• HIV cure: terminology and definitions

- Sterilizing cure
- Functional cure
- Sustained remission
- SVR (cf HCV)
HIV cure: clinical examples

- **Berlin Patient**: Stem-cell transplantation (CCR5Δ32) for treatment of AML. No detectable HIV.
- **Visconti cohort**: Cohort of post-treatment controllers (treated during AHI phase). Long term remission in absence of ART.
- **Mississippi Baby**: Infant treated within 30 hours. No viral rebound despite ART discontinuation.

Boston Patients: Bone-marrow transplantation

Viral rebound
Prospects for achieving sterilizing or functional cure of HIV infection

- Purging the HIV latently infected cells reservoir (responsible for residual viremia in cART treated patients)
- Targeting a residual virus-producing reservoir with immunotoxin (targeted cytotoxic therapy)
- Manipulating HIV-specific immune responses (including HIV therapeutic vaccine)
- Silencing the expression of HIV genes
- Gene Therapy
Ongoing HIV cure research: 7 priority areas

Cellular and viral mechanisms that maintain HIV persistence

Tissue and cellular sources of persistent SIV/HIV in animal models and in long-term ART-treated individuals

Origins of immune activation and dysfunction in the presence of ART and their consequences for HIV/SIV persistence

Host and immune mechanisms that control HIV/SIV infection but allow viral persistence

Assays to study and measure persistent infection: comparison and validation

Therapeutic agents or immunological strategies to safely eliminate latent infection in individuals on ART

Strategies to enhance the capacity of the host response to control active viral replication
HIV cure clinical trials

- Latency reversing strategies
- Gene therapy
- Stem cell transplantation
- Therapeutic vaccines
- Treatment intensification
- Antiretroviral therapy
- Combination approaches

http://www.treatmentactiongroup.org/cure/trials
European research programmes
ANRS HIV Cure research programme

- Understanding HIV reservoirs
- Post-treatment controllers • Visconti International Cohort
- Acceptability and Willingness of HIV patients
- Gene Therapy Approaches
- Therapeutic Vaccines
- HIV Controllers • Pediacam

- ANRS HIV Cure research programme
• Although no specific earmarked funds for HIV Cure, the ANRS funds numerous projects

• Funding, including basic research, preclinical studies and clinical research (therapeutic trials and cohorts)

• 2013 funding for specific HIV Cure research: \textbf{2.09 million € (2.82 M USD)}

• Total amount includes some post-doc salaries and PhD studentships, but excludes all other salaries
• **AC 32: Viral reservoirs**
  
  – Co-presidents: Christine Rouzioux, Hopital Necker, Paris and Asier Saez-Cirion, Institut Pasteur
  
  – Created in 2008, this group brings together research from basic sciences, preclinical and clinical studies.
  
  – 4 meetings per year

• **AC 5: Therapeutic clinical trials**
  
  – President: Jean-Michel Molina, St Louis Hospital, Paris
  
  – Review and discussion of all therapeutic clinical trials, including trials on primary infection, treatment intensification, etc...

• ANRS CO6 Primo cohort: some rare patients show persistent control of HIV following treatment interruption (Antiviral Therapy 2012)

• ANRS 147 Optiprim: Evaluation of treatment intensification at AHI on viral reservoirs (poster presentation at ICAAC 2012)

• ANRS CODEX CO21 - Multicentric Cohort of HIV Patient With Extreme Profile

• More than 30 ongoing projects in basic science
Collaborative HIV Eradication of viral Reservoirs: UK BRC

The aim of the CHERUB collaboration is to:

- Develop and promote a coordinated UK wide response to the need to explore strategies targeting HIV eradication and remission.
- Create a biobank of samples for use in scientific research by the collaborative parties, according to agreed study protocols.
- Undertake internationally competitive clinical and scientific research within a framework for sharing of data, resources and consumables.

HIV Cure RIVER trial:

- ART + HDACi + Vax
- ART + placebo
Danish research teams, Aarhus, Denmark

- Latency reversing strategies:
- Romidepsin (HDACi)
- Ongoing trial with therapeutic vaccine
International AIDS Society
Towards an HIV cure initiative
Towards an HIV Cure: Mission

- Facilitate scientific discussion, exchange and collaboration to promote and accelerate research towards a cure for HIV.
- Provide leadership in advocating for increased investment and resource optimization in HIV cure research.
- Provide clear and accurate information and disseminate knowledge to the broader community.
Global Scientific Strategy
Global Scientific Strategy

Seven Priority Research Areas:

1. Cellular and viral mechanisms that maintain HIV persistence

2. Tissue and cellular sources of persistent SIV/HIV in animal models and in long-term ART-treated individuals

3. Origins of immune activation and dysfunction in the presence of ART and their consequences for HIV/SIV persistence

4. Host and immune mechanisms that control HIV/SIV infection but allow viral persistence

5. Assays to study and measure persistent infection: comparison and validation

6. Therapeutic agents or immunological strategies to safely eliminate latent infection in individuals on ART

7. Strategies to enhance the capacity of the host response to control active viral replication
Initiative Structure
Towards an HIV cure
people focused science driven

- Int. scientific collaborations
- Data exchange platforms between pilot studies
- Interaction between Basic + Clinical Science
- Cross-talk with other scientific disciplines
- New concepts, new generation
- Cooperation public + privates sectors
- Community engagement

Working Groups

J. Martinez-Picado, AIDS 2012
Initiative Organisation

Advisory Board

- Industry Collaboration Group
- Cost-effectiveness Working Group
- Psychosocial Studies Working Group
- Ethics Working Group

Ethics now integrated throughout the entire initiative
Advisory Board

**Co-chairs:** Françoise Barré-Sinoussi (Institut Pasteur), Jack Whitescarver (NIH OAR)

Carl Dieffenbach, *NIAID/NIH, USA*
Clive Morris, NHRMC, Australia
Glaudina Loots, *Department of Science and Technology, South Africa*
Gottfried Hirnschall, *WHO*, Switzerland
Jean-François Delfraissy, *ANRS, France*
Marc Ouellette *CIHR, Canada*
Mark Harrington, *Treatment Action Group (TAG), USA*
Nikos Dedes, *EATG/ITPC, Global*
Paola de Carli, *Sidaction, France*
Paula Munderi *(UVRI/MRC), Uganda*
Peter Godfrey-Faussett, *UNAIDS, Switzerland*
Rowena Johnston, *amfAR, USA*
Subhasree Sai Raghavan *SAATHII, India*
Yiming Shao, *Chinese Center for Disease Control and Prevention, China*
Ethical considerations in HIV cure research: points to consider

Bernard Lo* and Christine Grady**, on behalf of the Working Group on Ethics of the International AIDS Society

Curr Opin HIV AIDS 2013, 8:243–249
Co-chairs: Guenter Kraus (Janssen), Sharon Lewin (Monash University), David Margolis (UNC CH), Andrew Spaltenstein (GSK)

Open forum for dialogue, exchange and interaction on HIV cure research between private and public sectors.

Private sector representatives include: GSK, Janssen, Merck, Gilead, ViiV Healthcare, Profectus Biosciences, BMS, Roche, Genetic Immunity, Monogram Biosciences, Bionor Pharma…

Ongoing focus points:

- Universal MTA
- Assay development and standardization
- Paediatric ARV formulations
Public Health Cost-effectiveness

Co-chairs: Kenneth Freedberg (Harvard), Yazdan Yazdanpanah (APHP, Paris)

• Opinion Article:
  • “The HIV cure research agenda: the role of mathematical modeling and cost-effectiveness analysis
    Freedberg, Possas, Deeks, Ross, Di Mascio, Collins, Walensky, Yazdanpanah.
Co-chairs: David Evans (Project Inform), Bruno Spire (Inserm, AIDES)

Ongoing Projects:
• Acceptability, expectations and preferences for HIV cure-related clinical trials among patients with undetectable viral load and caregivers. Marie Suzan, Bruno Spire (ANRS)
• Unintended and Intended Implications of HIV Cure: A Social and Ethical Analysis. Joseph Tucker, Stuart Rennie (UNC at Chapel Hill NIH)
• HIV cure patient perspective survey. Julie Fox (Kings College London)

Other members: David Evans, Michael Arnold, Fred Verdault, Joep Lange, Jo Watson (Napwha), Veronica Noseda (Sidaction), Dianne Rausch (NIMH), Clare Ojwang, Paul Newman, Marian Pitts, Nelson Vergel, Judith Auerbach.
HIV Cure Symposium
Towards an HIV Cure Symposium

2010: HIV Reservoirs Workshop, Vienna
2012: HIV Cure Symposium, Washington DC
2013: HIV Cure Symposium, Kuala Lumpur

2014: HIV Cure Symposium, July 19-20, Melbourne, Australia
2014 Symposium

- 2014 HIV cure Symposium
  - Co-Chairs: Françoise Barré-Sinoussi, Steve Deeks, Sharon Lewin
  - Melbourne, 19-20 July 2014
  - Over 250 registered delegates
  - 42 scholarships awarded for young researchers and community members worldwide

- Confirmed Speakers: Jeff Lifson, Miles Prince, Geoffrey Hill, Melanie Ott, Dan Barouch, Christine Rouzioux
Think-Tank meeting, Paris (May 2013)

The meeting convened a group of 25 researchers in the field of HIV cure and experts in other biomedical fields, including virology and cancer, met in Paris to discuss the problem of persistence with the notion of residual disease and how to either control it or eliminate it.
Provide leadership in advocating for increased investment and resource optimization in HIV cure research
Evaluating Investment

- Resource Tracking
  - Survey of global investment in HIV cure research and development in 2012
  - Collaboration with AVAC and HIV Vaccines & Microbicides resource tracking working group, with input from amfAR and TAG

In collaboration with AVAC.
Knowledge dissemination and information sharing

Provide clear and accurate information and disseminate knowledge to the broader community
Knowledge dissemination and information sharing

- General Media

- IAS HIV cure webpages (towardsanhivecure.org)
  - New features include:
    - HIV cure video
    - Quotes banner
    - Resource Tracking
    - HIV cure fact-sheet
    - Media Centre
Community Engagement

- Community Scholarships for the Symposium
- Call for Nominations for Community Representatives to ensure fair representation in working groups and throughout the initiative
- HIV fact-sheet developed in collaboration with community members
- Community Literacy Workshop, AIDS 2012, Washington DC
- Community Training Workshop, Chennai, January 2014
Thank you for your attention