

# Combination of Gram Stain, Sputum Culture, and Molecular Method for Diagnosis and Guiding Target Therapies of Bacterial Pneumonia

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Dear Prof. Guo, Thank you for your interest in our work. It is important to obtain qualified sputum specimen for accurate etiology diagnosis of bacterial pneumonia. In our study, all specimens were lower respiratory secretion samples, which means all the samples were detected by Gram stain before quantitative loop-mediated isothermal amplification (qLAMP) assay and only adequate samples (sputum containing >25 leukocytes per low power field) were enrolled. In fact, most of our samples were lower respiratory tract aspirations by bronchoscopy which were more accurate to reflect the pathogens of pneumonia.

Hospital-acquired pneumonia (HAP) contributes significantly to healthcare costs and is associated with prolonged hospital stays and increased mortality in critically ill patients. Patients with HAP are commonly exposed to broad-spectrum antimicrobial agents, which causes increasing prevalence of resistant pathogens, especially multidrug-resistant pathogens.<sup>[1]</sup> The emergence of multidrug-resistant pathogens in cases of HAP emphasizes the need for effective strategies to prevent and treat this disease, of which early pathogen target-driven therapy is an optimizing choice. With the rapid, sensitive, and specific features, qLAMP can be applied for the decision-making regarding whether we selected empirical antibiotic therapies or the target antibiotic therapies for HAP patients.

However, our qLAMP assay is not currently available for the drug sensitivity identification yet. Therefore, it is still important to refer to sputum culture information with molecular method for diagnosis and guiding target therapies of bacterial pneumonia in spite of the rapid diagnosis and high sensitivity of qLAMP. Currently, we have been focusing on the development of bacterial

drug-resistance gene assay with LAMP strategies. Different combinations of antibiotic resistant gene panels are designed for surveillance by LAMP to define the precise profiles of drug administration. However, patterns of resistance to antimicrobial agents have changed dramatically over the past decade.<sup>[2]</sup> Epigenetic inheritance, population structure and heterogeneity, high mutation rates, gene amplification, efflux pumps, and biofilm formation can all contribute to the development of bacterial drug-resistance. Among all the known types of resistance, adaptive resistance is particularly inconvenient, which has been repeatedly correlated with the appearance of multidrug resistance, yet the biological processes behind its emergence and evolution are not well understood.<sup>[3]</sup>

As a result, there is still a long way to go to make qLAMP as an ideal method for guiding early target therapy of HAP.

## REFERENCES

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