Research Priorities for an HIV Cure: IAS
Global Scientific Strategy

Steven Deeks, MD
Professor of Medicine
Division of HIV, Infectious Diseases, and Global Medicine
Zuckerberg San Francisco General
University of California, San Francisco
Towards an HIV cure: a global scientific strategy

The International AIDS Society (IAS) is committed to advancing our understanding of HIV infection and developing effective treatments. This commitment is exemplified by the IAS Initiative Towards an HIV Cure. The Initiative aims to develop a global scientific strategy and framework for research towards an HIV cure. This strategy recognizes the importance of addressing the unique needs of different populations, including those with drug-resistant HIV, and focuses on developing a comprehensive approach to HIV cure research.

The Initiative is spearheaded by a group of leading experts in HIV cure research and includes contributions from a diverse range of stakeholders, including researchers, clinicians, public health officials, and community members. The Initiative is supported by a grant from the Global Fund to Fight AIDS, Tuberculosis, and Malaria, which has made a significant investment in HIV cure research.

The Initiative is guided by a scientific advisory board, which provides strategic advice and oversees the implementation of the Initiative's goals. The Initiative's goals include conducting robust research to advance our understanding of HIV cure, developing new strategies for HIV cure research, and ensuring the effective implementation of these strategies.

The Initiative is committed to ensuring that research findings are translated into real-world impact, and that the results of research are shared with all stakeholders, including those affected by HIV. The Initiative is working to ensure that research findings are implemented in a way that is equitable and accessible to all populations.

The IAS Initiative Towards an HIV Cure is a vital contribution to the global effort to find a cure for HIV. By working together, we can accelerate our progress towards a cure for HIV and bring hope to those affected by the virus.
Online process: November 2020 - August 2021

Eight major topics and working groups formed

Steering committee (WG co-chairs, community member) generated draft

Draft strategy refined through an online stakeholder consultation (162 responses), and a review by experts and opinion leaders
Recommendations

1. Understanding HIV reservoirs
2. HIV reservoir measurement
3. Mechanisms of virus control
4. Targeting the provirus
5. Targeting the immune system
6. Cell and gene therapy
7. Paediatric remission and cure
8. Social, behavioural and ethical aspects of HIV cure

IAS Global Scientific Strategy 2021
Advances in the last 5 years

Remaining knowledge gaps

Research priority areas for next 5 years
Biology of the reservoir

- Define and characterize the sources of the rebound-competent viruses
- Define the phenotype of infected cells
- Define the clinical significance of defective proviruses
- Define the mechanisms of clonal proliferation
- Determine if infected cells are resistant to cell death
- Define the impact of sex and other factors on the reservoir
Measuring the reservoir

- Develop a high-throughput assay of the rebound-competent reservoir
- Develop assays that quantify integration sites
- Develop assays that account for qualitative differences in viral transcripts
- Develop methods to quantify HIV protein expression
- Develop imaging modalities of the reservoir in tissues
- Define the link between the cellular reservoirs, residual plasma viremia, and the rebounding virus
- Develop point-of-care and eventually at-home viral-load monitoring
Targeting the provirus

- Develop improved strategies to reverse latency
- Develop strategies to permanently silence the provirus
- Determine the impact of targeting the provirus at the time of initiation of ART
- Define the role of viral subtype on the effectiveness of interventions
Mechanisms of post-treatment control

- Identify the mechanisms that contribute to SIV/HIV control
- Define the role of HIV-specific antibodies, B cells, and the innate immune response in virus elimination or control
- Define the viral dynamics and biomarkers associated with post-treatment control
- Optimize human organoid models, as well as mouse and nonhuman primate models, for cure- and remission-related studies
Targeting the immune system

- Develop ‘reduce and control’ approaches
- Develop immune modulators
- Conduct clinical trials to determine whether combination immunotherapies will result in safe and durable HIV remission
Gene and cell therapies

- Define the level of antigen expression needed to enable direct targeting (CAR-T cells)
- Develop gene-editing strategies that target the provirus
- Develop strategies for sustained production in vivo of antiviral antibodies
- Leverage advances in other biomedical fields
Pediatric cure

- Characterize the establishment, persistence, and potential for preventing or reversing HIV latency in infants and children on ART
- Develop assays to monitor and identify biomarkers to predict the efficacy of HIV-1 cure therapeutics
- Test HIV immunotherapies and other strategies in infants and children
Social, behavioral, and ethical aspects of cure

- Expand community/stakeholder engagement and capacity building
- Develop HIV cure research with equity, representation, and scalability considerations
- Establish standards for the safe conduct of clinical research
- Integrate social, behavioral, and ethics research as part of HIV cure trials
- Build capacity for basic discovery research and clinical trials in high-burden, resource-limited settings
HIV Cure Research in Africa

- What do people want from a cure?
- What will it need to cost?
- What can be practically given in non-urban health care clinics?
- Will HIV subtype have an impact?
- Will host factors (genetics) unique to the dominant African population be important?
- Will common prevalent co-infections and chronic inflammation affect or preclude the use of immunotherapy?
Cure: Iterative and incremental progress expected

The first generation of cures are expected to be complex and difficult-to-scale, as were the initial antiretroviral regimens.