Nano Medical Engineering Laboratory
Chief Scientist: Yoshihiro Ito (D.Eng.)

(0) Research field

CPR Subcommittee**:** Chemistry and Engineering

Keywords:

Biomaterials, Evolutionary Engineering, Drug Delivery, Biochips, Regenerative Medicine

(1) Long-term goal of laboratory and research background

This laboratory aims to create new functional materials by a new method which will be developed by combination of chemical and biotechnological methodology. We use organic synthetic chemistry, combinatorial chemistry, molecular engineering, polymer engineering, hybrid materials engineering, gene and protein engineering, microfabrication technology, and nanotechnology to synthesize new materials and the systems for development of regenerative medicine, artificial organs, drug delivery systems, nanomedicine, molecular imaging, biochips, bioelectronics, artificial enzymes and artificial antibodies.

(2) Current research activities (FY2019) and plan (until Mar. 2025)

i) Development of biomaterials having biological activities

Biomaterials having biological activities such as cell adhesion, mobility, growth, and differentiation have been developed by immobilization of growth factors. In 2019, on silicone rubber micropatterned adhesion regions were prepared by using prepared photo-reactive gelatins. Cell morphology on the micropatterned rubber was investigated under mechanical stress. Micropatterned immobilization of nerve growth factor and vascular endothelial growth factor were carried out using the photoreactive gelatin, and neurocyte formation and growth and mobility regulation were investigated, respectively. In future, immobilization of bone morphogenic protein will be immobilized on metal and investigated as an artificial bone.

ii) Development of diagnostic and therapeutic peptides by molecular evolutionary engineering

Peptide aptamers containing functional groups as non-natural amino acids have been developed by molecular evolutionary engineering. Fluorescent group which is sensitive to environmental conditions was connected to amino acid and the amino acid was acylated with tRAN for incorporation into random sequence library of peptide through in vitro translation. From the prepared peptide library, peptide aptamer which binds to target substance has been in vitro selected. In 2019, allergens in food were chosen as the target and fluorogenic peptide were selected. The selected peptide emitted fluorescence only after mixing with target allergen without bound/free separation. In addition, peptide containing a low molecular weight inhibitor against an immune checkpoint pathway interaction PD-1/PD-L1 was designed by in silico selection and the activity was investigated.

In future, for diagnostic peptide probe, pathogen virus will be chosen as the target for clinical applications. For therapeutic peptide, targeting cancer cell will be designed and synthesized. In vitro selection of peptide inhibitor of PD-1/PD-L1 interaction is also planned.

iii) Nanostructure by self-assembled polypeptide conjugates

Various nanostructures have been developed by self-assembly of block-copolypetides and they were applied for drug delivery carriers. The coplypetides are composed of α-helix forming peptide segment and hydrophilic one and they form tubular and sphere structures. By mixing of different structures-forming copolypeptides, drug incorporated torpedo shape was formed. In 2019, lipid molecules were co-assembled with the copolypeptide and the shape control was performed by changing the hydrophilic segment. In addition, it was demonstrated that the immunological problem induced by hydrophilic poly(ethylene glycol) was reduced by using polysarcosine as the hydrophilic segment.

In future, conjugation with other components such as DNA origami and fusogenic lipid will be performed for various shape control or cytological drug delivery.

iv) Development of cell control systems

For regenerative medicine, stem cell technologies are investigated. Microfabricate devices or nanotube formation protein is used for development of cell fusion system to prepare stem cell. Large scale production of human iPS cells are also investigated. In 2019, some efficient cell fusion systems were investigated and a new component for efficient iPS cell culture was found. In future, new cell fusion for stem cell production and cell culture bioreactior for stem cells will be developed.

v) Development of biochip for diagnosis

Photo-reactive polymer is used for development of microarray biochip system. Since the polymer can stably immobilized various biological components by covalent bonding, various allergens were immobilized on one chip and applied for assay of IgE antibodies. In 2019, the allergy diagnosis system was approved as a medical insurance. A new type of photo-reactive polymer is also developed. In future, this system will further developed with artificial intelligence.

(3) Members as of March, 2020

(Chief Scientist)
Yoshihiro Ito
(Senior Research Scientist)
Takanori Uzawa, Masuki Kawamoto,
Takashi Isoshima, Hideyuki Miyatake,
Masashi Ueki
(Research Scientist)
Motoki Ueda
(Special Postdoctoral Researcher)
Hei Man Leung
(Postdoctoral Researcher)
Toru Itagaki
(Special Temporary Research Scientist)
Nobuhiro Morishima
(Visiting Researcher)
Hriday Bera
(Junior Research Associate)
Eunhye Kim, So Jung Park
(International Program Associate)
Liang-Chun Wu
(Student Trainee)
Xueli Ren, Mizuki Fujisawa,
Mohamed Elafify,
Roopa Dharmatti, Boyang Ning,
Mohammed Abosheasha、
(Assistant)
Kyoko Yamanaka
(Research Part-time Worker)
Eiko Kubo

(4) Representative research achievements

1. "Instantaneous Detection of α-Casein in Cow's Milk Using Fluorogenic Peptide Aptamers", C. Phadke, S. Tada, I. Kono, A. Hiyama, Y. Takase, S. Gayama, T. Aigaki, Y. Ito, T. Uzawa, Anal. Methods, 12, 1368-1373 (2020)
2. "Evasion of the Accelerated Blood Clearance Phenomenon by Polysarcosine Coating of Liposomes", K. Son, M. Ueda, K. Taguchi, T. Maruyama, S. Takeoka, Y. Ito, J. Control. Rel., 322, 209-216 (2020)
3. "Cell migration and growth induced by photo-immobilised vascular endothelial growth factor (VEGF) isoforms", X. Ren, J. Akimoto, H. Miyatake, S. Tada, L. Zhu, H. Mao, T. Isoshima, S. Mueller, S. M. Kim, Y. Zhou, Y. Ito, J. Mater. Chem. B., 7, 4272-4279 (2019)
4. "Disulfide-unit conjugation enables ultrafast cytosolic internalization of antisense DNA and siRNA", Z. Shu, I. Tanka, A. Ota, D. Fushihara, N. Abe, S. Kawaguchi, K. Nakamoto, F. Tomoike, S. Tada, Y. Ito, Y. Kimura, H. Abe, Angew. Chem. Int. Edn., 58, 6611-6615 (2019)
5. "Tubular network formation by mixing amphiphilic polypeptides with differing hydrophilic blocks", M. M. Rahman, M. Ueda, K. Son, S. Seo, S. Takeoka, T. Hirose, Y. Ito, Biomacromolecules., 20, 3908-3914 (2019)

Laboratory Homepage

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