Strategic Plan for Herpes Simplex Virus Research – Overview

- Four strategic priorities
  - Basic biology, pathogenesis, and epidemiology
  - More accurate and widely-available diagnostics
  - Improved HSV treatment and curative strategies
  - Prevention strategies for HSV infection



NOSI: Development of HSV Diagnostics, Therapeutics and Vaccines



Notice of Special Interest (NOSI): Research to Stimulate Development of Diagnostics, Therapeutics, and Vaccines for Herpes Simplex Virus (HSV)

Notice Number:
NOT-AI-24-028

Key Dates

Release Date:	March 27, 2024
First Available Due Date:	June 05, 2024
Expiration Date:	April 06, 2027

https://grants.nih.gov/grants/guide/notice-files/NOT-AI-24-028.html

FY24 SBIR Contract Topic

Development of a serological test for herpes simplex Types 1 and 2 infections

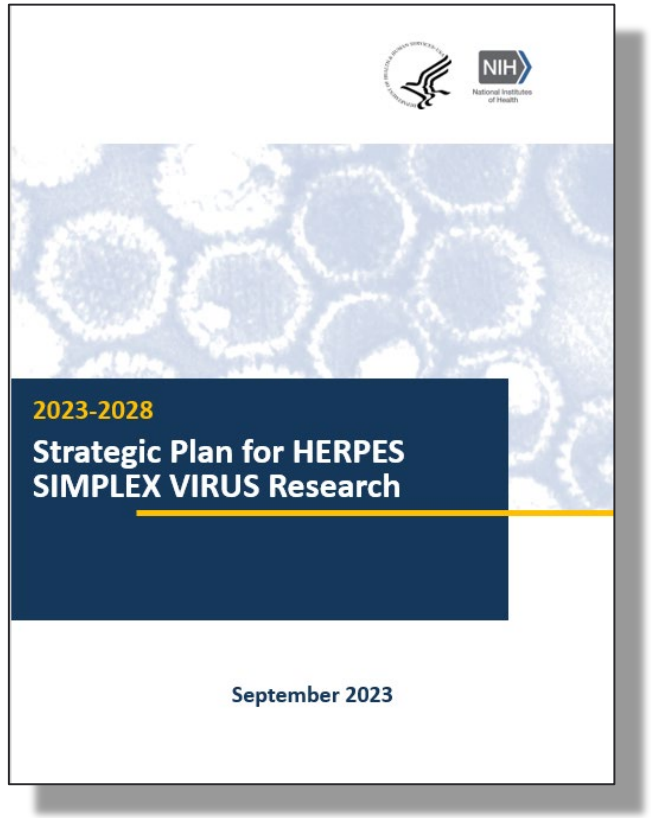
- **Significance**: Many persons with genital herpes are asymptomatic; therefore, a serological test is used to confirm HSV infection. Available serologic tests for HSV have high false positive rates.
- **Purpose:** To develop a serological test for genital herpes that retains high specificity, sensitivity and positive predictive values; distinguishes between HSV-1 and HSV-2; and uses technology such that the test could be distributed for broad use

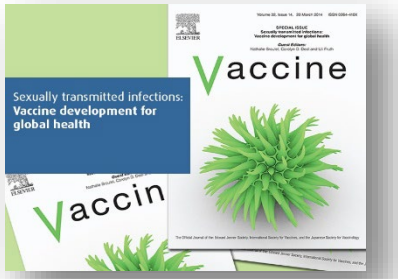
https://sam.gov/opp/f76f86b1206b4b6e9132c6cf9da3b6c0/view

NIH National Institute of Allergy and Infectious Diseases

Herpes Simplex Virus (HSV) Diagnostics

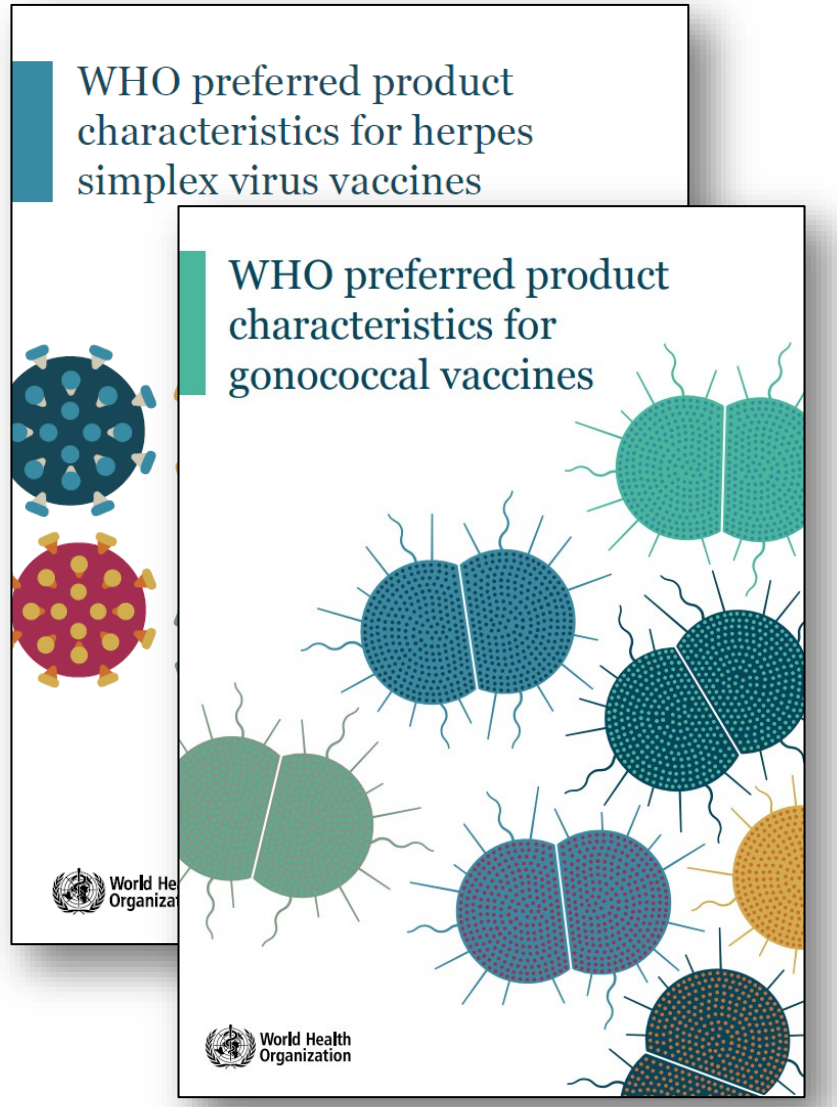
- SBIR Contract Awards
  - 3 Phase 1 awards:
    - Qoolabs,
    - Antigen Discovery, Inc. (ADI)
    - Kephera Diagnostics
  - Focus on HSV-1 / HSV-2 differentiation
  - Rapid or POC – 30 minutes or less
  - All 3 are serology-based, with the goal of improved sensitivity/specificity
- Goal: Serology test that is comparable to the gold standard Western blot





STI Vaccines - A Needed Intervention

- **Rationale:**
  - Despite diagnostics and treatment, epidemics of these diseases continue
  - Growing concern about antibiotic resistant *N. gonorrhoeae*
  - Limited commercial development (except for HBV & HPV)
- **WHO & NIAID developed an STI Vaccine Roadmap**
  - Collaboration with CDC & multiple international partners
  - Outlines need, development status, & future prospects for STI vaccines (HSV, *Chlamydia trachomatis*, gonorrhea, trichomanias, syphilis)
  - https://doi.org/10.1016/j.vaccine.2014.01.053
- **WHO Product Development Vaccine Advisory Committee**
  - HSV, chlamydia, & gonococcal infections highlighted at meetings
  - Published Preferred Product Characteristics (PPC) for HSV vaccines (https://www.who.int/reproductivehealth/publications/HSV-Vaccine-PPCs/en/)
  - Preferred Product Characteristics for Gonococcal Vaccines (https://www.who.int/immunization/research/ppc-tpp/Gonococcal_vaccine_PPCs_for-public-comment.pdf)



Benefits of a Prophylactic HSV Vaccine

HSV Negative Partner

Vaccine induces protective immunity

Individual Benefits

- Decreased risk of infection
- Remains free of negative psychosocial impact
- Decreased risk of acquiring HIV

Societal Benefits

- Decreased cost of medical care
- Interrupt the cycle of transmission
- Decreased risk of maternal transmission of HSV

Benefits of a Therapeutic HSV Vaccine

HSV Positive

Vaccine suppresses viral load

Individual Benefits

- Decreased shedding
- Decreased number of outbreaks
- Decreased probability of transmission to partners

Partner Benefits

- Decreased risk of infection
- Remains free of negative psychosocial impact

HSV Negative Partner

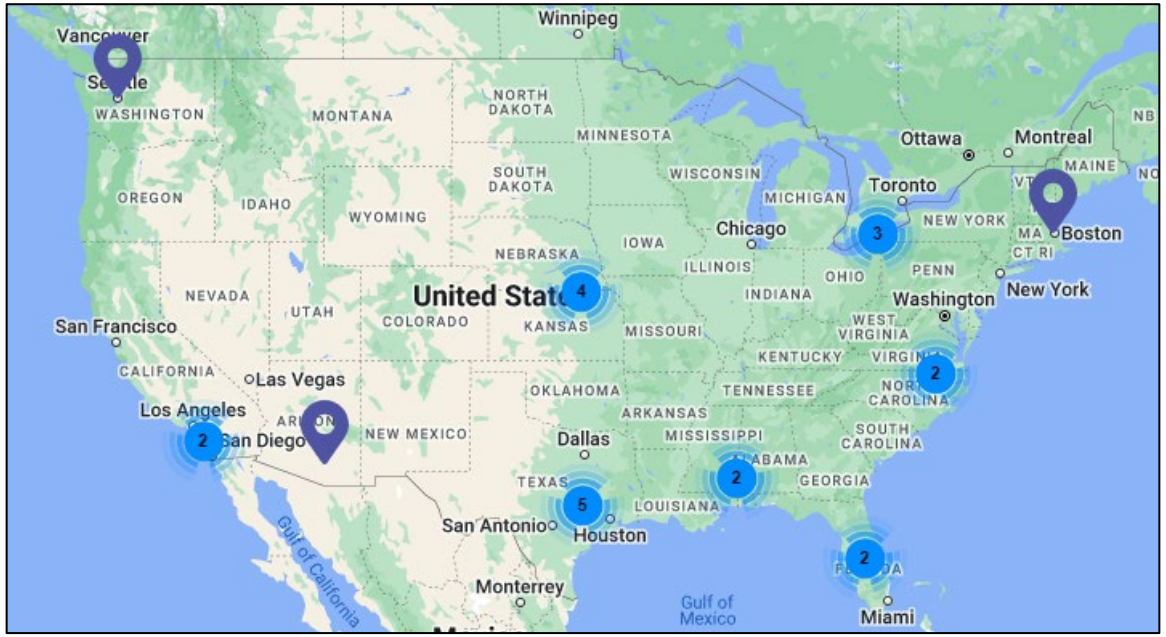
Societal Benefits

- Decreased cost of medical care
- Decreased risk of acquiring HIV
- Interrupt the cycle of transmission
- Decreased risk of maternal transmission of HSV and HIV

mRNA therapeutic HSV vaccine

moderna

- Healthy adults 18-55 years of age with recurrent HSV-2 genital herpes
- Phase 1/2 trial, 365 participants, Sept 2023-June 2025
- ClinicalTrials.gov ID NCT06033261

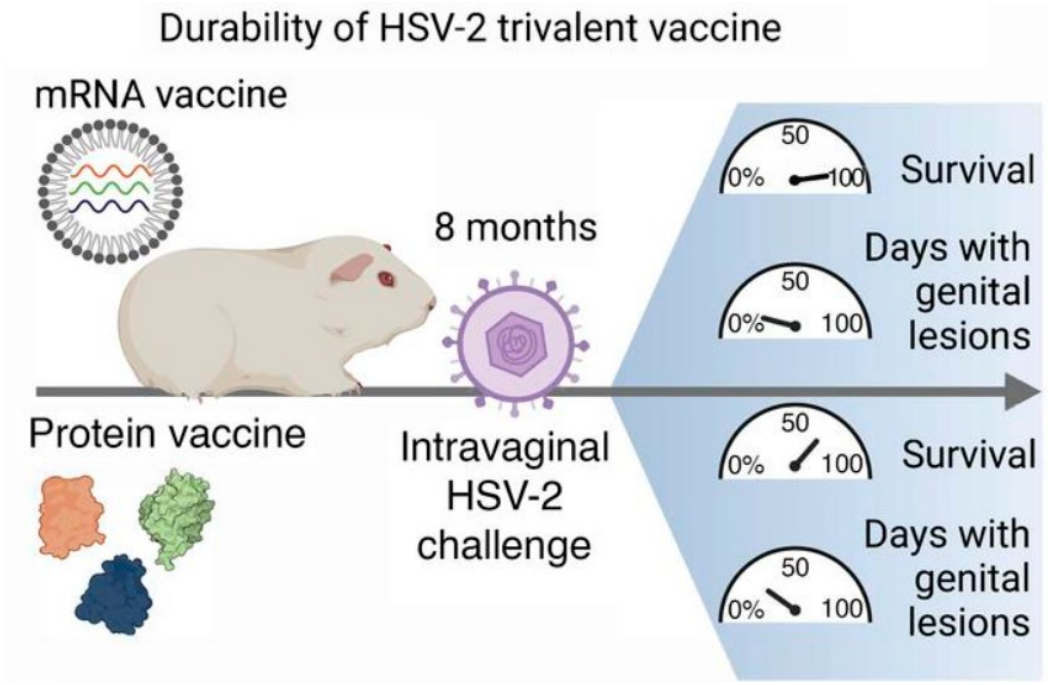


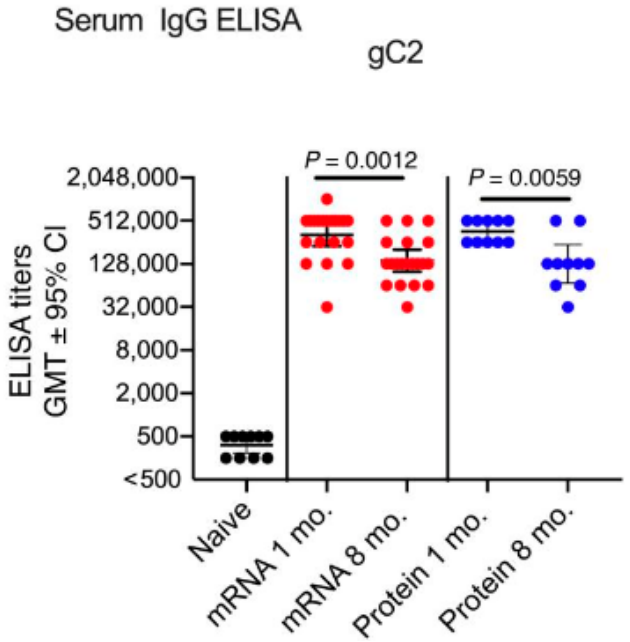
NIH National Institute of Allergy and Infectious Diseases

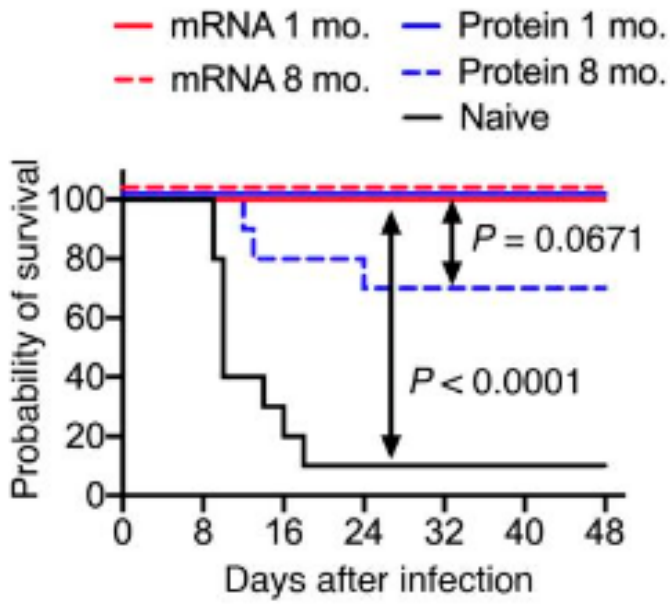
mRNA prophylactic HSV-2 vaccine

BIONTECH

ClinicalTrials.gov ID: NCT05432583





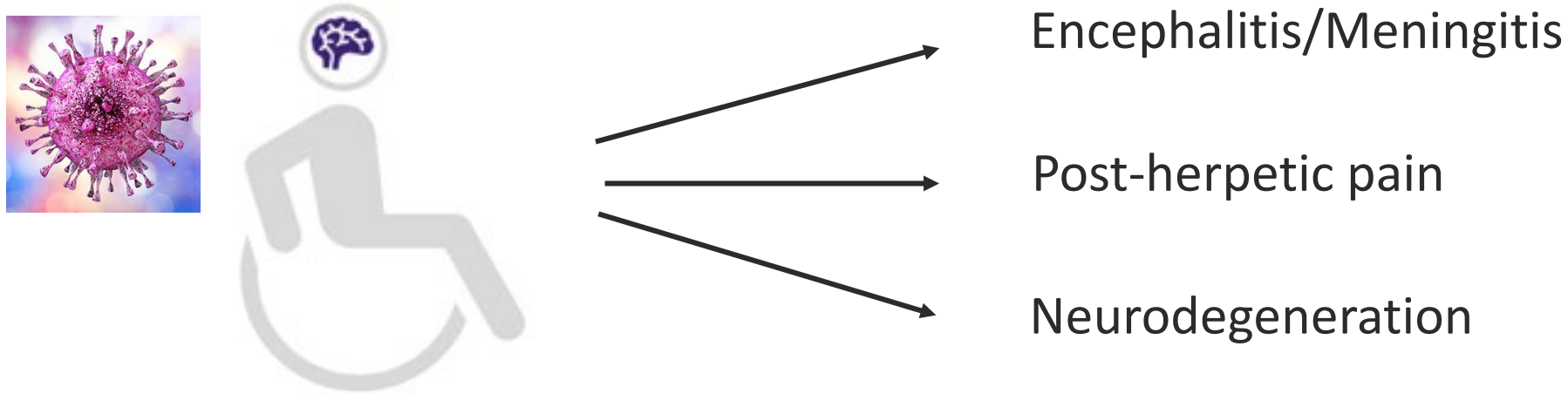


Awasthi *et al. Journal of Clinical Investigation.* 2021.

- mRNA vaccine against **glycoprotein D (gD2), gC2, and gE2 of HSV-2** stimulated greater serum and vaginal neutralizing titers than protein vaccine

NIH National Institute of Allergy and Infectious Diseases

Neurological Impacts of HSV



NINDS supports basic, translational, and clinical research focused on the nervous system pathogenesis of HSV in both the periphery and the CNS. Ongoing NINDS-funded efforts in this area are investigating:

- Molecular mechanisms of HSV reactivation from latency in neurons
- HSV transport within and between axons
- Effect of HSV infection on neural progenitor cells and CNS development
- Genetic factors which increase susceptibility to HSV encephalitis
- Interactions between HSV infection and neurodegenerative disorders such as Alzheimer's Disease

AD/ADRD-related NOFOs of interest

Currently Open: PAR-22-093

Research on Current Topics in Alzheimer's Disease and Its Related Dementias (R01 Clinical Trial Optional)

Currently Open: NOT-AG-21-043

Notice of Special Interest (NOSI): Infectious Etiology of Alzheimer's Disease

AD/ADRD-related applications can be funded beyond the NINDS general payline.

- FY2024 AD/ADRD Extended Payline- 17%ile (25%ile and 20%ile for ESI and NI R01s)
- NINDS AD/ADRD R01s in the general payline (8%ile) will have admin. cuts restored

New NINDS Initiative: Infection-Associated Chronic Illnesses

Notice of Intent to Publish a Funding Opportunity Announcement for Towards a Better Understanding of the Neurological Effects of Infection-Associated Chronic Illnesses (R01 - Clinical Trial Optional)

Notice Number:	NOT-NS-24-105
Key Dates	
Release Date:	July 08, 2024
Estimated Publication Date of Notice of Funding Opportunity :	October 28, 2024
First Estimated Application Due Date:	February 03, 2025

NOT-NS-24-105 (R01s): https://grants.nih.gov/grants/guide/notice-files/NOT-NS-24-105.html

NOT-NS-24-108 (R21s): https://grants.nih.gov/grants/guide/notice-files/NOT-NS-24-108.html

Guiding Collaborative HSV Efforts

- NIH HSV Working Group continues to hold meeting to coordinate research efforts
- Comprised of multiple ICs across NIH:
  - NINDS, NIA – neurodegenerative impacts
  - NIMH – mental health
  - NEI – ocular keratitis
  - NICHD – neonatal health
  - NIMHD – health disparities