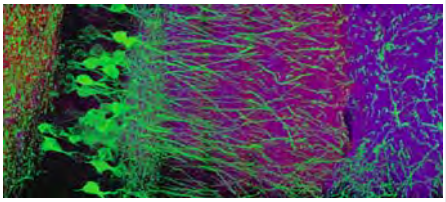
Making Small Things Large

02/06/2015
Kristie Nybo, PhD
Biological imaging at single nanometer resolution became possible with the introduction of super resolution microscopy. Can the same resolution be achieved by simply enlarging the sample? Find out...

Biochemical experiments have revealed many details about cell contents and function, but for understanding cell biology, nothing beats looking directly at the cell. Cell imaging has been possible since the seventeenth century, when the first microscopes were invented. But until recently, microscopists were unable to resolve the smallest cellular components, such as proteins, that really carry out the functions of a cell. Improvements in lens manufacturing and alignment advanced microscopes extensively, but light microscopy resolution remained limited because objects separated by a distance less than half the wavelength of light can't be distinguished from one another. It's a principle of physics.

Super resolution microscopy overcame the diffraction barrier, resolving structures at nanometer resolution by switching fluorophores on and off and recording signals one after another. For this accomplishment, inventors Eric Betzig, William Moerner, and Stefan Hell were awarded the 2014 Nobel Prize in Chemistry. However, while it is possible now to peer into the tiniest corridors of cells, super resolution microscopes are expensive and require significant expertise to operate. For these reasons, they aren't available to most labs. Now researchers from MIT present an alternative for super resolution imaging: enlarge the sample before imaging.

"Instead of acquiring a new microscope to take images with nanoscale resolution, you can take the images on a regular microscope. You physically make the sample bigger, rather than trying to magnify the rays of light that are emitted by the sample," said Ed Boyden, senior author of the study, in a press release.



Boyden's team first immunolabeled components of interest in their samples with antibodies linked to a fluorescent dye and a chemical anchor, which they would later covalently attach to a very absorbent polymer gel network formed within the tissue. After digesting the proteins that hold the sample together, they added water, swelling the tissue like a sponge to 100-times its original size. With the labeled proteins still anchored to the matrix, the expanded tissue actually maintained the relationships between the various elements of the cells.

Using a confocal microscope, Boyden's team imaged expanded cultured cells and brain tissue with an apparent ~70nm lateral resolution. "The other methods currently have better resolution, but are harder to use, or slower," said first author Paul Tillberg, a graduate student in Boyden's lab.

The new method, which the authors call expansion microscopy, offers a less expensive option for high resolution imaging and uses chemicals commonly found in research laboratories. While Boyden's group plans to focus on brain imaging, the method might also be suitable to imaging tumor metastasis, angiogenesis, or immune function.

Reference

Chen F, Tillberg PW, Boyden ES. Optical imaging. Expansion microscopy. Science. 2015 Jan 30;347(6221):543-8.

Recent News:

- Flu Viruses Cross Oceans
- Trapper Cuppers
- The Power to Program Life

Keywords: super resolution microscopy BRAIN initiative technology