Evaluation of the Innate Immune Modulator Acitretin as a Novel Strategy to Clear HIV Reservoir

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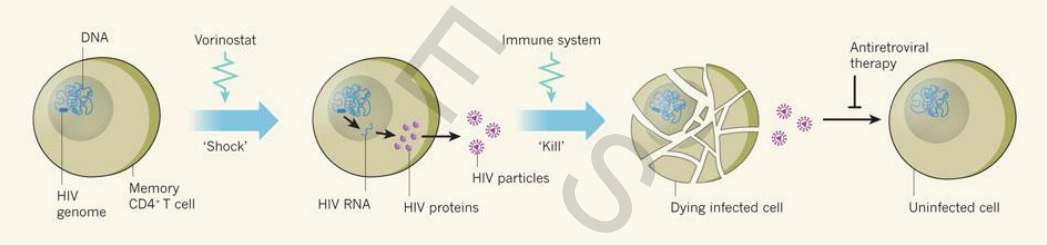
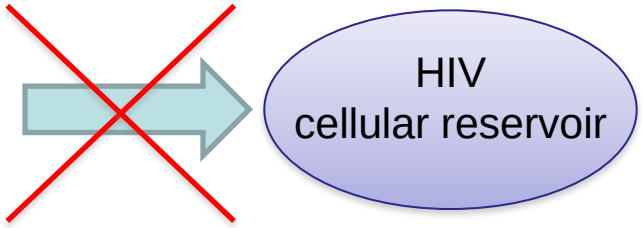
Clearing HIV reservoir: State of art and new approaches

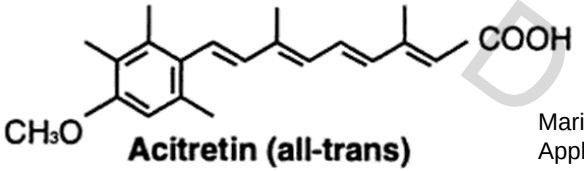
Current strategies to induce latent HIV expression: Shock and Kill





Steven G. Deeks, Nature. 2012;487:439–440.

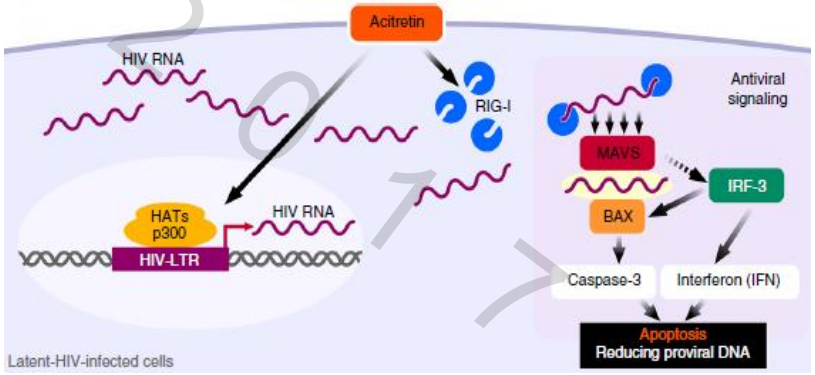
Acitretin



Maria A. Livrea, Lester Packer. 1993. Retinoids: Progress in Research and Clinical Applications. New York (NY): Marcel Dekker, Inc.

- Second-generation retinoid.
- Used to treat severe psoriasis (Soriatane®, Neotigason®).

- Recently, proposed as an innate immunity modulator able to reactivate latently HIV-infected cells and induce selective cell death (Peilin Li, et al. Nat Med. 2016; 22:807–811.).



Peilin Li, et al. Nat Med. 2016; 22:807–811.

Cheap and effective anti-HIV treatment

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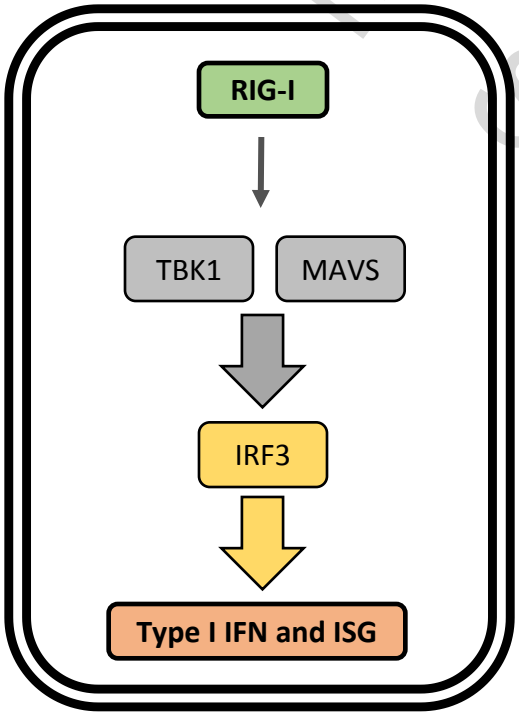
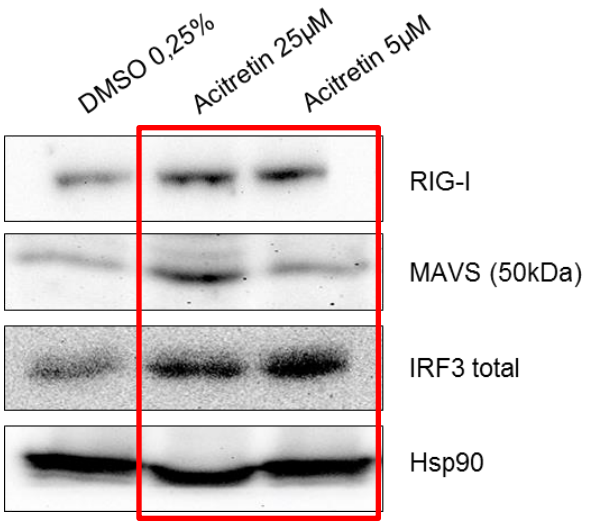
Our AIM:

To evaluate Acitretin as an agent to clear the HIV reservoir

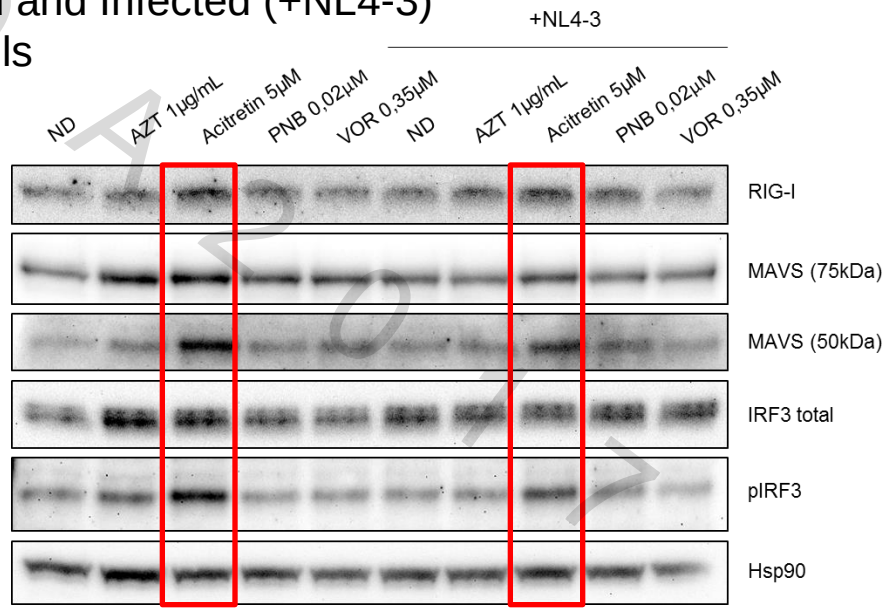
Acitretin as innate immune modulator



ACH-2 cells



Uninfected and Infected (+NL4-3)
TZM-bl cells



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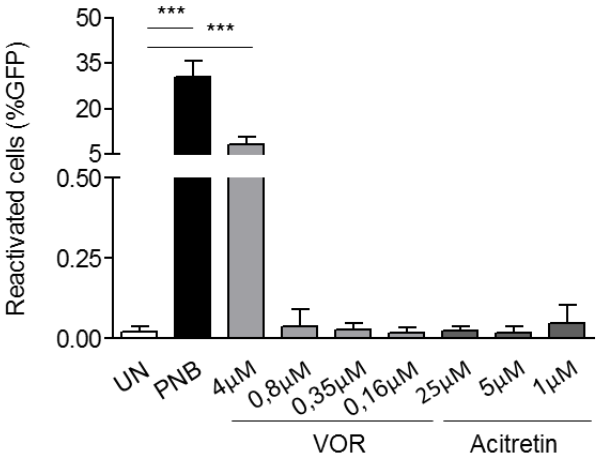
Acitretin as a latency-reversing agent (LRA): I

J-Lat. Clon 8.4

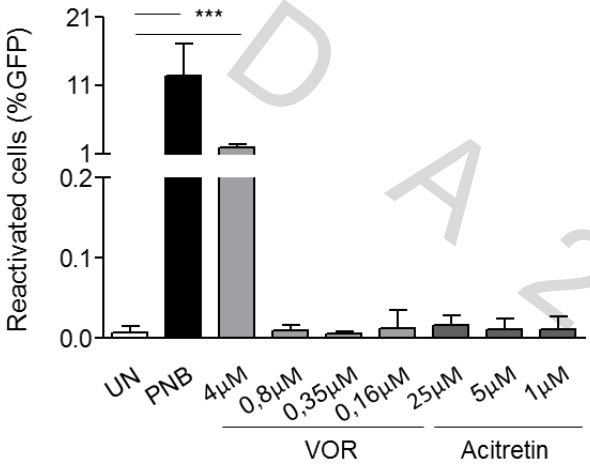
- 24h incubation
- Effect as a LRA alone



Did not reactivate

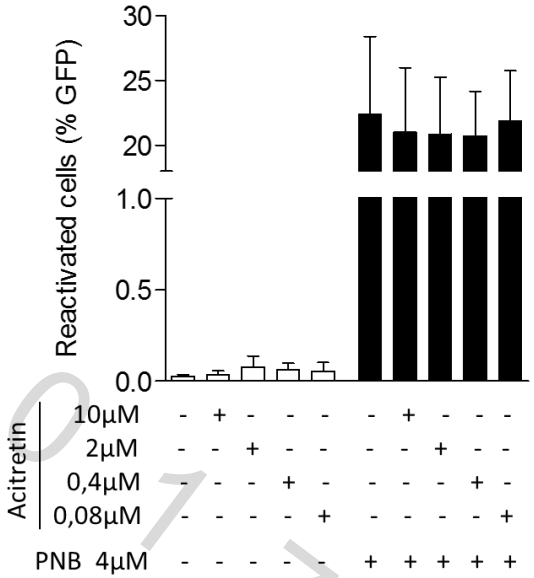
J-Lat. Clon 9.2

- 24h incubation
- Effect as a LRA alone



Did not reactivate

- 24h incubation
- Effect as a LRA alone and in combination with LRA panobinostat

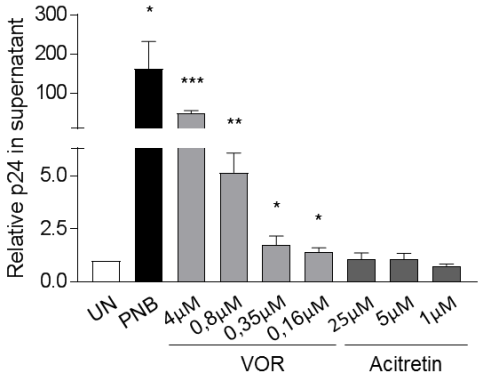


Did not reactivate

Acitretin as a latency-reversing agent (LRA): II

ACH-2

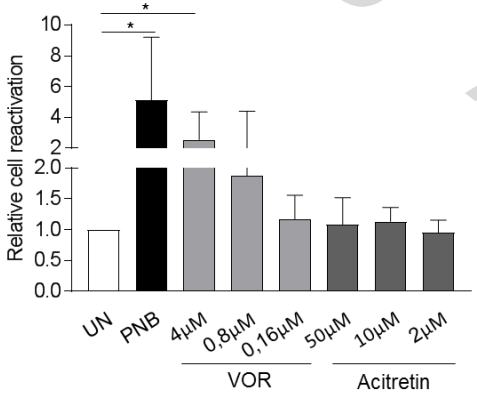
- 48h incubation
- Effect as a LRA alone



Did not reactivate

Latently infected primary CD4+ T lymphocytes

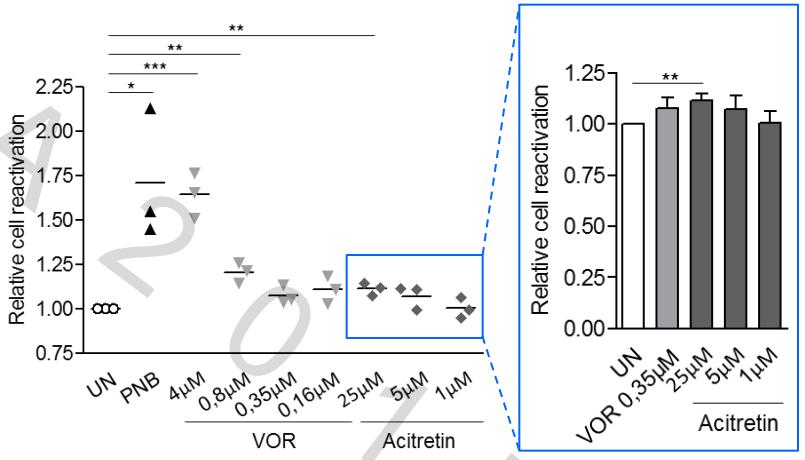
- Overnight incubation
- Effect as a LRA alone



Did not reactivate

Latently infected Jurkat cells

- 24h incubation
- Effect as a LRA alone



Did reactivate (slightly)

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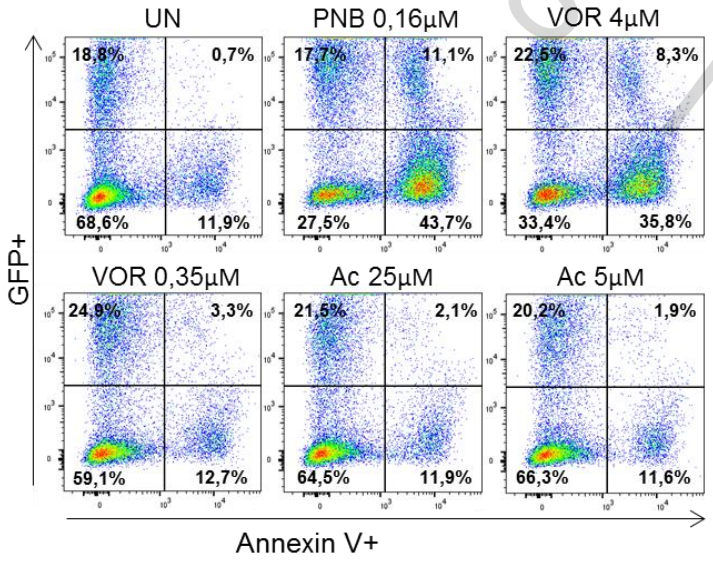
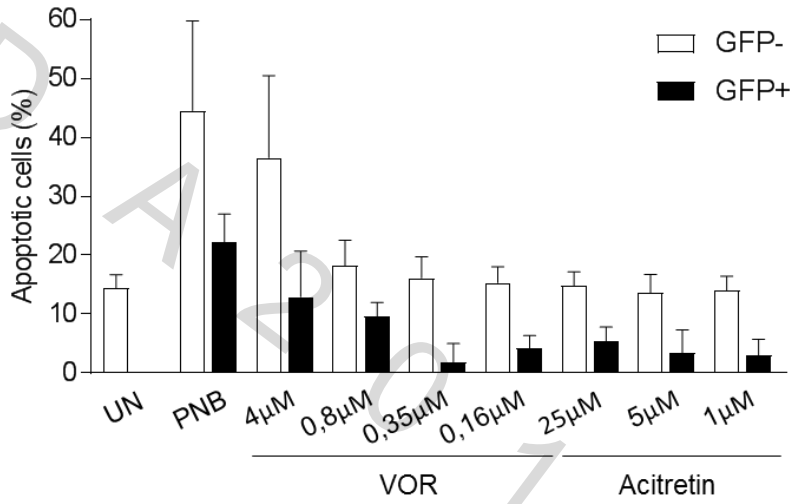
Acitretin as an apoptotic inducer of HIV-reactivated latently infected Jurkat (JHig) cells

JHig cell subpopulations dot plots:



JHig selective apoptosis:

- 24h incubation
- Effect as a LRA alone



GFP-: non-reactivated cells
GFP+: reactivated cells
Annexin V-: live cells
Annexin V+: apoptotic cells

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CONCLUSION:

- Acitretin is not able to induce HIV-reactivation in most of the tested models.
- Acitretin do not induce HIV-selective apoptosis in reactivated cells.

Thank you for your attention!

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HIV pathogenesis group

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