COMBINING EXPANSION MICROSCOPY AND LIGHT SHEET MICROSCOPY FOR FAST 3D IMAGING OF VIRUS-INFECTED HUMAN CELLS AT SUPER-RESOLUTION

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Viruses are small infective agents that require a host cell in order to replicate, and often lead to pathological conditions [1]. Dissecting the replication cycle of viruses in human cells is essential for developing effective antiviral drugs and vaccines. Here, we study the replication cycles of herpes simplex virus 1 (HSV-1, a wildtype pathogenic virus) and live attenuated influenza virus (LAIV, the basis of flu vaccines) by means of super-resolution optical imaging (<200 nm). To this aim, we employ the technique of expansion microscopy. Expansion microscopy is a sample preparation technique that physically magnifies biological specimens in order to increase the resolution achievable by a diffraction-limited microscope [2]. After staining and expanding virus-infected human cells, we image the expanded samples at either a widefield, confocal or light sheet microscope. The combination of expansion and light sheet microscopy has proved to be the best of the three in terms of contrast, signal-to-noise ratio, acquisition speed and 3D rendering quality. Importantly, we can reconstruct 3D models of the different stages of the replication cycles of both HSV-1 and LAIV by combining expansion and light sheet microscopy, revealing previously unknown virus-induced morphological changes in the host cell.

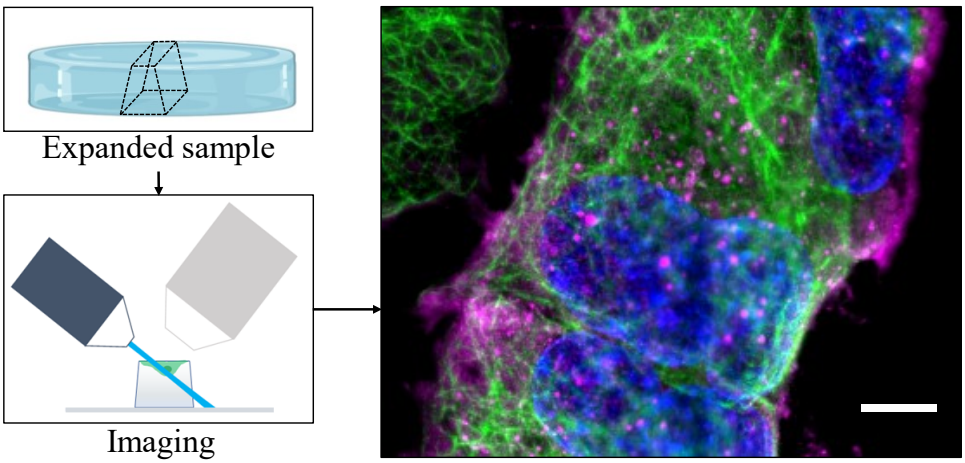

Figure 1: A549 cells infected with live attenuated influenza virus (LAIV) were magnified using expansion microscopy (left, top). A gel strip was cut to fit in between the objectives of a light sheet microscope (left, bottom). A maximum intensity projection of the infected cells was then rendered (right) to highlight the virus-induced morphological changes in the host cell. Blue: cell nuclei; green: cell microtubules; magenta: LAIV nucleoprotein. Scalebar: 5 µm.

REFERENCES

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