LightSheet super-resolution imaging of whole-kidney by tissue expansion

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Abstract

Optical imaging techniques provide much important information in understanding life science especially cellular structure and morphology. However, the resolution of optical imaging is limited by the Abbe diffraction limit. For the last 100 years, biologists and optical scientists were unable to obtain a clear optical image of biological entities down to molecular level that are smaller than the diffraction limit (around 200-nm in lateral resolution). With the discovery of green fluorescent protein, the winners of Nobel Prize in Chemistry 2014, E. Betzig, W. E. Moerner and S. Hell, innovated super-resolution microscopic techniques. Such techniques enable biologists to visualize nanoscale fluorophores that are beyond the diffraction limit. These techniques do not physically violate the diffraction limit of resolution but exploit the photoluminescence properties and labelling specificity of fluorescence molecules to achieve super-resolution imaging.

Instead of sweating on the super-resolution techniques to pursuit high spatial resolution, expansion microscopy (ExM) is invented to bypass the optical diffraction limit by physically expanding the samples to ~4 fold larger than original with swellable polymers [1]. In order to image such expanded renal samples, we use lightsheet microscopy, a separate excitation lens perpendicular to the widefield detection lens to confine the illumination to the neighborhood of the focal plane [2]. By combining intrinsic optical sectioning with widefield detection, lightsheet microscopy allows fast imaging speed to record multi-megapixel imaging of selected plane in a single exposure of the camera. Here we apply expansion technique and lattice light-sheet microscopy to understand subcellular details and its organ-scale intercellular connectivity in kidney, and provide renal tubule 3D imaging with higher resolution and deeper penetration.

References

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