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A probiotic capable to reduce sarcopenia in undernourished elderly, results from a pre-clinical study

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Backgrounds

In 2050, older adults (65+) will reach 20% of world population with sarcopenic individuals representing a third of them. Specific nutritional strategies based on proteins coupled or not with exercise have shown some beneficial effects to limit sarcopenia but depending of the physio-pathological state, they may not be optimal or not applicable in case of poor appetite or disabilities to perform exercise.

Objectives

Hence, complementary strategies independent of food intake need to be developed to limit sarcopenia. We recently observed on small intestine-resected patients a specific microbiota with a tremendous increase in *Lactobacilli* [1]. Following the transfer of this specific microbiota in axenic rats [2], we showed an improved energy metabolism regulation which could be an adaptation of the gut physiology and metabolism to optimize the challenged utilization of nutrients in those patients. We hypothesized that this microbiota could be of interest to optimize energy utilization in malnourished frail elderly and then to limit sarcopenia.

Methods

From feces of these patients, specific strains were selected on their capacity to preserve *Caenorhabditis elegans* survival and muscle integrity. *Lactocaseibacillus casei* CNCM I-5663 (LC-63) were then tested in old rats (18 months, n=25 per group) under moderate food restriction for 4 weeks (75% of *ad libitum* (AL group)) to experimentally mimic the development of sarcopenia with malnutrition. Body composition, muscle mass, and insulin sensitivity (OGTT, HOMA-IR, insulin signaling pathway in muscle) were assessed.

Results

Moderate food restriction induced a decrease in muscle mass (-10%, p <0.05, R *vs* AL) but concomitant daily intake of LC-63 (~10⁹ CFU) minimized the loss of lean mass (-51%, p<0.05, R+63 *vs* R) and the muscle protein content (-12%, p<0.05, R+63 *vs* R). An improvement in overall insulin sensitivity was

also observed in the R+63 group at whole body level and at the muscle level suggested by the 73% increased p-S6/S6 ratio ($p < 0.05$, R+63 *vs* R).

Conclusion

We observed the existence of a microbiota-gut-muscle crosstalk that could be modulated positively by LC-63 and then represents an interesting complementary approach to limit sarcopenia in the elderly. The inter-organ signals involved and the mechanisms involved in both insulin sensitivity and on muscle protein preservation remain to be determined.

1. Joly, F.; Mayeur, C.; Bruneau, A.; Noordine, M.-L.; Meylheuc, T.; Langella, P.; Messing, B.; Duée, P.-H.; Cherbuy, C.; Thomas, M. Drastic Changes in Fecal and Mucosa-Associated Microbiota in Adult Patients with Short Bowel Syndrome. *Biochimie* **2010**, *92*, 753–761, doi:10.1016/j.biochi.2010.02.015.
2. Gillard, L.; Mayeur, C.; Robert, V.; Pinget, I.; Le Beyec, J.; Bado, A.; Lepage, P.; Thomas, M.; Joly, F. Microbiota Is Involved in Post-Resection Adaptation in Humans with Short Bowel Syndrome. *Front. Physiol.* **2017**, *8*, doi:10.3389/fphys.2017.00224.