Light, x-rays or electrons for imaging malaria parasites?

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Imaging technologies have provided us with phenomenal insight into the micro- and nano-scopic domains and efforts to answer the major medical and biotechnology questions of the 21st century will be heavily reliant on the use of advanced imaging techniques. However there are limitations. Conventional light microscopy can be used with hydrated (in some cases, live) cells but has limited resolution, particularly for full-field imaging. Conventional electron microscopy offers very high resolution however the strong absorption of electrons by air and by the sample means that it can only be used with very thin, fixed, dehydrated samples. Imaging technologies that overcome some of the disadvantages of optical and electron microscopies are keenly sought.

We have used two “bridging” imaging modalities to explore sub-cellular topography. Three-dimensional structured illumination microscopy (3D-SIM) permits super-resolution fluorescence imaging of cells that are specifically labelled with fluorescent probes. Immunoelectron tomography offers high resolution imaging of individual ultrastructural features in a cellular context. Combined with serial sectioning and immunogold labeling it permits precise mapping of whole cell architecture.

The malaria parasite, *Plasmodium falciparum*, develops within human erythrocytes. As it grows the parasite establishes a membrane network outside its own limiting membrane in the cytoplasm of its host cell. These membrane structures play an important role in the trafficking of virulence proteins to the host cell surface, however their ultrastructure is only partly defined and there is on-going debate regarding their origin, organization and connectivity. Parasite endocytic processes are also poorly understood. The parasite consumes host haemoglobin in order to support its own growth. Small packets of haemoglobin are transferred from the host cell cytoplasm to a parasite digestive vacuole for haemoglobin digestion and heme detoxification however the precise mechanism for uptake is debated. Advanced imaging methods have provided novel insights into parasite cell architecture and functional cell biology.