Clarion Journal of Infectious Diseases and Therapy [CJIDT]

Volume 2021 Issue 02

Mini Review

Bacteriophage Φ6 as Surrogate and Human-Harmless Viruses to Study Anti-SARS-CoV-2 Approaches

Joana Barros[1,2], Maria Pia Ferraz[1,2,3]*, Fernando Jorge Monteiro[1,2,4]

[1]i3S – Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Porto, Portugal

[2]INEB – Instituto de Engenharia Biomédica, Universidade do Porto, Porto, Portugal

[3]FCS/UFP – Faculdade de Ciências da Saúde, Universidade Fernano Pessoa, Porto, Portugal

[4]FEUP – Faculdade de Engenharia, Universidade do Porto, Porto, Portugal

Received: January 8, 2021; **Accepted:** January 20, 2021; **Published:** January 23, 2021

Citation: Barros J, Pia Ferraz M, Monteiro FJ (2021) Bacteriophage Phi 6 as Surrogate and Human-Harmless Viruses to Study Anti-SARS-CoV-2 Approaches. *Clar J Infect Dis Ther* 02 (02): 126–128.

Abstract

Given safety challenges in conducting laboratory work with highly infectious human coronaviruses (pathogenicity, genetic mutations rate, biosafety level 3 and 4 requirements), many researchers have valued the potential of bacteriophages as appropriate viral surrogate to measure humans enveloped virus' survival, transfer and removal. The use of phage Φ6 seems to be useful as coronavirus surrogate to assess the effectiveness of anti-SARS-CoV-2 approaches, providing important insights concerning COVID-19 pandemic and human public health.

Keywords: SARS-CoV-2; COVID-19; bacteriophage Φ6

Review

The 2019 Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has emerged as a new respiratory pathogen and is responsible for large-scale morbidities and mortalities around the globe [1]. It is caused by a single positive-stranded RNA virus from the coronavirus (CoV) family of Coronaviridae, composed of four genera out of which α- and β-CoV can infect mammals including humans. SARS-CoV-2 is identified as β-CoV and is responsible for coronavirus disease 2019 (COVID-19) [1,2]. These viruses are wrapped in host cells derived lipid membranes where viral surface proteins are embedded. One of these surface proteins known as spike [S] protein protrudes out of membranes and gives a characteristic crown/halo-like appearance to the virus when observed under electron microscope, hence named coronavirus [1]. Once the virus gains entry into the respiratory tract, SARS-CoV-2 causes damage to epithelial cells of the airways making lungs unable to clear dirt and mucus which can lead to pneumonia [1,2]. In extreme cases, patients experience a dramatic increase in the levels of pro-inflammatory chemokines and cytokines including IL-6 and TNF-α, a condition known as "cytokine storm". This leads to the development of Acute Respiratory Distress Syndrome (ARDS), septic shock, metabolic acidosis, coagulation dysfunction, and even death [1,2].

Given safety challenges in conducting laboratory work with highly infectious human coronaviruses (pathogenicity, genetic mutations rate, biosafety level 3/4 (BSL-3 and BSL-4)), many researchers have valued the potential of bacteriophages (phages) as an appropriate viral surrogate to measure humans enveloped virus' survival, transfer and removal [3,4]. Phages seem to be good alternatives once they are relatively easy to produce in large quantities, and several purification procedures are laboratory available [3,5–8]. Bacterial viruses of biosafety level 1 (BSL-1), pose no risk to humans, being safe for laboratory workers, and their study does not require specialized biocontainment precautions. Moreover, their similarity with eukaryote viruses allow cross-study comparisons, making them interesting models for aerovirology research [6,7,9,10]. In 2020, several studies have shown the potential of phage Φ6, non-pathogenic viruses that infect specifically bacterium *Pseudomonas syringae*, as a surrogate virus to study infections caused by enveloped human viruses [6,7,9,10]. For instance, Turgeon *et al* compared the effects of the aerosolization and sampling on the infectivity of 5 phages and 2 pathogenic viruses: MS2 (a single-stranded RNA [ssRNA] phage of the *Leviviridae* family), Φ6 (a segmented double-stranded RNA [dsRNA] phage of the *Cystoviridae* family), ΦX174 (a single-stranded DNA [ssDNA] phage of the *Microviridae* family), PM2 (a double-stranded DNA [dsDNA] phage of the *Corticoviridae* family), PR772 (a dsDNA phage of the *Tectiviridae* family), human influenza A virus H1N1 (an ssRNA virus of the *Orthomyxoviridae* family), and the poultry virus Newcastle disease virus (NDV; an ssRNA virus of the *Paramyxoviridae* family)[11]. These authors showed that the behaviour of the influenza virus resembled that of phages PR772 and Φ6, providing critical information for the selection of appropriate phages models to mimic the behaviour of specific human and animal viruses in aerosols [11].

Phage Φ6 is a segmented RNA virus involved by a phospholipid envelope (fatty) with spike proteins at its surface, with ~80–100 nm size, structural features similar to several human viruses, namely Influenza (belongs to *Orthomyxoviridae* family), SARS-CoV-1, SARS-CoV-2 and Middle East Respiratory Syndrome-associated coronavirus (MERS-CoV) (belong to *Coronaviridae* family) [3,5–9]. Thus, phage Φ6 has been used as surrogate virus model to understand the relationship between environmental conditions and virus infectivity in order to improve strategies for predicting and controlling disease transmission, namely COVID-19 [3,5–9]. For instance, Casanova *et al* showed that recovery of phage Φ6 and *Influenza* virus from hands were comparable, with approx. 2–3 log10 loss after using protein and non-ionic detergent-based eluent solutions [3]. These authors concluded that viruses' inactivation was probably due those solutions with capability to destabilize the fatty envelope structure, a primary target for virus inactivation [3]. Dubuis *et al* showed that ozone at low concentration combined with high relative humidity was able to kill airborne viruses, such as phage Φ6 and murine norovirus MNV-1[12]. Rockey *et al* used phage Φ6 as surrogate model to evaluate the effectivity of heat and humidity treatments for N95 respirator de-contamination [9]. Buhr *et al* proved that phage Φ6 could be a useful indicator model to evaluate the inactivation and survival of an enveloped RNA virus on contaminated aircraft materials after exposure to hot, humid air [13]. Fedorenko *et al* showed that phage Φ6 presented a high survival rate in dry saliva deposited on glass surfaces, even when submitted to a wide range of relative humidity levels [6]. Phage Φ6 was considered a good model for virus respiratory pathogens, including SARS-CoV-2 [6].

Conclusion

Overall, the use of phage Φ6 may be useful as coronavirus surrogate to assess the effectiveness of anti-SARS-CoV-2 approaches, providing important insights concerning COVID-19 pandemic and human public health.

References

1. Zheng Y, Zhuang MW, Han L, Zhang J, Nan ML, Zhan P, *et al.* (2020) Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) membrane (M) protein inhibits type I and III interferon production by targeting RIG-I/MDA-5 signaling. *Signal Transduct Target Ther* 5: 299. [View]
2. Costela-Ruiz VJ, Illescas-Montes R, Puerta-Puerta JM, Ruiz C, Melguizo-Rodriguez L (2020) SARS-CoV-2 infection: The role of cytokines in COVID-19 disease. *Cytokine Growth Factor Rev* 54: 62–75. [View]
3. Casanova LM, Weaver SR (201) Evaluation of eluents for the recovery of an enveloped virus from hands by whole-hand sampling. *J Appl Microbiol* 118: 1210–6. [View]
4. Whitworth C, Mu Y, Houston H, Martinez-Smith M, Noble-Wang J, Coulliette-Salmond A, *et al.* (2020) Persistence of Bacteriophage Phi 6 on Porous and Nonporous Surfaces and the Potential for Its Use as an Ebola Virus or Coronavirus Surrogate. *Appl Environ Microbiol* 86: 01482–20. [View]
5. Prussin AJ 2nd, Schwake DO, Lin K, Gallagher DL, Buttling L, Marr LC (2018) Survival of the Enveloped

Virus Phi6 in Droplets as a Function of Relative Humidity, Absolute Humidity, and Temperature. *Appl Environ Microbiol* 84: 00551–18. [View]

6. Fedorenko A, Grinberg M, Orevi T, Kashtan N (2020) Survival of the enveloped bacteriophage Phi6 (a surrogate for SARS-CoV-2) in evaporated saliva microdroplets deposited on glass surfaces. *Sci Rep* 10: 22419. [View]
7. Fedorenko A, Grinberg M, Orevi T, Kashtan N (2020) Virus survival in evaporated saliva microdroplets deposited on inanimate surfaces. *bioRxiv* :2020.06.15.152983. [View]
8. Vatter P, Hoenes K, Hessling M (2020) Photoinactivation of the Coronavirus Surrogate phi6 by Visible Light. *Photochem Photobiol* 2020. [View]
9. Rockey N, Arts PJ, Li L, Harrison KR, Langenfeld K, Fitzsimmons WJ, *et al.* (2020) Humidity and Deposition Solution Play a Critical Role in Virus Inactivation by Heat Treatment of N95 Respirators. mSphere 15: 00588–20. [View]
10. Gendron L, Verreault D, Veillette M, Moineau S, Duchaine C (2010) Evaluation of Filters for the Sampling and Quantification of RNA Phage Aerosols. *Aerosol Science and Technology* 44: 893–901. [View]
11. Turgeon N, Toulouse MJ, Martel B, Moineau S, Duchaine C (2014) Comparison of Five Bacteriophages as Models for Viral Aerosol Studies. *Appl Environ Microb* 80: 4242–50. [View]
12. Dubuis ME, Dumont-Leblond N, Laliberte C, Veillette M, Turgeon N, Jean J, *et al.* (2020) Ozone efficacy for the control of airborne viruses: Bacteriophage and norovirus models. *Plos One* 15. [View]
13. Buhr TL, Young AA, Borgers-Klonkowski E, Kennihan NL, Barnette HK, Minter ZA, *et al.* (2020) Hot, Humid Air Decontamination of Aircraft Confirmed That High Temperature and High Humidity Are Critical for Inactivation of Infectious, Enveloped Ribonucleic Acid (RNA) Virus. *Front Bioeng Biotech* 8. [View]

[*]**Corresponding author:** Maria Pia Ferraz, Faculdade de Ciencias da Saúde, Universidade Fernando Pessoa, Rua Carlos da Maia, 296, 4200-150 Porto, Portugal;

Email: mpferraz@ufp.edu.pt