

Investigating immune cells in the brain using light sheet fluorescence microscopy

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Light sheet fluorescent microscopy (LSFM) and related techniques have become a recent trend. The fusion of fluorescence-based microscopy and non-invasive tomographic imaging creates a powerful tool to investigate intact organ structures. Even very large organs or whole organisms can be imaged in toto which allows three-dimensional histological examination without previous sectioning. The physiological integrity is maintained like known from computer tomography (CT) or magnetic resonance imaging (MRI) scans. But in combination with fluorescent dyes or proteins, LSFM allows a structural macro view as well as cellular resolution. Side-on planar illumination excites fluorescent structures selectively in the focal plane which leads to high sensitivity and specificity of detected signals.

In a recent study, LSFM is used to identify mast cells in the brain and investigate their functional role in immune cell entry across the blood brain barrier. Therefore, double reporter mice, expressing fluorescent proteins in mast cells and neutrophils, were infected with *Toxoplasma gondii*. These parasites enter the brain of the host, which leads to immune cell recruitment to the parenchyma and its structural and functional reorganization. The intact skulls of healthy and infected mice were cleared and imaged with a light sheet microscope. After a three-dimensional reconstruction, qualitative and quantitative analysis on a cellular level can reveal the immune cell distribution in the brain, immune cell interactions, entry routes or the impact on the pathological outcome.