In addition to helping us perform vital activities required for daily living, our skeletal muscles play a critical role in the way the body uses substrates like amino acids, glucose and fat. If they accumulate in body, diseases like obesity and diabetes can develop.

Nutrition and resistance exercise are the two most important non-medicinal factors that can regulate muscle mass and health. They do this in part by regulating muscle protein synthesis. However, their precise mechanisms of action are unknown.

Studying rat skeletal muscle, we examined the expression and regulation of a signalling molecule that had been shown to regulate protein synthesis in non muscle cells. It was not known if this regulator was expressed in muscle, or if it could be regulated by nutrition. We demonstrated the expression of this molecule in skeletal muscle and in muscle cells. We showed that when rats were deprived of nutrients, this molecule accumulated and its abundance correlated with reduced muscle protein synthesis. When the animals we fed, the molecule was degraded and muscle protein synthesis increased in parallel. Our results are consistent with a model whereby this molecule, called PDCD4, accumulates when nutrients are not available. When nutrients are provided, however, it is degraded, an event that allows protein synthesis to increase. Consistent with this model, we showed that protein synthesis remained high in muscle cells in which PDCD4 had been depleted, even in the absence of nutrients.

This study identifies this molecule as a critical repressor of skeletal muscle protein synthesis. Interventions that can deplete its abundance
may prove useful in maintain/ enhancing muscle mass, especially in conditions normally associated with muscle wasting.

Reference: Zargar S, Moreira TS, Samimi-Seisan H, Jeganathan S, Kakade D, Islam N, Campbell J, **Adegoke OA**. Skeletal muscle protein synthesis and the abundance of the mRNA translation initiation repressor PDCD4 are inversely regulated by fasting and refeeding in rats. Am J Physiol Endocrinol Metab. 2011 Jun;300(6):E986-92.

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