COINS

THE UNIVERSITY OF TOKYO

COINS Seminar #12

Cationic Nanohydrogel Particles as Safe Carriers for Therapeutic Oligonucleotide Delivery

N. Leber, L. Nuhn, R. Zentel

Institute of Organic Chemistry, Johannes Gutenberg-University of Mainz

Date:Friday,December 4,2015
Time:16:00～17:00

Venue:Room #56,Engineering building #5, The University of Tokyo
（会場：東京大学工学部 5 号館 56 号講義室）

—Abstract—

Pharmaceutically active oligonucleotides (e.g siRNA) require adequate carriers for targeted and safe transport through the body, crossing membrane barriers and controlled release of their payload at the site of action. In contrast to lipoplex or polyplex formulations, cationic nanogels can serve as alternative oligonucleotide carriers. Usually they have pre-adjusted superstructures independent from their polyanionic cargo and show great stability, especially in presence of further polyanionic competitors. To this respect, we developed a novel concept for synthesizing polymeric cationic nanohydrogels,[1] which provides a safe and stable environment for siRNA, avoids carrier aggregation under physiologically relevant conditions[2] and promotes size-dependent gene silencing *in vitro*.[3] *Via* RAFT polymerization well-defined block copolymers of pentafluorophenyl methacrylate and tri(ethylene glycol) methyl ether methacrylate were synthesized that self-assemble in polar aprotic solvents (*e.g.* DMSO) into nm-sized polymer micelles. The resulting superstructures were used to generate cationic nanohydrogel particles by covalently cross-linking the reactive ester cores with spermine providing cationic moieties for stable siRNA complexation.[2] Interestingly, the synthetic process offers possibilities to synthesize nanohydrogels of various sizes, which show a size-dependent gene silencing potential *in vitro*.[3] Presently, we are working on the introduction of groups for active targetting and degradable cross-linkers for stimuli-responsive siRNA release.[4] Looking ahead, these novel cationic nanohydrogel particles can also serve as platform for advanced therapeutic oligonucleotide delivery strategies in the field of cancer immunotherapy.[5]

[1] L. Nuhn, M. Hirsch, B. Krieg, K. Koynov, K. Fischer, M. Schmidt, M. Helm, M.; R. Zentel, *ACS Nano* **2012**, *6*, 2198.

[2] L. Nuhn, S. Gietzen, K. Mohr, K. Fischer, K. Toh, K. Miyata, Y. Matsumoto, K. Kataoka, K., M. Schmidt, R. Zentel. *Biomacromolecules* **2014**, *15*, 1526.

[3] L. Nuhn, S. Tomcin, K. Miyata, V. Mailänder, K. Landfester, K. Kataoka, R. Zentel, *Biomacromolecules* **2014**, DOI:10.1021/bm501148y.

[4] L. Nuhn, L. Braun, I. Overhoff, A. Kelsch, D. Schaeffel, K. Koynov, R. Zentel, *Macromol. Rapid Commun.* **2014,** *35*, 2057–2064

[5] S. Hartmann, L. Nuhn, B. Paliztsch, M. Glaffig, N. Stergiou,B. Gerlitzki, E. Schmitt, H. Kunz, R. Zentel, *Adv. Healthcare Mate*r. **2014**, 4, 522 -527

＊Organizer: Center of Innovation (COI program) by JST

Kazunori Kataoka, Research Leader, Kawasaki Institute of Industrial Promotion, Innovation Center of Nanomedicine (iCONM)

and Professor. Graduate Schools of Engineering / Medicine, The University of Tokyo

＊For Further Information Contact: COINS Research Support Office　E-mail: jimukyoku-coins@kawasaki-net.ne.jp
Web: http://coins.kawasaki-net.ne.jp

<Access>
Venue: Room #56,Engineering building #5,The University of Tokyo

Address: 7-3-1, Hongo, Bunkyo-ku, Tokyo 113-8654, JAPAN

Access by train:

Toudaimae Sta(Nanboku Line) Walk about 1 minutes (See below access map)

Hongo-Sanchome Sta(Ooedo Line) Walk about 6 minutes (See below access map)

Hongo-Sanchome Sta(Marunouchi Line) Walk about 8 minutes
(See below access map)

Nedu Sta(Chiyoda Line) Walk about 8 minutes

Access Map

東大正門を入って左折後直進し、工11号館(1F スターバックス)、
その先の工14号館を左に見ながら通過し、その突き当りが工5号館です。
入口すぐのピロティを左に入るとその奥に56、57講義室があります。