IDF INNOV

From invention to innovation

NEW SMALL MOLECULES TO PURGE HIV RESERVOIRS

Small molecule capable of reactivating latent HIV in reservoirs to be used in a «shock and kill approach».

HIV ▪ Infectious disease ▪ Reservoir cells ▪ Latent infection ▪ Shock and kill ▪ Small molecules

APPLICATIONS

- HIV treatment in combination with ART

DEVELOPMENT PHASE

- POC *ex vivo* on CD4+ T cells obtained from HIV infected, antiretroviral-treated and aviremic patients
- Ongoing studies: continuation of *ex vivo* studies, mechanism studies and *in vitro* toxicity profile of the two hits

INTELLECTUAL PROPERTY

International patent application
WO201581387

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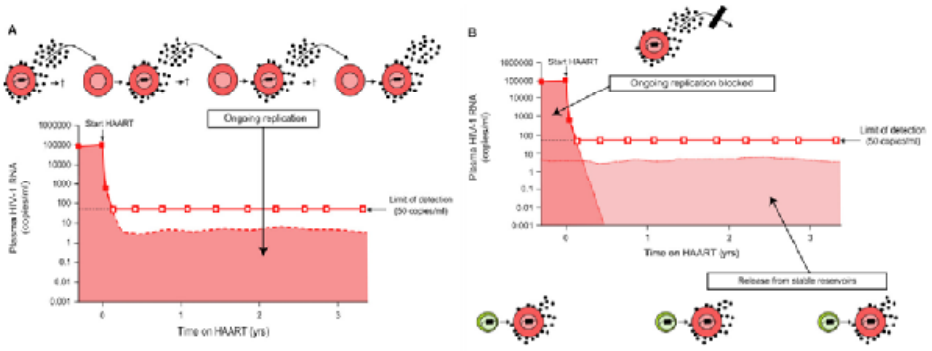
PRESENTATION

Significant progresses have been made in the treatment of HIV infection, in particular in the field of anti-retroviral therapies (ART). However, when ART are stopped or treatment resistance occurs, plasma viral load increases again. This rebound has been attributed to HIV reservoirs in which the pro-virus is in a non-expressing state. The present offer relates to the development of new drugs for the eradication of these HIV reservoir cells using the shock and kill approach. The aim of this approach is to induce expression of viral HIV genes in the latent cells. The cells may then be killed by the damaging effects of virus production (viral cytopathic effect), apoptosis, or may be recognized by the immune system or ART directed towards viral proteins.

Starting from a library screening, the team has optimized 2 hits thanks to the synthesis of 70 analogues and their evaluation *in vitro* (Structure-Activity Relationship approach). These compounds do not act as HDAC inhibitors and present no cytotoxicity up to 50 µM on a panel of cell lines. Their efficacy has been evaluated *ex vivo* on primary CD4+ T cells obtained from HIV infected, antiretroviral-treated and aviremic patients and were able to strongly increase the viral load detected.



VIH reservoirs mechanism *in vivo*

COMPETITIVE ADVANTAGES

- New small molecules
- Easy to synthetize in 3 or 4 steps without hard conditions
- Strong reactivation effect in *ex vivo* studies
- The compounds do not act as HDAC inhibitors