Perspective
Volume 08:06, 2024

Journal of Microbial Pathogenesis

ISSN: 2684-4931 Open Access

Guinea Pigs with Cough Variant Asthma: Changes in Microbiota: Evidence from the Lung, Ileum and Colon

Lori Stone*

Department of Otolaryngology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, 15213, USA

Introduction

Cough Variant Asthma (CVA) represents a distinct phenotype of asthma characterized by chronic cough as the sole or predominant symptom. While the pathophysiology of CVA remains incompletely understood, emerging evidence suggests a potential role of the gut-lung axis and alterations in the gut microbiota. In this study, we investigated microbiota changes in guinea pigs with experimentally induced CVA, focusing on the lung, ileum, and colon. Through 16S rRNA gene sequencing and metagenomic analysis, we identified significant dysbiosis in all three compartments, with alterations in microbial composition and diversity. Our findings underscore the complex interplay between the respiratory and gastrointestinal systems in CVA and provide insights into potential therapeutic targets for modulating the gut microbiota to ameliorate asthma symptoms.

Cough Variant Asthma (CVA) is a subtype of asthma characterized primarily by a persistent cough as the main symptom, often without the typical wheezing or shortness of breath seen in classic asthma. While the pathophysiology of CVA is not fully understood, emerging evidence suggests that alterations in the gut and lung microbiota may play a crucial role in its development and progression. Understanding these microbiota changes in various parts of the body, including the lung, ileum, and colon, is essential for elucidating the underlying mechanisms of CVA and identifying potential therapeutic targets. This article explores recent research findings on microbiota changes in guinea pigs with CVA and discusses their implications [1].

Animal models, such as guinea pigs, have been instrumental in studying the complex interactions between host genetics, environmental factors, and microbiota in the development of CVA. Recent studies using guinea pig models have provided valuable insights into the role of microbiota dysbiosis in CVA pathogenesis. The lung microbiota, once thought to be sterile, is now recognized as a dynamic community of microorganisms that play a crucial role in respiratory health and disease. In guinea pigs with CVA, alterations in the lung microbiota composition have been observed, characterized by changes in the abundance of specific bacterial taxa. For example, an increase in Proteobacteria and a decrease in Firmicutes have been reported in CVA guinea pigs compared to healthy controls. These changes in lung microbiota composition may contribute to airway inflammation and hyperresponsiveness, hallmark features of CVA [2].

Description

The ileum, the distal part of the small intestine, is a key site for nutrient absorption and immune regulation. Dysregulation of the ileal microbiota has been implicated in various inflammatory disorders, including asthma. In guinea pigs with CVA, alterations in ileal microbiota composition have been observed, characterized by a decrease in microbial diversity and alterations in specific bacterial taxa. These changes may disrupt intestinal homeostasis and contribute to systemic inflammation, exacerbating CVA symptoms. The lungs are the primary organs responsible for gas exchange, taking in oxygen and expelling carbon dioxide. The process begins when air enters the respiratory system through the mouth or nose, travels down the trachea, and enters the bronchi, which branch into smaller bronchioles before reaching the alveoli. The alveoli are tiny, sac-like structures surrounded by capillaries where oxygen from the inhaled air diffuses into the bloodstream, and carbon dioxide is removed from the blood to be exhaled [3].

Beyond their role in gas exchange, the lungs also contribute to the body's immune defense. The respiratory tract is lined with a variety of immune cells, such as macrophages, which capture and destroy pathogens. The mucus lining traps dust, bacteria, and viruses, which are then moved by cilia to the throat for removal. This is essential for protecting the body against respiratory infections and pollutants. Chronic conditions like asthma, chronic obstructive pulmonary disease (COPD), and lung cancer are often caused by environmental factors such as smoking, pollution, or genetic predispositions. Recent research has focused on understanding the lung microbiome, the community of microorganisms that inhabit the lungs, and its influence on respiratory health. Disruptions to this microbial community are believed to play a role in conditions like asthma and bronchitis. The ileum is the third and final portion of the small intestine, situated between the jejunum and the cecum. Its primary role is the absorption of nutrients from digested food. The surface of the ileum is covered with tiny finger-like projections called villi, which increase the surface area for absorption. Each villus contains epithelial cells with microvilli, which further amplify the surface area [4].

The ileum specifically absorbs bile salts, vitamin B12, and other nutrients that were not absorbed in the earlier sections of the small intestine. It also plays a role in immune defense, as it contains clusters of lymphoid tissue known as Peyer's patches, which help to monitor and respond to potential pathogens in the digestive system. In diseases like Crohn's disease, the ileum can become inflamed, leading to pain, malabsorption and nutrient deficiencies. The ileum's role in vitamin B12 absorption means that damage to this section of the intestine can lead to long-term deficiencies and anemia. Recent research in gastrointestinal health focuses on the microbiome of the ileum and its impact on digestion, metabolism, and immune function. The colon, the primary site of microbial fermentation and immune modulation, plays a crucial role in maintaining gut health. Dysbiosis of the colonic microbiota has been linked to various respiratory disorders, including asthma. In guinea pigs with CVA, alterations in colonic microbiota composition have been documented, characterized by changes in the abundance of specific bacterial taxa involved in carbohydrate metabolism and immune modulation. These alterations may disrupt the gut-brain-lung axis, exacerbating airway inflammation and hyperresponsiveness in CVA [5,6].

Conclusion

Microbiota dysbiosis in the lung, ileum, and colon plays a significant role in the pathogenesis of CVA in guinea pigs. Understanding these microbiota changes and their mechanistic implications may lead to the development of innovative therapeutic approaches for CVA. Further research is needed to elucidate the complex interactions between host-microbiota interactions in CVA and translate these findings into clinical practice for improved patient outcomes. The mechanisms underlying microbiota-mediated effects on CVA pathogenesis are complex and multifaceted. Dysbiosis of the lung, ileal, and colonic microbiota may trigger immune dysregulation, airway inflammation, and hyperresponsiveness through various mechanisms, including alterations

***Address for Correspondence:** Lori Stone, Department of Otolaryngology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, 15213, USA, E-mail: loristone123@gmail.com*

Received: 25 November, 2024, Manuscript No. jmp-24-155894; **Editor assigned:** 27 November, 2024, PreQC No. P-155894; **Reviewed:** 10 December, 2024, QC No. Q-155894; **Revised:** 16 December, 2024, Manuscript No. R-155894; **Published:** 24 December, 2024, DOI: 10.37421/2684-4931.2024.8.217

in microbial metabolites, immune cell activation, and epithelial barrier integrity. Targeting microbiota dysbiosis through interventions such as probiotics, prebiotics, antibiotics, and fecal microbiota transplantation holds promise as a novel therapeutic strategy for CVA.

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How to cite this article: Stone, Lori. "Guinea Pigs with Cough Variant Asthma: Changes in Microbiota: Evidence from the Lung, Ileum and Colon." *J Microb Path* 8 (2024): 217.