

# 'Shock and kill' research gives new hope for HIV-1 eradication

June 4 2009

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Latent HIV genes can be 'smoked out' of human cells. The so-called 'shock and kill' technique, described in a preclinical study in BioMed Central's open access journal *Retrovirology*, might represent a new milestone along the way to the discovery of a cure for HIV/AIDS.

Dr. Enrico Garaci, president of the Istituto Superiore di Sanità (the Italian Institute of Health) and Dr. Andrea Savarino, a retrovirologist working at the institution, worked with a team of researchers to study the so-called "barrier of latency" which has been the main obstacle to HIV eradication from the body.

Cells harbouring a quiescent HIV genome are responsible for HIV persistence during therapy. In other words, HIV-1 genes become pieces of the human organism, and many scientists have simply thought there is nothing we can do. Dr Savarino's team aimed to 'smoke out' the virus in order to render the latently infected cells targetable by the immune system or artificial means. They write, "This can be achieved using inhibitors of histone deacetylases (HDACs), which are a class of enzymes that maintain HIV latency. However, their effects on HIV are evident only when used in toxic quantities".

To overcome this problem, the Italian researchers tested a collection of HDAC inhibitors, some of which specifically target only certain enzyme isoforms (class I HDACs) that are involved in HIV latency. The toxicity of this approach, however, was not markedly decreased, although it compromises a more limited number of cellular pathways. Moreover, at

non-toxic quantities, class I HDAC inhibitors were able to induce the 'awakening' of a portion of cells within a latently infected cell population. The researchers then repeated the experiment adding a drug inducing oxidative stress, buthionine sulfoximine (BSO). The results showed that BSO recruited cells non-responsive to the HDAC inhibitors into the responding [cell population](#). An important result was that the infected cells' 'awakening' was followed by cell death, whereas the non-infected cells were left intact by the drug combination.

"I really hope this study may open new avenues to the development of weapons able to eliminate the HIV-infected cells from the body", says Dr. Andrea Savarino, "Such weapons, in combination with antiretroviral therapies, could hopefully allow people living with HIV/AIDS to get rid of the virus and return to a normal life. Of note, there are testable drug combinations composed of molecules that have passed phase I clinical trials for safety in humans". This type of approach has been dubbed 'shock and kill'. "Although this type of approach is largely accepted by the scientific community", adds Dr. Savarino, "to be honest, we have to take into consideration that some scientists are skeptical about this approach, and others even think that a cure for [HIV/AIDS](#) will never be found. Experiments using animal models will shed a new light on this difficult problem."

More information: "Shock and kill" effects of class I-selective histone deacetylase inhibitors in combination with the glutathione synthesis inhibitor buthionine sulfoximine in cell line models for HIV-1 quiescence; Andrea Savarino, Antonello Mai, Sandro Norelli, Sary El Daker, Sergio Valente, Dante Rotili, Lucia Altucci, Anna Teresa Palamara and Enrico Garaci; *Retrovirology* 2009, 6:52  
doi:10.1186/1742-4690-6-52

Article available at journal website:

[www.retrovirology.com/content/6/1/52](http://www.retrovirology.com/content/6/1/52)

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Citation: 'Shock and kill' research gives new hope for HIV-1 eradication (2009, June 4) retrieved 7 May 2024 from <https://medicalxpress.com/news/2009-06-hiv-eradication.html>

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