Microb Health Dis 2023; 5: e873

# RESPIRATORY MICROBIOME: EVIDENCE FROM BASIC AND CLINICAL STUDIES

V. Ankudavicius[1], J. Skieceviciene[2], D. Nikitina[2], R. Lukosevicius[2], S. Miliauskas[1], M. Zemaitis[1]

[1]Department of Pulmonology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania
[2]Institute for Digestive Research, Lithuanian University of Health Sciences, Kaunas, Lithuania

*Corresponding Author:* Vytautas Ankudavicius, MD; email: vytautas.ankudavicius@lsmu.lt

**Abstract – *Objective:*** In recent years, culture-independent methods led to provide a strong background to further microbiota studies, especially in lower respiratory tract investigation. Scientific research has focused more on studying and characterizing relationships between lung microbiota and various diseases, such as lung cancer, chronic obstructive pulmonary disease (COPD), asthma, sarcoidosis, acute respiratory infection, etc.
***Materials and Methods:*** The electronic search was performed on the PubMed database using the combination of the text words "respiratory microbiota" and "lung microbiome". Only research studies in humans published between March 2022 and March 2023 were eligible for inclusion.
***Results:*** The scientific search retrieved 124 results, from which 106 articles were excluded if they duplicate or did not fit the inclusion criteria. A total of 18 studies were included for review.
***Conclusions:*** These studies have shown that changes in lower respiratory microbiota composition are a variable characteristic of all the aforementioned conditions; the relationship between circulating biomarkers, clinical data, and dysbiosis also was found in several studies. However, some studies had limitations, and future investigations are needed to better understand lung microbiota involvement in the pathogenesis of respiratory diseases.

**Keywords:** Lung microbiota, Microbiome, Lung diseases.

## INTRODUCTION

Microorganisms along the human skin, upper respiratory tract, gastrointestinal tract, urinary and reproductive systems contain from ten to hundreds of trillions of symbiotic bacterial cells, which are called the human microbiota[1,2]. For a long time, scientists believed that the lower respiratory tract is sterile. However, the next-generation sequencing technologies led to announced controversial data that the unique microbial communities inhabit the lower respiratory tract[3]. The microbiota may assist in host metabolism, mucus barrier function, immune stimulation, and signalization to mainly all parts of the body[4]. Previous gastrointestinal tract studies[5,6] noted that dysbiosis could promote the development of various diseases. Following scientific progress, lower respiratory tract microbiota started to be investigated during the last few years. Lung microbiota research is a potential novel area, whose investigation is increasing. Recent studies[7,8] showed significant differences in bacte-

rial composition between healthy and patients with respiratory disease. In this review, we aimed to gather the latest results of lower respiratory tract microbiome studies and systematize the results, highlighting the future path of development of research in this field.

## MATERIALS AND METHODS

The aim of this article is to represent the latest scientific news on the literature published between March 2022 and March 2023 on respiratory microbiota. The electronic search was conducted on the PubMed database using the combination of the text words “respiratory microbiota” and “lung microbiome”. Papers were included if they presented data about any type of microbiological analysis of the human lower respiratory tract. Literature presenting results about animals, children, or not in English was excluded.

## RESULTS

The search retrieved 124 results, from which 44 articles were excluded if they duplicate or did not fit the inclusion criteria. A total of 80 studies were evaluated for eligibility. After analyzing the exclusion criteria, 18 papers were included. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) showed the final research strategy (Figure 1).

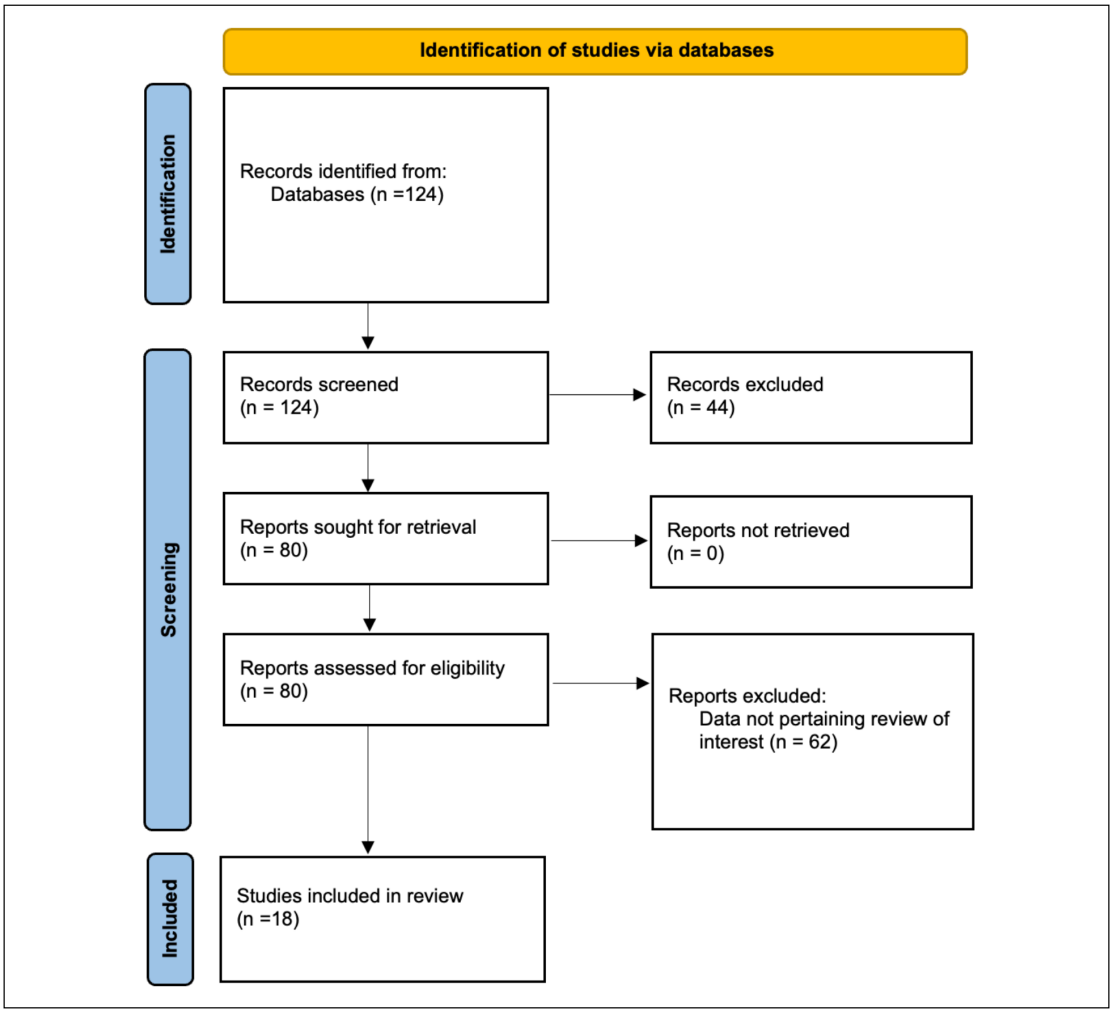


**Figure 1.** Baseline (T0) and after one month of treatment (T1) breath tests of patients treated with one monthly cycle of rifaximin (600 mg/day for 5 days).

The evidence from the review was divided into seven main topics. A summary of the included studies is presented in Table 1[9-26].

## DISCUSSION

### Microbiota and Lung Cancer

The chapter on microbiota and lung cancer has been deeply investigated by seven different research groups. Major studies investigated lung microbiota composition in BALF samples, except two studies that used malignant lung tissue samples. Studies[16,18] of lung tissue samples investigated only early stages lung cancer patients, while studies with BALF[14-15,17,19-22] investigated from early to advance stages diseases. All previously mentioned research distinguished differences between the bacterial composition of lung cancer patients and healthy volunteers. Zen et al[17] noted, that Firmicutes, Bacteroidetes, Fusobacteriota at the phylum level, and Prevotella, Alloprevotella, and Veillonella at the genus level were significantly enriched in NSCLC samples. Zheng et al[18] showed significant differences in alpha and beta diversities between malignant lung samples with adenocarcinoma, squamous cell carcinoma, and benign pulmonary nodules. The other studies also noted differences in the bacterial composition between patients with lung cancer and benign pulmonary nodules. Beta diversity was decreased in patient samples with lung cancer compared with benign pulmonary nodules. Several bacteria, such as Burkholderia cenocepacia, Corynebacterium accolens, Porphyromonas somerae, and Streptococcus mitis, were enriched BALF samples of NSCLC patients[22]. Another study investigated only patients with lung adenocarcinoma and noted that Bacteroidota, Prevotella, and Alloprevotella were the most abundant taxa in the BALF samples. Leptotrichia, and

**TABLE 1. SUMMARY OF ALL INCLUDED STUDIES.**

| Authors | Publication years | Topic | Sample type | Number of samples |
|---|---|---|---|---|
| Zhu et al[9] | 2022 | AIDS patients with pneumocystis pneumonia | BALF | 90 |
| Wang et al[10] | 2022 | Asthma | Sputum | N/A |
| Hardouin et al[11] | 2023 | Cystic fibrosis | Sputum | 6 |
| McKay et al[12] | 2023 | Cystic fibrosis | Swab/sputum | 82 |
| Yan et al[13] | 2022 | COPD | Sputum | 135 |
| Martinsen et al[14] | 2022 | COPD | BALF | 306 |
| Kullberg et al[15] | 2022 | COVID-19 | BALF | 114 |
| Wong-Rolle et al[16] | 2022 | Lung cancer | Malignant tissue | 12 |
| Zeng et al[17] | 2023 | Lung cancer | BALF | 75 |
| Zheng et al[18] | 2023 | Lung cancer | Malignant tissue | 82 |
| Liu et al[19] | 2022 | Lung cancer | BALF | 16 |
| Xia et al[20] | 2022 | Lung cancer/pulmonary tuberculosis/pneumonia | BALF | 78 |
| Guo et al[21] | 2023 | Lung cancer | BALF | 42 |
| Yuan et al[22] | 2023 | Lung cancer | BALF | 229 |
| Shajiei et al[23] | 2022 | Mechanical ventilation | BALF | 58 |
| Hérivaux et al[24] | 2022 | Pulmonary aspergillosis | BALF | 104 |
| Knudsen et al[25] | 2022 | Sarcoidosis | Washings/BALF/swab | 70 |
| Liu et al[26] | 2022 | Smoking | BALF | 55 |

AIDS – acquired immune deficiency syndrome, BALF – Bronchoalveolar lavage fluid, COPD – Chronic obstructive pulmonary disease, COVID-19 – Coronavirus disease 2019, N/A – not applicable.

Fusobacterium tended to increase in patients with advanced-stage of lung adenocarcinoma. Authors suggested that these bacteria may be associated with lung cancer progression[21]. Liu et al[19] showed that samples of NSCLC patients were enriched Lactobacillus, Massilia, and Lactococcus compared with controls. This study suggested that Cysteinyl-Valine, 3-Chlorobenzoic acid, and 3,4-Dihydroxyphenyl ethanol could be the predictive biomarkers for lung cancer identification.

Xia et al[20] analyzed BALF microbiota composition between three patient types: lung cancer, primary pulmonary tuberculosis, and community-acquired pneumonia. They found increased α-diversity only in samples of lung cancer patients. Beta diversity analysis showed that the microbiota composition of patients with primary pulmonary tuberculosis and lung cancer samples were very similar, except for Mycobacterium and Selenomonas, which were enriched in the tuberculosis group, and the other two genera, Sphingobium and Marseilla, increased in the lung cancer group. Meanwhile, patients with community-acquired pneumonia had different bacterial compositions compared with previously mentioned groups[20].

Wong-Rolle et al[16] represented a novel design microbiota study, which investigated intratumor bacteria burden with lung cancer cells. The authors used novel RNA detection technology, which allows them to identify the abundance of bacteria (16S rRNA), fungi (28S rRNA), and CMV (UL83) transcripts from human genes involved in immune and cancer pathways. Malignant tissue samples from early stages lung cancer patients showed significantly higher bacterial burden compared with control mouse germ-free samples. Furthermore, the maximum bacterial burden was found in the small airway tissue, lower in the malignant tumor tissue and further reduced in adjacent normal lung tissue. Interestingly, the lower bacterial burden was also observed in smokers' patient tissues. These results suggest that smoking may create an inhospitable environment for bacteria in general.

## Microbiota and Chronic Pulmonary Disease

Articles about the relationship between lung microbiota, COPD, and asthma were slightly less represented than the previous topic. Wang et al[10] noted that sputum samples from patients with asthma were enriched with Bacteroidetes, Fusobacteria, and Proteobacteria and a depleted of Actinobacteria and Firmicutes compared to healthy controls. The authors separated patients into several categories, which had different bacterial compositions. Sputum samples from older patients with lower blood transforming growth factor levels had an increased abundance of *Pasteurellaceae*, *Streptococcus*, and *Rothia*. Meanwhile, samples from patients with lower eosinophils and higher neutrophils count in sputa were enriched with Faecalibacterium and Bacteroides. Yan et al[13] investigated the sputum metagenome, metabolome, host transcriptome, and proteome from COPD patients and healthy volunteers. Authors suggested that neutrophilic inflammation in COPD may modify tryptophan metabolism in airway lactobacilli associated with epithelial cell apoptosis pathways. Martinsen et al[14] investigated oral washings and BALF samples in COPD patients and healthy volunteers. The study results showed that the lung mycobiome is less stable than the oral cavity mycobiome. Furthermore, COPD diagnosis and antibiotic use may not affect the microbiome stability. However, data from this study is limited and further analysis cannot be conducted.

## Microbiota and Cystic Fibrosis

Two studies investigated the lung microbiota relationship in patients with cystic fibrosis[11,12]. The review of Hardouin et al[11] described a novel and revolutionized technology called mass spectrometry, which proteotyping microorganisms at the species level. Study results showed 38 different and 9 similar bacterial genera in the six samples. Similar bacteria such as *Streptomyces*, *Bacillus*, *Clostridium*, and *Pseudomonas* were the most abundant and collectively represented almost half of the whole bacterial biomass in sputum samples. The authors remarked that cystic fibrosis patients have an individual microbiota signature in sputum samples. This innovative technology may be incorporated with bacterial cultural technology for personalized and predictive medicine by getting more information about the host microbiota.

This year, the research group of McKay et al[12] noted that alpha diversity was statistically significantly decreased in sputum and oropharyngeal swab samples of cystic fibrosis patients compared with healthy volunteers. Further analysis showed that the alpha and beta diversities of these samples from cystic fibrosis patients were similar. Due to this reason, data were investigated together. The bacterial composition of cystic fibrosis patients' samples compared with healthy volunteers was reduced in 26 genera, such as *Corynebacterium, Prevotella 2, Flavobacterium, Bergeyella, Gemella, Johnsonella, Peptococcus, Peptoclostridium, Selenomonas, Selenomonas 3, Megasphera,* etc. The authors also found a relationship in the gut-lung axis, where stool and airway samples from cystic fibrosis patients showed moderately positive correlations between *Intestinibacter* and *Aggregatibacter; Intestinibacter* and *Lachnoanaerobaculum; Prevotella 7* and *Alloprevotella; Bacteroidales and Corynebacterium.*

## Microbiota and Sarcoidosis

The research group of Knudsen et al[25] investigated the lung microbiota, including fungi and bacteria, in patients with sarcoidosis, compared with controls and the association between the microbiota and levels of the antimicrobial peptides in BALF samples. The study results showed that the fungus Aspergillus enriched BALF samples for sarcoidosis patients compared with controls. At the same time, bacteria *Abscondibacteria* were decreased in BALF of the same patient's group. Also, patients with sarcoidosis had decreased levels of antimicrobial peptides in the airways. The study findings suggested the presence of microbial dysbiosis of airways in patients with sarcoidosis. However, future investigations should be performed for a better understanding of how dysbiosis promotes sarcoidosis development.

## Microbiota in COVID-19 and Other Lung Infections

The impact of lung microbiota on the onset of lung infections was investigated in three different studies. Two of them investigated immunocompromised patients, and the other study investigated patients with coronavirus disease (COVID-19). The publication of Kullberg et al[15] investigated the relationship between lung microbiota and clinical outcomes of severe COVID-19-related acute respiratory distress syndrome (ARDS). The authors noted that COVID-19 patients with a higher bacterial and/or fungal burden might have a lower probability of extubation and spontaneous breathing. Also, the same group of patients with increased lung bacterial and fungal burden had a higher mortality ratio. These results demonstrated that lung bacterial and fungal burden is associated with clinical outcomes of COVID-19 and ARDS.

Hérivaux et al[24] determined the influence of the lung microbiota on invasive pulmonary aspergillosis development and course. Analysis showed that alpha diversity was decreased in BALF samples from patients with invasive pulmonary aspergillosis. Bacterial composition showed an increased abundance of *Escherichia, Finegoldia, Paraclostridium,* and *Staphylococcus*; decreased bacteria such as *Prevotella* and *Veillonella* genera. Further results demonstrated that the bacterial composition of the lung microbiota was affected by the neutrophil counts and associated with the concentration of alveolar cytokines. The authors established that the number of bacterial diversity when invasive pulmonary aspergillosis was diagnosed predicted the survival of patients.

The other investigation was conducted by Zhu et al[9], who investigated alterations of the gut and lung microbiota in patients who had acquired immune deficiency syndrome (AIDS) with pneumocystis pneumonia. The research is mainly focused on intestinal microbiota, although lung microbiota is shortly characterized. In this study, authors presented that intestinal and lung microbiota may be related to such factors as CD4+ T cells, CD4/CD8 ratio, and white blood cells count. Also, stool and BALF samples showed that human immunodeficiency virus infection and pneumocystis pneumonia significantly altered the microbiota composition of the lung and intestinal tract.

## Microbiota and Mechanical Ventilation

The review of Shajiei et al[23] analyzed the microbiome of sputum samples taken from mechanically ventilated patients in the intensive care unit. The study results showed that *Candida*

was the most common fungus in the sputum samples and suggested that fungus colonize the lungs of mechanically ventilated patients. Interestingly, other identified fungal species showed relationships with oral and nasal cavities microbiota. The authors concluded that culture methods alone are limited for the lung microbiota evaluation and additionally needed culture-independent methods for better management of fungi-associated respiratory diseases.

### Microbiota and Smoking

The review conducted by Liu et al[26] analyzed microbiota composition in 55 BALF samples from smokers and nonsmokers. The relative abundance of *Acinetobacter, Actinomycetes, Haemophilus, Neisseria, Porphyrins, Rothia,* and *Streptococcus* genera was highly increased in the smoking group samples. The authors noted that smoking may change the lung microbiota composition and it may promote smoking-related diseases. However, this study published only limited data. Due to this reason, we could not provide a deeper analysis of this topic.

## CONCLUSIONS

The standardized procedures and novel molecular analysis methods in microbiota let to increase the number of studies in the respiratory area. In recent years, a great number of research have been produced with the aim of increasing the knowledge between lung microbiota and various diseases. Our review has focused on the relationship between lung microbiota and respiratory tract diseases, such as lung cancer, COPD, asthma, sarcoidosis, and acute respiratory infection. These studies have shown that dysbiosis is a variable characteristic of all the aforementioned conditions; the relationship between circulating biomarkers, clinical data, and dysbiosis also was found in several studies. However, some studies had limitations due to the low number of samples, unclearly described methodology, and reporting contrasting evidence. Future studies are critically needed for a better understanding of lung microbiota involvement in respiratory diseases.

### Conflict of Interest

The authors declare no conflict of interest.

### Author Contributions

Writing - original draft preparation: V. Ankudavicius, D. Nikitina, R. Lukosevicius; Supervision and Conceptualization: M. Zemaitis, J. Skieceviciene, S. Miliauskas. All authors have read and agreed to the published version of the manuscript.

### Funding

This research received no external funding.

### Acknowledgments

Not applicable.

### Informed Consent

No additional consent is required for a review of published scientific literature.

## ORCID ID

Vytautas Ankudavicius: https://orcid.org/my-orcid?orcid=0009-0007-8447-0737
Jurgita Skieceviciene: https://orcid.org/0000-0002-4893-6612
Darja Nikitina: https://orcid.org/0000-0002-9942-5118
Rokas Lukosevicius: https://orcid.org/0000-0003-4584-9828
Marius Zemaitis: https://orcid.org/0000-0002-6633-5749

## REFERENCES

1. Ursell LK, Metcalf JL, Parfrey LW, Knight R. Defining the human microbiome. Nutr Rev 2012; 70: S38-44.
2. Kovaleva OV, Romashin D, Zborovskaya IB, Davydov MM, Shogenov MS, Gratchev A. Human lung microbiome on the way to cancer. J Immunol Res 2019; 2019: 1394191.
3. Zhang T, Joubert P, Ansari-Pour N, Zhao W, Hoang PH, Lokanga R, Moye AL, Rosenbaum J, Gonzalez-Perez A, Martínez-Jiménez F, Castro A, Muscarella LA, Hofman P, Consonni D, Pesatori AC, Kebede M, Li M, Gould Rothberg BE, Peneva I, Schabath MB, Poeta ML, Costantini M, Hirsch D, Heselmeyer-Haddad K, Hutchinson A, Olanich M, Lawrence SM, Lenz P, Duggan M, Bhawsar PMS, Sang J, Kim J, Mendoza L, Saini N, Klimczak LJ, Islam SMA, Otlu B, Khandekar A, Cole N, Stewart DR, Choi J, Brown KM, Caporaso NE, Wilson SH, Pommier Y, Lan Q, Rothman N, Almeida JS, Carter H, Ried T, Kim CF, Lopez-Bigas N, Garcia-Closas M, Shi J, Bossé Y, Zhu B, Gordenin DA, Alexandrov LB, Chanock SJ, Wedge DC, Landi MT. Genomic and evolutionary classification of lung cancer in never smokers. Nat Genet 2021; 53: 1348-1359.
4. Malard F, Dore J, Gaugler B, Mohty M. Introduction to host microbiome symbiosis in health and disease. Mucosal Immunol 2021; 14: 547-554.
5. Thursby E, Juge N. Introduction to the human gut microbiota. Biochem J 2017; 474: 1823-1836.
6. Lin L, Zhang J. Role of intestinal microbiota and metabolites on gut homeostasis and human diseases. BMC Immunol 2017; 18: 2.
7. Yagi K, Huffnagle GB, Lukacs NW, Asai N. The Lung Microbiome during Health and Disease. Int J Mol Sci 2021; 22: 10872.
8. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372: n71.
9. Zhu M, Liu S, Zhao C, Shi J, Li C, Ling S, Cheng J, Dong W, Xu J. Alterations in the gut microbiota of AIDS patients with pneumocystis pneumonia and correlations with the lung microbiota. Front Cell Infect Microbiol 2022; 12: 1033427.
10. Wang J, Chai J, Zhang L, Zhang L, Yan W, Sun L, Chen Y, Sun Y, Zhao J, Chang C. Microbiota associations with inflammatory pathways in asthma. Clin Exp Allergy 2022; 52: 697-705.
11. Hardouin P, Pible O, Marchandin H, Culotta K, Armengaud J, Chiron R, Grenga L. Quick and wide-range taxonomical repertoire establishment of the cystic fibrosis lung microbiota by tandem mass spectrometry on sputum samples. Front Microbiol 2022; 13: 975883.
12. McKay I, van Dorst J, Katz T, Doumit M, Prentice B, Owens L, Belessis Y, Chuang S, Jaffe A, Thomas T, Coffey M, Ooi CY. Diet and the gut-lung axis in cystic fibrosis - direct & indirect links. Gut Microbes 2023; 15: 2156254.
13. Yan Z, Chen B, Yang Y, Yi X, Wei M, Ecklu-Mensah G, Buschmann MM, Liu H, Gao J, Liang W, Liu X, Yang J, Ma W, Liang Z, Wang F, Chen D, Wang L, Shi W, Stampfli MR, Li P, Gong S, Chen X, Shu W, El-Omar EM, Gilbert JA, Blaser MJ, Zhou H, Chen R, Wang Z. Multi-omics analyses of airway host-microbe interactions in chronic obstructive pulmonary disease identify potential therapeutic interventions. Nat Microbiol 2022; 7: 1361-1375.
14. Martinsen EMH, Eagan TML, Wiker HG, Leiten EO, Husebø GR, Knudsen KS, Tangedal S, Sanseverino W, Paytuví-Gallart A, Nielsen R. A longitudinal study of the pulmonary mycobiome in subjects with and without chronic obstructive pulmonary disease. PLoS One 2022; 17: e0267195.
15. Kullberg RFJ, de Brabander J, Boers LS, Biemond JJ, Nossent EJ, Heunks LMA, Vlaar APJ, Bonta PI, van der Poll T, Duitman J, Bos LDJ, Wiersinga WJ; ArtDECO Consortium and the Amsterdam UMC COVID-19 Biobank Study Group. Lung Microbiota of Critically Ill Patients with COVID-19 Are Associated with Nonresolving Acute Respiratory Distress Syndrome. Am J Respir Crit Care Med 2022; 206: 846-856.
16. Wong-Rolle A, Dong Q, Zhu Y, Divakar P, Hor JL, Kedei N, Wong M, Tillo D, Conner EA, Rajan A, Schrump DS, Jin C, Germain RN, Zhao C. Spatial meta-transcriptomics reveal associations of intratumor bacteria burden with lung cancer cells showing a distinct oncogenic signature. J Immunother Cancer 2022; 10: e004698.
17. Zeng W, Zhao C, Yu M, Chen H, Pan Y, Wang Y, Bao H, Ma H, Ma S. Alterations of lung microbiota in patients with non-small cell lung cancer. Bioengineered 2022; 13: 6665-6677.
18. Zheng X, Lu X, Hu Y. Distinct respiratory microbiota associates with lung cancer clinicopathological characteristics. Front Oncol 2023; 13: 847182.
19. Liu B, Li Y, Suo L, Zhang W, Cao H, Wang R, Luan J, Yu X, Dong L, Wang W, Xu S, Lu S, Shi M. Characterizing microbiota and metabolomics analysis to identify candidate biomarkers in lung cancer. Front Oncol 2022; 12: 1058436.

20. Xia X, Chen J, Cheng Y, Chen F, Lu H, Liu J, Wang L, Pu F, Wang Y, Liu H, Cao D, Zhang Z, Xia Z, Fan M, Ling Z, Zhao L. Comparative analysis of the lung microbiota in patients with respiratory infections, tuberculosis, and lung cancer: A preliminary study. Front Cell Infect Microbiol 2022; 12: 1024867.
21. Guo Y, Yuan W, Lyu N, Pan Y, Cao X, Wang Y, Han Y, Zhu B. Association Studies on Gut and Lung Microbiomes in Patients with Lung Adenocarcinoma. Microorganisms 2023; 11: 546.
22. Yuan Q, Wang X, Li Z, Guo W, Cheng H, Cao Q. A Preliminary Study on Microbiota Characteristics of Bronchoalveolar Lavage Fluid in Patients with Pulmonary Nodules Based on Metagenomic Next-Generation Sequencing. Biomedicines 2023; 11: 631.
23. Shajiei A, Liu L, Seinen J, Dieperink W, Hammerschmidt S, van Dijl JM, Harmsen HJM. Specific associations between fungi and bacteria in broncho-alveolar aspirates from mechanically ventilated intensive care unit patients. Virulence 2022; 13: 2022-2031.
24. Hérivaux A, Willis JR, Mercier T, Lagrou K, Gonçalves SM, Gonçales RA, Maertens J, Carvalho A, Gabaldón T, Cunha C. Lung microbiota predict invasive pulmonary aspergillosis and its outcome in immunocompromised patients. Thorax 2022; 77: 283-291.
25. Knudsen KS, Lehmann S, Nielsen R, Tangedal S, Paytuvi-Gallart A, Sanseverino W, Martinsen EMH, Hiemstra PS, Eagan TM. The lower airways microbiota and antimicrobial peptides indicate dysbiosis in sarcoidosis. Microbiome 2022; 10: 175.
26. Liu X, Sun W, Ma W, Wang H, Xu K, Zhao L, He Y. Smoking related environmental microbes affecting the pulmonary microbiome in Chinese population. Sci Total Environ 2022; 829: 154652.