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# DHA-supplementation prior to fasting prevents muscle atrophy in mice

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## Background and aims

Muscle wasting prevails in numerous diseases (e.g. diabetes, cardiovascular and kidney diseases, COPD,...) and increases healthcare costs. A major clinical issue is to devise new strategies preventing muscle wasting. We hypothesized that a long-term docosahexaenoic acid (DHA) supplementation prior to fasting may preserve muscle mass in vivo.

## Methods

Six-wk-old C57BL/6 mice were fed a DHA-enriched or a control diet for 8 weeks and then fasted for 48 h. The effect of DHA on i) muscle energy stores (glycogen, triglycerides (TG)), ii) muscle mass, and iii) Akt and AMPK signaling pathways involved in the control of protein and energy metabolism has been addressed. The regulation of the formation and the fate of lipid stores has been also evaluated.

## Results

Feeding mice a DHA-enriched diet prior to fasting elevated muscle glycogen contents without any change in TG levels, reduced muscle wasting, blocked the 55 % decrease in Akt phosphorylation, and reduced by 30-40% the activation of AMPK, ubiquitination or autophagy. The DHA-enriched diet fully abolished the fasting induced-mRNA over-expression of the endocannabinoid receptor-1. Finally, DHA prevented or modulated the fasting-dependent increase in muscle mRNA levels for Rab18, PLD1 and perilipins, which determine the formation and fate of lipid droplets, in parallel with muscle sparing.

**Conclusion:** These data suggest that long-term DHA supplementation increased energy stores that can be efficiently mobilized, and thus preserved muscle mass in response to fasting through the regulation of Akt- and AMPK-dependent signaling pathways for reducing proteolysis activation. Whether a nutritional strategy aiming at increasing energy status may shorten recovery periods in clinical settings remains to be tested.