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Nutrition in cancer patients with cachexia: A role for the gut microbiota?

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SUMMARY

Cachexia is a multifactorial syndrome that includes muscle wasting and inflammation, and that is associated with chronic underlying diseases, such as cancer, chronic heart failure and chronic kidney disease. Since gut microbes influence host immunity and metabolism, we hypothesized a few years ago that the gut microbiota could be a potential therapeutic target to tackle cancer-related cachexia. In this review, we present evidence from animal and human studies suggesting that the gut microbiota and its crosstalk with the intestine might constitute unexpected targets in the therapeutic management of cancer and related cachexia. Finally, we discuss future research directions and hypotheses to progress in this new promising field, i.e. the role of the gut microbiota in cancer cachexia.

Abbreviations: CHF, chronic heart failure; CKD, chronic kidney disease; LPS, lipopolysaccharides; POS, pectic oligosaccharides; TLR, toll-like receptor.

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1. Introduction

Cachexia is defined as a multifactorial syndrome characterized by an ongoing loss of skeletal muscle mass (with or without fat mass loss), that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment [1]. This metabolic syndrome has been reported in patients with cancer, chronic heart failure (CHF), chronic kidney disease (CKD), chronic obstructive pulmonary disease and chronic sepsis [2]. Its prevalence ranges from 5 to 15% in end-stage CHF to 50–80% in advanced cancer [3]. In 2011, a panel of experts proposed to use the following criteria to diagnose cachexia: a weight loss greater than 5%, a weight loss greater than 2% in individuals already showing depletion according to current bodyweight and height (body mass index <20 kg/m^2), or skeletal muscle mass (sarcopenia) [1]. Combined weight loss and cachexia reduce tolerance to cancer treatment as well as the likelihood of response, and they both independently predict poor outcome [4]. It has been estimated that cancer-related cachexia could account for up to 20% of cancer deaths [5]. In addition to reducing length of life, cancer cachexia decreases the quality of life [6] and constitutes a not inconsiderable economical and health burden: the annual prevalence of cachexia in US community hospitals was recently estimated at over 160,000 cases [3].

Cachexia is a multifactorial syndrome resulting from the interaction of several pathological processes. Inflammation and metabolites generated directly by the tumour - or released by the body due to the presence of the tumour - alter host metabolism, leading to muscle atrophy, fat mass loss and in some cases insulin resistance. Reduced food intake and physical activity further contribute to the cachectic phenotype (Fig. 1) (for review on the aetiology of cachexia, see [2,5,7]).

Cachexia remains an often-neglected medical issue for which a clear therapeutic strategy is lacking. A multimodal approach is currently considered the best option to tackle cancer cachexia. This approach would combine nutritional support with anti-inflammatory/anti-atrophy drugs or nutrients and physical activity [7]. Several drug candidates are now under consideration to treat cachexia and associated muscle wasting, such as anamorelin (an oral ghrelin-receptor agonist with appetite-

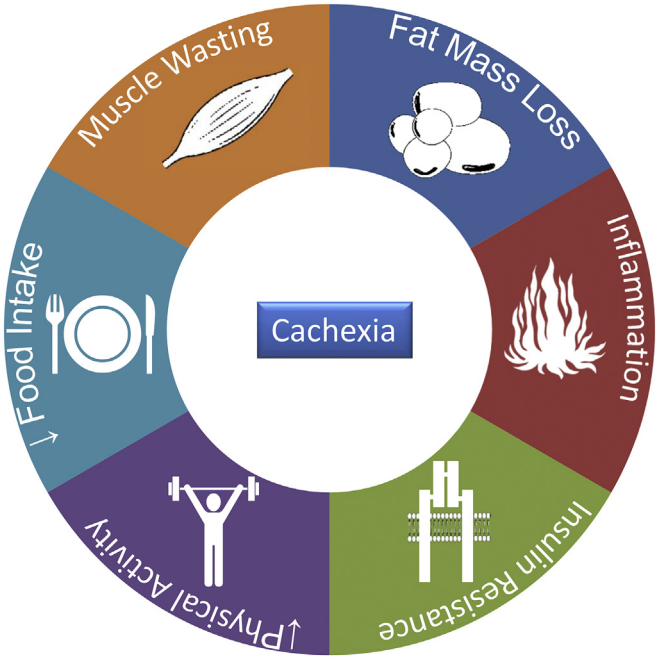

Fig. 1. Components of the cachexia syndrome. Diagram inspired from the hallmarks of cancer, Hanahan and Weinberg [53].