

## **Evaluating the Role of Dietary Polyunsaturated Fatty Acids on Long-chain Acyl-CoA Synthetase Isoform 4 (ACSL4) Expression**

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Long-chain acyl-CoA synthetases (ACSLs) are a family of enzymes that catalyze the rate-limiting thioesterification of a fatty acid and coenzyme A into a fatty acyl-CoA, which can then be further metabolized. ACSL isoform 4 has been shown to play an important role in beta-cell glucose-stimulated insulin secretion (GSIS); this isoform also specifically favors polyunsaturated fatty acids (PUFAs, linoleic acid (18:2) and arachidonic acid (20:4)) as substrates. We have previously observed that exposing beta-cells to PUFAs, specifically arachidonic and linoleic acids, specifically reduced ACSL4 mRNA expression and total acyl-CoA synthetase (ACS) activity. We hypothesize that a mixture of dietary fatty acids that contain PUFAs would result in similar reductions in ACSL4 expression and total ACS activity. Using a rat insulinoma cell line (INS 832/13), we examined the effects of different fatty acid exposures on ACSL4 expression by quantitative real time RT-PCR and western blot analysis, and total ACS activity. We found that after exposing INS 832/13 cells to arachidonic acid for 48 hours, there was a statistically significant reduction in ACSL4 mRNA expression. Though not statistically significant, exposure to linoleic acid by itself as well as exposure to combinations of dietary fatty acids that contain PUFAs for 48 hours also reduced ACSL4 mRNA expression. However, Western blot analysis showed increased relative ACSL4 protein expression with all fatty acid exposures. Total ACS activity was reduced across all individual fatty acid exposures, but contrary to our expectations, ACS activity was actually slightly increased with exposure to the combinations of dietary fatty acids with PUFAs. Ultimately, the data did not support our hypothesis that a mixture of dietary fatty acids with PUFAs would reduce ACSL4 expression and total ACS activity. Due to some findings inconsistent with previous studies, there is a need for further investigation.