



Acquired Immuno Deficiency Syndrome

Editorial

Towards an HIV Cure - a Myth or a Reality?

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Recent progress in HIV research has directed global scientific community to search for a 'cure' for HIV infection. The first evidence emerged from Timothy Brown, a Berlin patient. This HIV-infected patient received hematopoietic stem cells from an HLA-matched donor whose genome naturally lacked CCR5, the major receptor of HIV. Mr Brown appears to be cured of HIV as well as leukaemia as no infectious virus could be recovered from his blood and other tissues for over 6 years after the stem cell transplantation. The case has given direction to scientists to administer genetically modified stem cells lacking CCR5 receptors to HIV-infected person to provide a defence against HIV. However, this approach may be difficult to apply to all HIV-infected persons globally.

The second clue towards HIV cure came from a Mississippi infant, initiated ART at 31 hour of age for a period of 18 months who subsequently had undetectable plasma viral load for 27 months without ART. However, unfortunately the baby now at the age of four years have been detected HIV infected. The case nevertheless has given guidance to researchers to initiate ART very early in acute infection to reduce the size of HIV reservoir and achieve a long-lasting drug-free viral suppression (functional cure). Trials are in progress in Thailand that showed remarkable reduction in reservoir size following very early ART.

However, the resurgence of HIV after several years of discontinuation of ART suggests that the reservoir has been persisting though undetected that need to be tackled by innovative approaches. TAT is one of the first proteins produced by HIV infected cells that facilitate amplification of replication of HIV. Without TAT, the HIV-infected cells only produce new viruses very sluggishly. Didehydro-cortistatin A(dCA), a potent TAT inhibitor, has been discovered by Scientists at the Scripps Research Institute in California, which have potential to maintain the reservoir cells in a lifelong sleep such that no residual HIV replication is left. However, further research will be needed to understand therapeutic uses of dCA.

While CD4+ cells are the important reservoir and infected CD4+ cells undergo natural death, several studies have shown the presence of HIV in long-lived monocytes/macrophages, follicular dendritic cells, and cells of various organs. These cells can replicate the virus at a low level and not undergo any cell death. Hence to advance towards a cure, such viral reservoirs need to be taken to task by so called "kick and kill" strategy. Romidepsin, a Histone Deacetylase (HDAC) inhibitor, reactivate latent virus in the resting cells. Once the virus is "woken up" and starts replicating, it becomes visible to the immune system and is susceptible to antiretrovirals. However, HDAC inhibitors have unpredicted immune-suppressant effects.

The efforts to find an effective HIV vaccine have not been fruitful so far and require further continuous research. Hence the world scientific community has very rightly started searching for a cure for HIV-infection. Till then it is essential on our part to consolidate whatever we have gained so far through evidence based HIV research. The UNAIDS target of 90-90-90, which aims to diagnose 90% of people with HIV, treat 90% of people diagnosed with HIV and achieve undetectable viral load in 90% of people on treatment by 2020 should be given due emphasis and evidence based Option B+ PMTCT, PrEP and TasP approaches should be implemented globally.



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Citation: Gupta AK (2015) Towards an HIV Cure - a Myth or a Reality?. AIDS 1:1-2

Received: July 24, 2015
Accepted: July 30, 2015
Published: Aug 06, 2015

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