Nano Medical Engineering Laboratory（2020）
Chief Scientist: Yoshihiro Ito (D.Eng.)

(0) Research field
CPR Subcommittee: Engineering

Keywords: biomaterials, molecular evolutionary engineering, bioorganic chemistry, biochip

(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 (FY2020) and plan (until Mar. 2025)

(A) Creation of new biomaterials having biological activities

We are developing a new type of biomaterials which can promote cell growth or differentiation by immobilization of growth factor proteins. In 2020, we synthesized a photo-reactive gelatin and micropattern-immobilized it on silicone rubber. Some types of cells were cultured on the micropattern surfaces under periodic mechanical stretching. The behaviors of the cultured cells were investigated. In addition, we synthesized some growth factor polypeptide incorporated with amino acid which plays a main role in underwater adhesion proteins. In the case of modified bone morphogenic protein (BMP), it was coated on a titan material and implanted in animals for evaluation of stabilization of material in bones.

Future plan, 1) We will investigate the cell behaviors on the gelatin-micropattern-immobilized surface under periodic stress in detail. 2) We will investigate the BMP-immobilized materials in detail.

(B) Development of new diagnostic probe and therapeutic drugs by molecular evolutionary engineering

Peptide aptamers carrying non-natural amino acids are being developed. Environment-dependent fluorogenic groups or low molecular weight inhibitor, etc. was covalently connected with an amino acid and it was added on tRNA for *in vitro* translation which is for construction of ribosome display of peptide library of random sequences. From the library some peptide probe binding to target molecules were *in vitro* selected. In 2020, some fluorogenic peptide binding to pathogenic virus were found. The methodology for *in vitro* selection to find peptides carrying low molecular weight inhibitor of immune check point proteins for PD1/PD-L1 interaction was developed. In addition, cancer-targeting peptide aptamer project was started.

Future plan, 1) We will develop an assay system using the found fluorogenic peptide probe for pathogenic virus protein. 2) For development of therapeutic peptide, in vitro selection of cancer-targeting peptide and immune checkpoint inhibitor peptide will be performed..

(C) Creation of nano-assembled composited by supramolecular chemistry

We are developing a various form of nano-assembled architectures composed of block copolymer of peptides for drug delivery carrier. In 2020, we succeeded in the preparation of polypeptide assembly incorporated with cell fusion-accelerating lipids. In addition, it was found that addition of small organic molecule can regulate the molecular assembly of amphiphilic polypeptides according to the change of interaction of hydrophobic interaction of hydrophobic parts.

Future plan, 1) DNA origami will be combined and incorporated with the polypeptide assembly. 2) New shapes of polypeptide assembly will be developed for new medical applications.

(D) Systems for regulating cell functions

Stem cell preparation for regenerative medicine and new cell culture systems are being developed. Micro-fabrication of cell culture systems, stem cell preparation using nanotube protein, construction of somatic cell fusion system, and human iPS cell culture systems are investigated. In 2020, efficient cell fusion systems were developed and cell culture apparatus for human iPS cell was tested.

Future plan, 1) Further investigation on the development of cell fusion system for stem cell production will be performed.

(E) Development of biochips

A new type of microarray biochip using photo-reactive polymer is under development. In 2020, photo-reactive polymer containing poly(ethylene glycol) in the main chain was prepared and it reduced the non-specific binding biological components. SARS-CoV-2 proteins were also microarrayed by conventional photo-reactive polymer which had been developed in this laboratory and used for the antibody's detection.

Future plan, 1) The microarray detection system will be developed with AI functions for bioinformatics study using big data in future.

(3) Members

(Chief Scientist)
Yoshihiro Ito
(Senior Research Scientist)
Takashi Isoshima, Hideyuki Miyatake, Masashi Ueki, Masuki Kawamoto, Takanori Uzawa, Motoki Ueda
(Special Postdoctral Researcher)
Hei Man Leung
(Special Temporary Research Scientist)
Nobuhiro Morishima
(Visiting Researcher)
Hriday Bera, Toru Itagaki

(Junior Research Associate)
So Jung Park, Mohammed Abosheasha
(International Program Associate)
Liang-Chun Wu
(Student Trainee)
Eunhye Kim, Xueli Ren, Boyang Ning, Shin Woong Kim, Mahmoud Othman, Shohei Sekido, Mohamed Elafify, Mizuo Fujisawa
(Assistant)
Kyoko Yamanaka

(4) Representative research achievements

1. "Solvent effects on the self-assembly of an amphiphilic polypeptide incorporating α-helical hydrophobic blocks", A. Nandakumar, Y. Ito, M. Ueda, J. Am. Chem. Soc., 142, 20994-21003 (2020)
2. "Conjugation of biphenyl groups with poly(ethylene glycol) to enhance inhibitory effects on the PD-1/PD-L1 immune checkpoint interaction", E.-H. Kim, N. Boyang, M. Kawamoto, H. Miyatake, E. Kobatake, Y. Ito, J. Akimoto, J. Mater. Chem. B, 8, 10162-10171 (2020)
3. "Thermally induced switch of coupling reaction using morphological change of thermoresponsive polymer on reactive hetero-armed nanoparticle", S. J. Park, J. Akimoto, N. Sakakibara, E. Kobatake, Y. Ito, ACS Appl. Mater. Interfaces., 12, 49165-49173 (2020)
4. "Synthesis of photoreactive poly(ethylene oxide)s for surface modification", J. Akimoto, S. J. Park, S. Obuse, M. Kawamoto, M. Tamura, A. Nandakumar, E. Kobatake, Y. Ito, ACS Appl. Bio Mater., 3, 5941-5947 (2020)
5. "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)

Laboratory Homepage
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