

Bacteriophages: Foes or Friends?

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HIGHLIGHTS

- Bacteriophages are known for their roles in rapid development of the bacterial evolution and transfer of various genes.
- Safety issues have always been a great concern since primary uses of bacteriophages in medicine.
- Comprehensive studies are necessary to ensure safe uses of bacteriophages in medicine.

Keywords:

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Phage therapy

Antimicrobial resistance

Introduction

Foes or friends? This question frequently comes to mind when there are any footprints of bacteriophages in science. Since primary ideas of using these bacterial viruses in medicine, safety issues have always been a great concern. In recent decades, advances in molecular techniques significantly helped to address these issues. Bacteriophages, and in a further extend mobile genetic elements (MGE), are well-known for their roles in rapid development of the bacterial evolution through changes in bacterial genome structures (Lisch and Burns, 2018). The ability of these viruses to transfer various genes (however the exact capacity is unclear) makes them guilty of improving bacterial resistance to antimicrobials. In 2010, me and my colleagues at the University of South Australia fully sequenced an enterococcal bacteriophage and found that resistance genes to antibiotics with anticancer properties (e.g. daunorubicin), as well as other routine antibiotic resistance genes, could be transferred by these viruses (Mazaheri Nezhad Fard et al., 2010). Daunorubicin (AKA daunomycin) and its derivative doxorubicin are anthracycline antibiotics generally used as chemotherapy agents in neoplastic disorders, especially leukemias and some lymphomas. Up to that date, only one bacteriophage with enterococci origin had fully been sequenced; in which, no antibiotic resistance genes were found (Son et al., 2010). Although no strong evidence were available on transfer of genes between bacteriophages or prokaryotes to eukaryotic cells (including human somatic cells) and only a very few experiments demonstrated eukaryotic transfection by the bacteriophages, this finding was of importance. The frightening scenario of picturing spread of resistance to anticancer drugs in humans by the bacteriophages might remind readers of sci-fi movies. The major simulation regarded ability of eukaryotic viruses (both animal and plant viruses) to insert a part of their genomes or carried MGE in the host genome. However, before we could surely accuse bacteriophages for this, a long time should be awaited to find some proper proofs.

Back to the reality, we showed later in 2011 that enterococcal bacteriophages were more non-species specific than that previously thought (Mazaheri Nezhad Fard et al.,

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2011). Further studies by other researchers showed that bacteriophages could transfer antimicrobial resistance genes between relative genera and even distinct phyla! These included a wide variety of antimicrobials such as those used in human and veterinary medicines and recognized by the global authorities (e.g. WHO, JETACAR, EAGAR) as important in infection treatments. Since then and by popularizing next generation sequencing (NGS) platforms in microbial genetics, more and more bacteriophages have been wholly sequenced and much data have been added to the present data. Reviews of data in databases such as GenBank show that bacteriophages partially contain antimicrobial resistance genes as well as virulence genes, which can be transferred to bacteria through either general or specific transduction mechanism (Popa et al., 2017). In fact, the current research studies on bacteriophages are mostly limited to use of these viruses in infection cures and treatments while other dimensions and possible side effects of the bacteriophage clinical applications are neglected. Unfortunately, the antimicrobial oil wells have quickly been out of order, meaning that available antimicrobials have become ineffective more rapidly than what we primarily suggested (Li and Webster, 2018). Therefore, needs for novel substitutions such as short peptides, herbal essential oils and bacteriophages are urgently felt (Chouhan et al., 2017). Of these substitutions, the lovely bacteriophages are really good substitutive players in this field. Since public concerns are still rising on the capability of bacteriophages to co-transfer unwanted properties to microflora populations, further comprehensive studies seem necessary to overcome uncertainties and ensure safety of bacteriophages for medical uses. I, personally, believe that advantages of bacteriophages are much

more remarkable than their disadvantages, particularly in case of totally resistant infections. However, deeper investigations clarify this superiority.

Competing interests

The author declares no conflict of interest.

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