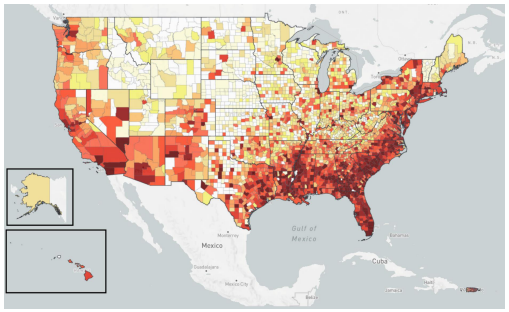
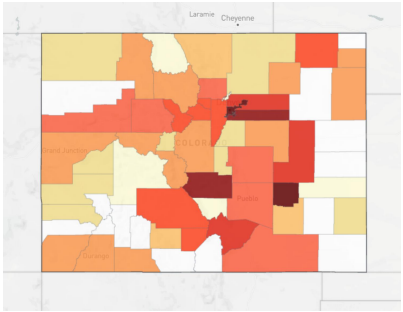
Why does HIV kill some CD4 T cells more than others?

Kaylee L. Mickens, Stephanie M. Dillon, Kejun Guo, Bradley S. Barrett, Mario L. Santiago, Cara C. Wilson
University of Colorado School of Medicine. Aurora, CO

Prevalence of Persons with HIV in the United States by County





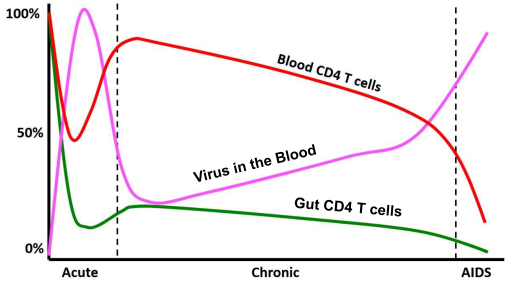
- 1.2 million people in the United States are living with HIV
- In Colorado there are over 13,000 people living with HIV

Rate of Persons Living with HIV per 100,000 (2020)

0 - 100	101 - 120	121 - 160	161 - 180	181 - 220
221 - 300	301 - 340	341 - 380	381 - 560	561+

HIV attacks gut immune cells more than those in other body sites

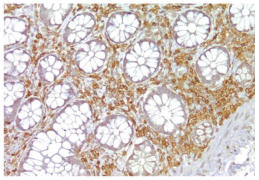
- HIV infects and kills **CD4 T cells**, immune cells that are important for protection against other diseases



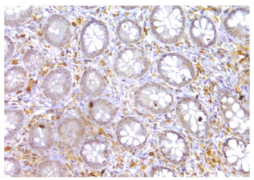
Small intestine tissue staining

CD4 T cell

Without HIV



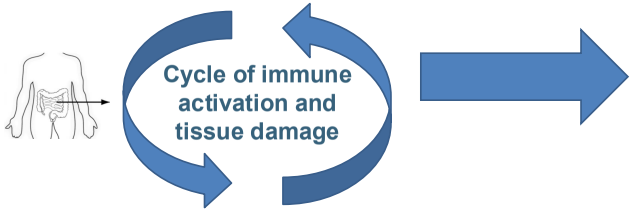
With HIV

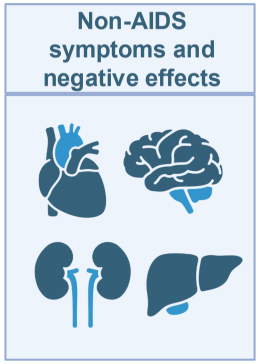


- During HIV infection, CD4 T cells **in the gut** are killed faster and in greater numbers than those from other body sites.

Loss of gut immune cells leads to other symptoms and diseases

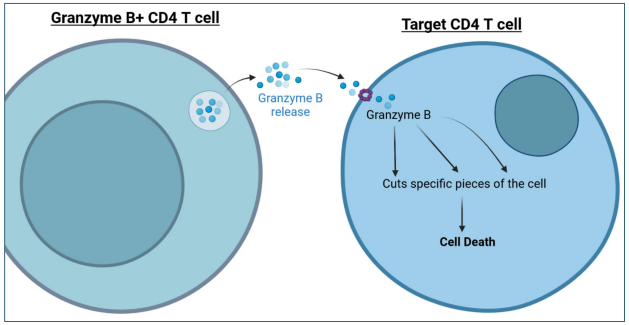
- When CD4 T cells are absent in the gut (due to HIV) it can lead to other problems like:
  - increased inflammation
  - Bacteria/bacterial products leaving the gut and entering the blood.

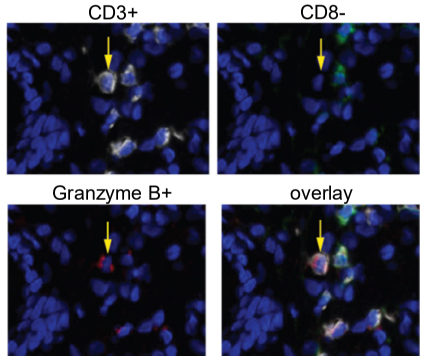




What makes gut immune cells more susceptible to HIV killing?

- Because the loss of gut CD4 T cells leads to continued negative effects for people with HIV, our main question is: why do gut CD4 T cells die in higher numbers when compared to other body sites?
- We know that when gut CD4 T cells see bacteria they produce a protein, called Granzyme B, that can kill other cells, including CD4 T cells.

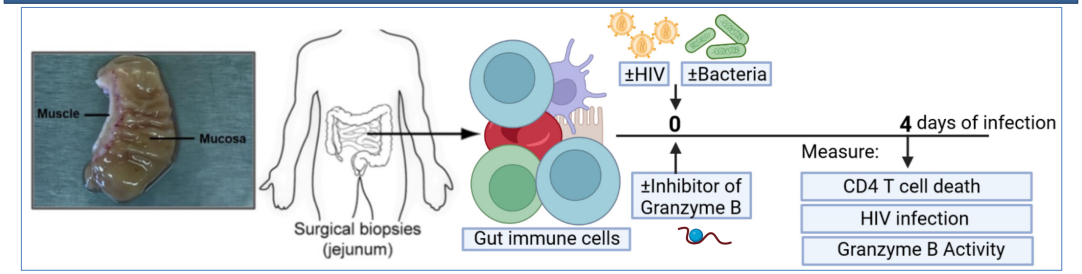


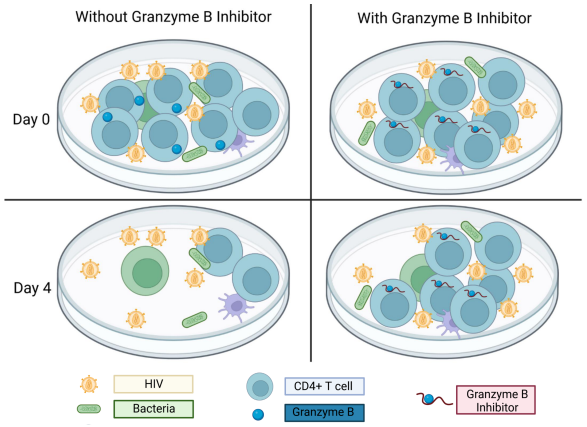


Marker on all T cells (CD3)
Marker on a subset of T cells (CD8)

Intestine tissue staining
CD3 CD8 Granzyme B

How do Granzyme B+ CD4 T cells affect HIV-mediated cell killing?





- Without Granzyme B activity HIV kills fewer gut CD4 T cells in culture
- Continued research on HIV mediated killing of gut cells will lead to a deeper understanding of how the virus causes disease and can better inform possible interventions for those living with HIV

Wilson Lab

ORCiD

University of Colorado Anschutz Medical Campus

NIH National Institute of Allergy and Infectious Diseases