Editorial

Respiratory infection: insights from assembly 10 of the European Respiratory Society 2018 Annual Congress

Cristina Calarasu[1], Aran Singanayagam[2]

[1]University of Medicine and Pharmacy of Craiova, Department of Medical Specialities, Craiova, Romania; [2]Airway Disease Infection Section. Imperial College London, UK

Correspondence to: Cristina Calarasu. University of Medicine and Pharmacy of Craiova, Department of Medical Specialities, Craiova, Romania. Email: calarasu.cristina@yahoo.com.

Submitted Sep 05, 2018. Accepted for publication Sep 05, 2018.
doi: 10.21037/jtd.2018.09.20
View this article at: http://dx.doi.org/10.21037/jtd.2018.09.20

Introduction

The European Respiratory Society Annual Congress featured an array of exciting research studies in the field of respiratory infections. In this article, we highlight three important studies featured at the Congress and discuss their impact on the field of respiratory infections.

Inhaled phage therapy for the treatment of acute Pseudomonas aeruginosa (PsA) lung infections

There is an urgent need for novel alternatives to antibiotic therapy due to evolving resistance. Inhaled bacteriophage (phage) therapy has recently gained renewed interest. Bodier-Montagutelli *et al.* (1) developed a phage cocktail for airways delivery and assessed its preclinical efficacy and resistance to aerosolization. A phage cocktail was initially tested against a 43-strain of a PsA reference panel in vitro, showing 95% efficacy. The authors then assessed the effects of inhaled phage therapy in a murine model of acute PsA infection. They demonstrated that 90% of animals treated with the phage cocktail survived versus 0% in the control group. These effects were associated with a concomitant reduction in bacterial loads in lung tissue. Phage suspension was aerosolized with 4 different nebulizers and aerosolized phage viability was assessed after aerosol collection. The study showed that mesh nebulization was less deleterious to phages, with 33.4% viability *vs.* 29.6% and 7.7% for ultrasonic and jet-nebulization. Previously published studies on different phage products for inhalation have also favoured mesh nebulization compared to jet and ultrasonic nebulizers because this method does not generate drug recycling or evaporation in the reservoir, limiting additional stresses and changes in drug formulation (2,3). These data suggest that the inhalation of phages as a novel antibacterial treatment could potentially be both clinically relevant and technically feasible. Phage product pharmacokinetics and immunogenicity still need to be studied in man. After regulatory and manufacturing guidelines are defined, randomized controlled clinical trials should be carried out to further characterise a potential therapeutic role for phage therapy.

The first experience of therapeutic dendritic cells (DCs) vaccine administration in patients with extensively drug resistant (XDR) lung tuberculosis

Drug resistant tuberculosis has become a major global public health problem due to lack of effective treatment, longer treatment duration using second line or experimental drugs, and the risk of further spread. Cellular therapy promises new potential adjunct therapeutic options for treatment of drug-resistant tuberculosis. Experimental DC based vaccines specific for viral, bacterial, fungal and protozoal infectious diseases are currently in development (4-6).

Starshinova *et al.* (7) described a study evaluating therapeutic DC vaccine administration in patients with confirmed XDR tuberculosis. They selected 13 patients with XDR-TB and administered therapeutic DC vaccination. In all patients, sputum smear positivity had been persisting without radiographic improvement before commencement

of immunotherapy. Immunotherapy was applied by administration of a suspension containing DCs, stimulated by the antigens ESAT-6 and SFP-10. Although a small sample size, the authors showed significant symptomatic improvement even after 60 days of therapy. Symptoms decreased in 61.5% of cases by day 60 and, by day 120, symptoms were observed only in 17.7% of cases. Sputum smear conversion was observed after 60 days in 61.1% of cases and after 120 days in 67.7% cases. The authors also reported radiographic improvement with resorption of focal and infiltrative changes noted in 41.7% and 70.0% cases. These preliminary data suggest that immunotherapy based on DCs could be an effective novel approach. This study now needs independent validation in larger cohorts and a more formalized controlled trial. The growing importance of DC therapies in cancer treatment and in other *in vivo* and *in vitro* studies for viral, bacterial, fungal and protozoal infectious diseases suggest that these approaches offer immense potential and could change treatment regimens in difficult-to-treat patients with TB.

Diagnosis of lower respiratory tract infections (LRTIs) using nanopore sequencing

Currently, routine culture is the "gold-standard" diagnostic test for LRTIs, but not all bacteria can be cultured and the process takes a minimum of 48 hours. Rapid molecular tests have been successful but the recent advances in bioinformatics and development of shotgun-metagenomic sequencing based approaches exceeded the shortcomings of culture and PCR, by combining speed with comprehensiveness, reducing turnaround time and improving diagnostic accuracy. Nanopore sequencing has been previously used to identify viral and bacterial pathogens from clinical samples mostly using samples with high pathogen loads (8,9). Respiratory specimens are a greater challenge due to variable pathogen load and the high ratio of host DNA present (10).

Using novel human DNA depletion, pathogen DNA extraction, library preparation and MinION sequencing, Charalampous *et al.* (11) developed a rapid metagenomics sequencing pipeline for the diagnosis of bacterial LRTIs directly from respiratory samples. Pathogens and antibiotic resistance genes were identified in real-time by MinION sequencing and Epi2ME analysis (an antimicrobial resistance pipeline) and were compared to routine microbiology testing results. They analysed 42 samples and found an 89% concordance rate with culture for pathogen detection. After improving turnaround and sensitivity, the pipeline was tested on a second sample set (n=13) and the result was 100% concordant with culture. The technique gives a rapid turnaround time of 6hrs from sample to pathogen and acquired-resistance gene identification. This novel rapid metagenomics sequencing pipeline presented by Charalampous *et al.* could potentially provide accurate pathogen and antibiotic resistance gene identification for LTRIs within six hours and raises speculation that metagenomic sequencing could have the potential to replace routine culture. Further studies in larger sample sets are now needed to evaluate this promising diagnostic approach.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Boldier-Montagutelli E, Pardessus J, Dalloneau E, et al. Inhaled Phage therapy for treatment of Pseudomonas aeruginosa lung infections. Eur Respir J 2018;52. [Epub ahead of print].
2. Respaud R, Vecellio L, Diot P, et al. Nebulization as a delivery method for mAbs in respiratory diseases. Expert Opin Drug Deliv 2015;12:1027-39.
3. Respaud R, Marchand D, Parent C, et al. Effect of formulation on the stability and aerosol performance of a nebulized antibody. MAbs 2014;6:1347-55.
4. Abate G, Hoft DF. Immunotherapy for tuberculosis: future prospects. Immunotargets Ther 2016;5:37-45.
5. Shnawa I. Dendritic Cell Based Vaccine for Human Tuberculosis. Int J Vac & Im Sys 2017;2:1-6.
6. Sinha A, Salam N, Gupta S, et al. Mycobacterium tuberculosis and dendritic cells: recognition, activation and functional implications. Indian J Biochem Biophys 2007;44:279-88.
7. Starshinova A, Nazarenko M, Burdakov V, et al. The first experience of therapeutic dendritic cells vaccine administration in patients with extensively drug resistant lung tuberculosis. Eur Respir J 2018;52. [Epub ahead of print].

8. Schmidt K, Mwaigwisya S, Crossman LC, et al. Identification of bacterial pathogens and antimicrobial resistance directly from clinical urines by nanopore-based metagenomic sequencing. J Antimicrob Chemother 2017;72:104-14.
9. Pendleton KM, Erb-Downward JR, Bao Y, et al. Rapid Pathogen Identification in Bacterial Pneumonia Using Real-Time Metagenomics. Am J Respir Crit Care Med 2017;196:1610-2.
10. Charalampous T, Richardson H, Kay GL, et al. Rapid Diagnosis of Lower Respiratory Infection using Nanopore-based Clinical Metagenomics. bioRxiv preprint first posted online 2018. Available online: https://www.biorxiv.org/content/biorxiv/early/2018/08/09/387548.full.pdf
11. Charalampous T, Richardson H, Kay G, et al. Diagnosis of lower respiratory tract infections using nanopore sequencing. Eur Respir J 2018;52. [Epub ahead of print].

Cite this article as: Calarasu C, Singanayagam A. Respiratory infection: insights from assembly 10 of the European Respiratory Society 2018 Annual Congress. J Thorac Dis 2018;10(Suppl 25):S3017-S3019. doi: 10.21037/jtd.2018.09.20