A Golden Ticket for Mass Spec Imaging, SEM, and MicroCT

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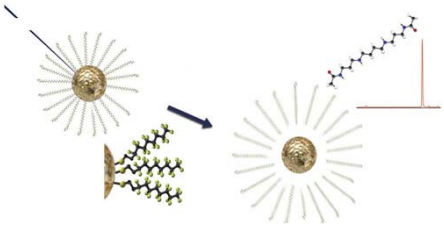
Mass spectrometry imaging (MSI) is an increasingly powerful tool for mapping metabolites and proteins in biological tissue, but the resulting pictures are devoid of structural detail. Now, a new multimodal MSI reagent may change how these experiments are done.

A research team led by Gary Siuzdak at the Scripps Research Institute developed the new imaging agent from gold nanoparticles, which are visible to X-rays and electron microscopes, and are also active in mass spectrometers. In the past, gold nanoparticles have been difficult to apply to MSI because the nanoparticles require so much energy to ionize that the metabolites of interest get destroyed in the process.



Schematic illustration of the possible desorption mechanism. On irradiation, the gold core efficiently absorbs the laser energy and transfers it to thermally release fluorinated ligands. The desorbed fluorinated ligands provide the kinetic energy (and driving force) for analyte desorption and serve to protect the analyte from thermal degradation (1).

To avoid that problem, Siuzdak's team modified the nanoparticles with fluorinated hydrocarbons. When applied to a tissue section surface and irradiated with a laser, these fluorinated gold nanoparticles (f-AuNPs) rapidly heat up to 2000°K. But rather than imparting that thermal energy directly to the sample, which would destroy the fragile metabolites, the structure seems to insulate them instead, causing the fluorocarbon ligands and nearby metabolites to vaporize into the gas phase where they can be analyzed. Siuzdak calls the process "nanostructure imaging mass spectrometry" (NIMS), redefining an acronym he first used in 2007 to describe another surface-phase imaging approach (nanostructure-initiator mass spectrometry), which also relied on fluorinated initiator molecules.

"We think the importance of the fluorinated hydrocarbons is they act like Teflon," Siuzdak explains. "The metabolites don't stick to them and are therefore more easily vaporized."

Using the f-AuNPs, the team performed mass spectrometry imaging and scanning electron microscopy (SEM) of bacterial biofilms grown under normal and stressed conditions. They found that synthesis of a particular diglyceride was downregulated under stress conditions, while bacterial density (measured by SEM) was elevated.

In another experiment, the team used a "breathable liquid" to perfuse f-AuNPs into mouse lungs through the trachea. They then imaged the lungs in 3-D via micro-computed tomography and sectioned the tissue to map the distribution of a particular phosphatidylcholine. The authors also demonstrated that they could suspend f-AuNPs in a fluorocarbon-based blood substitute to perfuse through the animals' circulatory systems.

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Because it requires no matrix, the f-AuNP approach produces cleaner spectra in the low molecular weight range, making it more amenable to metabolomic studies. f-AuNPs also require lower energy for ionization than MALDI, yielding more efficient ionization with lower fragmentation.

Jonathan Sweedler at the University of Illinois at Urbana-Champaign is "excited and intrigued" by the multimodal possibilities of the new f-AuNPs. Sweedler uses mass spectrometry imaging to map small molecules in neural tissue and noted that "There are molecules there that are hard to measure with our [current] approaches. So I'm going to explore this."

Reference

Kurczy, ME, et al., "Comprehensive bioimaging with fluorinated nanoparticles using breathable liquids," Nat Commun, 6:5998, 2015.

Keywords: mass spectrometry imaging scanning electron microscopy MicroCT nanoparticles