Impact of Excess Lipids on Naïve CD4 T Cell Activation and Differentiation
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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 µM oleic acid, 250 µM 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

Excess Lipid Decreases CD38 Expression

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.

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