Valorization

In almost every country, the proportion of people aged 60 y and over is increasing rapidly. Between 2015 and 2050, the proportion of the world’s population over 60 y will nearly double from 12 to 22%. The number of people aged 80 y and older is expected to rise from 125 million in 2015 to 434 million by 2050 (1). In the Netherlands, the total population will continue to grow over the next few decades to 18.1 million in 2060. The increase in population size is, at least partly, due to the increasing longevity. The current life expectancy is on average 80 and 83 y for boys and girls born in 2014, respectively. This life expectancy is predicted to increase by 7 years by 2060. The increasing life expectancy will contribute to the increase in the number of elderly individuals. The number of people aged over 65 years is expected to increase from 3.0 million in 2014 to 4.7 million in 2060. The number of people aged 80 years and older is expected to increase from 0.7 to 2 million in 2060 (2). The aging of the population can be seen as a success for public health policies and for socioeconomic development, but it also challenges society to improve health and functional capacity of older people and stimulate their social participation (1). Aging is accompanied by a decline in skeletal muscle mass, also known as sarcopenia. Loss of skeletal muscle mass may lead to a reduction in muscle strength and physical function, which increases the risk of falls and fractures. This could ultimately result in the loss of independence and an increase in nursing home admissions. Developing effective interventions to prevent or delay the onset of sarcopenia may reduce healthcare costs and improve the quality of life of older individuals.

In line with previous work, this dissertation provides further evidence that dietary protein intake directly stimulates muscle protein synthesis. In older individuals, the muscle protein synthetic response to protein intake is reduced (3), which may, at least partly, explain the age-related loss of skeletal muscle mass. The work presented in this dissertation used a novel stable isotope tracer methodology to assess certain aspects of postprandial protein handling in young and older individuals following various dietary interventions. We combined primed continuous intravenous infusions of stable isotope-labeled amino acid tracers with the ingestion of intrinsically labeled protein to assess dietary protein digestion and amino acid absorption kinetics, splanchnic amino acid retention, availability of dietary protein-derived amino acids in the circulation, basal and postprandial muscle protein synthesis rates, as well as the incorporation of dietary protein-derived amino acids into myofibrillar protein in vivo in humans (4). We demonstrate that dietary protein digestion and absorption may be impaired in the older population and that the postprandial increase in muscle protein synthesis is delayed in healthy older when compared with young men. These differences in postprandial protein handling may play important roles in the etiology of sarcopenia. We speculate that older people require more protein and/or higher quality protein to maximize postprandial muscle protein synthesis rates. Therefore, we studied dietary factors that may modulate the anabolic response to meal ingestion. Specifically, we investigated the role of carbohydrate and fat co-ingestion with protein, the impact of various dietary protein sources, and the relevance of habituation to a certain level of dietary protein intake. A better understanding of the various dietary factors that modulate the anabolic response to food intake enables us to develop dietary intervention strategies that maximize the postprandial muscle protein synthetic response and thereby compensate for the anabolic resistance with aging. The findings described in this dissertation provide the basis for defining alternative dietary intervention strategies that will help to preserve skeletal muscle mass in the older population.
Our diet provides protein from both animal-derived as well as plant-based protein sources. Though animal-derived proteins (e.g. dairy protein) are very potent in stimulating muscle protein synthesis, plant-based proteins are more cost-effective and sustainable, and may represent an alternative protein source for the stimulation of muscle protein synthesis rates. In this dissertation we demonstrate that the ingestion of wheat protein (one of the most predominant plant-based proteins in our diet) stimulates muscle protein synthesis provided that a relatively high dose of protein is consumed. The lower muscle protein synthetic response to lower doses of wheat protein might be due to a suboptimal amino acid profile of wheat protein, with a low lysine and leucine content in particular. We speculate that the combination of wheat protein and dairy protein may result in a protein blend with greater anabolic properties by providing a more preferred spectrum of essential and non-essential amino acids. These protein blends can contribute to the development of more sustainable and cost-effective nutritional strategies that support muscle mass preservation in people living in less privileged regions of the world.

Despite the necessity of studying the acute effects of various dietary factors on postprandial protein handling in controlled laboratory conditions, these findings need to be confirmed in more practical or applied settings. Recent advances in the field of muscle physiology introduced the use of deuterium-labeled water to assess muscle protein synthesis over days to weeks under free-living conditions. Studies using this methodology will be next to evaluate whether dietary strategies that apply the current findings can help to preserve muscle mass in the older population. It can be challenging to successfully implement such dietary intervention strategies into practice. To achieve such knowledge translation, a more interdisciplinary approach between scientists in the field of human nutrition and physiology, behavioral scientists, clinicians, and health care professionals should be pursued. The findings from ‘small’ experimental studies as presented in this dissertation need to be translated into larger cohort studies to evaluate the feasibility, applicability, and efficacy of changing food intake strategies to support muscle mass preservation in daily life. The research described in this dissertation defines the impact of a few dietary components that modulate the postprandial muscle protein synthetic response to meal ingestion. These findings can directly be applied to change food and food products as well as design more effective clinical nutrition products that should be part of dietary interventions to preserve muscle mass and prevent sarcopenia in both health and disease.

Consequently, the presented data provide many leads and targets for product development and innovations in the nutrition industry. Nutrition companies aim to improve current product formulations and/or develop new products or concepts to support healthy aging. Results from this dissertation provide clear insights on macronutrient composition and protein sources that need to be applied in the development or improvement of novel product formulations to maximally stimulate muscle protein synthesis and, as such, assist in the various strategies to combat the loss of skeletal muscle mass with aging. For example, we show that co-ingesting carbohydrate or fat with protein does not further improve the postprandial muscle protein synthetic response to protein intake. Clinical nutrition products generally contain a combination of all three macronutrients. We suggest that more protein-dense clinical nutrition products with lower amounts of carbohydrate and fat are preferred in interventional strategies aiming to preserve skeletal muscle mass where protein malnutrition is the main concern. Preservation of skeletal muscle mass is of major importance from a societal perspective regarding the quality of life of the individual, but also from an economic perspective regarding the enormous health care costs associated with sarcopenia. Besides the aging population, the results from this dissertation may be translated to other clinical conditions where progressive skeletal muscle mass loss is observed.
Cancer cachexia, chronic obstructive pulmonary disease (COPD), renal insufficiency, cardiovascular disease, and diabetes generally lead to a condition that resembles a state of accelerated aging. As strength and muscle loss seem to be accelerated in these more clinically compromised populations, it is evident that nutritional strategies should focus both on the prevention as well as treatment of muscle loss.

As individual scientists, we all work on just one piece of the puzzle. However, combining the knowledge gained from multiple studies conducted by different laboratories over the world within various fields of research will allow us to define (more) effective and sustainable dietary and physical activity intervention strategies to combat the age-related loss of skeletal muscle mass and strength and, as such, support healthy aging.

**References**