Team develops powerful new tool to aid in battle against cancer-causing bacteria in the stomach

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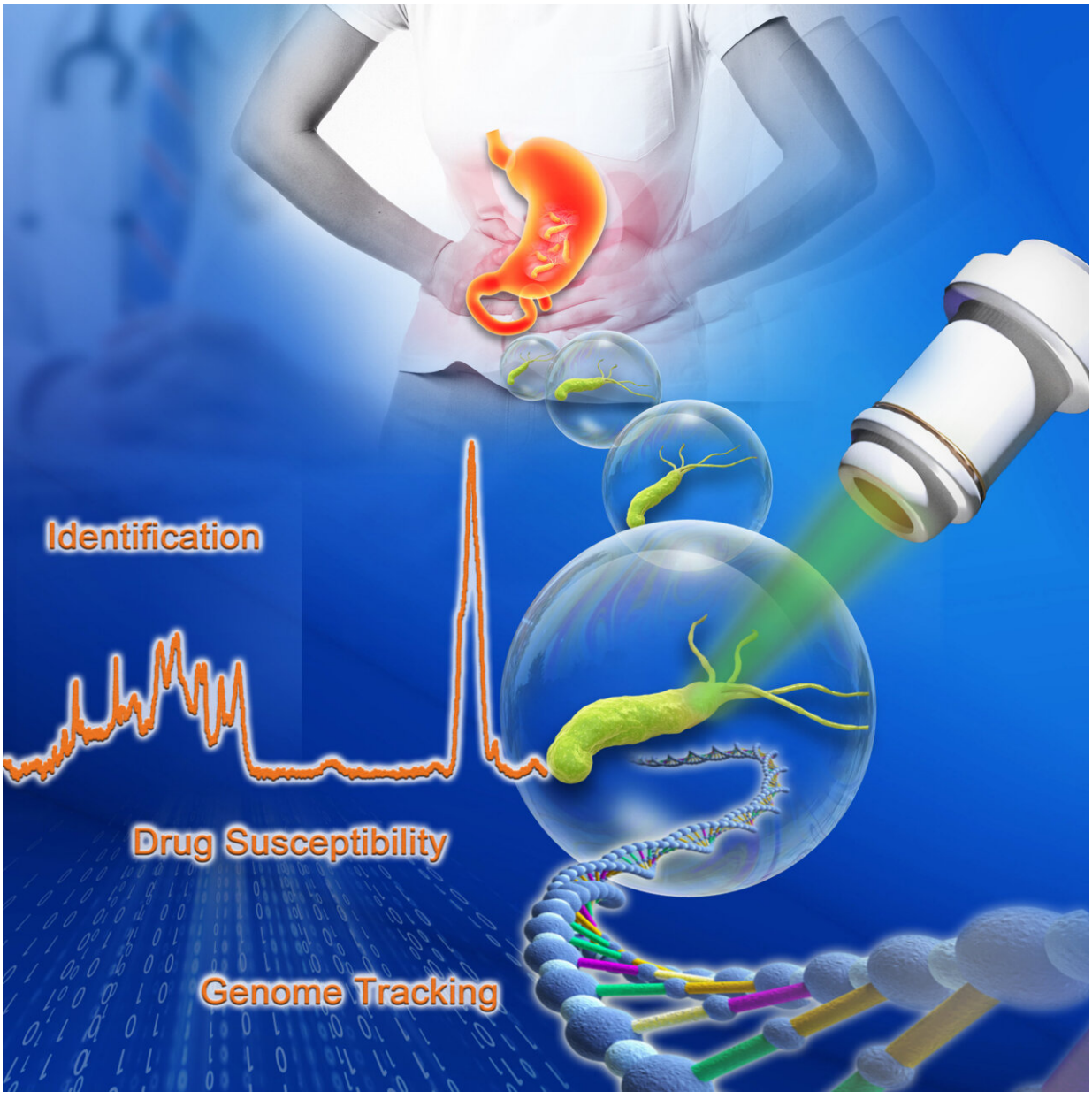

Clinical Antimicrobial Susceptibility Test Ramanometry for Helicobacter pylori (CAST-R-HP). Credit: Liu Yang

Helicobacter pylori (H. pylori), the bacteria that can cause human gastritis, peptic ulcers and stomach cancer, infects about half of the world's population. It is essential to quickly identify the infection and select the right combination of sensitive antibiotics. Current tools, however, are limited, mainly because H. pylori are slow-growing and hard to cultivate.

Researchers from the Qingdao Institute of Bioenergy and Bioprocess Technology (QIBEBT) of the Chinese Academy of Sciences (CAS) and their collaborators at State Key Laboratory of Infectious Disease Prevention and Control, National Institute for Communicable Disease Control and Prevention (ICDC) of China CDC and Qingdao Municipal Hospital have developed a medical instrument called Clinical Antimicrobial Susceptibility Test Ramanometry for Helicobacter pylori (CAST-R-HP) that holds promise as a powerful new tool in the diagnosis and treatment of H. pylori infections.

Their findings were published on June 18 in the journal *Clinical Chemistry*.

In battling H. pylori, researchers and health care professionals need tools that are fast, reliable and sensitive for pathogen identification and antimicrobial susceptibility tests, along with genome-wide mutation profiling that reveals the bacteria's resistance mechanisms.

Current methods for detecting H. pylori and identifying sensitive

antibiotics for eradication therapy are bacterial culture and drug sensitivity testing based on endoscopic gastric mucosal samples.

"The current culture-based antimicrobial susceptibility testing is too slow and requires at least a week of turnaround time," said Prof. Zhang Jianzhong from the State Key Laboratory of Infectious Disease Prevention and Control, ICDC of China CDC, a senior author of the study.

The team has devised an approach that performs rapid pathogen identification, metabolism inhibition-based antimicrobial susceptibility tests, and high-quality single-cell whole-genome sequencing for unveiling antimicrobial resistance mechanisms. Their approach provides greater than 98 percent accuracy and is successful at precise one-cell resolution working directly from biopsy samples.

The core technologies, called D2O-probed Ramanometry and Raman-activated Cell Sorting and Sequencing (RACS-Seq), are integrated in the CAST-R-HP instrument.

"The culture-independency, speed, high resolution and comprehensive information output suggest CAST-R-HP as a powerful tool for diagnosis and treatment of H. pylori infections, now at single-cell precision," said Xu Jian, another senior author of the study and Director of Single-Cell Center at QIBEBT.

Looking ahead to future research, the team will explore ways to further accelerate the CAST-R-HP, for example, by developing a microfluidics-based chip to enrich the trace number of cells directly from the H. pylori infected biopsy tissue. This chip development could further reduce the turnaround time of the metabolic-inhibition-based antimicrobial susceptibility test from roughly three days to less than 24 hours.

"Our next step would be to fully assess the utility of the workflow for all the first-line and second-line antibiotics in use for the treatment of H. pylori infections," said Liu Min from the Single-Cell Center at QIBEBT, the first author of the paper.

The team's CAST-R-HP could also be used to map H. pylori heterogeneity at the genome level. "By enabling identification, drug susceptibility tests, and whole-genome-based source tracking at single-cell resolution, CAST-R-HP should not just facilitate precise antibiotic administration for H. pylori infection, but reduce the risk of drug resistance in the general human populations," added Xu Jian.

More information: Min Liu et al, Single-Cell Identification, Drug Susceptibility Test, and Whole-genome Sequencing of Helicobacter pylori Directly from Gastric Biopsy by Clinical Antimicrobial Susceptibility Test Ramanometry, *Clinical Chemistry* (2022). DOI: 10.1093/clinchem/hvac082

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