## Ageing muscles: biomarkers and exercise

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The precise reasons for the onset and progression of age-related loss of skeletal muscle mass and function, called sarcopenia, are unclear. Time course throughout rodent life implicate a combination of denervation of myofibres, changes in myofibre metabolism and altered extracellular matrix. These changes are initiated sometime between 15-24 months (m) of age in mice. Our time course study in female C57Bl mice (aged 3,15,24,27 and 29m) identified increased mRNAs of genes associated with denervation as useful molecular markers of sarcopenia: these provide convenient readouts to test the capacity of various interventions to prevent sarcopenia.

It is difficult to identify the precise onset of these changes in aging human muscles, where sarcopenia is evident from around 60 years and progresses over 20-30+ years. We have now analysed a panel of molecular biomarkers in 120 muscle biopsies from elderly male humans, aged >70 years, from the Hertfordshire sarcopenia study (UK) to test their association with the severity of sarcopenia. Exercise is one of the most effective interventions to help maintain healthy muscles, yet the molecular basis for these benefits on older muscles is not clear. Such information could form the basis for specific drug and nutritional interventions to target aspects of sarcopenia.

We have tested 3 different exercise regimes in ageing mice using voluntary wheel running, to determine the impact on sarcopenia and the molecular biomarkers: (i) life long exercise from 3m (with muscles samples at 18, 24 and 28m); (ii) late-life onset of resistance exercise from 21m (sampled at 24m); and (iii) mid-life onset of resistance exercise from 15m (sampled at 24m). The capacity of ageing mice to undertake such exercise, the resultant muscle mass and phenotype, and gene expression data are combined to assess the benefits of introducing such exercise regimes at different stages of life.