TACSM Abstract

Fish-oils Increase BAMBI Expression to Protect Against Fibrotic Activity in LPS Stimulated Hepatic Tissue

MEGAN L. SCHALLER[1], MATTHEW P. HARRIS[1], DAKOTA R. KAMM[1], KENNETH A. WITT[2], KARIN E. SANDOVAL[2], and JOSHUA S. WOOTEN[1]

1. Exercise Physiology and Biochemistry Lab; Department of Applied Health; Southern Illinois University Edwardsville; Edwardsville, IL. 2. Department of Pharmaceutical Sciences; Southern Illinois University Edwardsville; Edwardsville, IL

Category: Masters

Advisor / Mentor: Wooten, Joshua (jwooten@siue.edu)

ABSTRACT

Non-alcoholic steatohepatitis (NASH), defined as excess hepatic lipid and chronic inflammation, provides an environment prone for the development of hepatic fibrosis. Recent evidence suggests that the antifibrotic protein BAMBI (BMP-Activin membrane bound inhibitor) is downregulated in the presence of inflammation, and may be central to the development of fibrosis. Diets rich in omega-3 (ω-3) fatty acids are known to provide anti-inflammatory effects; however, the effects of ω-3 fatty acids on hepatic fibrosis are not well-established. **PURPOSE:** To determine the effects of fish-oils on the hepatic fibrosis signaling cascade, following 32-weeks of high-fat feeding in a LPS-induced model of NASH. **METHODS:** Male C57BL/6 mice were randomly assigned to one of four diets for 32 weeks (n=9/group): low-fat lard based (LFL, 10% kcal fat), low-fat fish-oil based (LFFO, 10% kcal fat), high-fat lard based (HFL, 41% kcal fat), or high-fat fish-oil based (HFFO, 41% kcal fat). Following *in situ* LPS stimulation, liver mRNA expression of CD14, TLR4, MyD88, BAMBI, and TGF-β1 was quantified using quantitative RT-PCR. Differences between diets were identified using a one-way ANOVA with statistical significance set at $p<0.05$. **RESULTS:** Following LPS stimulation, CD14 was increased 2.5 fold ($p=0.020$) in HFFO when compared to HFL. Despite the increase in CD14, TLR4 showed no difference between groups. In contrast, MyD88 was 2.8 fold greater ($p<0.001$) in HFL compared to HFFO. In comparison to untreated tissue, BAMBI was 1.7 fold ($p=0.017$) higher in the HFFO LPS-stimulated tissue, which best explained the 1-fold ($p=0.004$) lower expression of TGF-β1 in HFFO when compared to HFL post-LPS stimulation. **CONCLUSION**: Despite the increase in extracellular LPS signaling receptor CD14, the consumption of fish-oils produced a protective intracellular response as observed by an increase in BAMBI and decrease in TGF-β1. These results suggest that a diet high in ω-3 fatty acids may protect against the development of hepatic fibrosis.