LIGHT SHEET FLUORESCENCE MICROSCOPY FOR WHOLE-BRAIN 3D MAPPING OF HUMAN NEURAL TRANSPLANT INNERVATION

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Rabies virus-based retrograde tracing has developed into a powerful approach for visualizing synaptically connected neurons. Combined with a refined tissue clearing technology [1], this approach enables e.g. the visualization of transplanted neurons and synaptically connected host cells in whole-mouse brain preparations. In order to visualize and 3D reconstruct such a transplant connectome depicted by rabies virus-based tracing we developed a light sheet fluorescence microscope (LSFM) for imaging complete mouse brains. The instrument features a field of view of 9 mm^2, a total magnification of 4, a numerical aperture of 0.234 and a maximum working distance of 20 mm. Due to its two-sided illumination the image quality in both brain hemispheres is identical. A pivoting of the scanned light sheets significantly reduced shadow artefacts. For a complete brain 12 sCMOS images were stitched together for a single optical slice, and 1700 optical sections were acquired. First biological data generated with this system show that the same human neural donor cell population grafted into different brain regions receives highly orthotopic input. These findings indicate that transplant connectivity is largely dictated by the circuitry of the target region and depict rabies-based transsynaptic tracing and LSFM as efficient tools for comprehensive assessment of host–donor cell innervation [2].

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