Welcome to the Cure RFI Webinar
May 28, 2014

Thank you for your patience, we will begin shortly.
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Having technical issues?

Contact our technical support specialist, Ricardo Ferrer, at ricardo.ferrer@nih.gov or by submitting a query in the Question pod.
Introductions

Moderator

Lynne Mofenson
NICHD

Presenters

Jack Whitescarver
Director, OAR, NIH

Carl Dieffenbach
Director, DAIDS, NIAID

Panel of Experts

Rohan Hazra
NICHD

Avindra Nath
NIAID

Diana Finzi
NIAID

Sarah Read
NIAID
The NIH HIV Cure Initiative

Jack Whitescarver, Ph.D.
NIH Associate Director for AIDS Research and Director,
Office of AIDS Research
OAR Cure Activities

- NIH has been building the portfolio of HIV cure research, which currently totals approximately $75 million.

- Annual trans-NIH strategic plan for HIV-related research identifies highest scientific priorities and opportunities – includes section on Research Toward A Cure

- Cure research tracked across ICs

- Worked with industry, international partners and stakeholders to advance cure research
The New NIH HIV Cure Initiative

- On World AIDS Day 2013, President Obama announced that NIH plans to refocus AIDS research funds to expand support for research directed toward a cure for HIV.

- To accelerate research focused toward sustained or lifelong remission, in which patients control or even eliminate HIV without the need for lifelong antiretroviral therapy.
NIH HIV Cure Initiative: Timeline

- December 2, 2013 -- White House Announcement
- February 5 to March 14, 2014 -- Request for Information Open
- May 28, 2014 -- report back to research community (through this Webinar)
- Early summer 2014 -- publication of first set of solicitations
- Late fall 2014 -- first round of funding
- Additional solicitations will be published in successive years
Analysis of the RFI—Areas of Research Aimed at a Cure or Lifelong Remission of HIV Infection

Proposed Next Steps

Carl W. Dieffenbach, Ph.D.
Director
Division of AIDS, NIAID
Request for Information (RFI): Areas of Research Aimed at a Cure or Lifelong Remission of HIV Infection

Purpose: To seek input from the scientific community regarding high priority research areas related to HIV persistence and the development of strategies for eradicating or controlling virus remaining despite optimal antiretroviral treatment

Notice Number: NOT-AI-14-034

Release Date: February 5, 2014

Response Date: March 14, 2014

RFI Responses

- 42 responses (6 international) representing 71 individuals or organizations
- Good mix of academic, non-profit community organizations, and community members
Overarching Comments --
Increase Emphasis on:

- Mechanistic understanding of latency and persistence
- Immunological mechanisms and strategies
- Novel interventions
- Improved assays and biomarkers
- Access to current state-of-the-art assays
- Curated reagents, samples and methods
- Focused clinical evaluation of strategies
- Clearing house for sharing information and methods
Overarching Scientific Goal -- Understanding Latency and Persistence

- Over half of responses listed this as a priority and described a specific line of research worth pursuing
  - In most cases the line of research was directly related to studies currently underway in the respondent’s laboratory
- Excellent agreement on defining the molecular mechanisms, the cell types and tissues involved, and the anatomical distribution
  - T-cells, macrophage, virus trapped on FDCs and neurological reservoir(s) were all repeatedly highlighted
- Role of possible persistent low level replication was mentioned
- *Half of respondents felt that activation (kick and kill) was over emphasized, half felt the topic was under supported*
Overarching Scientific Goal -- Immunological Mechanisms and Strategies

- Immune mechanisms in formation of the reservoir were highlighted
  - Defining the rapid developmental changes in the newborn immune system was a focus
  - Role of immunological memory
  - Are the resting memory T cells truly resting?
  - Adaptive immunity, CTL killing, improving killing, the role of the target viral or host antigen were mentioned

- Solicit for immunological strategies such as therapeutic vaccines, use of monoclonal antibodies or immune–based therapies that can find the reservoir and eliminate the latently infected cells
Overarching Scientific Goal--Improved Assays and Biomarkers

- Continue to support work on simple, accurate, and robust assays and biomarkers
- Seek to make the current QVOA more readily available
- Make relevant animal models more accessible
- Make curated reagents and samples available
  - Role of reagent program
  - Bank of typed CCR5 D32 cord bloods (already exists)
Overarching Scientific Goal -- Research Facilitation

- Grant mechanisms should be appropriate for the types of research
  - Need to have all mechanisms available
- Further enable pharmaceutical industry participation
- Create a means of rapidly sharing data and a virtual collaborator space
Advice on Clinical Evaluation

- Support focused proof of concept studies and set criteria for entry into expanded clinical evaluation
- Continue conversations on the criteria of analytical treatment interruptions
- For pediatric studies, answer the question of interest in the most relevant population/patient subsets first
Behavioral and Social Science Research

- What is the understanding of the risks and benefits of current clinical studies in eligible populations and communities?
- What are the expectations and understanding of clinical providers and how the risks and benefits of different intervention methods will be determined?
- What is the relationship between the risk benefit decision making across eligible populations, clinical providers, and researchers?
- What are the studies of social and demographic factors that are associated with entry and retention in clinical trials?
Implementation

- FY15 through FY17, solicit R01 and R21 for basic research on mechanisms of persistence and latency
  - This will be an inclusive solicitation covering the interests of the cure community, as well as the NIH Institutes
  - Include assay and biomarker discovery
  - CSR receipt and referral as well as review

- Solicit for immunological approaches
  - Consider a contract-based strategy to engage Pharma
    - Therapeutic vaccines
    - Monoclonal antibodies, bispecific or otherwise modified antibodies
    - Other immunological strategies
Implementation

- In FY16, revise and focus the Martin Delaney Collaboratory (MDC) solicitation
  - Provide support for additional, but smaller sized MDCs
- Targeted supplement solicitations on rapidly emerging questions
- Maintain flexibility to meet newly emerging challenges and opportunities
- Facilitate assay discovery
NIH Cure Contacts

New Assays
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Animal Models
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Finding a Cure

Research to find a cure for HIV/AIDS is among NIAID top priorities. NIAID supports a large portfolio of investigator-initiated grants in HIV cure research to identify where HIV hides, known as the HIV reservoir, and to determine how these hideouts are established and maintained. In addition, NIAID also funds research to control and eliminate the viral reservoir.

Goals of NIAID HIV Cure Research

- Identify HIV reservoirs throughout the body
- Determine the effects of antiretroviral therapy, chemotheraphy, and other strategies on the HIV reservoir
- Develop assays and model systems, including a nonhuman primate model, to quantify and study HIV latency
- Characterize viral reservoirs that cause rebounding of viral levels when antiretroviral therapy is stopped
- Determine the role of HIV integration in virus elimination strategies
- Determine the role of HIV in hematopoietic progenitor cells regarding cure strategies
- Investigate strategies that lead to purging of the latent reservoir and a cure for HIV/AIDS

Notices

- NOT-AI-14-034 Request for Information (RFI): Areas of Research Aimed at a Cure or Lifelong Remission of HIV Infection (Responses due March 14, 2014)
- NOT-AI-14-023 Notice of Change of Program Priorities to be Supported by PAR-12-109 "Targeting Persistent HIV Reservoirs (TaPHR) (R21/R33)"

Funding Opportunity Announcements

- Quantitative Viral Outgrowth Assay (QVOA) Service Resource, RFP-NIAID-DAIDS-NIH2013104 (Contract proposals due by 3pm EST on 8/14/2014)
- Targeting Latently Infected Cells Without Reactivation (R01). (LOI due 6/15/2014; applications due 7/15/2014)
- Innovative Technologies and Assays in Support of HIV Cure Research (ITAS-Cure), R41/R42, (Standard Submission dates for ADS and ADS-related Applications)
- Innovative Technologies and Assays in Support of HIV Cure Research (ITAS-Cure) R43/R44, (Standard Submission dates for ADS and ADS-related Applications)
- Beyond HAART: Innovative Approaches to Cure HIV-1 (U19) (LOI due 6/26/2014; applications due 7/28/2014)
- Improvement of Animal Models for Stem Cell-Based Regenerative Medicine, R24, (Standard Non-ADS Submission dates)
- Basic Research on HIV Persistence, R01, (Standard Submission dates for ADS and ADS-related Applications)
- Basic Research on HIV Persistence, R21, (Standard Submission dates for ADS and ADS-related Applications)
- Targeting Persistent HIV Reservoirs (TaPHR), R21/R33 (LOI due 3/25/2014; applications due 4/25/2014)
- Creative and novel ideas in HIV Research Awards program (CNHRA) (Concept Proposals due 10/16/12; selected proposals due 2/16/2012)
- Pilot Clinical Trials to Eliminate the Latent HIV Reservoir (U01) LOI due 6/15/2014; applications due 7/15/2014)

http://www.niaid.nih.gov/topics/hivaid/research/cure/Pages/default.aspx
1. What are the NIH basic science questions or priorities for cure research?
2. What additional activities is NIH going to support to facilitate the cure research agenda?
3. Cure research is broad topic area, how is NIH going to spread the applications and funding so I get my grants from the NIH Institute I am most familiar with?
4. How will decisions be made about which cure grants get support?
Q&A

5. How will funding be prioritized across large and small grant programs?
6. What are cure research priority areas at NIH with respect to targeting CNS Reservoirs?
Q&A

7. Is cure research in children and adolescents a priority for NIH? And if so, what are the cure research priority areas for NIH in pediatric cure?
8. Is the NIH funding research into cure strategies that would be applicable globally as opposed to just in developed, resource-rich, countries?
9. Will pediatric cure studies be limited to resource-rich countries?
10. What types of cure-related clinical trials will NIH support as a priority?
11. What mechanisms will be used to support cure-related clinical trials?
Q&A

12. How do you plan to engage the community in HIV cure research?
13. Who is addressing the ethical issues of cure research?
Questions?
Thank you for your participation in the Cure RFI Webinar.