S41-3 Bioimaging of intracellular elements by coherent X-ray microscopy (CXM) system

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A novel approach is potentially beneficial in the study of diseases of unknown etiology. Our work has focused on the role of intracellular element kinetics in disease, and previously established and demonstrated that the coherent X-ray microscopy (CXM) system for cellular observation could be successfully used to measure intracellular elements. The Long-Evans Cinnamon (LEC) rat is an animal model of human Wilson disease. ATP7B, a gene responsible for regulation of cellular export of heavy ions, is mutated in both Wilson disease and the LEC rat. Both are characterized by excessive accumulation of copper in the liver. The LEC rat is also a model of chronic hepatitis or hepatocirrhosis and subsequent hepatic cancer. However, the mechanism for carcinogenesis remains unknown. CXM can visualize multiple cellular elements with high resolution. Analysis by CXM showed high levels of Cu and Zn accumulation in liver cell nuclei. In an ATP7B transgenic LEC rat, which does not suffer from hepatic disease, no excessive accumulation of Cu and Zn was observed in the nuclei. These data suggested that nuclear Cu and Zn accumulation is likely critical for hepatic disease in the LEC rat. We also isolated a Cu/Zn binding protein from LEC rat liver nuclei by HPLC-ICP-MS, which was interestingly found to cause DNA damage in vitro. We discuss the possible relation between nuclear Cu and Zn accumulation and hepatic malignancy, and propose the usefulness of CXM in the study of diseases.