The harder you run, the longer (and smoother) the road: exercise, muscle and ageing

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Advances in the understanding of the biological mechanisms that underpin the ageing process have enabled biogerontologists to identify a number of interventions that may potentially impact upon how we age. These interventions include the repurposing of established small molecules including metformin (Anisimov et al. 2015) and rapamycin (Wilkinson et al. 2012; Karunadharma et al. 2015) alongside newer agents including the ‘senolytic’ drugs (Zhu et al. 2015). These drug-based therapies extensive research into the role of nutrition in ageing has suggested that ‘you are what you eat’ may be a phrase that rings true in biogerontology. Whilst these advances in understanding have revolutionised how we view the biology of ageing, there is potentially even greater impact to be gained by better understanding the long established role that exercise has in promoting healthy ageing and longevity (van Saase et al. 1990; Booth et al. 2012).

In this special issue some of the latest knowledge about exercise, physical activity, muscle and ageing is

reviewed. Witard et al. (2016) present the latest, evidence-based recommendations for physical activity and exercise in older adults that may help preserve muscle mass and strength, highlighting the role that different types of exercise must have in any future recommendations for older adults. This is supported by McPhee et al. (2016) who describe how regular physical activity is safe for healthy and for even frail older people and the risks of developing major diseases of ageing are decreased by regularly completing activities ranging from low intensity walking through to more vigorous sports and resistance exercises. Piasecki et al. (2015) take an interesting position on loss of muscle function in ageing, focussing on motor neurons and how remodelling of surviving motor units constitutes the major change in ageing muscles, probably contributing to muscle loss and functional impairments. McLeod et al. (2016) continue the theme of the importance of muscle in ageing as they critique the current literature relating to the maintenance of muscle mass across lifespan, discussing whether maintaining or reducing protein synthesis is the most logical approach to support musculoskeletal function and extension healthy human ageing.

The role of muscle in healthy ageing and age-related decline is covered in many of the articles presented here. Hughes et al. (2015) present novel data that the ability of testosterone to improve myoblast differentiation and myotube hypertrophy occurs

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predominately via increases in androgen receptor and Akt abundance, identifying a molecular mechanism that may be of importance in regulating muscle mass in older adults. Sharples et al. (2015) further demonstrate that muscle cells have the capability of retaining an elevated methylation state for at least 30 cellular divisions after a single TNF- α challenge, identifying an epigenetic memory that may have functional implications. Tomlinson et al. (2015) review some of the functional limitations in muscle performance associated with obesity and in a related review Ikwuobe et al. (2016) propose innovative biomarkers for frailty in type 2 diabetes, including plasma bilirubin, plasma urinary DPP4-positive microparticles and plasma pigment epithelium-derived factor. A review article by Soriano-Aroquia et al. (2016) highlights the role of microRNA in muscle biology, including focus on miR-181a as a regulator of the sirt1 gene expression in skeletal muscle and evidence that miR-181a and its target gene are disrupted in skeletal muscle from old mice. Turner (2016) approaches exercise and ageing from a different perspective, reviewing evidence that exercise might elicit an ‘anti-immunosenescence’ effect, reporting observations that some forms of exercise are anti-inflammatory, and that repetition over the lifespan is associated with a lower morbidity and mortality from diseases with an immunological and inflammatory aetiology.

Whilst promoting exercise is one approach to increase physical activity and promote health-span, a second approach is to switch the focus onto the reduction of sedentary behaviour. Two review articles shine a light on the role that sedentary behaviour may have in ageing. Wullems et al. (2016) critique the evidence that sedentary behaviour has negative health implications for older adults whilst Perkin et al. (2015) introduce the concept that increased systemic inflammation and reduced protein synthetic responses to protein feeding and muscle contraction might influence the severity of muscle protein loss during periods of total unloading compared with younger individuals.

Finally Professor Janet Lord, Cohen Medal winner at the British Society for Research on Ageing 2015 annual scientific meeting, reviews the impact of ageing upon innate immunity to *Streptococcus pneumoniae*, as well as age-related changes to the serotypes present in the adult nasopharyngeal tract which could further influence susceptibility to infection (Gonçalves et al. 2015).

It is hoped that the reviews, and original papers, presented within this special issue will be of significant interest to biogerontologists. It is clear from this collection of articles that exercise is a powerful tool in the arsenal of those studying ageing, and that exercise physiology and biogerontology are fields that contain significant overlap. Indeed we postulate that collaborations between biogerontologists and exercise scientists may indeed provide the best blueprint for strategies to attenuate many age-related pathologies. As research increasingly elucidates the precise mechanisms that underlie exercise-induced changes in ageing cells, we can, as a integrative scientific community, ensure that the road we all run continues to get longer, healthier and happier.

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