Irisin – a myokine potentially bridging muscle and fat tissue in cachexia

We read with great interest the recent article reporting muscle atrophy in heart failure animal models by Matsuo et al.¹ Cachexia is characterized by loss of muscle mass with or without fat mass.² Also, in patients with heart failure, muscle, fat and even bone loss were shown and reported to be associated with worse outcome.^{3,4} Although studies in muscle wasting attract much attention in heart failure,⁵ cross-talk among these three different tissues has been increasingly investigated and discussed⁶ as Matsuo et al. stated them in Introduction of this article.¹ Large number of muscle biomarkers are in development⁷⁻¹⁰ and mentioned in several issues of Journal of Cachexia, Sarcopenia and Muscle. Under these circumstances, myokines including irisin, myostatin, interleukin-6, follistatin, and so on, which are produced by muscle tissue and affect other organs, are highlighted as both biomarkers and hormonal substances, which may have therapeutic implication.¹¹ Irisin has been investigated as a key myokine, which has a bridging potential between muscle and fat.^{12,13} There are a number of articles reporting the plasma levels of irisin in patients with diabetes,¹⁴ chronic kidney disease,¹⁵ and myocardial infarction.¹⁶ However, there is almost no data about irisin levels in heart failure patients. In addition, recent reports have just been casting some doubt on the detection methods for human plasma irisin.^{17,18} In this context, further clinical studies in heart failure patients performed with improved assays are needed.

Acknowledgement

The authors certify that they have complied with the ethical guidelines for authorship and publishing of the

Journal of Cachexia, Sarcopenia and Muscle (von Haehling S, Morley JE, Coats AJS, Anker SD. Ethical guidelines for authorship and publishing in the Journal of Cachexia, Sarcopenia and Muscle. J Cachexia Sarcopenia Muscle. 2010;1:7–8).

Conflict of interest

Masaaki Konishi, Junichi Ishida, Masakazu Saito and Jochen Springer declare they have no conflicts of interest.

> Masaaki Konishi Institute of Innovative Clinical Trials

> Junichi Ishida Institute of Innovative Clinical Trials

> Masakazu Saito Institute of Innovative Clinical Trials

> > Jochen Springer

Institute of Innovative Clinical Trials Department of Cardiology and Pneumology, University Medical Centre Göttingen, Göttingen, Germany

References

- Matsuo Y, Gleitsmann K, Mangner N, Werner S, Fischer T, Bowen TS, et al. Fibronectin type III domain containing 5 expression in skeletal muscle in chronic heart failure-relevance of inflammatory cytokines. J Cachexia Sarcopenia Muscle 2015;6:62–72.
- Evans WJ, Morley JE, Argiles J, Bales C, Baracos V, Guttridge D, et al. Cachexia: a new definition. *Clin Nutr* 2008;27:793–799.
- von Haehling S, Lainscak M, Springer J, Anker SD. Cardiac cachexia: a systematic overview. *Pharmacol Ther* 2009;121: 227–252.
- von Haehling S. The wasting continuum in heart failure: from sarcopenia to cachexia. *Proc Nutr Soc* 2015;**12**:1–11.
- Josiak K, Jankowska EA, Piepoli MF, Banasiak W, Ponikowski P. Skeletal myopathy in patients with chronic heart failure: significance

of anabolic-androgenic hormones. *J Cachexia Sarcopenia Muscle* 2014;**5**:287–296.

- Loncar G, Fulster S, von Haehling S, Popovic V. Metabolism and the heart: an overview of muscle, fat, and bone metabolism in heart failure. *Int J Cardiol* 2013;**162**:77–85.
- Nedergaard A, Sun S, Karsdal MA, Henriksen K, Kjaer M, Lou Y, *et al.* Type VI collagen turnover-related peptides-novel serological

© 2015 The Authors. Journal of Cachexia, Sarcopenia and Muscle published by John Wiley & Sons Ltd on behalf of the Society of Sarcopenia, Cachexia and Wasting Disorders This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made. biomarkers of muscle mass and anabolic response to loading in young men. *J Cachexia Sarcopenia Muscle* 2013;**4**:267–275.

- Nedergaard A, Karsdal MA, Sun S, Henriksen K. Serological muscle loss biomarkers: an overview of current concepts and future possibilities. J Cachexia Sarcopenia Muscle 2013;4:1–17.
- Fragala MS, Jajtner AR, Beyer KS, Townsend JR, Emerson NS, Scanlon TC, et al. Biomarkers of muscle quality: Nterminal propeptide of type III procollagen and C-terminal agrin fragment responses to resistance exercise training in older adults. J Cachexia Sarcopenia Muscle 2014;5:139–148.
- Patel SS, Molnar MZ, Tayek JA, Ix JH, Noori N, Benner D, et al. Serum creatinine as a marker of muscle mass in chronic kidney

disease: results of a cross-sectional study and review of literature. *J Cachexia Sarcopenia Muscle* 2013;4:19–29.

- Basaria S, Bhasin S. Targeting the skeletal muscle-metabolism axis in prostate-cancer therapy. N Engl J Med 2012;367:965–967.
- Bostrom P, Wu J, Jedrychowski MP, Korde A, Ye L, Lo JC, *et al.* A PGC1-alpha-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. *Nature* 201226;**481**:463–468.
- 13. Pedersen BK. A muscular twist on the fate of fat. N Engl J Med 2012;**366**:1544–1545.
- Xiang L, Xiang G, Yue L, Zhang J, Zhao L. Circulating irisin levels are positively associated with endothelium-dependent vasodilation in newly diagnosed type 2 diabetic patients without clinical angiopathy. *Atherosclerosis* 2014;235:328–333.

- Ebert T, Focke D, Petroff D, Wurst U, Richter J, Bachmann A, *et al.* Serum levels of the myokine irisin in relation to metabolic and renal function. *Eur J Endocrinol* 2014;**170**:501–506.
- Emanuele E, Minoretti P, Pareja-Galeano H, Sanchis-Gomar F, Garatachea N, Lucia A. Serum irisin levels, precocious myocardial infarction, and healthy exceptional longevity. Am J Med 2014;127:888–890.
- Jedrychowski MP, Wrann CD, Paulo JA, Gerber KK, Szpyt J, Robinson MM, *et al.* Detection and Quantitation of Circulating Human Irisin by Tandem Mass Spectrometry. *Cell Metab* 2015;12: 00392–00397.
- Sanchis-Gomar F, Alis R, Lippi G. Circulating irisin detection: Does it really work? *Trends* in endocrinology and metabolism: *TEM* 2015;26:335–336.