Store operated calcium entry in diabetic macrophages is reduced in fasting conditions

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Background and Hypothesis:
In diabetic mice, intermittent fasting (IF) prevents diabetic complications by temporarily reducing inflammation during the fasting period. As calcium homeostasis is tightly connected to the inflammatory response, we hypothesize that IF regulates macrophage response by altering store-operated calcium entry (SOCE). SOCE, mediated by the STIM and ORAI families, is the primary form of calcium entry into the cell.

Experimental Design or Project Methods:
We assessed SOCE levels in control and diabetic ($INS2^{Akita}$) mouse primary macrophages stimulated with a metabolic stimulus (MET: insulin, high glucose, palmitate) to mimic feeding and a starvation stimulus (STARVE: low glucose, low FBS, oleate) to mimic fasting. SOCE levels were measured by a Flexstation using Calcium-6 dye. We also assessed gene expression of SOCE components by RT-PCR and STIM1 and ORAI1 proteins by western blot.

Results:
A decrease in SOCE was observed with MET stimuli and an increase with STARVE stimuli in control macrophages. Interestingly, gene expression and protein levels of all major SOCE components, including STIM1 and ORAI1, were increased in the MET and decreased with STARVE. While diabetic macrophages had similar SOCE function than control under basal and MET conditions, they showed significantly downregulated SOCE under starvation conditions.

Conclusion and Potential Impact:
These data show that diabetic macrophages have altered SOCE function in response to fasting. This could have potential impact on how diabetic individuals respond to nutritional interventions such as IF that are recently proposed for prevention of diabetic complications.