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Phage Therapy: Promising For *H.pylori* Infection

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Helicobacter pylori (*H.pylori*) is a widely distributed human pathogen with high prevalence in human population. Many researches showed *H.pylori* infection is closely related with chronic gastritis, ganstric duodenal ulcer, mucosa associated diseases such as lymphoma and gastric cancer [1,2]. It has been classified as the class I carcinogen in 1994 by the World Health Organization and the International Agency for Research on Cancer consensus group [3]. The prevalence in the human population is 50-80%, with an increasing rate of 1-2% annually. About 12 million new cases emerged every year. *H.pylori* infection has become an extrusive public problem.

Unlike more common infection, *H. pylori* are sensitive to only a few medications, including PPI, amoxicillin, clarithromycin, metronidazole and so on. Different combinations of these antibiotics such as PPI combined with two antibiotics have been applied to eradicate the bacteria. However, they usually cannot give an acceptable eradication rate and increasing antibiotic resistance is becoming a problem [4]. At the same time upleasant side effects usually generated along with antibiotic therapies. For example, PPI can change the acid environment in the stomach, however the effect varies in different individuals, and it can lead to liver and kidney damage and thus often have poor compliance for patients [5]. Since the effects of antibiotics cannot meet our needs and multidrug-resistant *H. pylori* increases greatly, new therapies for *H.pylori* is in need.

Phages are reported as the most abundant organisms on earth and are ubiquitous in the nature. Phage therapy uses phages or their products as biological factors to treat or prevent bacterial infectious diseases. As early as 1917, prelimilary research showed phages can be used as therapeutic agents for bacterial disease [6]. Thereafter, a variety of infections including: gastroenteritis, sepsis, suppurative wounds, dermatitis, osteomelitis, emphysemas and pneumonia were cured by phage therapy in humans. In these experiments, the success rates were about 80 to 95 percent and there was no undesirable reaction [7]. Recent studies also showed many antibiotic-resistant infections such as *Bacillus anthracis*, *Staphylococci*, *Escherichia*, *Klebsiella* and *Propionibacterium acnes* were successfully treated by phage therapy [8-11]. Phage therapy has the advantages other biological agents do not have, such as high specificity for target bacterium; safe to be utilized clinically; few side effects; the frequency of phage mutation is much higher than that of bacteria, so if a phage-resistant bacterium emerges, the phage responds quickly [12].

In recent years, more and more researchers began to study *H. pylori* phages which may be possible prophylactic and alternative therapeutic treatment. The first *H. pylori* phages was reported by Schimd et al who isolated a *H. pylori* strain which can produce phages in vivo [13]. This phages can lysogenized *H. pylori* strain SchReck 290 rather than virulent to the bacteria. In 1993, Heintschel et al documented the isolation, propagation, lytic cycle, morphology, and genome composition of HP1 phage, recovered from *H. pylori* strain SchReck 290 [14]. In 2008, Vale et al. described the release of phage-like particles by *H. pylori* following UV induction [15]. In 2011, Lehours et al. discovered that temperate phage of the Siphoviridae family was released from *H. pylori* strain B45 following induction[16]; Wan et al. isolated a wild-type virulent phage of *H. pylori* and studied its simulated treatments of gastrointestinal *H. pylori* in vitro [17]. Other studies characterized *H. pylori* phage 1961P and KHP30 and found they are dissimilar to any previously sequenced phages and should be a new type of phages[18,19]. All these studies bring new opportunity for *H. pylori* phage discoveries and phage therapy.

Considering the great troubles such as low eradication rate and antibiotic resistance in *H. pylori* therapy, lytic and virulent phages to *H. pylori* appears promising in the future. We believe that with more studies on *H. pylori* phages, we can get a better understanding to the treatment of *H. pylori*. Phage therapies will provide a new effective treatment options for *H. pylori* infections.

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