Phage Therapy as a Means to Combat Antibiotic Resistant Bacteria

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Dr. Paul Turner received his PhD in Zoology from Michigan State University. He was a National Science Foundation postdoctoral fellow at the University of Maryland and an NSF–NATO fellow at the University of Valencia in Spain. He has completed a molecular virology fellowship at the National Institutes of Health Laboratory of Clinical Investigation. Turner has held multiple committee positions with the National Research Council and NSF and has chaired the American Society for Microbiology’s Evolutionary and Genomic Microbiology Division.

Evolution of life involves compromises; the improvement in a trait comes at the cost of reduced performance on other traits. For example, *Pseudomonas syringae* evolves resistance to phage Phi6 by trading off type-IV pili, resulting in reduced virulence. Dr. Turner harnesses this evolutionary tradeoff mechanism in bacteria, mainly the antibiotic resistance ones, to make them vulnerable to phage/antibiotic attack. Phage therapy targets infectious bacteria using specific phages that attack the bacteria.

Recently, there is an alarming increase in the incidence of bacterial prone illnesses caused by Multi Drug Resistant bacteria. MDR bacteria are prevalent in hospitals, nursing homes and among people with implants. Phage is a self-amplifying drug, as it multiplies inside the host cell. Bacteria prone to phage attack will develop resistance to the phage by trading off its virulence factor or the receptor in its membrane specific to the phage.

Phages that bind to the efflux pumps can be used to target MDR bacteria. Efflux pumps are transporters in the cell membrane that help to transport toxic substances like antibiotics out of the cell. The cells gain antibiotic resistance when the efflux pumps transport antibiotics outside the cell. When drug resistant bacteria are treated with a cocktail of the phage and antibiotic, the bacteria is forced to give up the efflux pump, making it sensitive to the antibiotic.

*Pseudomonas aeruginosa*, a priority pathogen in the WHO list of antibiotic resistant pathogens, poses great risk to human health. This bacteria causes variety of diseases ranging from urinary tract infection, lung infection to dermatitis. Dr. Turner along with Dr. Benjamin Chan, a microbiologist in his lab discovered phage OMKO1 infects the MDR *P. aeruginosa* by binding to OPRM1 receptor in cell surface. The OPRM1 receptor is part of the efflux pump that offers antibiotic resistance. The team arrived at a therapeutic formulation, by mixing phage OMKO1 with an antibiotic.

The team was successful in treating four patients with these phage-antibiotic cocktails. First, a patient with artificial aortic arch was colonized by MDR *P. aeruginosa*. They used a cocktail of antibiotic ceftriaxone and phage OMKO1, directly on the bacterial colony. The patient recovered completely without side effects(1). They used the same mixture but as an inhaler in the second case to treat a patient with cystic fibrosis. Third, a patient with small cell lung cancer, treated with H4 phage and erythromycin and ciprofloxacin for 10-days administered through nebulizer. Fourth, a firefighter diagnosed with Bronchiectasis had MDR *P. aeruginosa* infection. They used Phage H6 with antibiotics to cure him.
In the future, Dr. Turner and his team aim at developing phage therapy mechanisms for the WHO list of priority pathogens. They continue their search for potentially useful phages in the Islands of Haiti, Caribbean, East Africa, Refugee trails and sewage treatment plants in USA. Overall, the amazing feature of the talk was the practicality of the research, and the fact that they have cured people with the concept they developed.

Reference