Infection and Drug Resistance

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LETTER

A Response to Article "Distribution of Mcr-1 Harboring Hypervirulent Klebsiella Pneumoniae in Clinical Specimens and Lytic Activity of Bacteriophage KpnM Against Isolates" [Letter]

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Dear editor

We really appreciate the authors and all collaborators who have recently reported their research results in an article entitled "Distribution of Mcr-1 Harboring Hypervirulent Klebsiella Pneumoniae in Clinical Specimens and Lytic Activity of Bacteriophage KpnM Against Isolates".[1] This study had shown very encouraging research results and important information regarding the use of bacteriophage; *KpnM* phage in this case, which could be further studied for combating the antibiotic resistance issues. However, first of all, this study lacks clear determination of "hypervirulent" bacteria.[2,3] The phenotypes of hypervirulent *K. pneumoniae* isolates could be observed via microscopic examinations.[4] Take the observation of thick capsules formation or hyperfimbriae formation on the bacterial cells as examples.[5,6] Since the authors would like to address the hypervirulence in *K. pneumoniae* isolated in this study, the measurement of CPS staining observed under microscope or EPS/eDNA quantification would give a more comprehensive explanation, instead of showing the mucoid colonies cultured on LB or MacConkey agar show. in Figure 1A and B, for most *K. pneumoniae* strains show a mucoid colony phenotype especially when cultured on MacConkey agar at 37 °C. In Figure 1C the string test was mentioned as the hypervirulence phenotype test of the clinical *K. pneumoniae* isolates. Although the string test was performed well on the MacConkey agar, the required controls; such as the classical *K. pneumoniae* strain or virulent gene deletion mutant of *K. pneumoniae*, were excluded. The extracellular polysaccharide (EPS) related gene deletion mutants which lose their ability to form the mucoid colony phenotype could be the proper control for this type of assay.[7,8] In addition, the string test result should also mention at least the average length of the string resulting from the hyper virulence in an understandable unit, thereafter being compared to the control, or at least being statistically compared to the antibiotic(s) susceptible *K. pneumoniae* isolates.[9]

This study also performed PCR to detect the *mcr-1* gene's existence in the isolates whose result was shown in Figure 2C. However, the gel electrophoresis itself looked poorly performed while the interpretation of the PCR results was poorly given both in Figure 2C and in the figure legend. There should be an explanation of the size of the targeted gene, the DNA marker and the necessary controls used in this experiment. The authors also excluded the required interpretation, therefore it was hard for us, as readers, to fully understand the results completely as the expected purpose of the published results of a research.

Among all 67 *K. pneumoniae* isolates in this study, the *KpnM* phage was chosen from the 30 bacteriophages isolated from water waste. The bacterial growth and biofilm inhibitions of the *K. pneumoniae* isolates, especially those with *mcr-1* gene in their genome, were significant. Taken together, these results showed how promising this study is. However, the

Received: 5 October 2022
Accepted: 10 October 2022
Published: 19 October 2022

method of biofilm formation detection or quantification used to show the result (Figure 6B) was not clearly mentioned and explained either.

A consideration for future study, the study regarding the molecular mechanism involved in the inhibition of the bacterial biofilm formation or the hypervirulence of *K. pneumoniae* by *KpnM* phage; either through the biofilm related genes or EPS/CPS production or through the regulation of fimbriae production, could be good study topics. In addition, the identification of any protein secreted by the *KpnM* phage could also be studied in future. The role of *KpnM* on *mcr-1* gene regulation and expression could be as important as other mentioned topics for being further explored.

Acknowledgments

We would like to acknowledge and give full appreciation for all of the support given to the authors of this study throughout the study and article preparation.

Disclosure

The authors report no conflicts of interest regarding this communication.

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https://doi.org/10.2147/IDR.S392356