ADRB2 Polymorphism and Muscle Mass Preservation During Weight Loss

Genetic Determinants of Lean-Mass Maintenance and Sarcopenia Risk — A Literature Review

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ABSTRACT

Background. **Lean-mass preservation during weight loss is an important clinical goal, because unintended muscle loss reduces resting energy expenditure, predisposes to weight regain and accelerates sarcopenia. The β2-adrenergic receptor (ADRB2) modulates both skeletal-muscle protein synthesis and lipolysis; the common rs1042714 (Gln27Glu) polymorphism modifies adipocyte and myocyte β2-adrenergic responsiveness.**

Methods. **Narrative review of ADRB2 genotype, skeletal-muscle physiology and protein/exercise strategies for lean-mass preservation during weight loss.**

Results. **Glu27 carriers have modified β2-adrenergic signalling that may reduce the anti-catabolic effect of circulating catecholamines on skeletal muscle during negative energy balance. Resistance training plus adequate protein intake (1.2–1.6 g/kg/day) reliably preserves lean mass across ADRB2 genotypes.**

Discussion. **Genotype-informed advice for lean-mass preservation during weight loss emphasises resistance training, adequate high-quality protein, and avoidance of excessive caloric deficit.**

Subjects: Genetics, Exercise, Sarcopenia. **Keywords:** ADRB2; rs1042714; skeletal muscle; protein; resistance training; weight loss.

INTRODUCTION

During weight loss from hypocaloric feeding alone, approximately 20–30 % of the lost mass is lean tissue. This loss reduces resting energy expenditure and compromises long-term weight maintenance. Preserving lean mass during weight loss is therefore a central component of evidence-based weight-management programmes.

Skeletal muscle mass is governed by the balance between muscle protein synthesis and breakdown. β2-adrenergic signalling has both anabolic (protein synthesis) and lipolytic effects, and ADRB2 variants modify both. The rs1042714 Gln27Glu variant produces altered receptor kinetics with measurable effects on adipocyte lipolysis and, to a lesser extent, skeletal-muscle hypertrophy.

ADRB2 AND SKELETAL MUSCLE

The Glu27 allele has been associated in some studies with blunted muscle anabolic response to β2-agonist stimulation and with modestly lower lean mass at baseline. However, effect sizes are small, and the dominant determinants of muscle preservation during weight loss are resistance training and protein intake.

Resistance training stimulates muscle protein synthesis independently of β2-adrenergic signalling and is the single most effective intervention for lean-mass preservation during weight loss. Adequate high-quality protein (1.2–1.6 g/kg/day during active weight loss, distributed across 3–4 meals) provides the substrate for synthesis. Vitamin D, leucine-rich protein sources and adequate sleep support anabolic signalling.

TABLE 1 — SUPPORTING HUMAN STUDIES

STUDY (AUTHOR, YEAR)	POPULATION	DESIGN · SNP / FOCUS	PRIMARY OUTCOME / KEY FINDINGS
Large et al., 1997	**Population:** Obese adults.	**Design:** Functional study. **SNP:** ADRB2 Gln27Glu.	Glu27 carriers had altered adipocyte β2-adrenergic function (Large et al., 1997).
Leitzmann et al., 2017 (systematic review)	**Population:** Adults in weight-loss trials.	**Design:** Systematic review of protein and lean-mass preservation. **Focus:** Protein intake during weight loss.	Higher protein intake (1.2–1.6 g/kg/day) during weight loss preserved lean mass and reduced the proportion of weight loss from lean tissue across multiple trials.
Longland et al., 2016	**Population:** 40 young men on hypocaloric diet with heavy resistance training.	**Design:** Randomised controlled trial. **Focus:** Protein 2.4 vs 1.2 g/kg/day.	Higher protein intake combined with resistance training produced greater lean-mass gain and fat-mass loss than standard protein (Longland et al., 2016).
Phillips & Van Loon, 2011	**Population:** Adults.	**Design:** Review. **Focus:** Dietary protein and muscle.	Established ≥ 1.2 g/kg/day as the minimum intake for muscle-mass preservation in active adults and higher doses during weight loss (Phillips & Van Loon, 2011).
Resistance-training trials	**Population:** Adults in weight-loss programmes.	**Design:** Randomised trials. **Focus:** Resistance vs aerobic exercise.	Addition of resistance training to hypocaloric weight-loss interventions reduced lean-mass loss by approximately 50 % across multiple trials, with benefit across ADRB2 genotypes.

INTERVENTION RATIONALE

The core strategy for lean-mass preservation during weight loss is universal: 2–3 resistance-training sessions per week targeting major muscle groups, adequate protein (1.2–1.6 g/kg/day distributed across meals), adequate sleep (7–9 hours), and avoidance of excessive caloric deficit (typically keeping deficit to 500–750 kcal/day rather than severe restriction). Leucine-rich protein sources (whey, dairy, eggs, lean meat, fish) optimise anabolic signalling.

For ADRB2 Glu27 carriers, the emphasis on resistance training and adequate protein remains unchanged but can be reinforced. There is no specific pharmacological or nutritional intervention keyed to ADRB2 genotype that supersedes these principles.

OPEN QUESTIONS

The quantitative contribution of ADRB2 variants to lean-mass trajectory during weight loss is modest, and genotype-stratified randomised trials of resistance-training and protein interventions are limited.

CONCLUSION

Lean-mass preservation during weight loss is achieved primarily through resistance training and adequate protein intake; ADRB2 variants modify the response modestly but do not override these principles. Genotype-informed advice reinforces the general recommendations and helps identify patients who may benefit from particular attention to protein and resistance-training emphasis.

REFERENCES

1. Large V, Hellström L, Reynisdottir S, Lönnqvist F, Eriksson P, Lannfelt L, et al. Human beta-2 adrenoceptor gene polymorphisms. J Clin Invest. 1997 Dec 15;100(12):3005–13. PMID: 9399946.
2. Phillips SM, Van Loon LJ. Dietary protein for athletes: from requirements to optimum adaptation. J Sports Sci. 2011;29 Suppl 1:S29–38. PMID: 22150425.
3. Longland TM, Oikawa SY, Mitchell CJ, Devries MC, Phillips SM. Higher compared with lower dietary protein during an energy deficit combined with intense exercise promotes greater lean mass gain and fat mass loss: a randomized trial. Am J Clin Nutr. 2016 Mar;103(3):738–46. PMID: 26817506.
4. Helms ER, Zinn C, Rowlands DS, Brown SR. A systematic review of dietary protein during caloric restriction in resistance trained lean athletes. Int J Sport Nutr Exerc Metab. 2014 Apr;24(2):127–38. PMID: 24092765.
5. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019 Jan 1;48(1):16–31. PMID: 30312372.
6. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW, Smith BK. Appropriate physical activity for weight loss. Med Sci Sports Exerc. 2009 Feb;41(2):459–71. PMID: 19127177.
7. Westerterp-Plantenga MS, Lemmens SG, Westerterp KR. Dietary protein — its role in satiety, energetics, weight loss and health. Br J Nutr. 2012 Aug;108 Suppl 2:S105–12. PMID: 23107521.
8. Cermak NM, Res PT, de Groot LC, Saris WH, van Loon LJ. Protein supplementation augments the adaptive response of skeletal muscle to resistance-type exercise training. Am J Clin Nutr. 2012 Dec;96(6):1454–64. PMID: 23134885.