EuroSciCon

10th Edition of International Conference on

Advanced Microbiology & Education

June 14-16, 2018
London, UK

Manal Mohammed, Arch Clin Microbiol 2018, Volume 9
DOI: 10.4172/1989-8436-C2-007

TOWARDS THE TREATMENT AND PREVENTION OF INVASIVE NON-TYPHOIDAL SALMONELLA INFECTIONS

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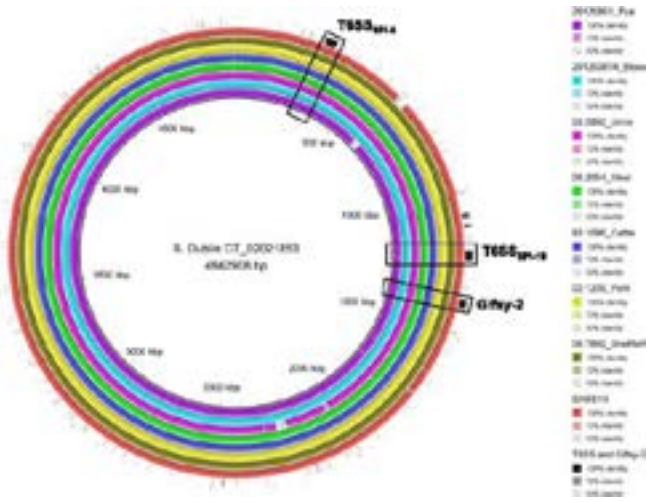
This lecture will address strategies to develop novel therapeutics against invasive non-typhoidal *Salmonella* infections. Salmonellosis is one of the most common foodborne diseases worldwide that causes a huge burden of morbidity and mortality in humans. Although non-typhoidal *Salmonella* serovars including *Salmonella* Typhimurium and *Salmonella* Dublin are associated primarily with self-limiting gastrointestinal illness they have adapted to cause invasive disease in humans particularly children, elderly and immunocompromised people. It is estimated that 680,000 people die every year as a result of infection by invasive non-typhoidal *Salmonella*. Interestingly, non-typhidal *Salmonella* have developed multi-drug resistance against current antibiotics including the last resource, colistin. Bacteriophage therapy is therefore the hope for the treatment of multidrug resistant infections however one of the key limitations to therapeutic use of phages, in particular for empiric therapy of infections, is the limited host range of many phages and the ease of development of bacterial resistance to phages. A solution may be to develop one or a cocktail of engineered phage that overcome some of these limitations. An essential step towards this goal is greater understanding of the complex dynamics of bacteria-phage interaction. We therefore use Anderson phage typing scheme of *Salmonella* Typhimurium as it provides a valuable model system for study of phage-host interaction and it will help us to characterize all bacterial antiviral systems and phage evasion strategies. The project will provide new insights into phage biology and strategies for genetic modification of phages and designing of effective broad spectrum engineered phages to overcome the limitations of bacteriophages as therapeutic agents. There is no vaccine against non-typhoidal *Salmonella* however our understanding of the molecular basis of virulence in invasive *Salmonella* Dublin using next generation sequencing technologies and associated bioinformatics associated tools will provide insights into the development of an effective vaccine through identification of novel virulence-attenuated strains with a potential for use as vaccine candidates for high-risk groups.



Complete genome alignment of Salmonella Dublin isolates showing the presence of Gifsy-2 like prophage and two different T6SSs that might contribute to virulence in Salmonella Dublin

Recent Publications

1. Mohammed M (2017) Phage typing or CRISPR typing for epidemiological surveillance of *Salmonella* Typhimurium?. BMC Res. Notes 10(1):578.
2. Mohammed M et al. (2017) The invasome of *Salmonella* Dublin as revealed by whole genome sequencing. BMC Infect. Dis. 17(1):544.
3. Mohammed M and M Cormican (2016) Whole genome sequencing provides insights into the genetic determinants of invasiveness in *Salmonella* Dublin. Epidemiol. Infect. 144(11):2430-2439.
4. Mohammed M et al. (2016) Whole genome sequencing provides an unambiguous link between

Salmonella Dublin outbreak strain and a historical isolate. Epidemiol. Infect. 144(3):576-81.

5. Mohammed M and M Cormican (2015) Whole genome sequencing provides possible explanations for the difference in phage susceptibility among two *Salmonella* Typhimurium phage types (DT8 and DT30) associated with a single foodborne outbreak. BMC Res. Notes. 8:728.

Biography

Manal Mohammed (BVSc, MVSc, PhD, FHEA) did her PhD in medical microbiology at University of Liverpool where she studied the molecular evolution of incurable Japanese encephalitis virus associated with high morbidity and mortality in humans. She tested the efficacy of intravenous immunoglobulins on inhibition of virus growth, she also discovered a new genotype of the virus. After she got her PhD Manal's research interests now include application of next generation sequencing technologies and associated bioinformatics analyses tools in investigating the molecular basis of virulence of non typhoidal salmonellosis in humans and understanding the complex dynamics of bacteria-phage interaction aiming to develop phage therapy as an alternative to antibiotics.

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