Entry point for curbing the evolution of antibiotic resistance discovered

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The team of Professor Tobias Bollenbach from the Institute for Biological Physics at the University of Cologne has published a study on a new approach to improving the effectiveness of antibiotics in bacterial

infections. The study 'Highly parallel lab evolution reveals that epistasis can curb the evolution of antibiotic resistance,' on ways to controlling antibiotic resistance through targeted gene interactions has appeared in *Nature Communications*.

'We wanted to know how genetic disorders in the bacterium E. coli interact with the later evolutionary adaptation to the drug,' said Bollenbach. Doctoral researcher Marta Lukačišinová developed a robotic platform together with Bollenbach and the technician Booshini Fernando with which hundreds of genetically altered Escherichia coli populations could be created simultaneously, and the course of their evolution investigated. "Our most important result was that we found an entry point for suppressing the spontaneous development of resistance to the administered drug," Lukačišinová added.

At first, the team identified a prototypical pattern in the development of resistance: Those bacterial strains that initially reacted more sensitively to drugs developed a greater resistance to the drug during the course of the evolutionary experiment. However, the researchers were particularly interested in the conditions under which this pattern is broken and virtually no resistance develops.

The study showed that this happens when the bacterium exhibits certain functional disorders. The researchers identified the areas of membrane transport and chaperones, which play a decisive role in the error-free production of proteins. If these functions are not fully intact in the bacterium, an antibiotic can attack these areas much more effectively and improve its effectiveness in the long term. In the future, these molecular targets may help to improve antibiotics.

As head of the Biological Physics and Systems Biology research group at the University of Cologne, Tobias Bollenbach is investigating new ways to minimize or even prevent the development of drug resistance.

More information: Marta Lukačišinová et al, Highly parallel lab evolution reveals that epistasis can curb the evolution of antibiotic resistance, *Nature Communications* (2020). DOI: 10.1038/s41467-020-16932-z