J Antivir Antiretrovir 2016, 8:2(Suppl)
http://dx.doi.org/10.4172/1948-5964.C1.028

Functional Remission of HIV-Infected cells Treated with ABX464 or its human metabolite ABX464 N-glucoronide

J. Tazi
University of Montpellier, France

Background: ABX464 represents a novel class of small molecule for oral administration targeting HIV that is in phase II clinical trials. It neutralizes the expression of the proviral genome in infected immune cells, including macrophages, and causes a prolonged reduction in viral load after a course of treatment in humanized mice. Macrophages have been proposed to be part of the long-lived HIV reservoir and to spread infection through cell to cell contact. Infected macrophages may account, at least in part, for viral rebound after stopping ART. Here, we tested the durability of ABX464 treatment on infected monocyte-derived macrophages (MDMs) and on the ability of these cells to transfer HIV-1 to autologous CD4+ T cell co-cultures after treatment cessation. To document the cellular changes behind ABX464 activity, we monitored the transcriptomic program of infected-MDMs that were treated or not with ABX464 or its human metabolite ABX464 N-glucoronide.

Methods: We used CD34+ hematopoietic stem cells (HSCs) isolated from human cord blood to differentiate them into lymphoid and myeloid lineages. PBMCs and MDMs were isolated from buffy coats of HIV-negative individuals using standard procedures. Cells were infected with the YU2 viral strain and treated with ABX464 or ABX464 N-glucoronide. HIV-1–infected MDMs treated or not were cultured with autologous CD4+ T cells, followed by p24 and flow cytometric analyses. Transcriptomic changes analyzed by high-throughput RNA-seq sequencing using an Illumine Genome Analyze

Results: Using CD34+ HSCs, ABX464 and its human metabolite ABX464-N-glucoronide had no effect on lymphoid and myeloid lineage differentiation and proliferation. However, in contrast to untreated HIV-1–infected MDMs, treatment with ABX464 or ABX464-N-glucoronide prevented HIV-1 spread to autologous CD4+ T cell cultures after one week treatment cessation. Furthermore, flow cytometric analysis of treated samples revealed an increased CD4+ Th1 central memory T cell population, suggesting that ABX464 or ABX464 N-glucoronide treatment triggered activation of an adaptive T cell response. Consistently, the analysis of gene expression profiles shows that treatment of infected MDMs with ABX464 or ABX464 N-glucoronide revert expression of several genes altered by HIV-1 infection

Conclusion: ABX464 and its predominant metabolite ABX464 N-glucoronide are potent antiviral agents that can prevent HIV-infected macrophages in culture from spreading viral infection. This effect may explain the long-lasting antiviral activity of ABX464 observed in humanized mice.

jamal.tazi@igmm.cnrs.fr

St Augustine and Theodicy in the face of HIV/AIDS in Africa- A Practical theology analysis

Joachim Kwaramba
Christian Theology Lecture, University of Zimbabwe, Zimbabwe

God has been viewed to have made and created all things; including HIV/AIDS. Church fathers have had battle in trying to explicate the biblical manuscripts in light of the pandemic. They try to vindicate God in the face of evil in the world. But, in this era of HIV/AIDS in Africa, do their teachings still hold? This paper selects St Augustine, one of the early and celebrated church father, (who lived between 354-430) in a bid to explore the relevance of his teachings to the prevalent pandemic. Augustine argues to put grace of God as priority for freedom from sin but some refuse or move away from grace hence they become victims of sin, and in this paper's focus, victims of HIV/AIDS. Augustine's concept of theodicy (problem of evil) seems to demonize God. This paper provides some theological and social insights on the problem of HIV/AIDS as an evil affecting Africans. It provides the proof of the irrelevance of Augustine's theory in light of HIV/AIDS in Africa. A survey of some biblical scriptures will help provide a theological position relevant to the 21st century scholar. The paper will exonerate God from the pandemic and loss of human life but place responsibility to humanity.

jokwazw1@gmail.com