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A high-resolution correlative light and X-ray 3D cryo-imaging platform for cells and tissue at near-native physiological conditions.

High-resolution imaging of the cellular world in recent years has underpinned a revolution in high-content volume data accumulation resulting in a new understanding of cell organization and behaviour. Amongst the highlights of microscopy developments in cellular imaging has been the emergence of new correlative imaging modalities that incorporate Soft X-ray Tomography (SXT) of cryopreserved cells and tissue. At the correlative cryo-imaging beamline B24 of the UK synchrotron, we have devised and refined such a correlative imaging platform to a high level of automation and throughput by focusing not only on technique development but also on the accessibility of ease or use.

SXT is a high-resolution 3D mesoscale imaging technique for cells and tissues up to 12 μm in thickness in the fully hydrated state without using chemical fixation, sectioning or milling, or the use of contrast-enhancing agents. Under cryogenic conditions, vitrified samples are irradiated with 'water-window'X-rays to achieve a lateral resolution of structures within cells to 25 nm depending upon the optical set-up of the SXT microscope. At B24, a 3D super-resolution fluorescence microscope based on structured illumination microscopy (SIM) principles was developed as a complementary tool to match molecular localisation with high-resolution structural data acquired in SXT under cryogenic conditions leading to the development of a unique same-sample correlative light and X-ray tomography (CLXT) platform.

Here we will highlight representative B24 data from current biomedical areas and disease developments in both methodology and applications alongside new results in infection and immunity that have been only recently discovered through the CLXT platform.

Primary author: Dr JADHAV, Archana (Diamond Light Source Ltd)

Co-authors: Dr OKOLO, Chidinma (Diamond Light Source Ltd); Dr NAHAS, Kamal (Diamond Light Source Ltd); Mr FISH, Thomas (Diamond Light Source Ltd); Mr TAYLOR, Adam (Diamond Light Source Ltd); Prof. HARKIOLAKI, Maria (Diamond Light Source Ltd)

Presenter: Dr JADHAV, Archana (Diamond Light Source Ltd)