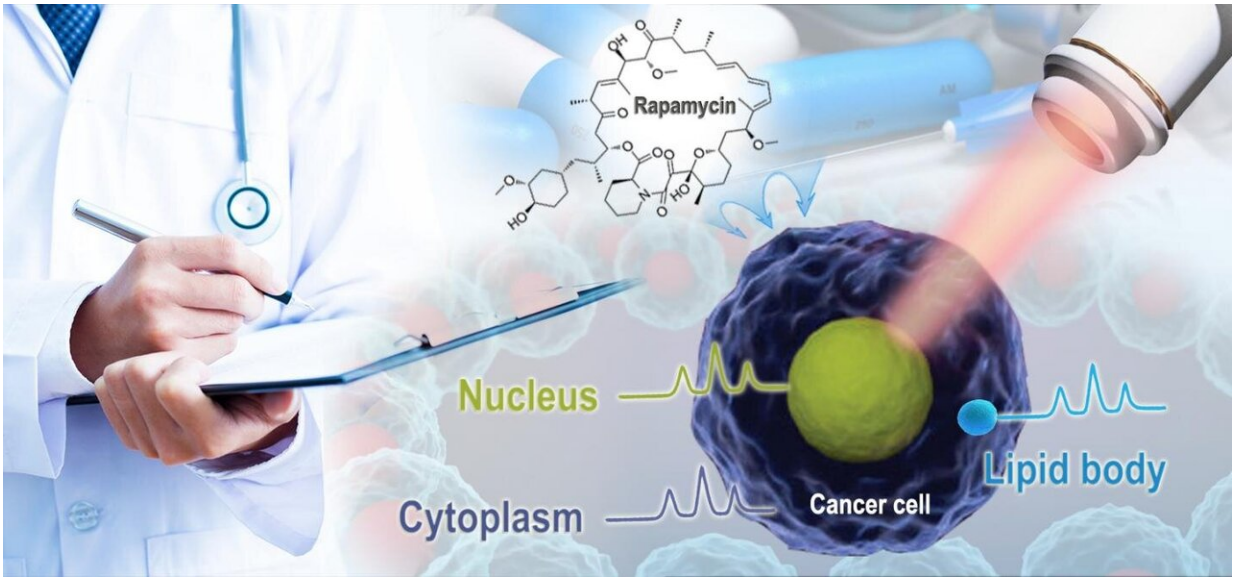
Single-cell test can reveal precisely how drugs kill cancer cells

January 19 2021



D_2O-probed CANcer Susceptibility Test Ramanometry (D_2O-CANST-R) Credit: LIU Yang

Cancer cells are smart when it comes to anti-cancer drugs, evolving and becoming resistant to even the strongest chemotherapies over time. To combat this evasive behavior, researchers have developed a method named D_2O-probed CANcer Susceptibility Test Ramanometry (D_2O-CANST-R) to see, at the single-cell/organelle level, how pharmaceuticals induce cancer cell death and how cancer cells adapt.

The research, conducted by the Qingdao Institute of Bioenergy and Bioprocess Technology (QIBEBT) of the Chinese Academy of Sciences (CAS), was published on Jan. 12 in *Analytical Chemistry*, a journal of the American Chemical Society.

"Understanding the mechanism of cellular response to drugs and pharmaceutical therapies is crucial to improving cancer treatment," said paper author Xu Jian, director of the Single-Cell Center at QIBEBT. He explained that cancer cells can resist chemotherapy by changing metabolic activity for adaptation to drug stress, but exactly how this happens is poorly understood. "Approaches are needed to rapidly illuminate the particular effects of a drug on metabolic activity of cancer cells. This is clinically important as precise and personal administration of cancer chemotherapy is crucial for saving cancer patients' lives."

Maryam Hekmatara, a Ph.D. student of Xu, and her workmates paired a powerful algorithm with Raman spectroscopy, which involves using a laser to excite photons in a sample to reveal structural information, including interactions. They examined how rapamycin, an anti-cancer drug, changed the metabolic activity in a human cancer cell line and in yeast.

Their method revealed the changes small organelles inside the cells made in energy use and consumption. With a resolution capability of less than one micrometer—the width of a human hair is typically 80 to 100 micrometers, for comparison—the approach has the potential to reveal the metabolism in a cancer cell with very fine details.

"The method is able to rapidly and precisely track and distinguish changes in lipid and protein metabolic-inhibitory effect of rapamycin," Hekmatara said, noting the method takes just days compared to traditional tests that can take much longer to see if an individual patient's cells will respond favorably to a drug. "It is also very precise, as it can

distinguish cancer cell responses to drugs at the single cell and single organelle resolution, which is crucial for understanding why the drug is—or is not—effective."

The researchers plan to further study how cells become resistant, as well as further develop their method as a personalized approach to determine the most effective anti-cancer drug for a patient.

More information: Maryam Hekmatara et al, D2O-Probed Raman Microspectroscopy Distinguishes the Metabolic Dynamics of Macromolecules in Organellar Anticancer Drug Response, *Analytical Chemistry* (2021). DOI: 10.1021/acs.analchem.0c03925

Provided by Chinese Academy of Sciences