DAYZERO DIAGNOSTICS

# Multi-copy qnrA1 Plasmid Causes Elevated Quinolone Resistance in E. coli

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Large multi-drug resistance (MDR) plasmids are often challenging to assemble and circularize due to repetitive sequences, numerous insertion elements, and regions sharing homology with the bacterial chromosome. These complications are exacerbated by copy number variation introduced by large duplication events involving multiple genes. In this work, we emphasize the utility of nanopore long-read sequencing to overcome these challenges by producing a complete sequence of a 200kb MDR plasmid containing a duplication event mediated by insertion sequence ISCR1 transposition. The 20kb multi-duplication introduced four additional copies of the *qnrA1* quinolone resistance gene. The qnrA1 copy number appears to have a dosage effect significantly increasing resistance to ciprofloxacin in *E. coli* strains carrying the plasmid. To our knowledge this is the first report of a resistance mechanism associated with a stable qnrA1 duplication in an *E. coli* plasmid.

 