SENSORS AND PROBES

Laser particles in hundreds of colors

The development of biologically compatible microdisk lasers enables massively multiplexed cell tracking.

Studying multiple cells or factors at a time is often necessary for understanding complex biological systems. With conventional probes for fluorescence microscopy, there is a 'color barrier' that arises from spectral overlap among fluorophores, which practically limits most experiments to studying fewer than ten different targets.

Probes that address this limitation are under constant development, and one type that is very promising is intracellular lasers. These are structures that are small enough to be taken up into typical cells and lase following appropriate excitation. Apart from being bright, a major benefit of intracellular lasers is their sharp emission profile, which makes them well-suited for multiplexed imaging.

Seok-Hyun Yun and his research group at Harvard Medical School have developed a series of 'laser particles' for multiplexed cell tagging and tracking applications. Their work builds on established technology for microdisk lasers, but extends it to make biocompatible laser particles in hundreds of colors from 1,170–1,580 nm, with sub-nanometer linewidths. The researchers chose semiconductor materials that are known to be biocompatible and then used lithography to make microdisks in a range of sizes corresponding to different lasing wavelengths. The microdisks were then covered in a silicon dioxide coating, which protects the material and makes the lasers less sensitive to changes in external refractive index.

The authors showed that the laser particles emit laser light as expected, are stable in biological solutions, and are biocompatible in mammalian cells. For cellular imaging applications, the team developed a microscope that combines the pump laser and spectrophotometer used for imaging the lasers with a confocal microscope, which allows rapid imaging of the intracellular lasers and fluorescence imaging.

The researchers generated breast cancer organoids using cells labeled with a huge set of laser particles. They showed that they could accurately track thousands of cells for over 24 h, and a smaller subset of these for over five days. Using their data, they identified regions of high and low mobility within the organoid.

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