Novel nutritional interventions to counteract frailty and wasting

R. Koopman, Department of Physiology, The University of Melbourne, VIC 3095, Australia.

Aging is associated with a progressive loss of skeletal muscle mass that leads to reduced functional capacity, impaired quality of life and increased morbidity and mortality (Koopman, 2011). Systemic inflammation during ageing and acute illness reduce skeletal muscle protein synthesis as increased amounts of circulating inflammatory cytokines impair the normal anabolic response to food intake. Therefore, treatments that modulate inflammation may have potential to counteract muscle wasting in older individuals and patients.

Amino acids are powerful regulators of protein synthesis and skeletal muscle cells are highly sensitive to fluctuations in amino acid availability. mTORC1 is crucial for amino acid-induced changes in protein synthesis and growth. In skeletal muscle, it has been clearly demonstrated that of all the amino acids, leucine is the most potent stimulator of mTORC1 and protein synthesis. Recent research highlights the negative impact of inflammation on amino acid sensing, mTORC1 activation and stimulation of protein synthesis and challenges the idea that leucine, as a standalone nutritional intervention, is effective in the prevention of muscle wasting (Ham *et al.,* 2014). We have therefore focussed on utilising other nutrients or treatments that sensitize skeletal muscle to leucine, thereby enhancing its therapeutic potential for muscle wasting conditions.

Glycine, a non-essential amino acid, is an effective anti-inflammatory agent that can reduce cytokine production and whole-body inflammation. Since inflammation is central to the development of muscle wasting in many conditions, glycine supplementation represents a simple, safe and promising treatment. Recent studies from our laboratory have demonstrated that supplemental glycine effectively protects muscles in a variety of wasting models including cancer cachexia, sepsis and reduced caloric intake (Koopman *et al.*, 2017). The underlying mechanisms responsible for the effects of glycine remain unclear but likely involve receptor mediated responses and modulation of intracellular metabolism, as it is a precursor for a range of important metabolites including creatine, heme, purines and glutathione (Koopman *et al*., 2017).

In summary, amino acids have major roles in modulating cellular metabolism and homeostasis and are not just simple building blocks for protein synthesis. Despite the lack of a definitive mechanism of action, glycine supplementation has therapeutic potential as an effective nutritional intervention for improving health by protecting muscles during different wasting conditions.

Koopman R. (2011) *Proceedings of the Nutrition Society* **70,** 104-113.
Ham DJ, Caldow MK, Lynch GS, Koopman R. (2014) *Clinical Nutrition* **33**, 937-45.
Koopman R, Caldow MK, Ham DJ, Lynch GS. (2017) *Curr Opin Clin Nutr Metab Care* **20**, 237-242

Supported by Project grant funding from the NHMRC.