



## Exercise Biochemistry Review

---

Proceedings of IBEC 2018, Beijing, China, October 23-25

PL-017

### High-fat overfeeding increases intramuscular triglyceride content and perilipin protein expression in human skeletal muscle.

Katie Whytock<sup>1</sup>, Siôn Parry<sup>2</sup>, Mark Turner<sup>2</sup>, Lewis James<sup>2</sup>, Richard Ferguson<sup>2</sup>, Carl Hulston<sup>2</sup>, Juliette Strauss<sup>2</sup>, Matt Cocks<sup>2</sup>, Anton Wagenmakers<sup>1</sup>, Sam Shepherd<sup>1</sup>

1.Liverpool John Moores University

2.Loughborough University

**Objective** High-fat high-calorie diets can induce whole body insulin resistance (IR) whilst increasing stores of intramuscular triglyceride (IMTG) contained within lipid droplets (LD). Perilipin (PLIN) proteins assist in IMTG storage. Synaptosomal-associated protein (SNAP23) may support LD growth and also direct IMTG-derived fatty acids (FA) to mitochondria for  $\beta$ -oxidation. The objectives of this study were: 1) to test the hypothesis that 7 days of high-fat overfeeding increases IMTG content to prevent lipid induced muscle IR and 2) identify changes in PLINs, SNAP23 and mitochondria content and colocalisation of PLINs with LD, and SNAP23 with LD and mitochondria.

**Methods** Muscle biopsies were obtained from the *vastus lateralis* of thirteen healthy individuals (age:  $23 \pm 1$  years, BMI:  $24.4 \pm 0.7 \text{ kg.m}^{-2}$ ) before (0min) and during (30min) an oral glucose tolerance test (OGTT), pre and post 7-days consuming a high-fat (65% energy) high-calorie (+50% kcal) diet. IMTG, PLIN2, PLIN3, PLIN5, SNAP23 and mitochondria content were measured using (semi)-quantitative confocal immunofluorescence microscopy. PLIN2, PLIN3 and PLIN5 colocalisation to LD was measured using object-based colocalisation analyses. Pearson's correlation coefficient quantified colocalisation between SNAP23 and plasma membrane (PM), mitochondria and LD. Phosphorylation of intermediates of the muscle insulin-signalling cascade (Akt and AS160) were measured at 0 and 30 min of the OGTT before and after the dietary intervention.

**Results** Following overfeeding phosphorylation of Akt and AS160 in muscle was not impaired during the OGTT, however Matsuda index of whole-body insulin sensitivity decreased (-23%;  $P < 0.01$ ). IMTG content increased in type I fibres (+100%;  $P < 0.001$ ) due to both an increase in LD number (+43%;  $P < 0.001$ ) and size (+44%;  $P < 0.001$ ). Of the PLINs investigated, only PLIN3 content increased (+50%;  $P < 0.01$ ) exclusively in type I fibres. PLIN2-associated LD increased (+80%;  $P < 0.01$ ) in type I fibres only, whereas PLIN3 and PLIN5-associated LD were unaltered. SNAP23 and mitochondria content did not change, nor did the colocalisation of SNAP23 with the PM, mitochondria or LD.

**Conclusions** Our data confirm the hypothesis that following high-fat overfeeding IMTG stores increased whilst activation of key muscle insulin signalling components were maintained. The increase in IMTG stores is likely supported by the concurrent increase in total PLIN3 content and a redistribution of existing stores of PLIN2 to the expanded LD pool in type I fibres. To confirm if increased IMTG storage protects muscle from IR future research should determine whether meal-derived FAs are directed to IMTG rather than ceramides and diacylglycerol.