

Do commonly consumed prescription drugs affect human LINE-1 retrotransposition?

Abstract

Transposons are mobile pieces of DNA that can jump to different places of the genome. LINEs are a type of Transposable Element that move by a copy and paste mechanism using a Reverse Transcriptase activity in the human genome. LINEs are very abundant in genomes, including our own (they comprise 20% of our genome). Because of their mobility, they can create mutations, as they can insert themselves in genes. This can be either beneficial, neutral or harmful for the organism, and in this project we want to determine whether commonly used prescription drugs affect the rate of mobilization of human LINE-1 retrotransposons.

To do that, we used an *in vitro* retrotransposition assay using human HeLa cells. The following were the drugs selected in our experiments, using two concentrations of each drug:

- Bisoprolol: β 1-adrenergic blocker and renin (hormone that constricts blood vessels) inhibitor (slow heartbeat and lower blood pressure), β 2-adrenergic blocker in high concentrations affecting bronchi blocker.
- Dramina: histamine receptors blocker (anti-allergens) and acetylcholine synthesis inhibitor.
- Acyclovir: virus DNA-polymerase blocker (used to treat herpes virus).
- Tenofovir: a nucleoside analog that can inhibit the reverse-transcriptase activity of HIV/AIDS.

Our results indicate that while Tenofovir acts to reduce the mobilization of human LINE-1s, both Dramina and Bisoprolol increase the rate of human LINE-1 retrotransposition in cultured cells.

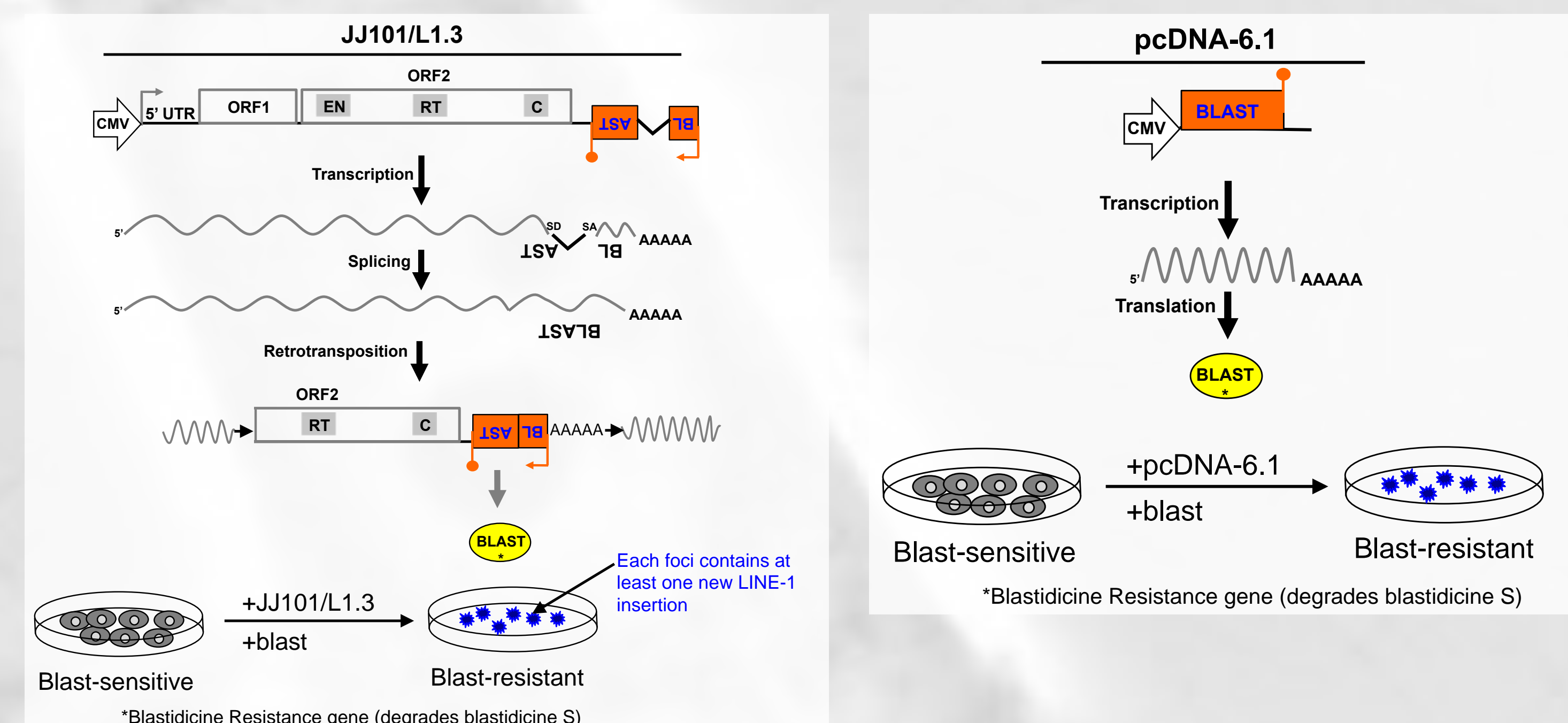


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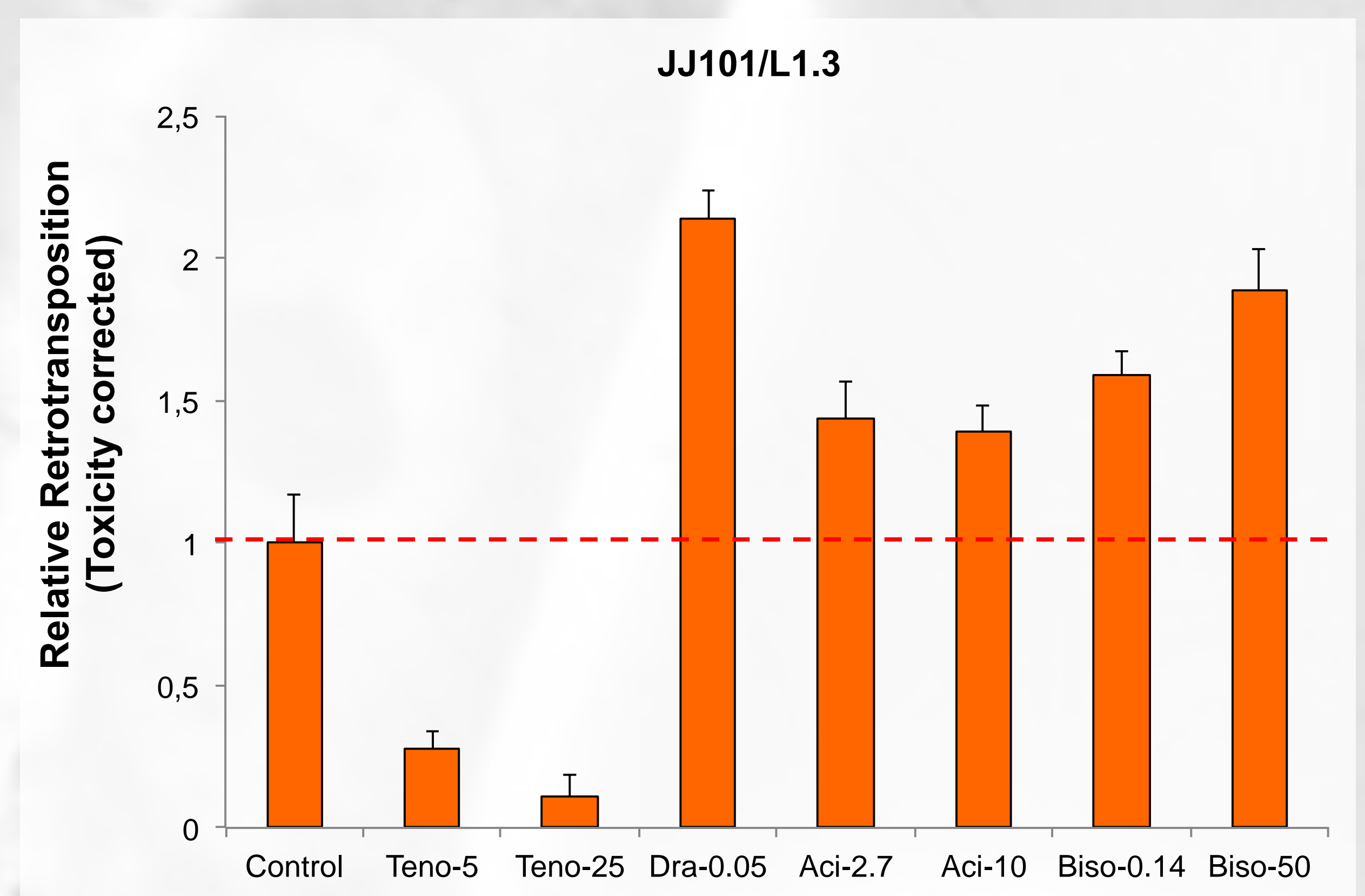
Hypothesis

It is known that the rate of human LINE-1 retrotransposition in cultured HeLa cells can be influenced by cellular host factors. However, the effect of these commonly used prescription drugs on human LINE-1 retrotransposition is unknown. To test their effect, we used an *in vitro* LINE-1 mobilization assay on cultures of HeLa cells.

Methods



Results



Discussion

TENOFOVIR: used to treat HIV/AIDS. Is a nucleoside analog that inhibits the reverse transcriptase activity of HIV. It also reduces the retrotransposition rate of a human LINE-1 in cultured HeLa cells and its inhibitory effect is dose-dependent.

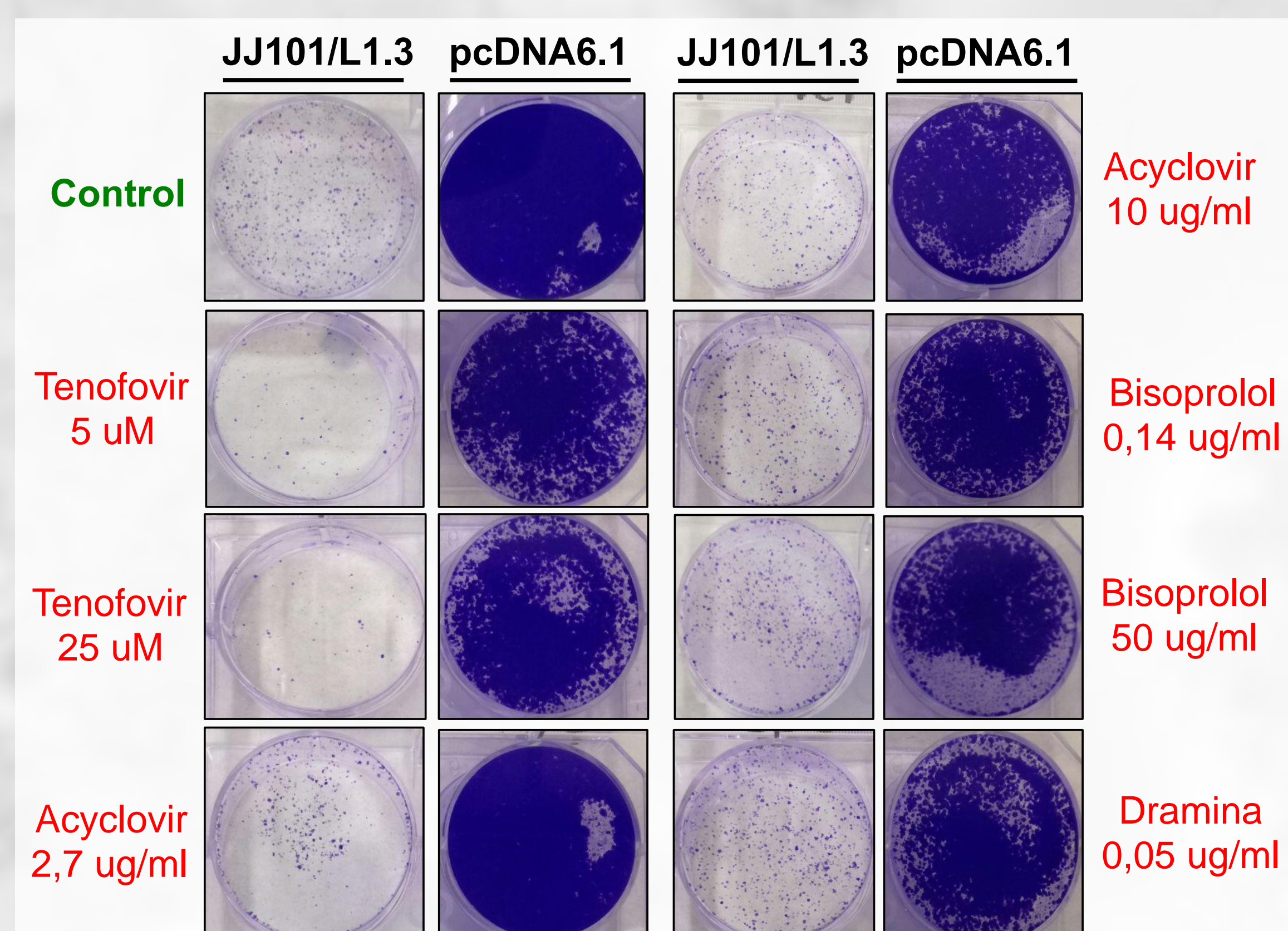
BISOPROLOL: reduces blood pressure and heart rate. This drug is used to reduce high blood pressure levels. In our assay, Bisoprolol increased the rate of human LINE-1 retrotransposition in cultured cells in a dose-dependent manner.

ACYCLOVIR: it is used to treat infection by herpes simplex virus and acts by blocking DNA polymerase. In our assay, we observed a minor increase in LINE-1 retrotransposition but the effect was not dose dependent. Thus, we can conclude that Acyclovir has a minor effect on LINE-1 retrotransposition.

DRAMINA: This drug inhibits the synthesis of acetylcholine and is widely used to prevent nausea, vomiting and/or dizziness associated with travelling (that is, motion sickness). In our assay, Dramina increased human LINE-1 retrotransposition but we only tested one concentration. We used a higher dose of Dramina (50 ug/ml), but we observed significant toxicity and we could not evaluate the effect at a higher doses.

These data indicate that: i) people consuming Bisoprolol and Dramina may accumulate more LINE-1 insertions during their life, and ii) HIV-patients taking Tenofovir would have less LINE-1 insertions accumulated during their life. While the inhibitory effect of Tenofovir could be explained by its ability to inhibit human LINE-1 Reverse Transcriptase, the stimulatory effect of Dramina and Bisoprolol requires further studies.

Results



Conclusions

- Tenofovir inhibit human LINE-1 retrotransposition in a dose dependent manner, likely by inhibiting the Reverse Transcriptase encoded by human LINE-1s.
- Dramina increases human LINE-1 retrotransposition; we also observed that this drug is toxic at high concentrations.
- Bisoprolol increases LINE-1 retrotransposition in a dose dependent manner, although we don't know the mechanism of action of this drug on LINE-1 retrotransposition.

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