P33 & FP – **Age-dependent effect of whey protein on body weight, lipid metabolism and gut microbiota in high-fat diet fed mice**

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Background: Whey proteins are present in the serum during milk manufacture. They are considered as a dietary solution to the obesity problem thanks to their beneficial effect on energy balance and lipid metabolism [1]. However, the mechanism of action of these proteins is poorly understood.

Objective: Determine the impact of duration of WPI intake on intestinal mechanisms and adipose tissue metabolism related to energy balance.

Methodology: Three-week-old C57BL/6J mice were housed four per cage and were divided into 6 groups. Groups 1 (n=16) and 2 (n=16) were provided with 45% energy high fat diet containing 20% whey protein isolate (HFD-WPI) or casein (HFD-CAS), respectively, for 5 weeks. Groups 3 (n=16) and 4 (n=16) were provided with 10% energy low fat diet containing 20% WPI (LFD-WPI) or CAS (LFD-CAS), respectively, for 5 weeks and then their diets were switched from LFD to HFD for another 5 weeks (tot=10 weeks) (HFD-Later WPI and HFD-Later CAS groups). The control groups, 5 (n=8) and 6 (n=8), received LFD-WPI and LFD-CAS, respectively, for 10 weeks. During the trial, body weight and energy intake were recorded weekly. At 5 and 10 week time points, faecal samples were collected and organs were harvested to carry out shotgun metagenomic analysis and gene expression using qPCR (ileum, liver and adipose tissue).

Results: The HFD-WPI group showed a significant decrease in body weight compared to the HFD-CAS group, after 5 weeks. Conversely, no differences in body weight were observed between the HFD-Later CAS and WPI groups. Despite this, both HFD-WPI and HFD-Later WPI fed mice intake significantly more energy than the respective HFD-CAS groups.

In the epididymal adipose tissue, we observed a decrease in expression of the gene encoding for leptin (ob) and an increase in the expression of two genes involved in fatty acids β-oxidation (*cpt1a* and *ucp2*) in the HFD-WPI group, relative to the HFD-CAS group. These differences did not persist In the HFD-Later groups.

From the shotgun metagenomic analysis, higher proportions of *Lactobacillus*, and the related species *Lactobacillus murinus*, were evident in the HFD-WPI fed mice compared to the HFD-CAS groups. Again, this difference was no longer observed in the HFD-Later groups.

Conclusions / Implications for practice: These results suggest that the effect of whey proteins on body weight, adipose tissue and intestinal related mechanisms depend on the stage of life of the mice and on diet duration. Whey proteins influence the gut microbiota composition, which might orchestrate the observed metabolic and physiological modification.

References

1. McAllan, L., P. D Cotter, and H. M Roche, *Bioactivity in Whey Proteins Influencing Energy Balance*. Journal of Metabolic Syndrome, 2012. 01(02).