VIRTUAL-SLIDE ASSISTED TARGETING OF A NEUROFIBRILLARY TANGLE FOR CORRELATIVE LIGHT AND PRE-EMBEDDING IMMUNOELECTRON MICROSCOPY USING QUANTUM DOT NANOCRYSTALS

Miho Uematsu 1,2,3, Kyoei Mikami 2, Momoko Ebashi 1, Katsuki Hirokawa 2, Eijiro Adachi 2, Ryosuke Takahashi 2, Toshihiko Uchihara 1
1. Laboratory of Structural Neuropathology, Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan
2. Department of Neurology, Kyoto University Graduate School of Medicine, Kyoto, Japan
3. The Japan Society for the Promotion of Science (JSPS), Tokyo, Japan
4. Department of Pathology, Nitobe-Memorial Nakanoko General Hospital, Nakanoko-ku, Tokyo, Japan

Abstract
Background Quantum dot (QD) nanocrystal is a nanometer-scale fluorophore, which is detectable both as a fluorescent signal by light microscopy and as an electron-dense particle under electron microscopy. It can be utilized for coregional light and electron microscopy of a diseased brain specimen, as we established previously. Objective The merit of QD for light and electron microscopic correlation was further boosted by introducing virtual slide system in the identification process of whatever target at any part of the specimen for immunoelectron microscopy. Patients and Methods Material and Methods A target on a floating section of the Alzheimer disease brain were immunofluorolabeled with QD nanocrystals. The specimen underwent fluorescence virtual slide capturing. A targeted structure was subsequently subjected to electron microscopic observation to identify immunolabeling on the ultrastructure. Results The virtual slide image identified fluorescent labeling of the QD nanocrystals, which labeled the tau-positive fibrils, at 60X magnification with multiple virtual z-planes. Using a virtual slide image as a guide for the identification, ultrastuctural study of the targeted neurofibrillary tangle was performed, which demonstrated the presence of the QD on the paired helical filaments. Conclusion Virtual slide imaging facilitated the exact correlation of the same structure by light and electron microscopy and demonstrated how its ultrastructural details are related to its surroundings, providing further insights into how molecules in specific pathological ultrastuctures are at work in situ.

References