



HOKKAIDO UNIVERSITY

Title	Design of Quantum Dot-Based High Performance Nanoparticle Platform for Nanoparticle-Based Drug Delivery (NDD) system [an abstract of dissertation and a summary of dissertation review]
Author(s)	TAN, ROGER SALVACION
Degree Grantor	北海道大学
Degree Name	博士(生命科学)
Dissertation Number	甲第12011号
Issue Date	2015-09-25
Doc URL	https://hdl.handle.net/2115/60373
Rights(URL)	https://creativecommons.org/licenses/by-nc-sa/2.1/jp/
Type	doctoral thesis
File Information	ROGER_SALVACION_TAN_abstract.pdf, 論文内容の要旨



学 位 論 文 内 容 の 要 旨

Abstract of Doctoral Dissertation

博士の専攻分野の名称 博士 (生命科学) 氏 名 _____.
Degree requested Doctor of Life Science Applicant name ROGER SALVACION TAN

学 位 論 文 題 名

Title of Doctoral Dissertation

Design of Quantum Dot-Based High Performance Nanoparticle Platform for Nanoparticle-Based
Drug Delivery (NDD) system

(ナノ微粒子による薬物送達システム

ー量子ドット型高性能ナノ微粒子プラットフォームの設計)

Nanoparticle drug delivery (NDD) platforms have emerged as a promising approach to enhance the efficacy of the existing drugs and potent therapeutic agents through encapsulation of poorly soluble agents. However, the early design of NDD vehicles was governed by the intrinsically poor pharmacokinetic properties of conventional chemotherapeutics. Low drug solubility, rapid metabolism and clearance, and most importantly a lack of selectivity regularly lead to therapeutic failure by causing severe systemic toxicity in healthy neighboring tissues, thus prohibiting the dose escalation necessary to eliminate tumor cells. Prime pre-requisite to a successful NDD is the ability to mediate the facile and efficient delivery of the nanoparticles to the cell to ultimately deliver various drugs towards the target intracellular space and various specific subcellular compartments of mammalian cells. The traceability of the delivered drug is also a crucial aspect in monitoring the biodistribution, intracellular trafficking, and long-term fate of drugs and NP-drug delivery vehicles in order to assess and characterize the pharmacokinetic properties as well as the targeting specificity of the delivered drug, which are lacking in the current NDD platforms.

In this study, a novel strategy for the development of high performance nanoparticle platform was established by means of cell surface mimetic quantum dots (QDs)-anchored peptides/glycopeptides as a model system for NDD vehicles with defined functions facilitating intracellular trafficking after initial endocytosis. This study describes the standardized protocol for the preparation of multifunctional QDs that allow for efficient cellular uptake and rapid escape from endolysosomal entrapment followed by subsequent molecular delivery to the target cellular compartment. The established protocol took advantage of the facile chemoselective ligation of ketone-functionalized

peptides and glycopeptides onto the surface of the aminoxy/phospholcholine self-assembled monolayer coated QDs (AO/PCSAM-QDs) in mild reaction condition. Displaying ketone-functionalized hexahistidine derivative onto the AO/PCSAM-QD surface during intracellular delivery facilitated both endocytic entry and rapid endolysosomal escape of the conjugates in various human cell lines. Combined use of hexahistidylated AO/PCSAM-QDs with serglycin-like glycopeptides, a proteoglycan initiators (PGIs), elicited an entry, controlled intracellular trafficking, golgi localization and subsequent excretion of the QD conjugates, as also observed in the real-time live cell imaging. The results suggested that this approach can potentially provide an ideal platform for the design of high performance NDD system that could track every stages of NDD.

Therefore, it is noteworthy that PCSAM coating strategy could become a universal tool for spatially oriented immobilization of engineered proteins including antibody and antibody-drug conjugates on various metal-based nanoparticles.