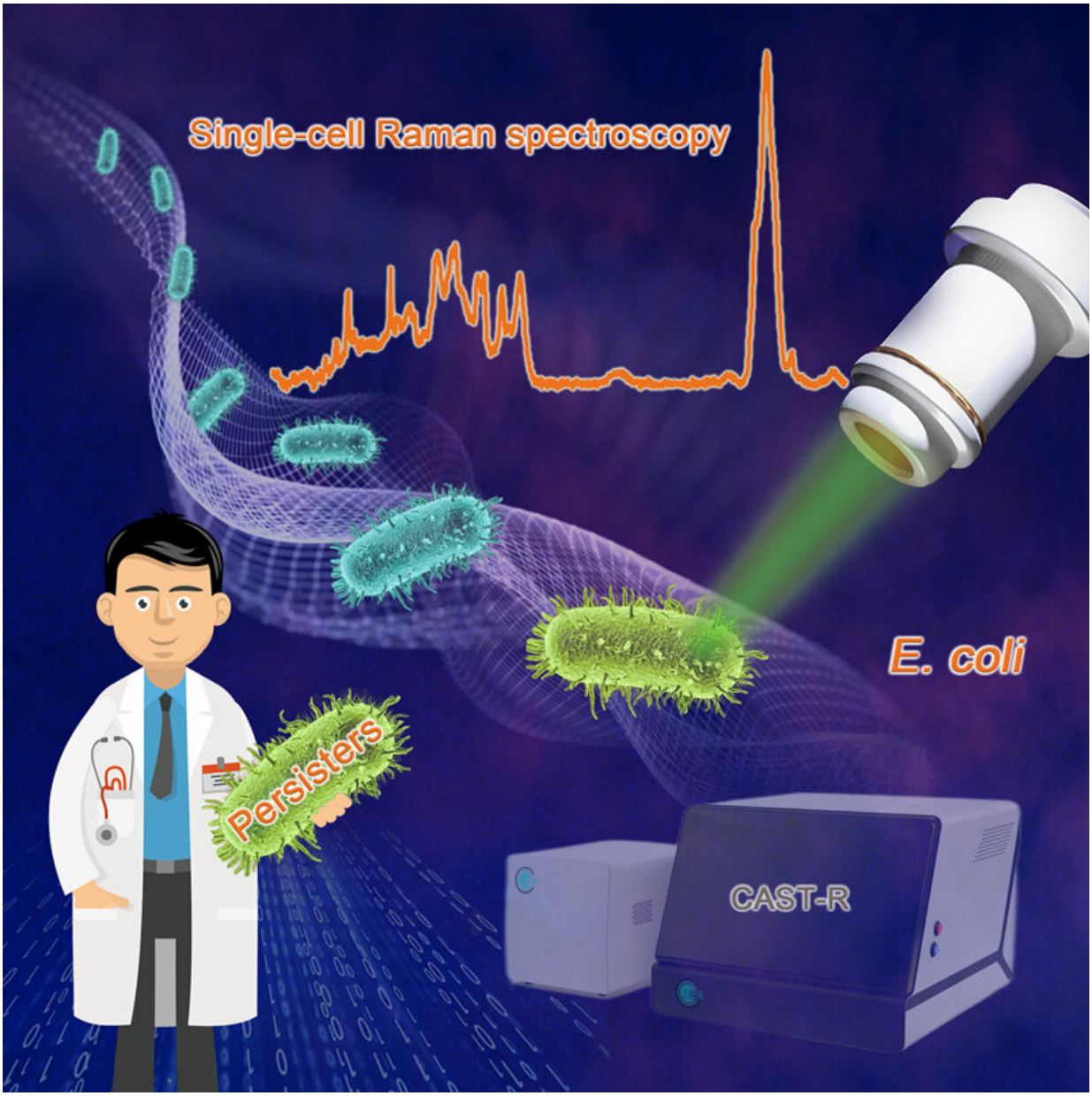
# New study reveals how E. coli cells evade antibacterial treatment

September 22 2022, by Zhang Nannan



Raman spectroscopy identifies E. coli persisters at single-cell level. Credit: Liu Yang

The formation of persisters is an important feature of bacteria like Escherichia coli (E. coli). These noxious cells, which are able to go dormant, are highly resistant to antimicrobial treatments and account for various relapsing chronic infections with common symptoms such as severe stomach pain, vomiting and bloody diarrhea.

Formation of persister cells is thought to be one of the most important strategies of bacteria like E. coli for survival under drug treatment and harsh conditions. But little is known about how they form and work, primarily due to technical limitations in previous studies.

In a recent paper published in *Frontiers in Microbiology* on Aug. 4, researchers have used a technique called "Raman spectroscopy" to identify the key characteristics of E. coli persister cells.

"Currently, the majority of the work deals with persisters at the whole population level," said Dr. Wang Chuan from The University of Hong Kong. "There are two significant improvements in our study. Firstly, the biochemical synthetic and metabolic activities of E. coli persister cells are analyzed on the basis of their molecular quantity, instead of merely observing the dividing rate and/or growth state. Secondly, our observations arise from investigations on single cells rather than the 'average' level of the whole population of bacterial persisters." This focus on individual cells has been proved to be important for understanding how the persister cells work.

The technique that researchers have applied to understand the persister cells is Raman spectroscopy. It is a well-known method of light-based

chemical analysis. The light excites the sample via creating a vibration. That vibration can be read and interpreted precisely. Raman spectroscopy results are often described as a "fingerprint" of the molecules inside the cells. Through the Raman spectroscopy technique, researchers are able to create a profile of the persister cells that can be used to subsequently identify similar cells.

Traditionally, persister cells have been considered to exist in a dormant state, as they do not grow while undergoing stress like an antimicrobial treatment. However, researchers find that the metabolic activity of the E. coli persister cells is significantly higher than the reference strains of E. coli. "This important new finding implies that persister cells remain to be active even in their dormant state, and this could be one of the crucial ways they are able to survive a high-dose antimicrobial treatment," said Prof. Jin Lijian from The University of Hong Kong.

"Based on the advanced Raman spectroscopy technology, our study has assessed for the first time the relative levels of biochemical synthesis in E. coli persister cells during their formation and resuscitation, indicating that these persister cells may develop intrinsic strategies via downregulating the replication rate while enhancing biosynthesis for survival and subsequent recovery," said Chen Rongze, co-first author of the paper and a doctoral student from the Single-Cell Center, Qingdao Institute of Bioenergy and Bioprocess Technology (QIBEBT) of the Chinese Academy of Sciences.

Importantly, this novel study further reveals the metabolic activity of E. coli persisters under different conditions and an increased level of their metabolic activities as compared to the reference strains of E. coli.

The researchers hope that the current findings could lead to additional discoveries in the near future. "Indeed, we have developed a new instrument called CAST-R (Clinical Antimicrobial Susceptibility Test

Ramanometry) to identify and characterize the persisters, so that the investigations can be extended to other pathogens and eventually applied in clinics, by disclosing the mechanisms of microbial pathogenicity for developing novel, personalized therapeutic strategies and approaches," said Prof. Xu Jian at the Single-Cell Center who co-led the study.

**More information:** Chuan Wang et al, Single-cell Raman spectroscopy identifies Escherichia coli persisters and reveals their enhanced metabolic activities, *Frontiers in Microbiology* (2022). DOI: 10.3389/fmicb.2022.936726

Provided by Chinese Academy of Sciences