

Kazunari Akiyoshi

1 .Topic in Research Achievements in the Year 2006

We can develop tailor-made functional nanogels to create novel nanobiomaterials (nanogel engineering) by the self-assembly of functional associating polymers as building blocks. Macrogels with well-defined nanostructures can be obtained by self-assembly using these nanogels as building blocks. In tissue engineering, hydrogels have been intensively studied to deliver the appropriate amount of growth factors to a target site on desired time scale. Recently, we modified CHP nanogel with methacryloyl groups and polymerized with other hydrophilic polymer to prepare the hybrid hydrogel with nanogel domains. The immobilized nanogels retained their ability to encapsulate proteins. In addition, the trapped proteins can be released from hydrogel in an active form (chaperon like activity). We cross-linked acryloyl-group modified CHP (CHPA) nanogels with thiol-group modified poly (ethylene glycol, PEGSH) to prepare a biodegradable hydrogel (CHP-PEG gel). Nanogel-based delivery system is expected to serve as a preferable hydrogel with the efficient drug-loading capacity for tissue engineering. The CHP-PEG hydrogel delivery system was an efficient delivery system of bone anabolic agent, PGE₂.

2 .Publications in the year 2006

○Sugawara A, Yamane S, Akiyoshi K, "Nanogel-template mineralization: Polymer-calcium phosphate hybrid nanomaterials", *Macromol. Rapid Commun* 2006;27:441-446.

Iwasaki Y, Akiyoshi K, "Synthesis and characterization of amphiphilic polyphosphates with hydrophobic graft chains and cholesteryl groups as nanocarriers", *Biomacromolecules* 2006; 7:1433-1438.

Sumida E, Iwasaki Y, Akiyoshi K, Kasugai S. "Platelet separation from whole blood in an aqueous two-phase system with water-soluble polymers", *J Pharmacol Sci* 2006;101:91-97.

Hatsuno K, Mukohyama H, Horiuchi S, Iwasaki Y, Yamamoto N, Akiyoshi K, taniguchi H, "Poly(MPC-co-BMA) coating reduces the adhesion of *Candida albicans* to poly(methyl methacrylate) surfaces", *Prosthodont. Res. Pract.* 2006; 5: 21-25.

Iwasaki Y, Akiyoshi K, "Highly wettable polyethylene films generated by spontaneous surface enrichment of perfluoroalkylated phosphorylcholines", *J Appl Polym Sci* 2006; 102: 2868.

○Sawada S, Nomura Y, Aoyama Y, Akiyoshi K, "Heat shock protein-like activity of nanogel artificial chaperone for citrate synthase", *J Bioact Compat Pol* 2006; 21:487-501.

Kitano S, Kageyama S, Nagata Y, Miyahara Y, Hiasa A, Naota H, Okumura S, Imai H, Shiraishi T, Masuya M, Nishikawa M, Sunamoto J, Akiyoshi K, Kanematsu T, Scott A M, Murphy R, Hoffman E W, Old J L, and Shiku H, "Induction of HER2-specific T Cell Immune Responses in Patients with HER2-expressing Cancer Vaccinated with Truncated HER2 Protein 1-146 Complexed with Nanogels of Cholesteryl Pullulan",

Clinical Cancer Research 2006; 12: 7397-7405

Ikeda K, Okada T, Sawada S, Akiyoshi K, and Matsuzaki K, "Inhibition of the formation of amyloid β -protein fibrils using biocompatible nanogels as artificial chaperones" FEBS Lett. 2006; 580: 6587-65958.

○Morimoto N, Nomura S M, Miyazawa N, Akiyoshi K. "Nanogel Engineered Designs for Polymeric Drug Delivery" S. Svenson Ed., Polymeric Drug Delivery Volume II - Polymeric Matrices and Drug Particle Engineering ACS Symposium Series 924. American Chemical Society pp.88-101,2006.

Morimoto N, Winnik F M, Akiyoshi K, "Botryoidal assembly of cholesteryl-pullulan/poly(N-isopropylacrylamide) nanogels" Langmuir, 2007; 23: 217-223

Morimoto N, Ogino N, Narita T, Kitamura S, and Akiyoshi K, Enzyme-Responsive Molecular Assembly System with Amylose-Primer Surfactants", Journal of the American Chemical Society 2007; 129: 458 – 459.

Wachiralapphaithoon C, Iwasaki Y, Akiyoshi K, Enzyme- degradable phosphorylcholine porous hydrogels cross-linked with polyphosphoesters for biocompatible cell matrices, Biomaterials, in press

○Kato N, Hasegawa U, Morimoto N, Saita Y, Nakashima K, Ezura Y, Kurosawa H, Akiyoshi K ,and Noda M, "Nanogel-based Delivery System Enhances PGE₂ Effects on Bone Formation, " J. Cellular Biochemistry, in press

3. Abstracts in the year 2006

1. Wachiralapphaithoon C, Iwasaki Y, Akiyoshi K. Preparation of biodegradable porous hydrogels cross-linked with polyphosphates. Society for Biomaterials 2006, Pittsburgh, Apr, 2006.
2. Maie H, Iwasaki Y, Akiyoshi K. Polymeric nanoparticles as cell-specific drug carriers. Society for Biomaterials 2006, Pittsburgh, Apr, 2006.
3. Iwasaki Y, Akiyoshi K. Spontaneous enrichment of photophorylcholine groups on polyolefin surface with perfluoroalkylated lipids additives . Society for Biomaterials 2006, Pittsburgh, Apr, 2006.
4. Morimoto N, Yamazaki M, Akiyoshi K. Enzymatic Synthesis And Characterization of Nanogels By Self-Assembly Of Hydrophobized Poly(L-Lysine)-Amylose Conjugates. Particles 2006, Florida, May, 2006.
5. Akiyoshi K. Novel Cellular Novel Cytosolic Delivery System Through Gap Junction Between Liposomes and Cells. 33rd Annual Meeting of the Controlled Release Society, Vienna, July, 2006.
6. Morimoto N. Hybrid Hydrogels with Self-Assembled Nanogels as Cross-Linkers: Protein Reservoir with Chaperon-like Activity. 33rd Annual Meeting of the Controlled Release Society, Vienna, July, 2006.
7. Ayame H, Asayama W, Morimoto N, Akiyoshi K. Self-Assembled Cationic Nanogels as Protein Carriers. 33rd Annual Meeting of the Controlled Release Society, Vienna, July, 2006. □
8. Hasegawa U, Toita S, Akiyoshi K. Nanogel-Quantum Dot Complex for Bioimaging. 33rd Annual Meeting of the Controlled Release Society, Vienna, July, 2006.
9. Ayame H, Asayama W, Morimoto N, Akiyoshi K. Designn of Cationic Nanogel as a

Protein Carrier. The Second International Symposium on Biomolecular Chemistry(ISBC2006), Kobe, August, 2006.

10. Hasegawa U. Nanogel-Cross-Linked Hydrogel with Chaperon-like Activity for Drug Delivery System. Gordon Research Conferences, Montana, August, 2006.
11. Akiyoshi K, Ayame H, Hasegawa W. Nanogel Engineering for DDS: Cationic Polysaccharide Nanogels for Intracellular Protein or Quantum Dot Delivery. 232nd American Chemical Society National Meeting, San Francisco, September, 2006.
12. Asayama W, Nomura Y, Sawada S, Morimoto N, Akiyoshi K. Nanogel Artificial Chaperone: Refolding And Cell-free Protein Synthesis. 232nd American Chemical Society National Meeting, San Francisco, September, 2006. □
13. Yamane S, Sugawara A, Akiyoshi K. Nanogel-Inorganic Hybrid: Synthesis of Polysaccharide-Calcium Phosphate Nanomaterials. 232nd American Chemical Society National Meeting, San Francisco, September, 2006. □
14. Iwasaki Y, Takamiya M, Iwata R, Akiyoshi K. Surface Modification of Silicone with Well-Defined Phospholipid Polymer. 20th European Conference on Biomaterials, Nantes, September, 2006.
15. Iwata R, Iwasaki Y, Akiyoshi K. Covalent Immobilization of Nanoparticle Uptake by Endothelial Cells. 20th European Conference on Biomaterials, Nantes, September, 2006.
16. Iwasaki Y, Akiyoshi K. Amphiphilic Biodegradable Polyphosphoesters. The Annual Hamburg Macromolecular Symposium, Hamburg, October, 2006.
17. Iwata R, Iwasaki Y, Akiyoshi K. Protein Immobilized Block Copolymer Brushes for Well-defined Biointerface. The Annual Hamburg Macromolecular Symposium, Hamburg, October, 2006.
18. Nomura M S, Asayama W, Akiyoshi K. Functional GAP Junctions between Liposomes and Cells. EABS&BSJ2006, Okinawa, November, 2006. □
19. Hasegawa U, Morimoto N, Akiyoshi K. Design of Biodegradable Hydrogel by Nanogel Engineering. The AIChE 2006 Annual Meeting, San Francisco, November, 2006.