Nano Medical Engineering Laboratory（2021）
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 (FY2021) 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 2021, some types of cells were cultured on the gelatin-modified silicone surfaces under periodic mechanical stretching. The behaviors of the cultured cells were analyzed and the data were summarized. In addition, as another physical stimulation, ultrasonic treatment was applied on cultured cells. Bone morphogenic protein (BMP) was connected with a peptide carrying dihydroxyphenylalanine and lysine residues and coated on a titan wire and screw. The modified wire and screw were implanted in animals and they showed the high performance in the titan-bone binding.

Future plan, 1) We will investigate the effect of ultrasonication on the cell behaviors cultured on the BMP-immobilized materials. 2)The effect of culture matrix on the immobilized biological signals will be inverstigated.

(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 2021, some fluorogenic peptide binding to pathogenic virus were found and we started to develop a diagnose system using them. We also found candidate peptides carrying low molecular weight inhibitor of immune check point proteins for PD1/PD-L1 interaction and started to analyze them. Cancer-targeting peptide aptamers were also found.

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, the candidate peptides for cancer therapy and immune checkpoint inhibitor will be analyzed and further improved.

(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 2021, we succeeded in the preparation of polypeptide assembly with a precisely controlled cubic shape by combining two amphiphilic polypeptides. The cubic vesicle has an ability to encapsulate hydrophilic dye and drug. 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. This research was developed more.

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-fabricated system constructed with a membrane having direct pores were fabricated to achieve cytosol fusion. By the cytosol fusion we aimed stem cell preparation from somatic cell fusion, as human iPS preparation. In 2021, cytosol fusion was observed using two stained cells.

Future plan, 1) Further investigation on the development of ceytosol 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 2021, SARS-CoV-2 proteins of wild and mutant types were microarrayed by developed photo-reactive polymers and used for the rapid automatic 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, Masuki Kawamoto, Takanori Uzawa, Motoki Ueda
(Senior Research Scientist)
Nandakumar Avanashiappan
(Special Postdoctral Researcher)
Hei Man Leung
(Special Temporary Research Scientist)
Nobuhiro Morishima
(Visiting Researcher)
Toru Itagaki, Eunhye Kim

(Junior Research Associate)
Mohammed Abosheasha
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Fang Kun、Mohamed Elafify
(International Program Associate)
Fumiharu Eiyo
(Student Trainee)
Xueli Ren, Boyang Ning, Shin Woong Kim, Mahmoud Othman, Mohamed Elafify, DianDian Dong, Shohei Sekido, Mizuo Fujisawa, Ken Takahashi,
(Assistant)
Kyoko Yamanaka

(4) Representative research achievements

1. "Tubular Assembly Formation Induced by Leucine Alignment along the Hydrophobic Helix of Amphiphilic Polypeptides", Mohammed A. Abosheasha, Toru Itagaki, Yoshihiro Ito, and Motoki Ueda, Int. J. Mol. Sci., 22(21), 12075 (2021)
2. "SARS-CoV-2 proteins microarray by photoimmobilization for serodiagnosis of the antibodies", Hiroharu Kashiwagi, Nobuhiro Morishima, Sei Obuse, Takashi Isoshima, Jun Akimoto, and Yoshihiro Ito, Bull. Chem. Soc. Jpn., 94, 2435-2443 (2021)
3. "Etherified pullulan-polyethylenimine based nanoscaffolds improved chemosensitivity of erlotinib on hypoxic cancer cells", Hriday Bera, Mohammed A. Abosheasha, Yoshihiro Ito, and Motoki Ueda, Carbohydr. Polym., 271, 118441 (2021)
4. "Versatile mitogenic and differentiation-inducible layer formation by underwater adhesive polypeptides", Seiichi Tada, Xueli Ren, Hongli Mao, Yun Heo, Shin-Hye Park, Takashi Isoshima, Liping Zhu, Xiaoyue Zhou, Reiko Ito, Shino Kurata, Megumi Osaki, Eiry Kobatake, and Yoshihiro Ito, Adv. Sci., 2100961 (2021)
5. "Development of a non-IgG PD-1/PD-L1 inhibitor by in silico mutagenesis and an in-cell protein-protein interaction assay", Boyang Ning, Xueli Ren, Kyoji Hagiwara, Shinji Takeoka, Yoshihiro Ito, and Hideyuki Miyatake, ACS Chem. Biol., 16, 3161-323 (2021)

Laboratory Homepage
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