Day Zero Diagnostics Announces Publication of Research Describing Plasmid-Mediated Mechanisms of Antibiotic Resistance Using Nanopore Long-Read Sequencing

Novel sequencing and analysis technique will advance the development of the company's technologies for rapidly diagnosing severe infections and investigating suspected outbreaks

Boston—June 2, 2020—Day Zero Diagnostics, Inc., an infectious disease diagnostics company using genome sequencing and machine learning to combat the rise of antibiotic-resistant infections, today announced the publication of research on two *E. coli (Escherichia coli)* strains with unusually high resistance to broad-spectrum, quinolone-based antibiotics.

Day Zero Diagnostics' research collaborators at Massachusetts General Hospital (MGH) identified the two unique, highly quinolone-resistant *E. coli* strains, but found that they lacked typical resistance markers associated with resistance to quinolones. Using nanopore long-read sequencing to assemble the full genomes of the strains along with advanced computational analysis, Day Zero's team helped MGH's researchers discover unusual plasmid-mediated resistance mechanisms in each strain.

Plasmids are small, mobile, DNA molecules within a bacterial cell that are physically separate from chromosomal DNA. Plasmids frequently carry antibiotic resistance and virulence determinants and are often swapped between individual bacterial cells, allowing for rapid transmission of antibiotic resistance. Plasmids can pose numerous challenges for sequencing and computational analysis since they contain large repetitive elements and can be present in multiple copies within a pathogen. In two recently published articles, Day Zero's work revealed new insights into the genomic complexity of antibiotic resistance, which can be used to predict the resistance of a particular infection and to aid in hospital-acquired infection transmission analysis.

Research on the first strain was published in Antimicrobial Agents and Chemotherapy and described a plasmid with a large duplication event introducing four additional copies of a quinolone resistance gene.[1] The research suggests a novel dosage effect from the introduction of multiple copies of the same gene that resulted in an 8-fold increase in resistance to quinolones.

Research on the second strain, published in International Journal of Antimicrobial Agents, found four different resistance genes carried on multiple plasmids which appear to collectively contribute to the strain's high quinolone resistance.[2] Resolution of the mechanism of resistance required assembly of the genome using both short and long read sequencing and careful bioinformatics analysis for this complex case that included a plasmid cointegration event.

"Sequencing and analyzing plasmid DNA is challenging but this research helps us better understand the important role that plasmids play in the spread of antibiotic resistance," said Mohamad Sater, Ph.D., Director of Computational Biology at Day Zero Diagnostics. "The novel techniques used in this research are helping us advance the development of our new diagnostic system that is intended to help physicians rapidly diagnose severe infections and determine the most effective antibiotic for treatment, as well as enhance our epiXact® service for investigating suspected hospital-acquired infection outbreaks."

About Day Zero Diagnostics

Day Zero Diagnostics, Inc., based in Boston, is pioneering a new class of infectious disease diagnostics using whole-genome sequencing and machine learning to revolutionize how the world fights the growing threat of antibiotic resistance. The company's mission is to change the way infectious diseases are diagnosed and treated by rapidly identifying both the species and the antibiotic resistance profile of severe infections without the need for a culture. By using sequencing, Day Zero also enables big data approaches for managing healthcare-associated infection outbreaks. Day Zero Diagnostics was founded in 2016 by a team of clinicians and scientists from Harvard University and Massachusetts General Hospital. The company has been recognized as a leading innovator by MedTech Innovator, TedMed Hive, Xconomy, HealthTech Arkansas, and MassChallenge HealthTech. For more information visit www.dayzerodiagnostics.com or follow us on Twitter at @dayzerodx.

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[1] Vinué L, Sater MRA, Herriott I, et al. Multiple Copies of qnrA1 on an IncA/C2 Plasmid Explain Enhanced Quinolone Resistance in an Escherichia coli Mutant. Antimicrobial Agents and Chemotherapy. 2019 Aug;63(8). DOI: 10.1128/aac.00718-19.
[2] L. Vinué, M.R.A. Sater and I.C. Herriott et al., Plasmids and genes contributing to high-level quinolone resistance in Escherichia coli, International Journal of Antimicrobial Agents. 2020 - Note full dated citation available once published