The interconnectedness of ageing: does the convoy principal apply?

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The convoy principal states that any system is only as functional as its 'slowest' unit. As organisms are made up of interconnected networks of physiological systems, it is possible that this principle applies to the biology of ageing. Often biogerontology will focus either on organismal ageing (mechanisms associated with increased longevity of a lower model organism for example), ageing of an individual organ system (such as the cardiovascular/musculoskeletal/immune) or ageing at the cellular level (from telomere length to cellular senescence, with many different cell types being studied) without considering the interconnectedness between the three and importantly, between the separate units of the convoy; the different organs systems. Conceptually, research that aims to identify 'anti-ageing' therapies is often deemed to be reaching for a panacea that will arrest or slow down the ageing process as a whole, whereas the more realistic aim is to first identify how we can improve the performance of systems that are 'the slowest in the convoy'. This concept of improving the biological performance of individual ageing systems should be seen as achievable in the short term. Recent evidence on the use of rapamycin in improving the immune performance of older adults is an excellent case in point (Mannick, Del Giudice et al. 2014) and provides evidence of the first small steps towards an 'anti-ageing' drug in humans.

In this special issue the latest knowledge about ageing of several systems is reviewed. Cobley et al (Cobley, Moult et al. 2014) provide fascinating insight into how exercise can support muscle function in older adults in their review of mitochondrial responses to physical activity in ageing muscle, providing a potential mechanism for the protective effect of exercise training on age-related musculoskeletal decline. This is supported by the review from Pararasa et al (Pararasa, Bailey et al. 2014) describing evidence for the role of adipose tissue and circulating free fatty acids in the increased insulin resistance, cardiovascular disease risk and inflammation in older adults. In a related article describing the mechanisms behind regulation of longevity role by the C. elegans FOXO transcription factor ortholog DAF-16 (Tullet 2014). These articles collectively provide novel insight into the role that energy homeostasis has on ageing and longevity.

The interconnectedness of biological systems is key in maintaining normal function as we age. These connections can be physical or chemical and recent advances in the knowledge regarding extracellular vesicles and brain ageing are discussed (Smith, Leonardi et al. 2014). Additionally, the oft-ignored concept of circadian rhythm and ageing, specifically the most common joint disease of ageing osteoarthritis, is discussed here (Gossan, Boot-Handford et al. 2014) highlighting how

chondrocyte rhythm dampens with age and how clock gene expression changes during the initiation stage of osteoarthritis.

In two related articles the importance of normal intestinal function in ageing is examined. Firstly, the mucosal immune system provides the first line of defence against pathogens acquired by ingestion, but its function is reduced in the elderly. This immunosenescence is discussed here by Mabbott et al (Mabbott, Kobayashi et al. 2014) along with a discussion of the evidence for ageing-induced neuronal dysfunction that can lead to neurogenic forms of incontinence in the elderly from Ranson and Saffrey (Ranson and Saffrey 2015). The immune system in ageing is further discussed by Hazeldine et al (Hazeldine and Lord 2014) who discuss the role of the innate immune system in immunesenescence.

Finally, as such a proportionally large amount of ageing research is performed in animal models, Smithey et al (Smithey, Uhrlaub et al. 2014) discuss the difficulty in extrapolating data from these models to people using the example of the ageing immune system, reinforcing the important observation that when performing basic and translational science that mice are indeed not men!

It is hoped that readers will find the reviews in this special issue to be of interest. It is evident from all the contributions made here that whilst excellent progress is being made in the understanding of the ageing process in these interconnected systems, further research is needed to fully appreciate the mechanisms that underlie changes in function as we age and the way in which ageing can affect systems differentially. If the biogerontology community can identify interventions that can improve the 'slowest systems' in the convoy or even multiple systems at the same time then we will be one step closer to improving the ageing experience for all.

Cobley, J. N., P. R. Moult, et al. (2014). "Exercise improves mitochondrial and redox-regulated stress responses in the elderly: better late than never!" Biogerontology.

Gossan, N., R. Boot-Handford, et al. (2014). "Ageing and osteoarthritis: a circadian rhythm connection." Biogerontology.

Hazeldine, J. and J. M. Lord (2014). "Innate immunesenescence: underlying mechanisms and clinical relevance." Biogerontology.

Mabbott, N. A., A. Kobayashi, et al. (2014). "Aging and the mucosal immune system in the intestine." Biogerontology.

Mannick, J. B., G. Del Giudice, et al. (2014). "mTOR inhibition improves immune function in the elderly." Sci Transl Med **6**(268): 268ra179.

Pararasa, C., C. J. Bailey, et al. (2014). "Ageing, adipose tissue, fatty acids and inflammation." Biogerontology.

Ranson, R. N. and M. J. Saffrey (2015). "Neurogenic mechanisms in bladder and bowel ageing." Biogerontology.

Smith, J. A., T. Leonardi, et al. (2014). "Extracellular vesicles and their synthetic analogues in aging and age-associated brain diseases." Biogerontology.

Smithey, M. J., J. L. Uhrlaub, et al. (2014). "Lost in translation: mice, men and cutaneous immunity in old age." Biogerontology.

Tullet, J. M. (2014). "DAF-16 target identification in C. elegans: past, present and future." Biogerontology.