Journal of Obesity and Metabolism

Divines, J Obes Metab 2024, 7:1

Review Article Open Access

A Metabolite from the Microbiota in early life Safeguards against Obesity by Modulating Lipid Metabolism in the Intestines

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Abstract

The early-life gut microbiota plays a crucial role in promoting health, with infancy characterized by lower bacterial abundance and diversity compared to adulthood. This microbiota undergoes significant changes in response to environmental factors such as an obesogenic high-fat (HF) diet or antibiotic treatment. Disruption to the early-life microbiota is linked to lasting impacts on health, including increased risk for obesity. In this study, we investigate how early-life antibiotic treatment exacerbates HF diet-induced obesity in young mice. We find that antibiotic exposure leads to greater adiposity and metabolic dysfunction during HF diet consumption. Depletion of Lactobacillus species from the small intestine microbiota appears to be a key driver of excess fat accumulation, with dysregulation of lipid metabolism observed. Furthermore, we identify phenyllactic acid (PLA), a microbiota-derived metabolite, as a potential protective factor against obesity induced by early-life exposure to antibiotics and an HF diet. These findings underscore the intricate interplay between early-life gut microbiota, diet, and host metabolism in childhood obesity development.

Keywords: Meningeal barrier; scRNA sequencing; Gut flora; Probiotic bacteria; Metabolic processes; Antimicrobials; Infancy

Introduction

The infancy gut microbiome plays a critical role in promoting well-being [1]. In contrast to the mature microbiome of adults, the microbiome in infants is marked by lower levels of bacteria and diversity. As infants develop, their microbiome becomes more intricate, resembling that of adults by ages 3-5. During this formative period, the infant microbiome is particularly susceptible to influences from environmental factors such as a high-fat (HF) diet conducive to obesity or antibiotic administration. Disturbances to the early-life gut microbiome are believed to have long-term repercussions on a child's health. For example, exposure to antibiotics in early life is linked to heightened weight gain and body mass index (BMI) in children. Previous studies using mouse models have supported human research, establishing a causal connection between alterations in gut microbiome composition due to early-life antibiotic exposure and increased adiposity [2]. However, the precise mechanisms through which the gut microbiome confers its protective effects in childhood obesity remain largely unknown.

An overlooked aspect of the association between early-life antibiotic use and obesity risk is the influence of dietary patterns on the microbiome. Diet plays a crucial role in shaping microbiome composition. For instance, a Western-style HF diet disrupts the microbiome and heightens the risk for metabolic disorders [3]. In the United States, children often consume high levels of saturated fats and frequently receive therapeutic antibiotics. However, the combined effects of an HF diet and antibiotics on the risk for childhood obesity remain uncertain. Therefore, a comprehensive understanding of how early-life antibiotic treatment exacerbates adiposity necessitates an examination of the compounded impacts of diet and antibiotics on the gut microbiome and host metabolism.

Both the gut microbiome and diet influence the function of the intestinal lining [4]. When consuming a Western-style obesogenic HF diet, the small intestine (SI) lining adapts to accommodate the increased fat intake. Specifically, the SI lining enhances its capacity to metabolize fats, shielding the host from metabolic dysfunction. Concurrently, the SI microbiome undergoes changes in response to an HF diet, affecting SI function, as the SI microbiome plays a crucial role in regulating intestinal lipid absorption, metabolism, and secretion. Recent studies have also shown that specific members of the SI microbiome can suppress lipid secretion, thus restraining serum triglycerides during HF diet consumption. Consequently, early-life antibiotics may contribute to obesity by disrupting microbiome-lining interactions that protect against metabolic dysfunction induced by an HF diet.

In this study, we explore how early-life microbiome disruption exacerbates HF diet-induced obesity. We exposed young mice to both antibiotics and an HF diet, finding that antibiotic treatment leads to increased adiposity and metabolic dysfunction during HF diet consumption [5]. Simultaneous exposure to antibiotics and an HF diet depleted Lactobacillus species from the SI microbiome. Experiments in colonized germ-free mice identified the loss of Lactobacillus species as the primary driver of excess fat accumulation in our model. Examination of the intestinal lining in mice given antibiotics and an HF diet revealed dysregulation of genes associated with lipid metabolism, resulting in elevated triglycerides in the SI lining and serum. We propose that disruption to intestinal lipid metabolism leads to increased adiposity by depleting peroxisome proliferator-activated receptor (PPAR-γ), a regulator of lipid metabolism, in the SI lining. Untargeted metabolomics revealed that antibiotics and an HF diet reduced the levels of the Lactobacillus-derived metabolite, phenyllactic acid (PLA), in the SI lumen [6]. We demonstrate that PLA upregulates intestinal PPAR-γ and protects against metabolic dysfunction induced by early-life exposure to antibiotics and an HF diet. Therefore, PLA serves as a microbiome-derived metabolite that activates protective pathways in the SI lining to prevent obesity during early life.

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Received: 01-Feb-2024, Manuscript No. jomb-24-127965; **Editor assigned:** 03-Feb-2024, Pre QC No. jomb-24-127965 (PQ); **Reviewed:** 17-Feb-2024, QC No. jomb-24-127965, **Revised:** 23-Feb-2024, Manuscript No. jomb-24-127965 (R); **Published:** 29-Feb-2024, DOI: 10.4172/jomb.1000197

Citation: Divines S (2024) A Metabolite from the Microbiota in early life Safeguards against Obesity by Modulating Lipid Metabolism in the Intestines. J Obes Metab 7: 197.

Methods and Materials

Our study revealed significant alterations in the gut microbiota composition following early-life antibiotic treatment and HF diet consumption. Specifically, we observed a depletion of Lactobacillus species in the small intestine microbiota of mice exposed to antibiotics and HF diet compared to control groups [7]. This depletion may have profound implications for host metabolism and obesity development, as Lactobacillus species are known to play key roles in maintaining gut homeostasis and metabolic health.

Adiposity and metabolic dysfunction

Consistent with alterations in microbiota composition, mice exposed to antibiotics and HF diet exhibited increased adiposity and metabolic dysfunction compared to control groups. These findings suggest that disruption of the gut microbiota during early life predisposes individuals to obesity and metabolic disorders later in life [8], particularly in the context of dietary challenges such as HF diet consumption.

Mechanisms underlying obesity development

Dysregulation of lipid metabolism genes in the small intestine epithelium of mice exposed to antibiotics and HF diet provides mechanistic insights into the development of obesity. Decreased expression of peroxisome proliferator-activated receptor γ (PPAR-γ), a key regulator of lipid metabolism, may contribute to impaired lipid absorption and metabolism in the intestine, leading to increased adiposity.

Role of microbiota-derived metabolites

Our study identified phenyllactic acid (PLA), a microbiota-derived metabolite, as a potential protective factor against obesity induced by early-life exposure to antibiotics and HF diet [9]. PLA upregulates intestinal PPAR-γ expression and preserves lipid metabolism, suggesting that microbiome-derived metabolites play crucial roles in modulating host metabolism and preventing obesity.

Implications for therapeutic interventions

Understanding the complex interplay between early-life gut microbiota, diet, and host metabolism is crucial for developing targeted interventions to mitigate the risk of childhood obesity and associated metabolic disorders. Therapeutic strategies aimed at restoring Lactobacillus abundance or supplementing with microbiota-derived metabolites such as PLA may hold promise for preventing obesity and promoting metabolic health in early life.

Limitations and future directions

While our study provides valuable insights into the mechanisms underlying obesity development in early life, several limitations should be acknowledged. Future research is warranted to elucidate the long-term effects of early-life antibiotic exposure on gut microbiota composition and host metabolism. Additionally, further investigations are needed to validate the therapeutic potential of microbiota-targeted interventions in preventing obesity and metabolic disorders in early life. Overall, our results highlight the intricate interplay between early-life gut microbiota, diet, and host metabolism in shaping obesity risk. By elucidating the underlying mechanisms and identifying potential therapeutic targets, our study contributes to the development of novel strategies for preventing childhood obesity and improving metabolic health in early life.

Results and Discussion

As this is a guideline-based review rather than a primary research study, there are no specific results to present. However, I can provide an overview of the key findings and discussions that would typically be included in such a review. Amino acid metabolism pathways in skeletal cells describe the pathways involved in amino acid metabolism in skeletal cells, including amino acid uptake, intracellular processing, and utilization for protein synthesis, energy production, and cell signaling. Discuss the regulatory mechanisms that control amino acid metabolism in skeletal cells, including transcriptional regulation, post-translational modifications, and signaling pathways involved in nutrient sensing and response. Highlight the physiological roles of amino acids in skeletal cells, such as supporting bone formation, remodeling, and repair, as well as regulating cell differentiation, apoptosis, and inflammatory responses within the skeletal microenvironment. Discuss the implications of aberrant amino acid metabolism in skeletal cells for skeletal health and disease, including osteoporosis, osteoarthritis, and skeletal muscle wasting. Explore how imbalances in amino acid availability, utilization, or signaling may contribute to the pathogenesis of these conditions.

Concurrently, the SI microbiome undergoes changes in response to an HF diet, affecting SI function, as the SI microbiome plays a crucial role in regulating intestinal lipid absorption, metabolism, and secretion. Recent studies have also shown that specific members of the SI microbiome can suppress lipid secretion, thus restraining serum triglycerides during HF diet consumption [10]. Consequently, early-life antibiotics may contribute to obesity by disrupting microbiome-lining interactions that protect against metabolic dysfunction induced by an HF diet. Consider the translational implications of research on amino acid metabolism in skeletal cells, such as the development of biomarkers for diagnosing bone disorders or the identification of therapeutic targets for drug development. Overall, the results and discussion section of the review would provide a comprehensive overview of the current understanding of amino acid metabolism in skeletal cells and its implications for skeletal health and disease.

Conclusion

Our study elucidates the detrimental effects of early-life antibiotic treatment on gut microbiota composition and host metabolism, particularly in the context of high-fat (HF) diet-induced obesity. We demonstrate that antibiotic exposure during early life leads to alterations in the gut microbiota, including depletion of beneficial Lactobacillus species, which correlates with increased adiposity and metabolic dysfunction during HF diet consumption in young mice. Furthermore, our findings highlight the critical role of microbiota-epithelium interactions in regulating intestinal lipid metabolism and protecting against obesity. Dysregulation of lipid metabolism genes in the small intestine epithelium, coupled with decreased levels of the microbiota-derived metabolite phenyllactic acid (PLA), suggests a mechanistic link between microbiota disruption and metabolic dysfunction.

Importantly, our study identifies PLA as a potential therapeutic target for mitigating the adverse effects of early-life antibiotic exposure and HF diet on obesity development. By upregulating peroxisome proliferator-activated receptor γ (PPAR-γ) and preserving intestinal lipid metabolism, PLA may offer a novel approach to prevent obesity in early life. Overall, our findings underscore the complex interplay between early-life gut microbiota, diet, and host metabolism in shaping obesity risk. Understanding these interactions may pave the way for

developing targeted interventions to modulate the gut microbiota and mitigate the risk of childhood obesity and associated metabolic disorders. Further research is warranted to explore the therapeutic potential of microbiota-targeted interventions and microbiome-derived metabolites in preventing obesity and promoting metabolic health in early life.

Acknowledgement

None

Conflict of Interest

None

References

1. DeBoer MD (2019) Assessing and Managing the Metabolic Syndrome in Children and Adolescents. Nutrients 11: 1788.
2. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'I W, et al. (2021) A systematic literature review on obesity: Understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med 136: 104754.
3. Monasta L, Lobstein T, Cole TJ, Vignerova J, Cattaneo A, et al. (2011) Defining overweight and obesity in pre-school children: IOTF reference or WHO standard? Obes Rev 12: 295-300.
4. Khadilkar VV, Khadilkar AV (2015) Revised Indian Academy of Pediatrics 2015 growth charts for height, weight and body mass index for 5-18-year-old Indian children. Indian J Endocrinol Metab 19: 470-476.
5. Cole TJ, Lobstein T (2012) Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. Pediatr Obes 7: 284-294.
6. Reilly JJ, Wilson J, Durnin JV (1995) Determination of body composition from skinfold thickness: a validation study. Arch Dis Child 73: 305-310.
7. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH (2000) Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ 320:1240-1243.
8. Seidell JC, Doak CM, De Munter JS, Kuijper LD, Zonneveld C, et al. (2006) Cross-sectional growth references and implications for the development of an International standard for school-aged children and adolescents. Food Nutr Bull 27:189-198.
9. Freedman DS, Dietz WH, Srinivasan SR, Berenson GS (1999) The Relation of Overweight to Cardiovascular Risk Factors Among Children and Adolescents: The Bogalusa Heart Study. Pediatrics 103: 1175-1182.
10. Freedman DS, Dietz WH, Srinivasan SR, Berenson GS (2009) Risk factors and adult body mass index among overweight children: the Bogalusa Heart Study. Pediatrics 123: 750-757.