High Resolution Soft X-Ray Microscopy of Medically Important Protozoa

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Some of the most pernicious diseases afflicting humankind are caused by parasitic protozoa, such as *Plasmodium falciparum*, the parasite that causes malaria. The 1-5 micron malarial parasite spends a large part of its life cycle within a red blood cell, where it metabolizes hemoglobin in its digestive vacuole, elaborates a tubulo-vesicular network for protein transport within the red cell cytosol, and inserts neoantigens in the red cell membrane to alter its antigenicity, morphology and function. The results of these processes have been detected and investigated using the soft x-ray microscope developed by the Center for X-Ray Optics at the Advanced Light Source in Berkeley. Our earliest studies established the morphology and structural development of parasites in normal erythrocytes and enabled us to then study aberrations in parasites that developed either in abnormal erythrocytes or in the presence of antimalarial drugs.[1] We made an important advance recently by utilizing an immunogold labeling technique that is compatible with soft x-rays for localizing antigens on the red cell surface.[2-4] We are evaluating whether this method can be used quantitatively, and we are developing novel labeling techniques to examine the alterations of phospholipid asymmetry in sickle cells infected with malarial parasites.[5] Our progress over the past two years and the promise of recent innovations in soft x-ray microscopy of intraerythrocytic malarial parasites demonstrates the value of this approach for biomedical research.

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[1]Magowan, C., Brown, J.T., Liang, J., Heck, J., Coppel, R.L., Mohandas, N., and Meyer-Ilse, W. 1997. Intracellular structures of normal and aberrant *Plasmodium falciparum* malaria parasites imaged by soft x-ray microscopy. Proc. Natl. Acad. Sci. USA 94:6222-6227.

[2]Chapman, H.N., Fu, J., Jacobsen, C., Williams, S. 1996. Dark-field x-ray microscopy of immunogold-labeled cells. J. Micro. Soc. Am. 2:53-62.

[3]Chapman, H. N., Jacobsen, C., Williams, S. 1996. A characterization of dark-field imaging of colloidal gold labels in a scanning transmission x-ray microscope. Ultramicroscopy. 62:191-213.

[4]Yeung, J., Brown, J.T., Nair, A., Meites, E., Coppel, R.L., Narla, M., Meyer-Ilse, W. and Magowan, C. 1998. X-ray microscopic visualization of specific labeling of adhesive molecule CD36 and cytoadherence by *Plasmodium falciparum* infected erythrocytes. Res Commun Mol Pathol Pharmacol. 99: 245-258.

[5]Kuypers, F.A., Lewis, R.A., Hua, M., Schott, M.A. Discher, D., Ernst, J.D. and Lubin, B.H. 1996. Detection of altered membrane phospholipid asymmetry in subpopulations of human red blood cells using fluorescently labeled annexin V. Blood 87:1179-1187.