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Introduction



- People living with HIV (PLWH) enrolled in the NOAH study have a lower healthy eating index than the population at large.
- Previous preclinical studies were conducted in simian immunodeficiency virus (SIV) infected macaques fed a healthy control diet.
- The impact of a high fat diet (HFD) on immune activation and differentiation is not known.
- CD4 T cell differentiation is metabolism dependent.

Hypothesis

High lipid media dysregulates CD4 T cell activation and differentiation.

Objective

- To better model the altered nutritional environment prevalent in PLWH. Specifically, to determine the impact of high lipid concentrations on T cell activation and differentiation.

Methods

- Naïve CD4 T cells were isolated from healthy blood bank samples.
- Sorted Naïve cells were separated into different media compositions:
 - Normal RPMI media
 - Low Lipid Media (100 μ M oleic acid, 250 μ M palmitic acid)
 - High Lipid Media (1 mM oleic and palmitic acid)
- Cells were stimulated on anti-CD3 coated plates using IL-12 and anti-CD28.
- After 3-day incubation period, cells were stained.
- Endpoints were assessed using flow cytometry.

Results

Excess Lipid Decreases CD4 T cell Differentiation to Th1 and Treg subsets

Tbet Expression

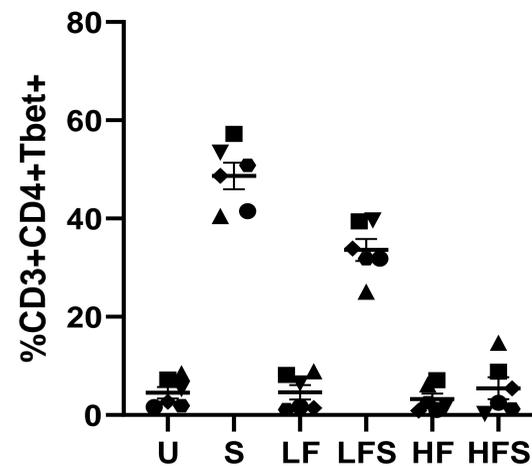


Figure 1a. Expression of Th1 master transcription factor, Tbet, in the presence or absence of excess lipids and stimulation.

FOXP3 Expression

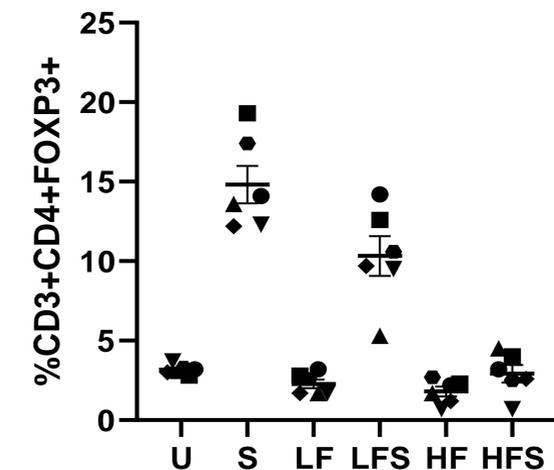


Figure 1b. Expression of Treg master transcription factor, FOXP3, in the presence or absence of excess lipids and stimulation.

Excess Lipid Decreases CD38 Expression

CD38+ Expression

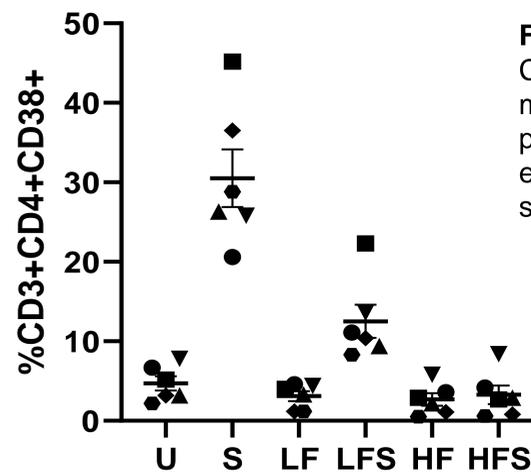


Figure 2. Expression of a CD4 T cell activation marker, CD38, in the presence or absence of excess lipids and stimulation.

U= Untreated S= Stim
LF= Low Fat LFS= Low Fat Stim
HF= High Fat HFS= High Fat Stim

Discussion

- Expression of Th1 master transcription factor, Tbet, decreased in a dose-dependent manner.
- Expression of Treg master transcription factor, FOXP3, decreased in a dose-dependent manner.
- CD38 expression decreased in a dose-dependent manner in the presence of palmitic and oleic acid.

Conclusions

- These preliminary analyses suggest that high lipid media significantly dysregulates CD4 T cell activation and differentiation.
- Further studies to determine the profile of activation in the presence of high lipid/high sugar levels are warranted. In addition, the impact of alcohol on cell responses remains to be examined under these conditions.