REACTIVATION OF HIV-1 GENE EXPRESSION TO TREAT PERSISTENT HIV INFECTION

STATE OF THE ART

Despite current effective and life-prolonging cART, HIV-1 can still not be cured. Indeed, the persistence of latently-infected resting CD4+ T cells harboring transcriptionally silent but replication competent HIV-1 proviruses seriously challenge the hope of HIV-1 eradication from cART-treated HIV-1 infected patients. Reactivation of HIV-1 expression in reservoirs together with an efficient cART has been proposed as an adjuvant therapy aimed at reaching a functional cure.

Several studies have identified individual compounds that are capable of reversing HIV-1 latency and several clinical trials have started. However, these studies question the efficiency of these drugs used alone and underly the importance to further test other classes of HIV-1 inducers, alone or in combination, to reduce the HIV-1 reservoirs.

THE INVENTION

The combined use of two drugs to activate latent HIV could cause a synergistic reactivation of HIV-1 production. Indeed, a proof-of-concept has been demonstrated by inventors for the coadministration of two different types of therapeutically promising HIV-1 inducers [DNA methylation inhibitors in combination with histone deacetylase inhibitors (HDACis) or histone methyltransferase inhibitors (HMTis) in combination with HDACis or NF-kappaB inducers] together with efficient cART as a therapeutic perspective to decrease the pool of latent HIV-1 reservoirs.

COMMERCIAL INTEREST

As selected molecules are already promising candidates or accepted in human clinical trials or therapies for other diseases, a clinical phase Ib/II has been launched. The cART therapy is the only treatment currently available for AIDS and our current approach is innovative, no competition exists for the moment in this competitive market.

KEY ADVANTAGE OF THE TECHNOLOGY

> Obtaining a regimen to eliminate the latent compartment of HIV-1 and stop cART therapies may:
  • limit exposure to the anti-AIDS molecules, thereby limiting side effects and the life quality of the patients would be greatly improved.
  • reduce the care costs for HIV+ patients.

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KEYWORDS

• HIV latency
• Anti-latency therapies
• Epigenetic drugs

Collaboration type
Partnership
License agreement
IP Status
WO2013050422
(Published in 2013-04-11)
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THE INVENTORS

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**Sophie Bouchat** is a PhD Student supervised by Carine VAN LINT at ULB and funded by the Belgian 'Fonds pour la Recherche dans l’Industrie et l’Agriculture' (FRIA). She studies HIV-1 reactivation from latency and potential therapeutic implications. She received a prize for the best Poster presentation at the ISHEID 2012 meeting.

**Jean-Stéphane Gatot** has performed a post-doctoral fellowship at ULB in Carine VAN LINT’s lab and was funded by the “CIBLES” Excellence program of the Walloon Region.

THE TEAM

The major research goal in the ULB laboratory is the study of the molecular and epigenetic mechanisms regulating transcriptional latency and reactivation from latency in 3 retroviruses: HIV-1 and two oncogenic retroviruses HTLV-I and BLV. Regarding HIV-1, a major objective of the laboratory is to design, based on the understanding of viral transcriptional mechanisms, novel strategies to reduce the pool of latent reservoirs to a level bearable by the host immune system.

Olivier ROHR’s Lab from the University of Strasbourg collaborates with Carine Van Lint for the study of the molecular mechanisms regulating HIV latency.

MAIN PUBLICATIONS (RELATED TO THIS TECHNOLOGY)

- **Histone methyltransferase inhibitors induce HIV-1 recovery in resting CD4+ T cells from HIV-1+ HAART-treated patients.** Bouchat S., Gatot JS., Kabeya K., Cardona C., Colin L., Herbein G., de Wit S., Clumeck N., Lambotte O., Rouzioux C., Rohr O., Van Lint C. Aids 2012, 26:1473-82. IF : 6,245
- **HIV-1 transcription and latency: an update.** Van Lint C., Bouchat S., Marcello A. Retrovirology 2013, 10: 67. IF: 5,660