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Department of Biofunction Research

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Recovering and reconstructing sensorimotor functions

1. **mRNA-based therapeutics as a new paradigm for gene therapy**
2. **Regenerative medicine using gene and oligonucleotide therapeutics**
3. **Cell therapy using genetically modified spheroid transplantation**
4. **Creating osseointegrated dental implants by regulating micro/nano structure**

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2. Anraku Y, Kuwahara H, Fukusato Y, Mizoguchi A, Ishii T, Nitta K, Matsumoto Y, Toh K, Miyata K, Uchida S, Nishina K, Osada K, Itaka K, Nishiyama N, Mizusawa H, Yamasoba T, Yokota T, Kataoka K: Glycaemic control boosts glucosylated nanocarrier crossing the BBB into the brain, Nature Communications 8, 1001, 2017.
3. Lin CY, Perche F, Ikegami M, Uchida S, Kataoka K, Itaka K: Messenger RNA-based therapeutics for brain diseases: An animal study for augmenting clearance of beta-amyloid by intracerebral administration of neprilysin mRNA loaded in polyplex nanomicelles, J Control Release 235, 268-275, 2016.
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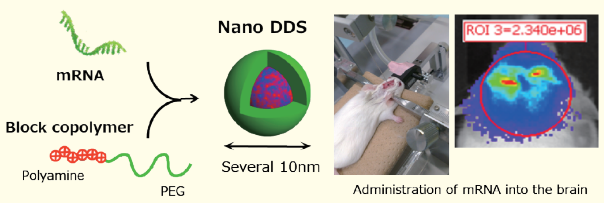
5. Itaka K, Uchida S, Matsui A, Yanagihara K, Ikegami M, Endo T, Ishii T, Kataoka K: Gene transfection toward spheroid cells on micropatterned culture plates for genetically-modified cell transplantation, J Vis Exp 10, e52384, 2015.

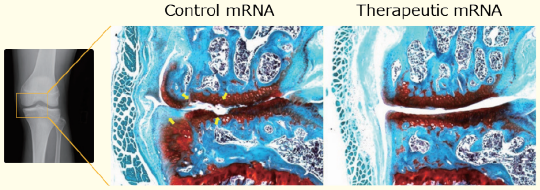
Itaka Laboratory focuses on the development of innovative medical technologies based on the science of biomaterials, drug delivery systems (DDS), and molecular biology. We aim at regulating the biofunctions of host cells and biomaterials, obtaining proof-of-concept of therapeutic strategies through animal studies, and pursuing their clinical applications in collaboration with hospitals and companies.

mRNA-based therapeutics: a new paradigm of gene therapy

Gene therapy is defined as introducing genetic information for therapeutic purposes. Gene therapy may have wide application, including: vaccination against cancer and infectious diseases; regenerative medicine through *in situ* cell regulation by introducing "therapeutic" gene(s); and, the ultimate goal of "gene" therapy, through the technology of gene editing. Messenger RNA (mRNA) is a new tool for introducing genetic information. Direct delivery of mRNA into cells is highlighted as a safe and effective method that avoids the risk of random integration into the genome. Despite the fact that mRNA delivered in the body would be susceptible to highly active RNases that are ubiquitous in extracellular space, we have established a drug delivery system (DDS) based on synthesized polymers -- polyplex nanomicelles -- to transport mRNA into target cells while preventing its degradation. We achieved *in vivo* mRNA administration for therapeutic purposes to various organs and tissues, including brain, spinal cord, bone, articular cartilage, skeletal muscle, and liver. This mRNA-based therapy is indicated for the treatment of various diseases within the fields of gene therapy, cell therapy, and regenerative medicine.



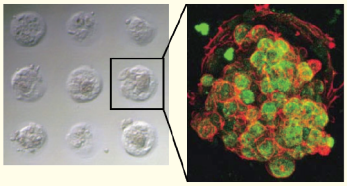
Administration of mRNA into the brain



Treatment of osteoarthritis by intra-articular injection of mRNA

Genetically-modified spheroid cell culture system for cell transplantation

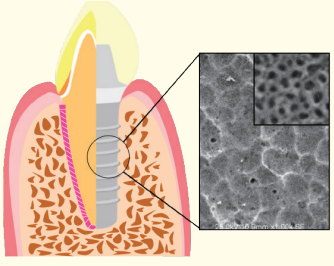
Cell transplantation therapy is an attractive strategy for various medical fields. We are developing an injectable spheroid system for cell transplantation therapy that preserves cell-to-cell interaction. It is based on a 3D spheroid cell culture system using micropatterned plates coated with a thermosensitive polymer. In addition, we have augmented the therapeutic effects of cell transplantation by integrating the genetic modification of the cells using a biocompatible non-viral gene carrier.



Micropatterned substrate for spheroid culture

Osseointegrated dental implants created by regulating micro/nano structure

Although dental implant treatment has already been clinically applied and excellent clinical progress has been reported, some cases demonstrate unexpected disorders. Because natural teeth integrate with bone via periodontal ligaments to perform their functions, the osseointegration, which occurs during healing in current dental implants, is thought to be one of the causes of disorders. In this department, we are working on the development of periodontal ligament-bonded dental implant materials, and we are trying to elucidate the mechanism of periodontal tissue homeostasis.



Micro/nano structure for controlling cell cycle of osteoblasts