Scientists illustrate role of novel chromosomal mutations in fosfomycin resistance

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Researchers identified novel chromosomal mutations and described their role in the development of resistance of *Escherichia coli* (*E. coli*) to broad-spectrum antibiotic fosfomycin, according to research presented at the 28th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID).

Researchers from France studied the genetic basis of fosfomycin resistance in a panel of *E. coli* isolates and found that certain mutations rendered fosfomycin ineffective at lower doses compared with other mutations. They obtained four mutants in vitro and used a set of 20 clinical isolates, 11 of which were susceptible to antibiotics and nine of which were resistant. The team analysed the minimum inhibitory concentration (MIC) of fosfomycin, which is the concentration at which bacterial growth was prevented. A low MIC means that a smaller amount of the antibiotic was needed to stop growth compared to samples with high MICs.

“In this study, we have identified novel chromosomal mutations both selected in vitro and in vivo and experimentally determined their role in fosfomycin resistance,” explained presenting author Prof. Vincent Cattoir. “Mutations in uhpB and uhpC appear to be more frequent than those in already known genes.”

Researchers found no genetic mutations in the 11 *E. coli* isolates that responded to fosfomycin, with MICs ranging from 0.5 to 8 mg/L. However, they found several mutations in each of the nine fosfomycin-resistant isolates, which exhibited

MICs in the range of 64-256 mg/L.

Cattoir’s team obtained two mutants that corresponded with mutations in two novel genes, uhpB and uhpC. Additional mutations were noted on genes galU and Ion. When researchers introduced the uhpB and uhpC mutations, the amount of fosfomycin needed to stop the visible growth of *E. coli* was 64-fold. Single mutations in the galU and Ion genes only caused a two-fold increase in the MIC. Three other uhpB/uhpC mutations each led to a 128-fold increase in fosfomycin MICs.

Fosfomycin is an antibiotic used to treat bladder and urinary tract infections. Fosfomycin resistance results from a set of known chromosomal mutations or the acquisition of mutated genes from elsewhere, such as other bacterial species. But resistance is also observed in some strains that do not have these known mutations or acquired genes.