ANALYSIS OF FECAL MICROBIOTA AND THE EXPRESSION OF GENES RELATED TO HUMAN METABOLIC SYNDROME IN ANIMAL MODELS

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INTRODUCTION

The gut microbiota plays an important role in metabolic homeostasis and epigenetic regulation and may be related to the development of diseases such as metabolic syndrome (MetS) and obesity[1].

AIMS

To identify genetic variants associated with obesity in the South Brazilian Mennonite population and to evaluate their gene expression in animal models, as well as regarding the intestinal microbiota and in adipose tissue.

METHODS

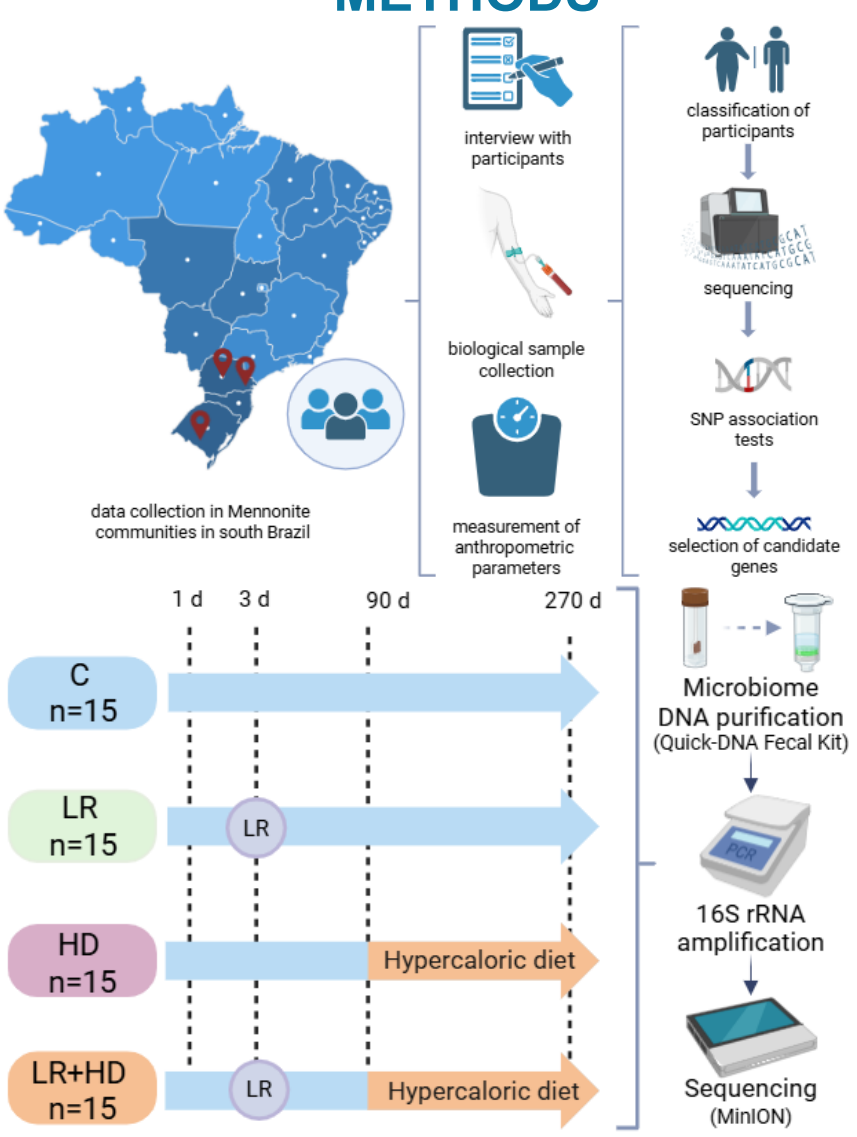

Figure 1: Data collection and subsequent analyses in the Mennonite population. Concurrently, male Wistar rats were divided into control (C), litter reduction (LR), high-calorie diet (HD), and combined LR+HD groups. Research approved by CAAE 55297916.6.0000.0102 and CEUA (1513/2023).

RESULTS AND DISCUSSION

Gene	N.Marker.All	N.Marker.Test	N.Marker.Rare	N.Marker.Common	pcorr[1]	pcorr[3]
ZGLP1	4	4	0	4	**0.0018**	**0.0018**
TAS2R4	6	3	0	3	**0.003**	**0.0059**
MESP1	10	9	0	9	**0.0044**	**0.013**
ATP23	7	6	0	6	**0.011**	**0.045**
ATOH1	5	4	0	4	**0.047**	0.23
KRT5	12	12	6	6	**0.0034**	**0.0034**
FANK1	20	19	8	11	**0.015**	**0.046**
FADS3	13	12	4	8	**0.015**	0.082
TAS2R3	7	7	3	4	**0.015**	0.084
SSBP1	21	18	9	9	**0.015**	0.092
CTBP1	43	36	19	17	**0.025**	0.18
ENDOV	19	17	8	9	**0.03**	0.24
DGKG	67	54	21	33	**0.035**	0.31

Table 1: Association between gene polymorphisms and obesity in the Mennonite population.
pcorr[1] = corrected by the FDR; pcorr[3] = corrected by the Bonferroni N.Marker.All = total number of available variants; N.Marker.Test = total number of variants used for gene association; N.Marker.Rare = total number of rare variants; N.Marker.Common = total number of common variants.

After genetic association analyses and subsequent filtering methods, 34 genes were associated with MetS and 95 genes with obesity (13 after SKAT analyses) (table 1).

LR+HD presented the highest percentage of retroperitoneal and mesenteric fat among the groups, followed by HD and LR (figure 2).

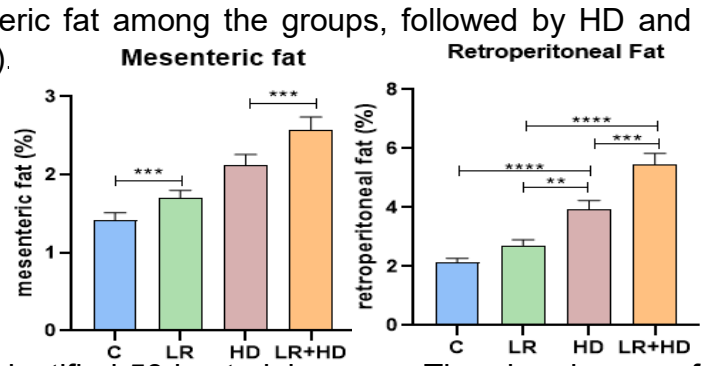

Figure 2: Fat percentage between groups

In total we identified 58 bacterial genera. The abundances of certain bacterial genera differed between the groups (table 2 and figure 3).

	Mean (%)			pcorr (FDR)		
Genera	C	HD	LR	C vs HD	C vs LR	HD vs LR
Prevotella	3.07	0	0.0	0,02*	0,01*	>0,99
Limosilactobacillu	4.47	0	4.17	0,02*	0.91	0,02*
Lactobacillus	19.91	0	23.00	0,008**	0.91	0,008**
Ligilactobacillus	6.84	0	11.64	0.09	0.31	0,02*
Marvinbryantia	2.42	0	0.0	0,03*	0,03*	>0,99
Clostridium	0.77	11.69	0.0	0,002**	0.47	0,0006***
Blautia	2.29	22.50	5.30	0,005**	0.3	0,03*

Table 2: Comparison of means between groups.

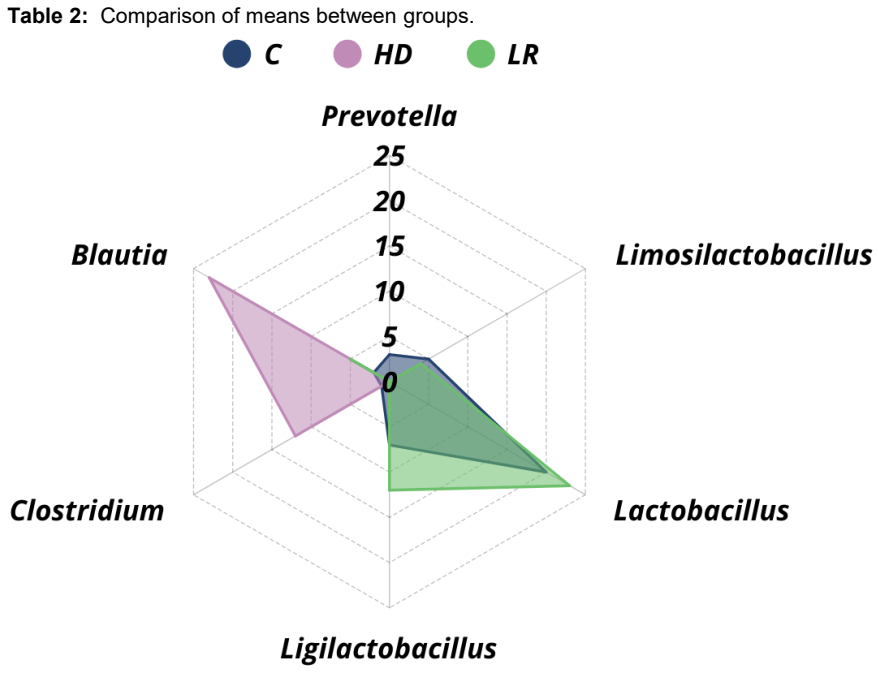

Figure 3: Radar graph representing the difference in abundance of genera. control (C), litter reduction (LR), high-calorie diet (HD).

While *Blautia sp*. have an ambiguous correlation with obesity[2], species of the genera *Lactobacillus, Ligilactobacillus* and *Lomosilactobacillus* (reduced in the HD group, possibly because of the diet) are known as probiotics and may be used to prevent obesity[3].

DISCUSSION AND CONCLUSION

Early metabolic programming increased adiposity, followed in parallel by significant changes in the bacterial microbiome. These components may affect host gene expression through microbiota-induced epigenetic changes, causing obesity. The expression of genes with variants associated with human obesity will also be assessed in animal tissues, allowing the evaluation of their function across different contexts.

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REFERENCES:
1- Lee CJ, Sears CL, Maruthur N. Gut microbiome and its role in obesity and insulin resistance. Ann N Y Acad Sci. 2020. 2- Chanda W, Jiang H, Liu SJ. The Ambiguous Correlation of Blautia with Obesity: A Systematic Review. Microorganisms. 2024. 3- Song W, Song C, Li L, Wang T, Hu J, Zhu L, Yue T. Lactobacillus alleviated obesity induced by high-fat diet in mice. J Food Sci. 2021.