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REPLY

Role of microRNAs in wasting in heart failure

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We thank Bei and Xiao for their Correspondence (MicroRNAs in muscle wasting and cachexia induced by heart failure. *Nat. Rev. Cardiol.* http://dx.doi.org/10.1038/nrcardio.2017.122; 2017)[1] on our Review (Muscle wasting and cachexia in heart failure: mechanisms and therapies. *Nat. Rev. Cardiol.* **14**, 323–341; 2017)[2]. Bei and Xiao raise an important issue in drawing our attention to microRNAs and their role in body wasting. Current understanding of microRNAs in regulation of skeletal muscle is limited, and most studies have been performed in the field of endurance and resistance exercise training[3]. Interestingly, microRNAs not only inhibit the insulin-like growth factor I (IGF1)–RACα serine/threonine-protein kinase (Akt)–mechanistic target of rapamycin (mTOR) pathway and induce the expression of E3 ligases in the context of muscle wasting, as mentioned by Bei and Xiao, but can also induce or regulate the expression of pro-inflammatory cytokines such as tumour necrosis factor ligand superfamily member 12 (TWEAK) and *vice versa*[4]. In addition, microRNAs negatively regulate myogenesis under catabolic conditions; for example, miR-1, miR-206, and miR-486 restrict satellite cell proliferation and promote differentiation of satellite cells by inhibition paired-box protein Pax-7 expression[5,6]. In cancer, microvesicles derived from tumour cells have been shown to induce apoptosis of skeletal muscle cells, which is caused by miR-21 that is contained in these vesicles and which activates Toll-like receptor 7 (encoded by *TLR7*), resulting in apoptosis[7]. Unfortunately, data on the regulation of muscle mass in patients with heart failure, or even heart diseases generally, remain scarce. However, we agree that microRNAs have enormous appeal as biomarkers of muscle wasting or adipose tissue wasting that might help in early identification and treatment of affected patients. This point is important, because no biomarkers are currently available that have both high sensitivity and high specificity for muscle wasting. Furthermore, weight changes help with the diagnosis only in cachexia, and not in muscle wasting without weight loss. C-terminal agrin fragment has been evaluated as a potential biomarker of muscle wasting in patients with chronic heart failure, but its specificity was low[8]. Many other biomarkers have been evaluated, but none has so far had sufficient sensitivity or specificity[9]. As our understanding of microRNAs develops, therapeutic interventions might be possible in this exciting field.

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Competing interests statement

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