EDITORIAL

Aged Muscle

Although aging represents a fundamental biological process, the evolutionary role of senescence in nature is not understood [1]. Cellular aging triggers a progressive decline in the function of vital tissues and organs thereby disturbing overall body homeostasis. Some of the most striking features of the aging process are a depletion of lean body mass, the functional decline of the neuronal and muscular apparatus and a drastic decrease in an appropriate immune response to invading pathogens [2]. It is not clear what kind of molecular hierarchy exists within pathophysiological pathways leading to age-related abnormalities and what molecular and cellular alterations trigger secondary changes. The role of compensatory adaptations and repair mechanisms is not well understood. Most likely numerous cellular factors are involved in the complexity of the aging process. Recent studies suggest that the nutritional status [3] and extent of physical activity [4] may play a central role in delaying age-related diseases [5]. From a biomedical point of view, in order to better comprehend frailty and functional impairment in the elderly, it is essential to study the effects of aging both at the molecular and anatomical level. This may lead to the development of new treatment strategies to counter-act insufficient mobility, high susceptibility to chronic and infectious diseases and poor recovery after traumatic injury [6].

With respect to skeletal muscle fibres, the most common group of specialised tissues in the human body, age-associated alterations trigger the functional decline of fibres and an overall loss of muscle mass. The now generally accepted medical term for this phenomenon is sarcopenia [7]. The complete elucidation of the factors involved in sarcopenia will be an extremely difficult task, since skeletal muscle fibre type and tissue mass is modulated by various biological factors, including muscle loading, fuel supply, innervation pattern, fibre utilisation and capacity for cellular regeneration. Besides its central physiological role in the contraction-relaxation cycle, the muscle protein complement is a metabolically highly active component. Hence, a biochemical imbalance between the rates of protein synthesis and degradation has been implicated in the age-related loss of skeletal muscle mass [2, 5]. Research over the last decade has clearly shown that sarcopenia is the final result of a variety of molecular and cellular changes and involves loss of motor units, a shift to slower fibre types, progressive denervation, decreased protein synthesis of myofibrillar components, decreased capillarisation, abnormal ion homeostasis, mitochondrial alterations, oxidative stress, increased apoptosis, impaired metabolism and a progressive decline in energy intake, as well as an altered equilibrium of hormones and growth factors essential for the proper maintenance of skeletal muscle function [8].

This issue of Basic and Applied Myology contains two reviews discussing the involvement of denervation and excitation-contraction uncoupling in sarcopenia, and two research articles on the characterisation of satellite cells. The authors are partners in a research network on muscle ageing funded by the European Commission. Bruce Carlson points out the striking similarities of the effect of denervation on mammalian skeletal muscle as compared to the cellular processes that naturally occur during fibre aging. Hence, certain pathological changes that take place during normal aging may be attributable to primary abnormalities in the central and/or peripheral nervous system. In the most extreme case, motor axons completely degenerate during the normal aging process thereby eliminating the neuronal supply to skeletal muscle fibers causing muscle weakness. The review gives a comparative overview of the changes in denervated versus aged fibres on the cellular level, discusses the responsiveness of satellite cells and the role of cell and nuclear death, as well as describes the paradoxical feature of neo-myogenesis and crucial changes in gene expression. Michelle Ryan and Kay Ohlendieck review the potential involvement of excitation-contraction uncoupling in sarcopenia. Reduced levels of calcium ion supply to the contractile apparatus via excitation-contraction uncoupling may lead to muscle weakness associated with normal aging. It is proposed that impaired signal transduction at the triad junction is a result of a larger number of internal calcium release channels being uncoupled to the voltage-sensing receptor units of the fibre periphery. The review compares recent findings from the biochemical and physiological analysis of aged animal versus human muscles. The assumption that abnormal triadic signal transduction is

responsible for sarcopenia appears not to be completely transferable from animal models to senescent human muscle without modifications.

The two research papers associated with this issue focus on the analysis of satellite cells. This important group of muscle-precursor cells is responsible for fibre growth, cellular maintenance and repair of postnatal skeletal muscle following injury or disease-associated degeneration. Although during adult life the percentage of satellite cells remains relatively constant, most studies have shown that a drastic decrease in satellite cell numbers occurs during aging. Ida Erzen and colleagues examined the satellite cell frequency in cross-age transplanted rat EDL muscles. Their examination of the relative frequency of satellite cells in cross-age transplanted muscles showed a doubling of the satellite cell count and a higher incidence in old-into-young transplants. However, the influence of the host environment does not appear to be as influential on this property of the regenerated muscle as it is for certain other biological characteristics. Although the manuscript by Anton Wernig and co-workers did not directly analyse the responsiveness of satelitte cells in the ageing process, this paper represents a very important finding with respect to establishing M-cadherin as a reliable marker of quiescent satellite cells in mouse skeletal muscle fibres. There is an ongoing search for specific cellular markers for the proper identification of satellite cells by cell biologists. For ease of preparation, molecular markers detectable by light microscopy are the preferred markers. Satellite cells are involved in fibre growth, muscle maintenance, ageing and repair processes, making the establishment of a reliable marker a central issue in muscle biology. Their research shows that the calcium-dependent cell adhesion molecule is expressed in almost all satellite cells demonstrating that M-cadherin as a reliable marker of quiescent satellite cells.

The papers presented in this issue are a valuable contribution to the field of 'Muscle Aging' and may encourage young myologists to engage in studies analysing the age-related progressive decline in muscle that adversely affects muscle fibre structure, isoform expression patterns and the physiological control of the excitation-contraction-relaxation cycle.

References

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