1520100 - **Composition of Dietary Fat Source Shapes Gut Microbiota Architecture and Alters Host Inflammatory Mediators in Mouse Adipose Tissue**

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Background: A rapidly emerging area of study is the role of the commensal gut microbiota in the progression of obesity and inflammation. The use of germ-free mice has demonstrated a direct link between the consumption of a high-fat diet, the intestinal microbes, and adiposity. Studies have also shown that dietary factors dramatically alter the microbial architecture within the host. Previous work has suggested that mesenteric adipose tissue, due to its close proximity to the portal vein, possesses substantial pro-inflammatory potential. Moreover, these depots are situated adjacent to the intestine suggesting an inherent reciprocity between commensal microbes and mesenteric-derived adipokines. However, this relationship has not been well characterized. Since gut microbiota have a direct effect on host metabolism, it is of significant interest to define a precise mechanism linking diet-induced obesity, inflammation, and the gut microbiota. We sought to address two key areas of study: 1) How dietary fat consumption and fat source, particularly high saturated (SFA) and polyunsaturated (PUFA) fat, shapes the intestinal microbiota, and 2) To identify how observed perturbations in the microbiota due to dietary fat source are reflected in host adipose tissue-mediated inflammation.

Methods: Adult male C57Bl/6 mice were fed milk fat-, lard- (SFA sources), or safflower oil (PUFA)- based high fat diets for four weeks. Body mass, food consumption, and stool samples were collected throughout the study. Bacterial 16S rRNA was isolated and analyzed via T-RFLP; bacterial DNA sequencing libraries were run through massive parallel sequencing (HiSeq). In addition, mesenteric and gonadal adipose depots were excised and analyzed for both lipogenic and inflammatory gene expression via qRT-PCR.

Results: Mice fed high-fat diets gained more weight with a concomitant increase in caloric consumption relative to low-fat diet controls. Additionally, consumption of high-fat diets was associated with a dramatic shift in gut microbiota phyla architecture and stratified based on the specific source of dietary fat (Figure 1). These changes also led to significant differential

expression of inflammatory markers (e.g. MCP-1, CD192, resistin, LPL) in mesenteric and gonadal fat depots (Table 1).

Conclusions: These initial findings support the notion that dietary fat composition can both shape the dynamics of structure of gut microbiota as well as alter host adipose tissue-mediated inflammation. Germ-free studies are currently underway to define the direct and indirect roles of gut microbiota induced by specific dietary fat source. Collectively, results from this study may delineate a potential mechanism by which dietary fat, inflammation, and the commensal gut microbiota are intertwined.

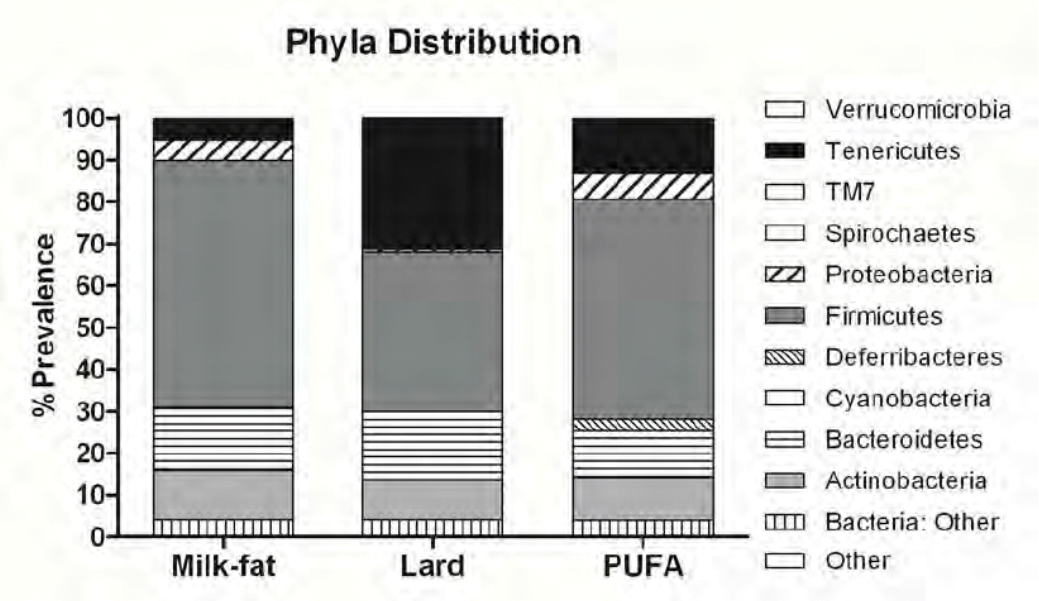

Figure 1. Average phyla distribution of microbiota after high-fat feeding.

Table 1. Gene expression levels of inflammatory markers in mesenteric and gonadal adipose tissues.

Inflammatory Gene Expression (relative to B-actin)	Tissue type	Milk-fat	Lard	PUFA	Low-fat Control	*P-value*
MCP-1	Mesenteric adipose ± SEM	5.11E-03[a] 1.10E-03	9.80E-03[b] 7.52E-03[a]	1.12E-02[b] 1.61E-02[b]	3.07E-03[a] 7.25E-03[a]	*P < 0.01* *P < 0.001*
	Gonadal adipose ± SEM	5.37E-04 6.20E-03[a] 5.45E-04	8.88E-04	7.73E-04 1.52E-03	7.24E-05 2.63E-04	
CD192	Mesenteric adipose ±	5.38E-04[a] 5.03E-05	5.22E-04[a] 3.76E-05	6.53E-04[a] 2.08E-05	2.77E-04[b] 1.95E-05	*P < 0.01*

	SEM Gonadal adipose ± SEM	7.12E-04[a] 3.50E-05	5.00E-04[a] 4.96E-05	1.29E-03[b] 1.13E-04	5.45E-04[a] 2.14E-05	*P < 0.001*
Resistin	Mesenteric adipose ± SEM Gonadal adipose ± SEM	2.80E+00[a] 3.04E-01 6.70E+00[a] 4.33E-01	1.79E+00[a] 3.79E-01 6.28E+00[a] 8.91E-01	4.36E+00[b] 4.58E-01 4.84E+00[a] 3.41E-01	1.01E+00[c] 7.74E-02 3.19E+00[b] 9.97E-02	*P < 0.05* *P < 0.001*
LPL	Mesenteric adipose ± SEM Gonadal adipose ± SEM	2.25E+00[a] 2.45E-01 5.81E+00[a] 4.84E-01	1.30E+00[a] 1.27E-01 5.42E+00[a] 8.42E-01	3.28E+00[b] 4.06E-01 3.42E+00[b] 3.02E-01	9.71E-01[a] 4.78E-02 3.27E+00[b] 7.50E-02	*P < 0.01* *P < 0.01*