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Phage antimicrobials, promises and challenges

The rise of bacterial variants in the presence of lytic phage has been one of the basic grounds for evolution studies. However there are serious concerns regarding bacteria acquiring phage resistance and the possible implications of this event bacterial fitness and virulence. We developed phage-coated surface and investigated the development of phage resistance and associated variations in virulence and biofilm formation for the resulting phage-resistant PA phenotypes. Experimental evolution was used to generate Pseudomonas aeruginosa variants under selective pressure from different homogeneous and one heterogeneous phage environment. Studying phenotypic traits of the variants revealed significant changes in various fitness and virulence determinants such as growth, motilities, biofilm formation, resistance to oxidative stress and production of siderophores and chromophores compared to the control. Variants resistant to a bacteriophage mixture were observed to suffer a greater change in phenotypic traits. Furthermore, the appearance of melanogenic variants and the increase in pyocyanin and pyoverdin production for some variants is believed to affect the virulence of the population. The choice of therapeutic phage (or phage cocktail) allowed for the control of evolution of resistant phenotypes (i.e., selective pressure). Choosing a mixture of phages that directly or indirectly use known PA virulence factors as receptors led to direct killing, or selected for inactivation of the receptors, causing loss of those virulence determinants and impeding the mutants' ability to invade cultured skin cell lines (keratinocytes). This work is currently being followed up by invivo experiments on various models and also using microfabricated microenvironments for a more mechanistic investigation. The knowledge gained from this study will fundamentally contribute to our understanding of the evolutionary dynamics of bacteria under phage selective pressure, which is crucial for the efficient utilization of bacteriophages as antimicrobials.

Biography

Zeinab Hosseini-Doust is an assistant professor in the Departments of Chemical Engineering and Biomedical Engineering at McMaster University. For the past 10 years, he has been working on bacteriophage biotechnologyon bacteriophage biotechnology. The overarching goal of this research program is to employ the remarkable properties of bacteriophages (or phages), combined with the powerful tools of biotechnology, to design solutions that tackle global challenges in human health and the health of the environment. Her work particularly focused on three applications of bacteriophage biotechnology, namely: (1) alternative antimicrobials, (2) novel biosensors and diagnostic assays, and (3) multifunctional biomaterials and bioactive nanoparticles for biomedical engineering..

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