AMORPHOUS NANOSILICA INDUCES MHC CLASS I-RESTRICTED PRESENTATION OF EXOGENOUS ANTIGENS

T. Yoshikawa[1,2], H. Nabeshi[1,2], N. Itoh[1,2], Y. Yoshioka[2,3], Y. Tsutsumi[1,2,3,4]

[1]*Department of Toxicology and Safety Science, Graduate school of Pharmaceutical Sciences, Osaka University*
[2]*Laboratory of Biopharmaceutical Research, National Institute of Biomedical Innovation (NiBio)*
[3]*The Center for Advanced Medical Engineering and Informatics, Osaka University*
[4]*Ministry of Education, Culture, Sports, Science and Technology (MEXT)*
Osaka, Japan

Nanoparticle-based vaccine (Nanovaccine) is anticipated as a promising technology for the treatment of prostate cancer. Biocompatible nanoparticles are suitable carriers that are capable of delivering prostate cancer-derived antigenic proteins or peptide into antigen presenting cells, and eliciting potent immune responses based on MHC class I-restricted antigen-specific cytotoxic T lymphocytes. However, the fundamental information which is essential for the design of safe and effective nanovaccines, such as relationship between physicochemical properties of nanoparticles and immunomodulating effect, are insufficient. Here we explored the immunomodulating effect of nanoparticles in terms of transdermal absorption and MHC class I restricted cross-presentation of co-exposed antigenic proteins using nanosilicas as model particles. We evaluated the distribution of nanosilicas in the dermis after topical application of silica particles with diameters of 1000, 300, and 70 nm (designated nSP70, nSP300, and mSP1000, respectively). Transmission electron microscopy revealed that only nSP70 reached Langerhans cells and draining lymph nodes. We then evaluated the influence of nSP70-treatment on antigen processing in terms of cross-presentation of ovalbumin. We demonstrated that the efficiency of cross-presentation was substantially enhanced in the dendritic cell when exogenous antigens were loaded with nSP70. In contrast, cross-presentation was not detected when antigens were loaded with nSP300 and mSP1000. Thus, particles size is a point which should be well taken for the development of innovative nanovaccine.