PERSONALIZED PHAGE THERAPY: PROVING TO BE A VALUABLE THERAPEUTIC APPROACH AGAINST DIFFICULT-TO-TREAT INFECTIONS IN HUMANS

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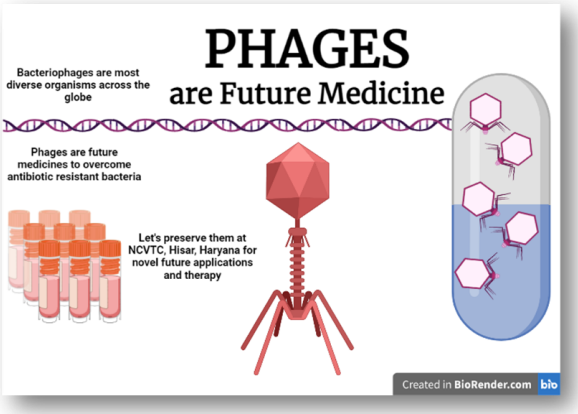

Dear Editors

We would hereby like to draw the attention of the research community and healthcare professionals towards the re-emergence of phage therapy as a life saving therapeutic intervention against difficult-to-treat and acute infections. As evidenced, recently a Multidisciplinary Phage Task Force (MPTF) reported standardized treatment pathway for curing severe musculoskeletal infections by using phage therapy concomitantly with antibiotics[1]. In recent times, chronic infections including burn wound, urinary tract infections, chronic otitis and diarrhoea have also been cured using phage therapy[2-6]. There is a reported case of a 76 year old male patient (year 2018) who was treated successfully using phage therapy for an aortic graft infection caused by *Pseudomonas aeruginosa* using phage OMKO1 and ceftazidime[7]. Amongst other recent popular cases is a 68-year old patient infected with multidrug resistant (MDR) *Acinetobacter baumanii* who was treated with phage therapy[8]; successful curing of lung infection caused by resistant *Burkholderia cepacia*[9] and treatment of chronic skin infection caused by resistant *Staphylococcus aureus*. Extraordinarily, the **Phage Therapy**" is being applied as personalized medicine against MDR, XDR, pan-drug resistant - difficult-to-treat infections. Researchers are using the phage cocktail prepared on a custom basis against emergent strains and are exploiting Phage-Antibiotic synergy (PAS) to treat the infections remaining uncured otherwise. As such, the role of phage banks needs to be highlighted to benefit the scientific community and the end users. The role of the phage banks is important to timely present bacteriophages for overcoming infection in patients as well as to tackle any resistant developed strains later during due course of treatment.

The '**Eliava Phage Therapy Center**' in Georgia (established year 1923) by Georgian scientist Georgi Eliava and French Canadian phage pioneer Felix d'Herelle is the oldest known repository of bacteriophages. Since olden times, the Eliava Institute has produced phage preparations after extensive preclinical and clinical trials for the treatment and prophylaxis of septic and intestinal infections which may be applied orally, locally, rectally, intravenously or as aerosols by nebulizer.

Simultaneously on the other hand, '**Phage Therapy Unit**' at Ludwik Hirszfeld Institute of Immunology and Experimental Therapy, Wroclaw, Poland (Est. 1952) operates as an out-patient clinic for phage therapy for severe cases of infections worldwide. Later in year 1982, **Felix d'Herelle Reference Centre for Bacterial Viruses**, Canada remained a major provider of phages for research applications.

However, now with the advent of emerging antimicrobial resistance, the entire globe has recognized the potential of bacteriophages and many international culture collections have initiated maintining bacteriophage deposits including:

American Type Culture Collection (ATCC), USA; Biological Resource Centre, NITE (NBRC), Japan; Deutsche Sammlung von Mikroorganismen und Zellkulturen (DSMZ), Germany; The Netherlands Culture Collection of Bacteria (NCCB), Netherlands; China Center for Type Culture Collection (CCTCC), National Centre for Veterinary Type Cultures (NCVTC), India, etc.

Bacteriophages have a critical edge in therapeutics owing to their inherent properties of comparative easy isolation, rapid growth kinetics, survivability till availability of host and increase in number during therapy without disturbing the natural microflora besides being plentiful in nature. After having a critical face-off with **Emerging Antimicrobial Resistance** due to antibiotic usage in the mainstream medical practice and complete deportation of phage therapy from the Western world since middle of the last century, personalized therapies are on a rise. Phage therapy is re-emerging and countries like Georgia and Russia which have never abandoned Phage Therapy now have a stronghold over it. "**Magistral formula"** is being implemented by the Federal Agency for Medicines and Health Products in Belgium. On the other hand generation of engineered phages with improved efficacy, safety or novel functions are being explored and it may even generate the interest of pharmaceutical agencies. Novel means of phage therapy in preliminary results have demonstrated even antiviral and antifungal results apart from the antibacterial action Concerns about increasing the robustness at every involved production step of phage formulations are being addressed and the Western countries are also pursuing Phage therapy on personalized basis. Application of phage therapy on compassionate grounds is being pursued so, with all the elaborated groundwork and scientific evidences related to therapeutic and immunomodulatory effects, in the current scenario of increased incidences of treatment failures, we believe that introduction of bacteriophages at clinician levels will offer practicable approach for treatment of MDR-infected, immunocompromised and critically ill-patients. Efforts should be made to percolate the phage research from bench to bedside by collaborating with medical practitioners who may serve as key resource persons in case of debilitating infections such as diabetic foot and infections leading to amputation. It has become urgent to explore alternate means of treatment and Phage Therapy offers a feasible & possibly best understood option.

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