Association between the respiratory microbiota and response to antibiotic therapy in children with macrolide-resistant *Mycoplasma pneumoniae* pneumonia

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INTRODUCTION

- A community outbreak of macrolide-resistant *M. pneumoniae* (MRMP) has been observed in Taiwan during 2017 to 2019. However, some patients were clinically responsive to macrolide which can't kill MRMP and is not an effective treatment.

- We aimed to investigate whether respiratory microbiota at the beginning of hospitalization was associated with disease severity and response to antibiotic treatment in children with MRMP pneumonia

METHOD

- A prospective study of 66 children < 18 years old hospitalized with confirmed MRMP infection at Chang Gung Memorial Hospital Lin Kou and Kaohsiung branches, Saint Paul's Hospital between April 2017 and March 2020 was conducted.

- Total 66 samples were performed 16S rRNA gene sequencing to identify respiratory microbiota.

- The difference in microbial composition among groups were examined using microbial community analysis and functional prediction of respiratory microbiota.

- Clinical data were obtained and stratified by two groups according to with or without effective treatment.

RESULT

- The predominant bacterial composition in respiratory samples (on average >2% of the total sequences) at the genus level. comprising 78.7% and 83.6% of the respiratory microbiota in the without effective treatment group and doxycycline treatment group, respectively (Figure 1)

- WET = Without effective treatment
- DT = Doxycycline treatment

RESULT

- Age, gender, and bacterial loads between these two groups were similar. The group of DT had a significantly longer duration of total febrile days (p<0.001) and total hospitalization days (p=0.002) than those in the group WET. (Table 1).

- Higher respiratory microbial diversity is associated with MRMP patients without effective treatment than MRMP patients who need doxycycline treatment (Figure 2).

- From the list of most relatively abundant species in MRMP patient without doxycycline, *Fusobacterium periodonicum* most negatively correlated with total febrile days and severity score (Figure 3).

- Classification of samples to detect patients with effective treatment or not based on these selected microbiota genera features achieved AUC of 0.861(Figure 4).

CONCLUSION

- Respiratory dysbiosis was associated with persistent fever and disease severity in patients with MRMP pneumonia.

- Respiratory microbiota might modulate the anti-inflammatory effects in response to M. pneumoniae infection and have important implications on the treatment and prevention of M. pneumoniae infection.

- *Fusobacterium periodonticum* may indicate no need doxycycline treatment.

Figure 1 Fraction of predominant microbiota with a relative abundance of at least 2% at the genus level in all sample.
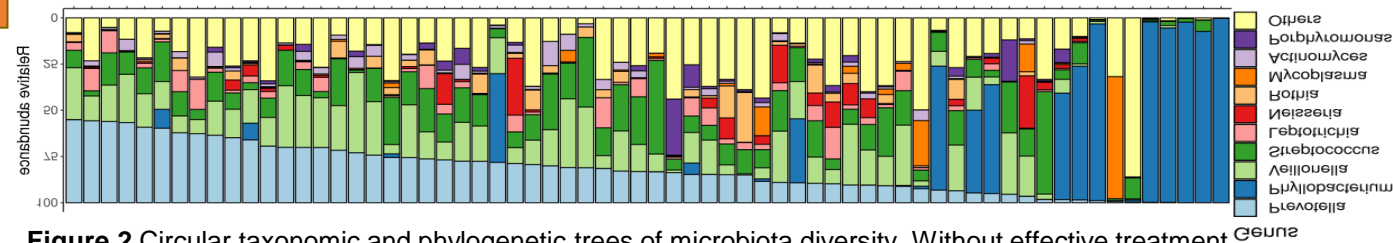

Figure 2 Circular taxonomic and phylogenetic trees of microbiota diversity. Without effective treatment (blue) and doxycycline treatment (red)
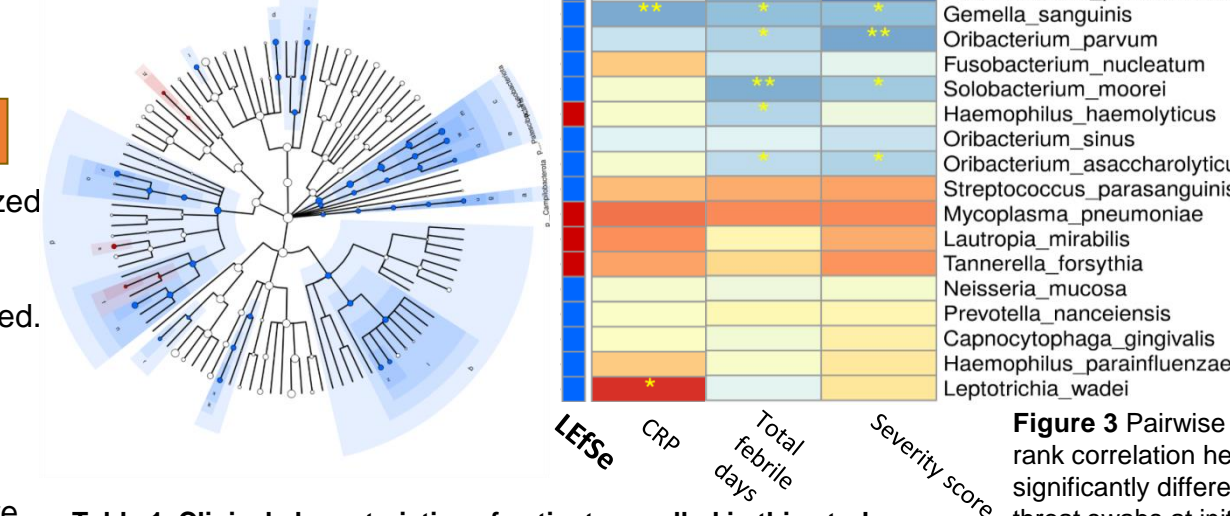

Figure 3 Pairwise Spearman rank correlation heat map of significantly different taxa in throat swabs at initial sampling and clinical severity score in MRMP patients WET/DT at the species level. The correlation was indicated by color gradient
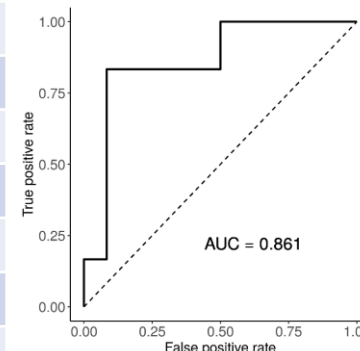
Table 1 Clinical characteristics of patients enrolled in this study

MRMP patients	WET (n=23)	DT (n=43)	P value
Age, years	7.6 ± 2.2	7.9 ± 2.9	0.5
Sex, male	10 (43.5%)	11 (25.6%)	0.2
Total fever days	6 (1.6)	9 (2.9)	<0.001 *
Hospitalization days	3.3 (1.9)	5.6 (3.1)	0.002 *
Ct value at diagnosis	29.2 ± 3.98	29.3 ± 3.5	0.9
Hypoxemia	0 (0%)	6 (14%)	0.08
WBC (/uL)	7115.9±2238.5	8051.8±2748.9	0.2
CRP (mg/L)	41.7±52.8	70.6±81.02	0.09
Infiltration (CXR)	9 (39.1%)	8 (18.6%)	0.08

Figure 4 ROC curves of ASVs to predict MRMP patients WET or DT