Venetoclax treatment decreases intact proviral DNA in SIV infected, Rhesus Macaques.

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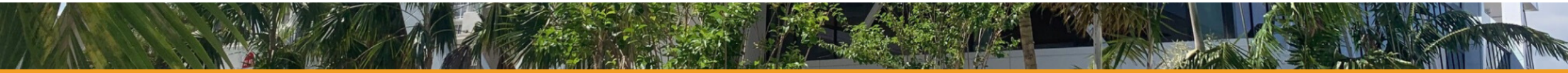


CONFLICTS OF INTEREST

No conflicts of interest to disclose.

Plain Language Summary

Goals of our study

Latency reversing agents are part of “shock and kill” strategies. Their efficacy in reducing the reservoir requires death of cells with reactivated virus production. Venetoclax may promote the death of these cells.

What did we learn from this study?

By combining the BCL-2 inhibitor, cell death promoting drug Venetoclax, with LRAs in SIV macaque model, we observed a reduction of cells containing intact proviral DNA under long-term ART.

Why is this important in the search for an HIV cure?

“Shock and kill” strategies will not be successful unless they induce death of cells that have reactivated virus production in PLWH treated with ART.

BCL-2 antagonism in long-term ART suppressed SIV-infected Rhesus macaques to decrease the intact proviral reservoir

- MT807R1 Ab CD8α Depletion
  50 mg/kg
- Rh-heterodimeric IL-15
  10-40 ug/kg
- Venetoclax
  300 mg/dose
- αSIV-*env* mAb cocktail
  ITS102.01-LS
  ITS103.01-LS
  ITS109-LS
  ITS113.01-LS

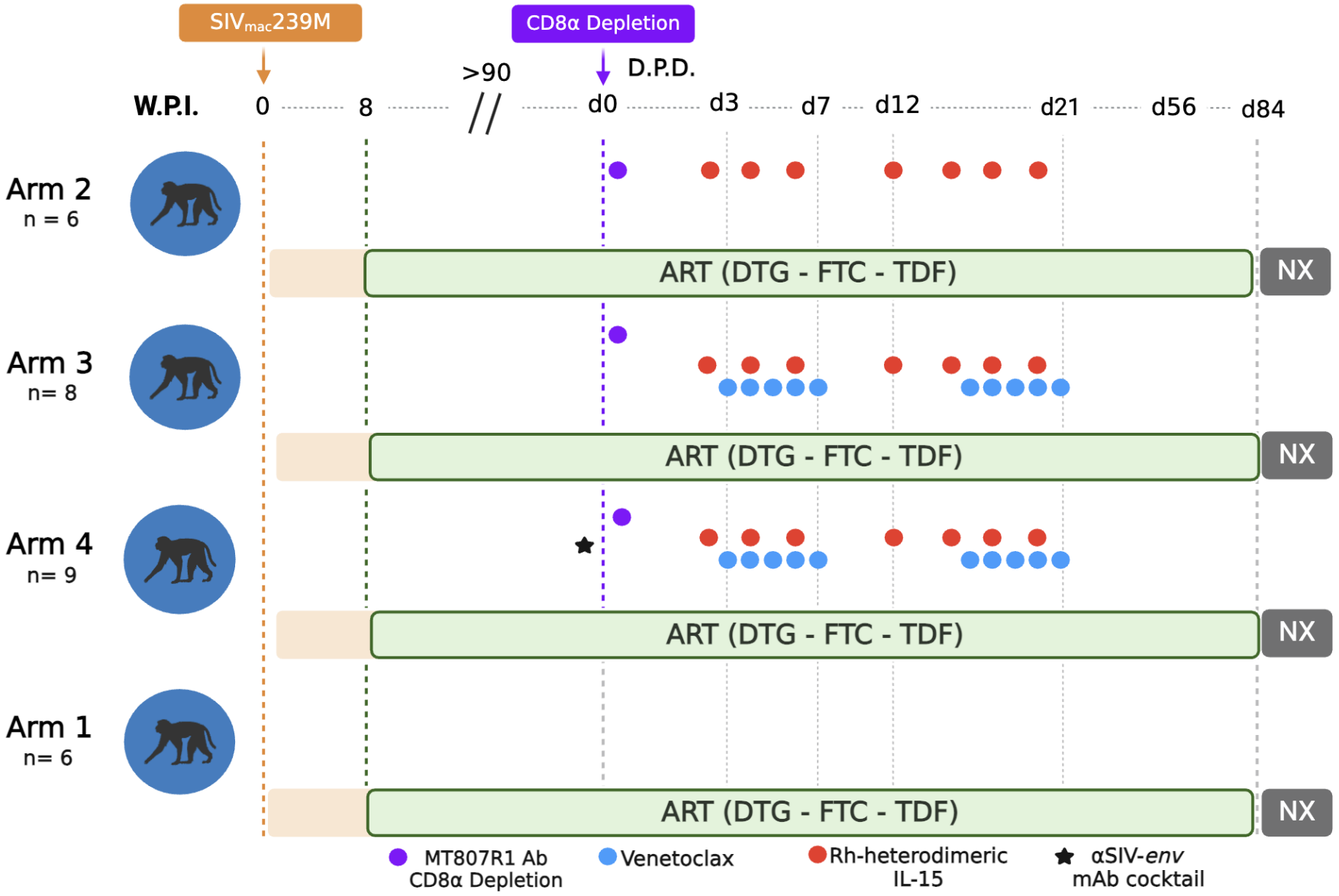
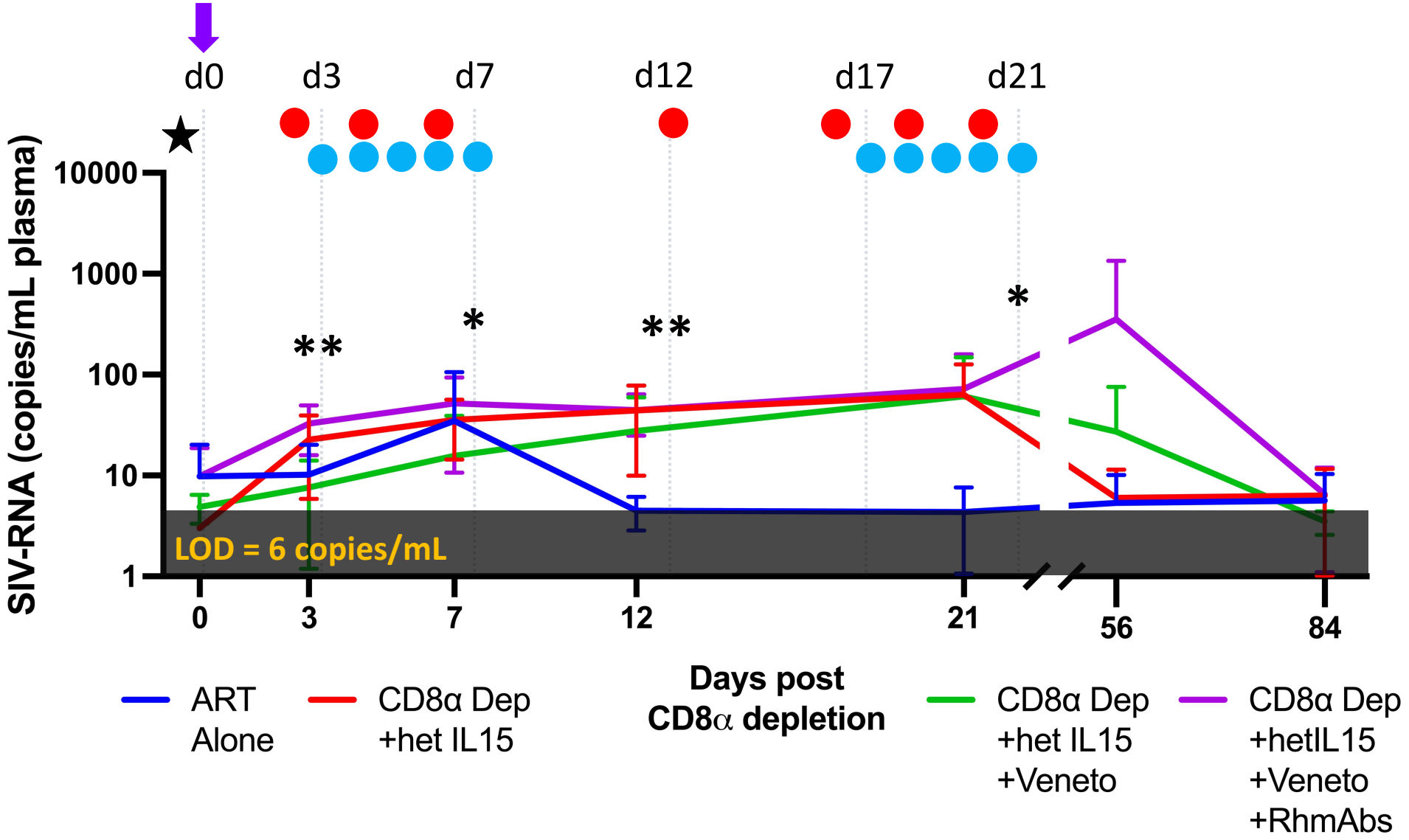


Figure made with Biorender

CD8α depletion + hetIL-15 induces on ART viremia +/- Venetoclax



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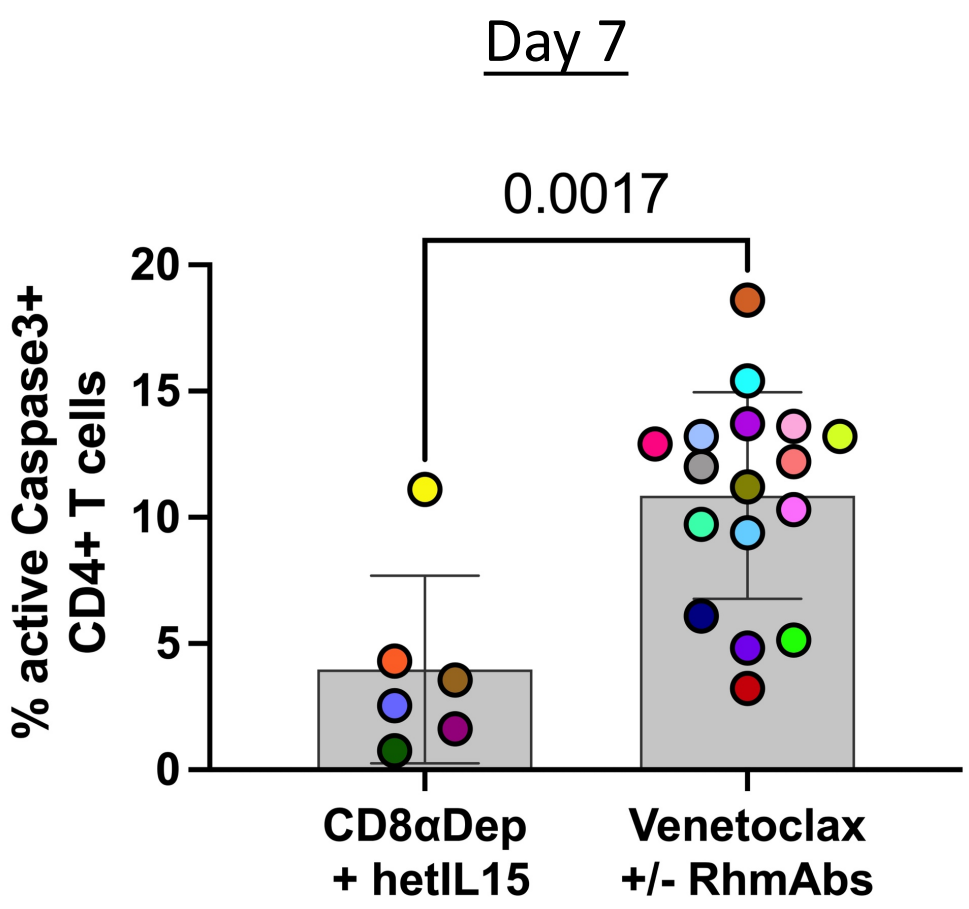
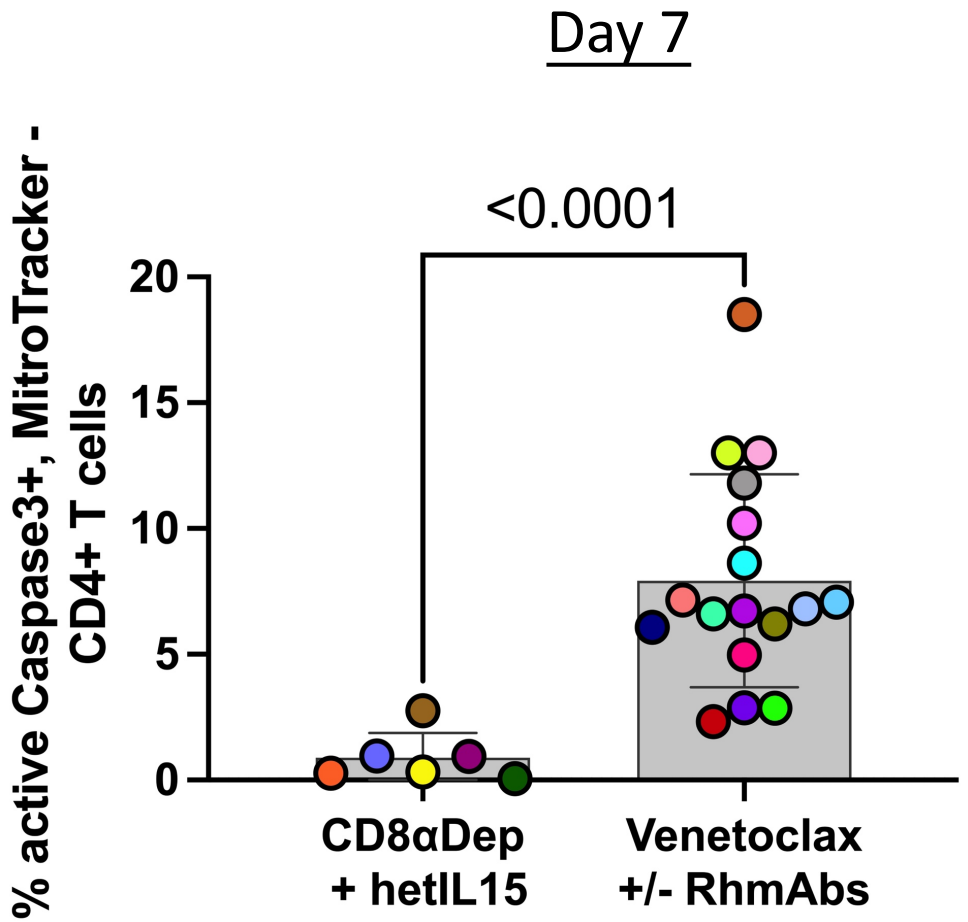
Caspase3 activation and inhibition of mitochondrial respiration observed in CD4+ T cells 4-hours post Venetoclax treatment





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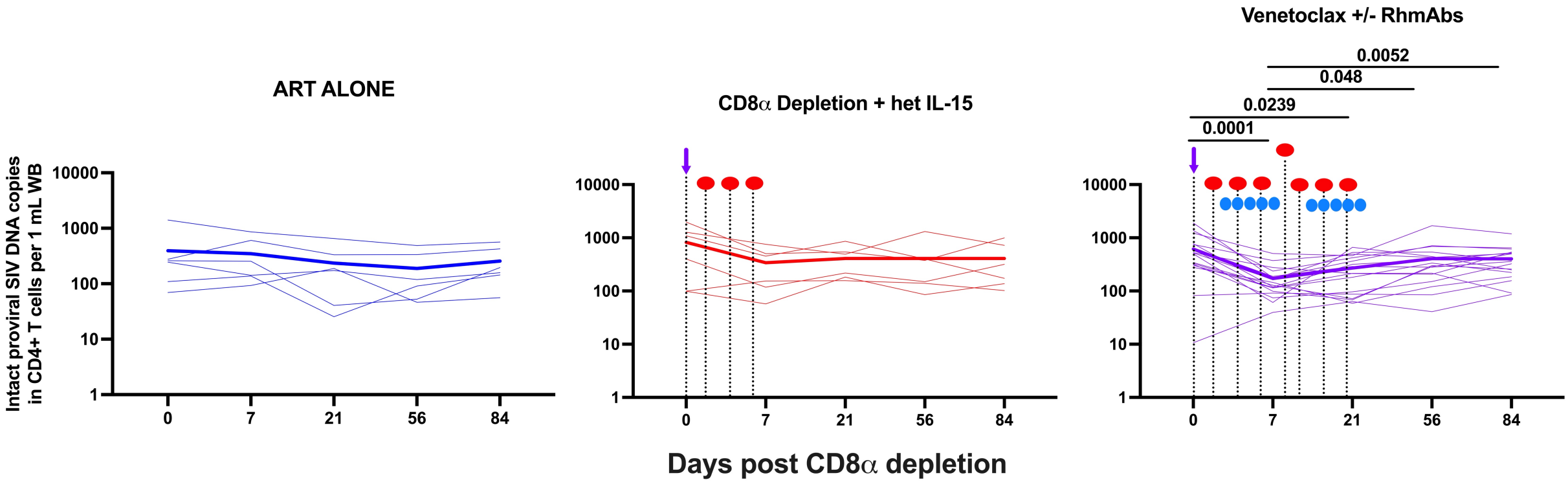
Decrease of intact SIV proviral DNA observed in peripheral CD4+ T cells is observed following Venetoclax treatment



MT807R1 Ab CD8α Depletion

Venetoclax

Rh-heterodimeric IL-15

αSIV-*env* mAb cocktail

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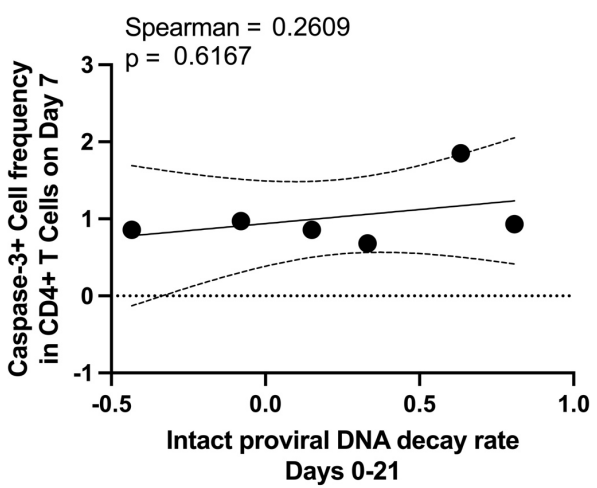
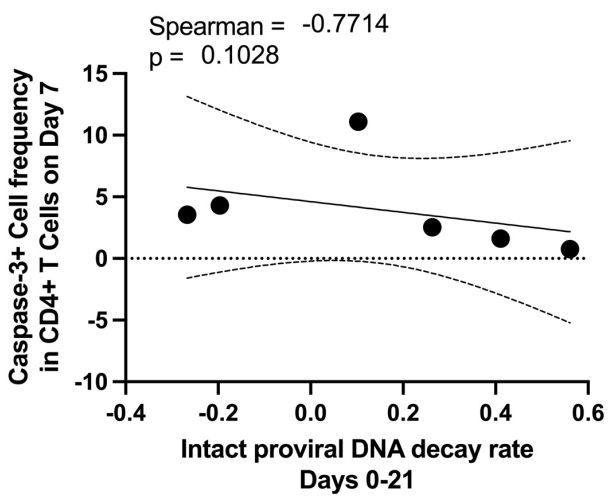
Caspase-3 frequency correlates with the decay of intact proviral SIV DNA

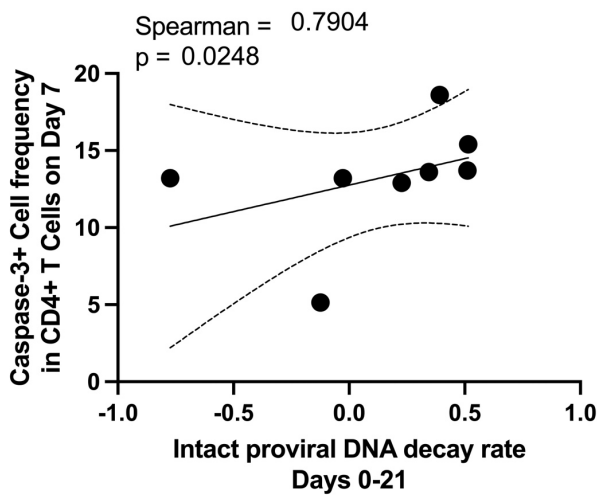
ART ALONE



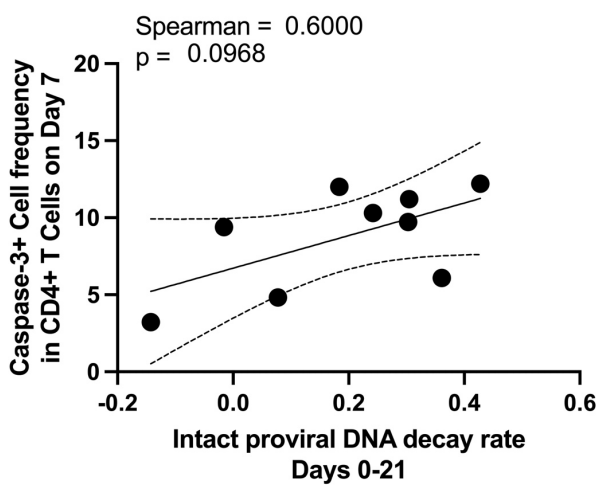
CD8α Depletion + het IL-15



+Venetoclax



+Venetoclax +RhmAbs



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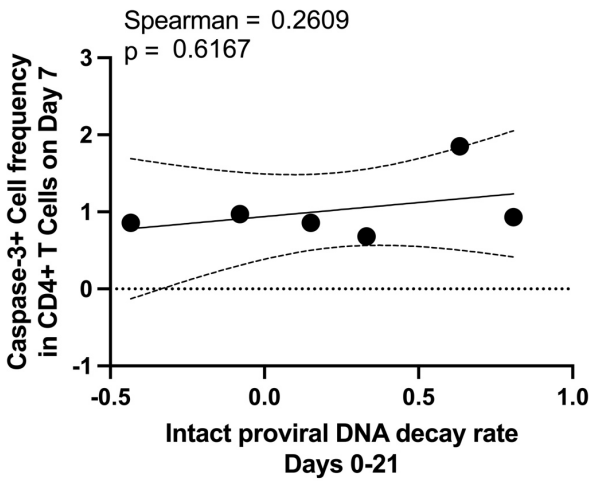
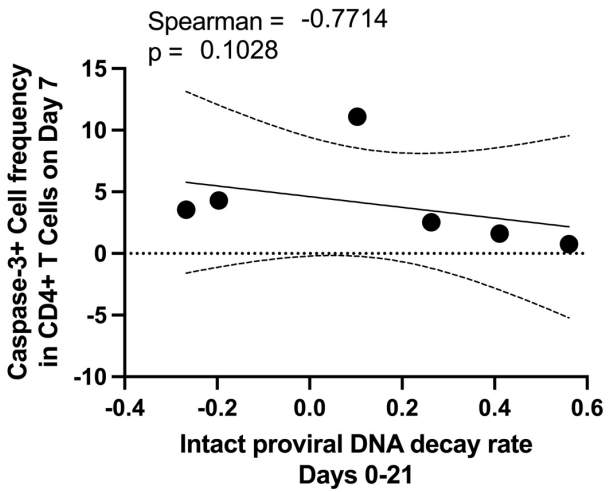
Caspase-3 frequency correlates with the decay of intact proviral SIV DNA

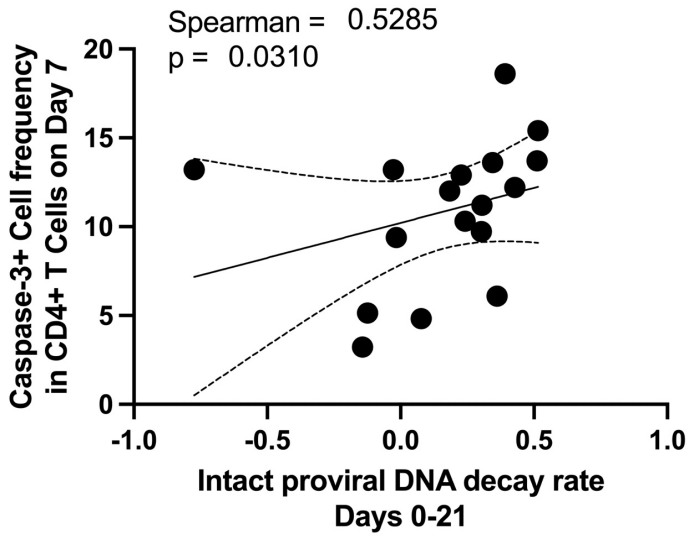
ART ALONE



CD8α Depletion + het IL-15



+Venetoclax +/-RhmAbs



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