Engine of Improving Health

大阪大学橋渡し研究支援機関・革新的医療技術シーズ
The University of Osaka Translational Research Support Hub, Innovative Medical Seeds

Drugs

Medical devices

Regenerative medicine

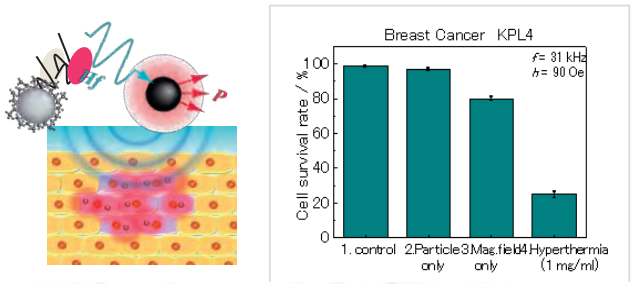
Diagnostics

Development of magnetic nanoparticles for theranostics

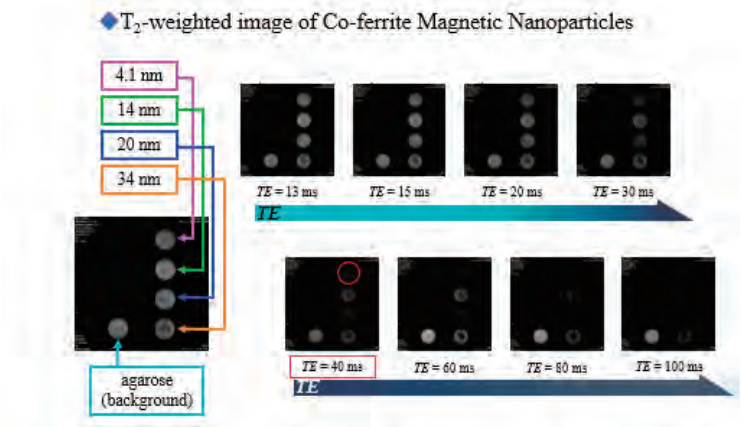
Principal Investigator	Yokohama National University
	Professor Yuko ICHIYANAGI

Project Outline

Theranostics is a coined word that combines the words "therapy" and "diagnostics". We create magnetic nanoparticles and give them the ability to selectively pass into cancer cells. We have previously shown that by modifying magnetic nanoparticles with folic acid, they can be selectively introduced into cancer cells. We will develop cancer cell-selective magnetic nanoparticles, by developing this technology. As a first idea, we will develop a method for modifying the nanoparticles with glucose based on the idea of learning from FDG, a PET imaging agent. We will then attempt to use magnetic particles that can generate a temperature increase of 6 degrees or more above body temperature even in a weak magnetic field to perform thermotherapy. We will also develop magnetic hyperthermia + imaging techniques with a view to creating a method for detecting cancer using the same particles and performing "theranostics", therapy and diagnosis simultaneously.



An image of hyperthermia therapy for cancer using magnetic nanoparticles and an alternating magnetic field, and the results of an in vitro hyperthermia experiment using human breast cancer
cells. When a very weak magnetic field of f=31 kHz, h=90 Oe was applied for just 30 minutes, the number of cancer cells was suppressed by around 20%.



Phantom images of *T2* relaxation measured by MR using magnetic nanoparticles with a particle size of 4-34 nm. For the 4 nm sample, a clear contrast was obtained compared to the background agarose gel with an echo time of only 40 msec.

Target disease: Cancer, Patent information: PCT/JP2019/008494,
Technical features: Magnetic nanoparticles that can be used for both diagnosis and treatment.
Cancer thermotherapy, imaging materials,
Marketability and development issues: Marketability is high in countries with a long life expectancy.Issues include establishing dispersibility in water and surface modification,
Desired Collaboration: contrast media manufacturers and companies developing alternating magnetic field devices. Technology consignment for mass production.

Development of anti-cancer drug with immunomodulators

Principal Investigator	Initiative for Advanced Research, Gunma University
	Professor Keisuke NIMURA

Project Outline

Characteristics of the Novel Anticancer Drug Under Development

- Inactivated Sendai virus (HVJ-E) demonstrates a strong anti-tumor effect when administered directly into tumors but faces challenges in formulation.
- We have elucidated the mechanism of the anti-tumor effect of HVJ-E and further discovered that by enhancing the effectiveness of this mechanism, we can amplify and activate cancer-specific T cells in the body.
- We are implementing this mechanism as mRNA and introducing it into tumors using lipid nanoparticles, thereby inducing systemic anti-tumor immunity.

Targeted Diseases

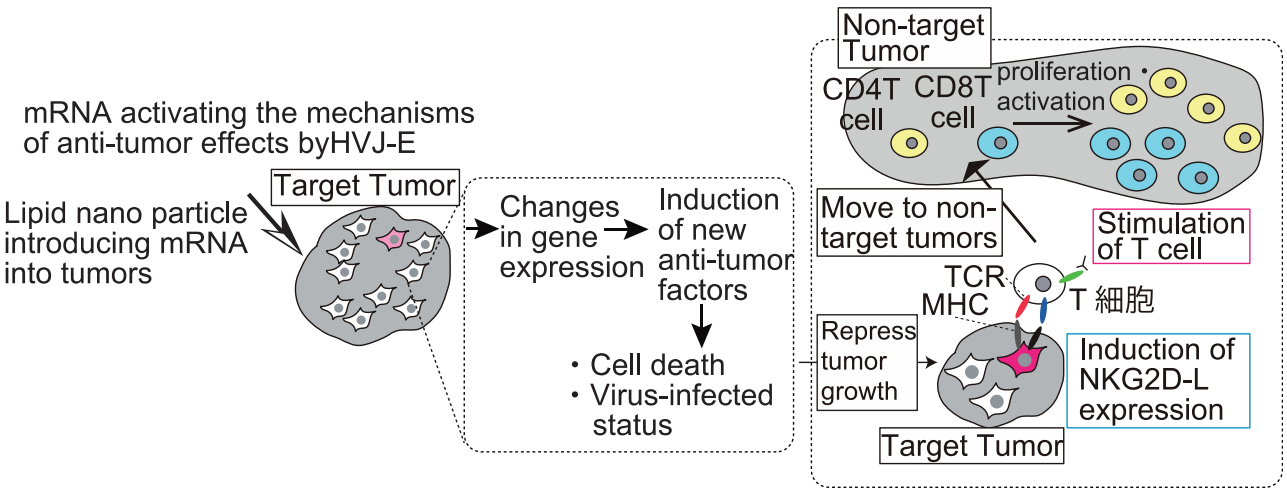
- Inoperable tumors with metastasis
- Infectious diseases

Market Viability

- Leveraging a novel mechanism, and the ability to induce cancer-specific immunity, we consider the market viability to be high.

Challenges in Development

- Optimization of lipid nanoparticles and mRNA sequences.



Targeted Diseases: Cancers that can be administered directly into the tumor. It is desirable if it can be administered to several metastatic lesions.
Patent Information: Patent application 2020-155901
Technical Features: Expressing proteins in tumor cells using mRNA/LNP to induce tumor immunity.
Market Viability and Development Challenges: It is highly unique as it is based on an unprecedented new mechanism. The challenges in development include the optimization of lipid nanoparticles and mRNA sequences.

Research aiming to develop refractory cancer therapeutics using protein-based drug delivery systems with drug release control function

Principal Investigator

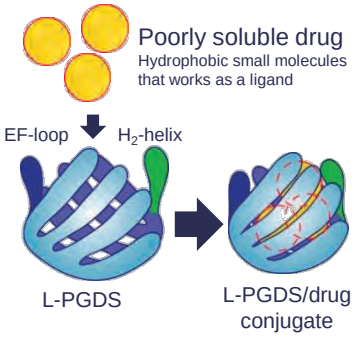
Graduate School of Agriculture, Osaka Metropolitan University

Professor Takashi INUI

Project Outline

◆Description

The researchers found lipocalin-type prostaglandin D synthase (L-PGDS), a protein existing in human cerebrospinal fluid and physiologically transporting hydrophobic substances, to be applied for an innovative drug delivery system (DDS). L-PGDS has a unique barrel-like structure and hydrophilic properties as a whole, meanwhile, its internal hydrophobic domain can incorporate various hydrophobic small molecules such as poorly water-soluble chemical drugs. L-PGDS reduced its spatial size about 10% with capsulated drugs and acts as a drug carrier exhibiting favorable properties such as control release and well-distribution of capsulated drugs at the site of drug acting (e.g. tumor tissue). Interestingly multimerization of L-PGDS markedly improved its pharmacological activity of the capsulated drug suggesting a significant contribution of enhanced EPR effect.



◆Advantages

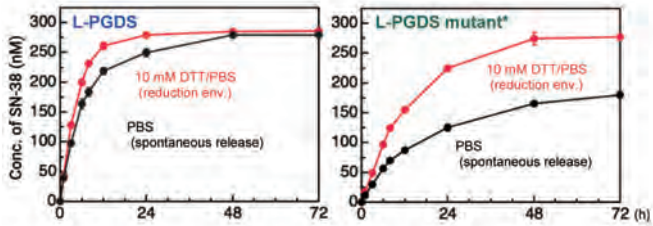
- Solubilizes poorly water-soluble chemical drugs (M.W.< 850)
- Prevents unwanted release of capsulated drug in blood circulation by amino acid substitutions of L-PGDS
- Enhanced drug exposure in tumor tissue by multimerization of L-PGDS
- Tissue specific drug targeting can be achievable by adding specific peptide motif
- Long-term storage by freeze drying
- Applicable for oral administration and intravenous injection

Name	Therapeutic target	Drug concentration (μM) +PBS	+HP-β-CD* (1 mM, 1.5 mg/mL)	+L-PGDS (1 mM, 19 mg/mL)
Telmisartan (Mr : 514.6)	Hypertension	9.0	15.2	1230
SN-38 (Mr : 392.4)	Colon cancer Stomach cancer	6.3	19.1	126
Lapatinib (Mr : 581.1)	Breast cancer	Insoluble	Insoluble	234
MCC-555 (Mr : 381.4)	Diabetes	3.3	73.0	784

*HP-ß-CD(2-Hydroxypropyl-ß-cyclodextrin) Currently-available solubilizing agent that has higher solubilizing ability than ß-cyclodextrin.

【 Drug release profiles of L-PGDS mutant capsule *in vitro* 】

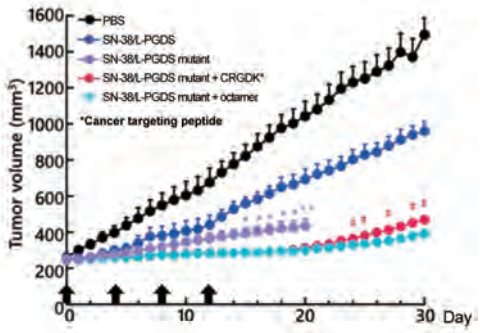
L-PGDS mutant capsule suppressed spontaneous release of encapsulated SN-38** and promoted its release in a reduction environment.



***L-PGDS mutant** A certain amino acid in the opening of barrel-like L-PGDS structure was replaced with a sterically bulky amino acid to act as a temporary lid.

****SN-38**: Active metabolite of CPT-11 (irinotecan), poorly water soluble

【 *In vivo* anti-tumor evaluation using L-PGDS mutant capsule】



Each L-PGDS sample (L-PGDS sample encapsulating PBS or SN-38) was administered to prostate cancer model mouse by tail vein injection every 4 days (4 times in total). The tumor volume was measured every day. As a result, both **L-PGDS mutant group** and **L-PGDS mutant + octamer group** inhibited the tumor growth from the beginning of the measurement. Even some time after day 12 (=last administration), the tumor growth was completely inhibited. It is suggested that the enhanced EPR effect allowed the drug to be retained in the cancer tissues, resulting in long-lasting efficacy.

- **Target disease:** Intractable cancers (e.g. glioma, pancreatic cancer)
- **Patent information:** ① [Title] Compound solubilizing agent and composition containing the same [Patent number] Patent No. 5099545, ② [Title] Capsule protein and its multimer composition and pharmaceutical composition using the same [Application number] PCT/JP2020/019827
- **Features of technology:** DDS technology for poorly water-soluble drugs
- **Marketability and development issues:** We expect to receive poorly water-soluble compounds owned by pharmaceutical companies that are difficult to develop, and develop them as new drugs by combining them with the relevant technology, and introduce them into the market. We are looking for a pharmaceutical company that will receive a license agreement and aim to put this invention into practical use.

Development of innovative antibody therapy against ovarian cancer by controlling lipid metabolism
(Acquisition of non-clinical POC for novel antibody therapy using anti-LSR antibody for ovarian cancer)

Principal Investigator

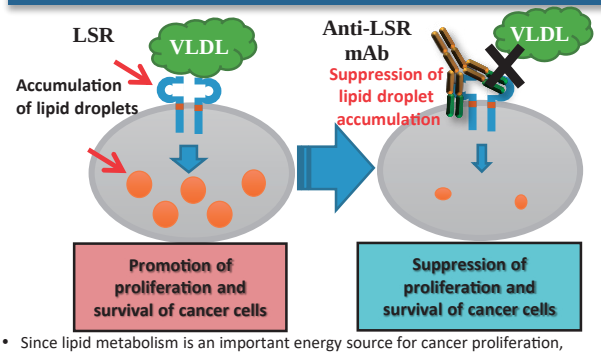
Institute for Biomedical Sciences, Division of Drug Discovery and Medical Device Development, Iwate Medical University

Professor Tetsuji NAKA

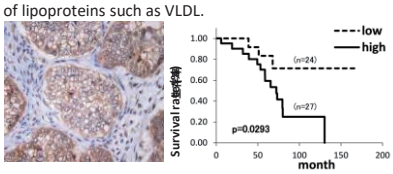
Project Outline

Sixty percent of ovarian cancers are diagnosed as advanced cancer, and the 5-year survival rate is 20-30%, which is a poor prognosis. The effect of chemotherapy on ovarian cancer is limited, and the development of anticancer agents with new mechanisms of action is required. We identified the lipolysis-stimulated lipoprotein receptor (LSR) as a novel target antigen for ovarian cancer. So far, we have clarified that a chicken-mouse chimeric anti-LSR antibody exhibits excellent antitumor effects in ovarian cancer cell lines and animal models. In this project, we will create a humanized chicken/mouse chimeric anti-LSR antibody and conduct non-clinical trials to evaluate its efficacy and safety.

Image of mechanism of action of anti-LSR antibody

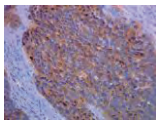


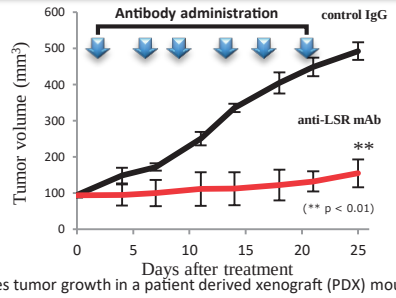
- Since lipid metabolism is an important energy source for cancer proliferation, peritoneal dissemination, and metastasis, lipid metabolism control is considered to be a good target for new therapies.
- LSR is involved in the cellular uptake of lipoproteins such as VLDL.
- LSR expression levels are associated with prognosis in ovarian cancer.
- Inhibition of lipoprotein uptake by anti-LSR antibodies reduces intracellular lipids and suppresses the growth and survival of cancer cells.



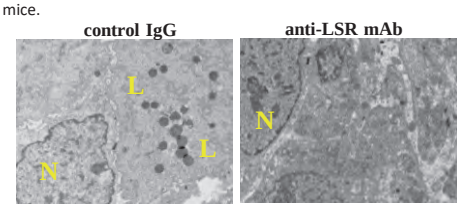
Tumor growth inhibitory effect of anti-LSR antibody on ovarian cancer

PDX (case 1)



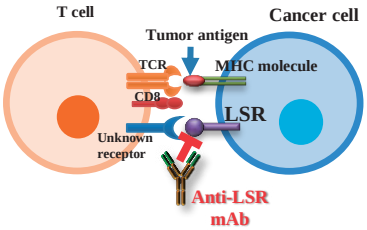


Anti-LSR antibody suppresses tumor growth in a patient derived xenograft (PDX) mouse model in which LSR-positive human ovarian cancer tissue is transplanted into immunodeficient mice.

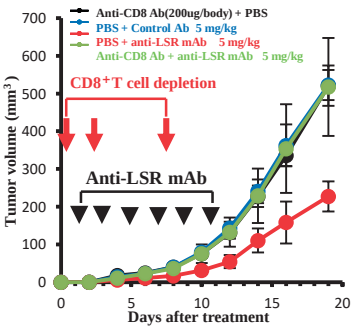


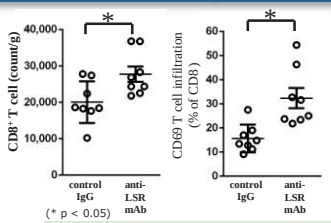
Anti-LSR antibody reduces intracellular lipids in tumor tissue of ovarian cancer PDX model.

The antitumor effect exerted by anti-LSR antibodies also has immune checkpoint inhibitory activity



LSR has an Ig super family domain that is conserved in the B7 family, so it may function as an immune checkpoint molecule.





Anti-LSR antibodies also exert antitumor effects on 4T1 syngeneic mice through CD8⁺ T cells. Administration of anti-LSR antibody increases the number of CD8⁺ T cells infiltrating into the tumor and the percentage of activated CD8 T cells.

References)
Hiramatsu K, Naka T et al., LSR Antibody Therapy Inhibits Ovarian Epithelial Tumor Growth by Inhibiting Lipid Uptake. *Cancer Research.* 2018;78:516-727
FunauchiM, Naka T et al., Tumor cell-expressed lipolysis-stimulated lipoprotein receptor negatively regulates T-cell function. *Int J Cancer* 2023 In Press

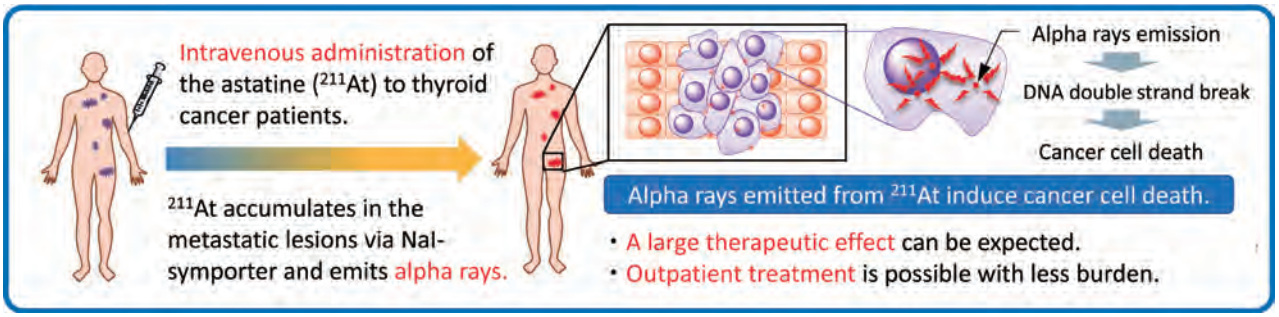
Target disease: Ovarian cancer
Patent information: Patent application 2015-554577, 2022-179712
Technology features: A new molecular-targeted drug that exerts an antitumor effect by regulating lipid metabolism.
Marketability and development issues: Simultaneous development of a companion diagnostic that predicts the efficacy of anti-LSR antibodies may increase the therapeutic efficacy of anti-LSR antibodies.
Details of desired corporate collaboration: Licensing-out after phase I investigator-initiated clinical trials
Current corporate collaboration: ONSSI Co., Ltd. (venture company launched by R&D representatives)

Targeted alpha-ray therapy for refractory thyroid cancer

Principal Investigator	Institute for Radiation Sciences, The University of Osaka
	Associate Professor Tadashi WATABE

Project Outline

Cancer treatment using alpha rays has garnered attention, with excellent therapeutic effects reported in the treatment of advanced cancers. In the treatment of differentiated thyroid cancer, beta-ray therapy involving radioactive iodine (^{131}I) is commonly employed, but the therapeutic effect may prove insufficient. In addition, it needs isolated hospitalization in dedicated rooms due to regulation. Conversely, alpha rays emit a substantial amount of energy within a short range and have minimal radiation impact on their surroundings, making them suitable for outpatient treatment. Astatine (^{211}At) is an alpha-emitting nuclide that exhibits properties similar to iodine and accumulates in thyroid cancer cells. In preclinical studies, we have confirmed the efficacy and safety of [^{211}At]NaAt and have successfully established stable production as an investigational drug at Osaka University Hospital. Furthermore, we have completed an investigator-initiated clinical trial using astatine (^{211}At) in patients with refractory thyroid cancer and confirmed its tolerability and efficacy.



Outline of Investigator-Initiated Clinical Trial

A phase I investigator-initiated clinical trial (Alpha-T1 study) was conducted as a first-in-human study to evaluate the safety, pharmacokinetics, and preliminary efficacy of [^{211}At]NaAt in patients with differentiated thyroid cancer refractory to radioactive iodine (^{131}I). The study started with a low dose of 1.25 MBq/kg, followed by stepwise dose escalation to 2.5 MBq/kg and 3.5 MBq/kg. A total of 11 patients received a single administration.

Among patients in the mid- and high-dose groups (2.5 or 3.5 MBq/kg; n = 9), three patients achieved a ≥50% reduction in the tumor marker thyroglobulin compared with baseline. In addition, three patients showed disappearance of ^{131}I uptake in metastatic lesions on ^{131}I imaging (complete disappearance in one patient and near disappearance in two patients) . These results demonstrate the therapeutic potential of targeted alpha-particle therapy using astatine, even in patients refractory to conventional treatments.

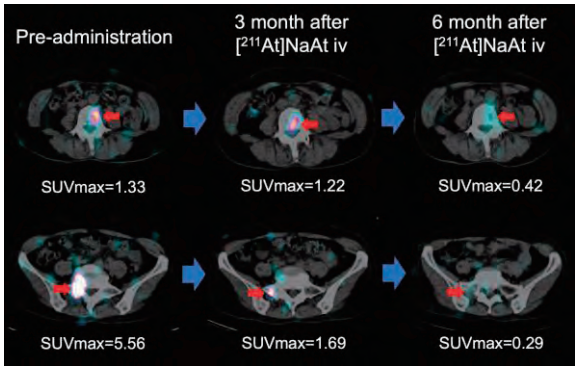


Figure 1. ^{131}I-SPECT image after administration of astatine (^{211}At): The lesions have almost completely disappeared (arrow).

- Astatine, a novel cancer therapeutic that emits alpha particles in the body, is being administered to patients with refractory thyroid cancer. Even in cases where standard treatment with radioactive iodine (^{131}I) is ineffective, alpha particles—characterized by high energy and a very short tissue range—can selectively target cancer cells and show higher therapeutic efficacy.
- As astatine can be produced using accelerator , a domestic supply network can be established and it can expand the development of targeted alpha-ray therapies for a wide range of cancers in the future.

Development of a new treatment for chemotherapy-resistant triple-negative breast cancer

Principal Investigator	Department of Advanced Molecular Therapy, Graduate School of Medicine, The University of Osaka
	Professor Yoshiaki TANIYAMA

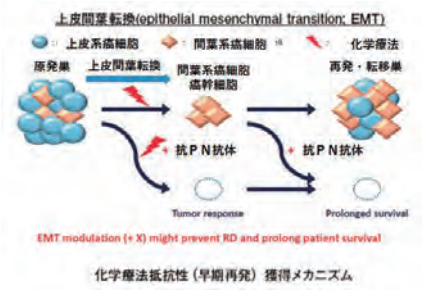
Project Outline

Epithelial-to-mesenchymal transition (EMT) is currently considered to be a major mechanism responsible for chemoresistance. It is thought that mesenchymal cancer cells that are resistant to anticancer drugs later undergo mesenchymal-epithelial transition and become stagnant (figure on the right). Next, in order to search for specific targets, we conducted a joint research with UCSD in US, using tissue samples from more than 1,000 cases of malignant tumors to comprehensively identify the gene of eight mesenchymal markers that have the strongest correlation.

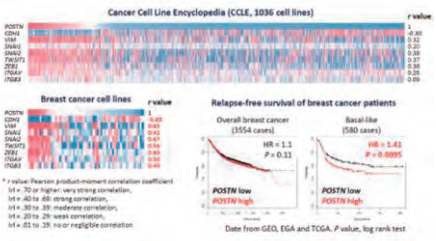
As a result, we discovered the periostin gene. In particular, in breast cancer, there was a clearer relationship between periostin gene expression and EMT. Furthermore, it was found that there is a strong correlation with the prognosis of basal type (mainly TNBC). The periostin gene has a splicing variant in which an exon is dropped, so when we investigated which exon's expression was strongly altered in a chemotherapy-resistant model, we found that it was periostin exon 21 (see figure on the right).

Therefore, we administered a pathological periostin-neutralizing antibody that uses exon 21 as an antigen to a chemotherapy-resistant model of TNBC, and confirmed that it significantly suppressed recurrence. (Patent already obtained) Furthermore, we have developed a diagnostic agent to measure blood pathological periostin (patent applied for), and plan to study its potential as a companion diagnostic agent.

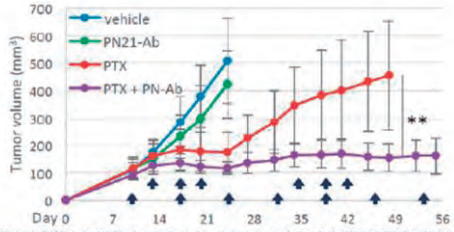
On the other hand, in addition to TNBC, many cases of HER2-negative breast cancer develop into TNBC due to metastasis or recurrence, and the prognosis is similarly poor. Therefore, in 2025/3, an investigator-initiated clinical trial Phase 1/2a is started at four institutions led by the Department of Breast Endocrine Surgery, UOsaka targeting metastatic and recurrent HER2 -negative breast cancer. The market size is large as shown in the figure on the right.



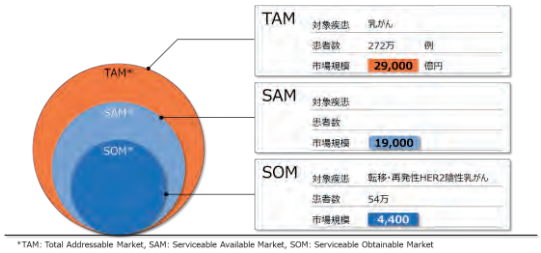
化学療法抵抗性（早期再発）獲得メカニズム



抗がん剤治療後に残存する治療抵抗性乳がん（間葉系転換した癌）ではペリオスチンの発現が亢進しており、予後と逆相関する。



抗がん剤投与後再発はペリオスチンエクソン21中和抗体併用で著明に抑制され、同時にEMTの抑制を伴う。



Target disease: HER2 negative breast cancer

Patent information: PCT applied Technology features: Release existing chemoresistance and safely induce effective results Marketability and development issues: There is a sufficient market, but Phase I/IIa development is required for FIH Desired corporate collaboration details: We are looking for a licensing-out corporate collaboration.

Innovative alpha therapy targeting PSMA for refractory prostate cancer

Principal Investigator	Institute for Radiation Sciences, The University of Osaka
	Associate Professor Tadashi WATABE

Project Outline

Unmet needs in prostate cancer

- Patient data (2018, Japan)
  - Number of new patients: 92,021/year (1st in male)
  - Number of deaths: 12,544/year
- Castration-resistant prostate cancer
  - Five-year survival rate: 42% (low risk), 24% (intermediate risk), 5% (high risk)

(National Cancer Center Cancer Information Service https://bettert bayer.jp/ , Armstrong AJ, et al. Eur Urol. 2020.)

PSMA theranostics

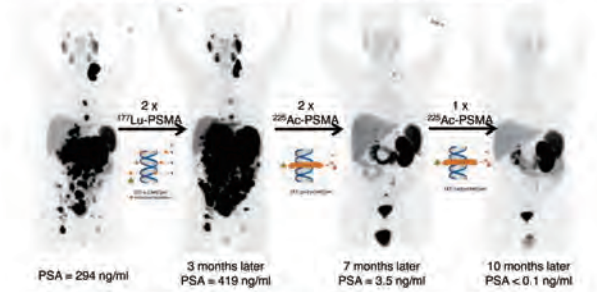
(Prostate specific membrane antigen)

- Membrane protein highly expressed on the membrane surface of prostate cancer cells
- Expressed in most of prostate cancers, including castration-resistant prostate cancer

(F. Giesel et al. EJNMMI. 2016)
(* Approved by FDA and EMA)

Alpha-ray therapy with actinium(^{225}Ac)-PSMA

Advanced prostate cancer with multiple metastases

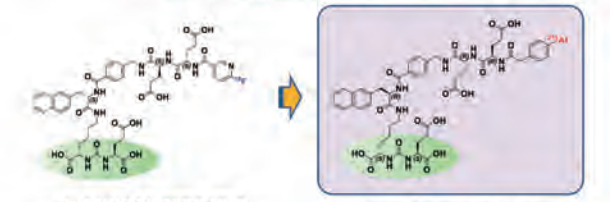


α-therapy (^{225}Ac) is remarkably effective in refractory cases in β-therapy (^{177}Lu).

(C.Kratochwil et al. J Nucl Med. 2016)

^{211}At-PSMA5: new alpha therapy

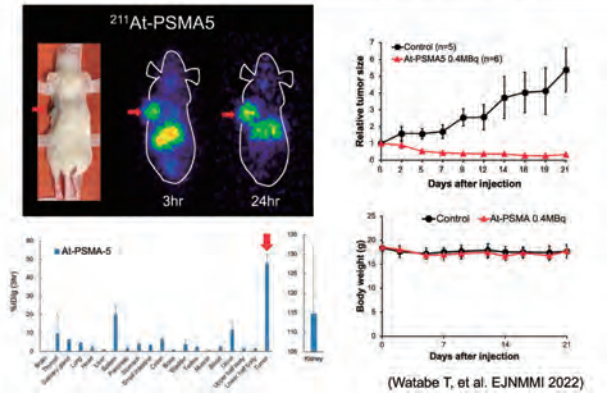
Green area: Specific binding site to PSMA (Ureido structure)



In Osaka University, we developed a new drug ^{211}At-PSMA5 by replacing the radionuclide with ^{211}At. ^{211}At is an alpha-emitting nuclide that can be produced in an accelerator, which can be used on an outpatient basis and manufactured domestically.

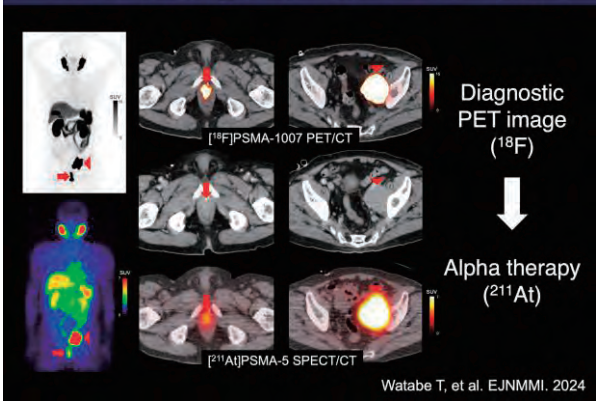
(Watabe T, et al. EJNMMI 2022)

^{211}At-PSMA5: new alpha therapy



(Watabe T, et al. EJNMMI 2022)

1st in human Image of [^{211}At]PSMA-5 in mCRPC



Target disease: prostate cancer　　Patent information: Application number: JP 2021-125774

Technology features: An anticancer drug that emits alpha rays for advanced cancer with multiple metastases

Current status: Under AMED translational research (seeds F) in 2022-2026, and Phase I investigator-initiated clinical trial is being conducted at the University of Osaka Hospital.

Development of ASOs for multiple system atrophy

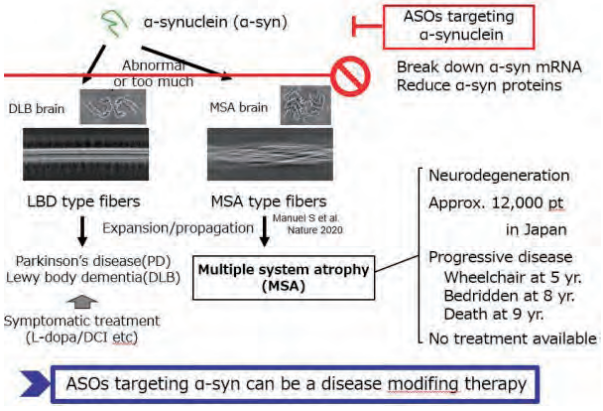
Principal Investigator	1. Department of Neurology, Graduate school of Medicine, The University of Osaka 2. Osaka Toneyama Medical Center
	Specially appointed Lecturer Yasuyoshi KIMURA[1], Director Hideki MOCHIZUKI[2]

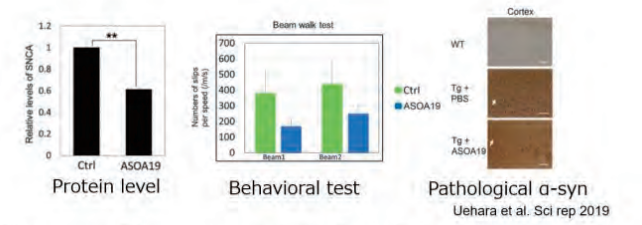
Project Outline

Multiple system atrophy (MSA) is the neurodegenerative disorder affecting about 12,000 people in Japan. Multiple symptoms including motor and autonomic symptoms progress, and patients eventually become bedridden. Currently, no effective treatment is available, thus vigorous researches have been conducted to elucidate the mechanism and develop treatment of MSA all over the world. Cumulative evidences indicate that pathological alpha-synuclein aggregates accumulate in oligodendrocytes and spread through brain, leading to neuronal death in MSA. That's why therapies targeting alpha-synuclein are considered as one of the promising strategies, and among them is the antisense-oligonucleotide(ASO).

We have developed ASOs targeting the coding sequences of alpha-synuclein. We've already had patents and found sequences that effectively suppress human alpha-synuclein *in vitro* and *in vivo*. The prototype ASO ameliorated the Parkinson's disease phenotype in transgenic mice model and suppressed alpha-synuclein expression in primates. Recently, we have developed next-generation ASOs that may be safer and more potent than the original version. We now test these ASO(s) to reveal whether they can suppress human alpha-synuclein in transgenic mice and ameliorate the disease progression and phenotype of mutant alpha-synuclein preformed fibrils-injected mice model with MSA-like parkinsonian pathology. Once we prove the concept that these modified ASO(s) are effective against aipha-synucleinopathy, we will transfer this seed to the stage of clinical evaluation.

Finally, our seeds could be applied to Lewy body diseases including Parkinson's disease and Lewy body dementia which suffer more than 6 million people worldwide.





Prototype ASO suppress α-syn and ameliorate related pathology

Targeted disease：Multiple system atrophy (approx. 12,000 persons in Japan)
Patent information：Application submitted
Characteristics of the technology ：Antisense oligonucleotide containing modified nucleic acids with optimized sequences
We are seeking for：Collaboration, license-out, and/or support for transfer to investigator-initiated clinical trial(s)

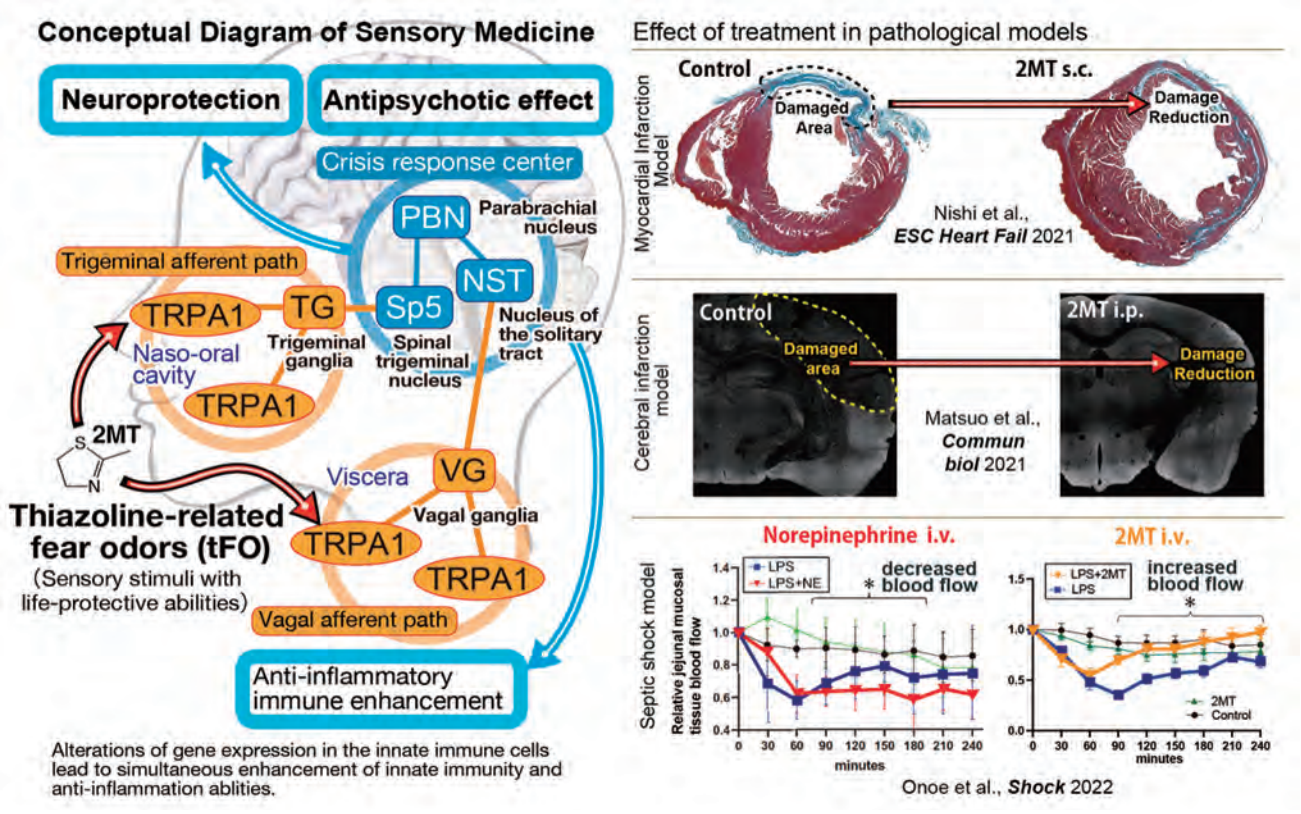
Sensory medicine: Innovative therapeutics based on the principle of inducing the artificial hibernation / life-protective state by TRPA1 - activating odor molecules

Principal Investigator	Kansai Medical University
	Associate Professor Ko KOBAYAKAWA

Project Outline

Organisms have evolved latent life-protective capabilities and survived the race for existence. The whole picture of these life-protective abilities is unknown, and the drugs that artificially induce these abilities have yet to be developed. Innate fear is thought to have evolved as a function of the brain that integrates physiological responses to increase the chance of survival in crisis situations. Given the evolutionary link between life-protective abilities and innate fear emotions, it is hypothesized that some sensory stimuli may induce latent life-protective effects by transmitting information to the central regulatory system of innate fear emotions in the brain.

Based on this hypothesis, we have discovered combinations of odor molecules and their receptor that artificially interfere with the innate fear system to induce life-protective effects that can determine life-or-death in critical situations. Activation of TRPA1 in the trigeminal and vagus nerves with thiazoline-related odor molecules activated the central crisis pathway in the brain, resulting in life-protective effects, including a dramatic increase in survival rate in a lethal hypoxic environment and in septic conditions. In this research and development, we are developing emergency drugs for sepsis, ARDS, ischemia-reperfusion injury, etc., and organ preservation drugs by using "sensory medicine" technology, a method to induce innate fear-induced life-protective effects through sensory stimulation.



Simultaneous induction of immune-enhancing and anti-inflammatory effects is desirable for the treatment of inflammatory infections such as COVID-19, but drugs with such medicinal properties have yet to be developed. Thiazoline-related odorants modulate gene expression of immune cells through the brain circuit to enable simultaneous induction of innate immunity enhancement and anti-inflammatory effects. Sensory medicine utilizes a new route of drug administration, in which drugs are delivered in the nasal cavity as odors, and can be applied to treat various diseases. In order to put this technology to practical use, we would like to promote partnerships with pharmaceutical manufacturers, companies that develop functional gas generators, and companies that develop organ preservatives.

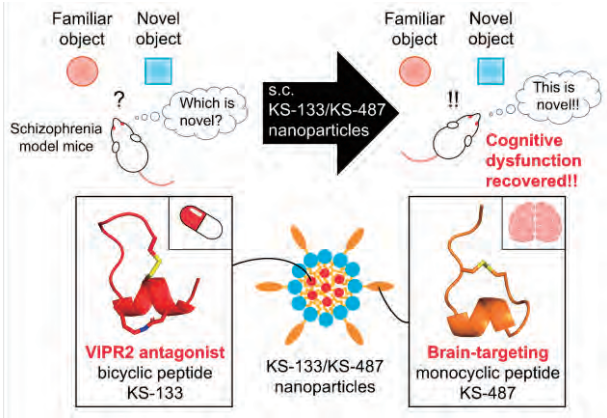
Development of a novel therapeutic drug for schizophrenia

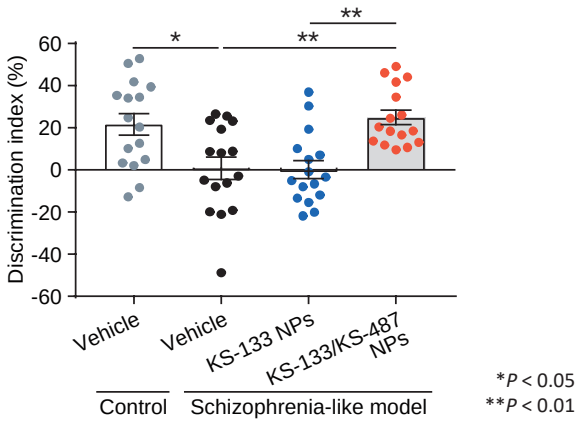
Principal Investigator	Graduate School of Biomedical and Health Sciences, Hiroshima University
	Professor Yukio AGO

Project Outline

Schizophrenia is a psychiatric disorder characterized by positive symptoms, negative symptoms, and cognitive dysfunctions. It affects approximately 1% of the population, with an estimated 900,000 patients in Japan and over 24 million worldwide. Existing drugs only target mechanisms related to neurotransmitter regulation, offering limited therapeutic effects, particularly in addressing cognitive dysfunction. Recent clinical and preclinical research has revealed that excessive activation of the neuropeptide receptor VIPR2 is involved in schizophrenia. This research group previously identified KS-133, the first selective VIPR2 inhibitory peptide usable in vivo (Front Pharmacol 2021, 12:751587), but its low brain permeability posed a challenge.

In this study, the aims are (1) the development of a nanodrug formulation to deliver KS-133 to the brain, and (2) the identification of low-molecular-weight VIPR2 antagonists using docking simulations. For (1), the LRP1 protein expressed at the blood-brain barrier is known to facilitate the transfer of substances from the bloodstream into brain tissue. This research group had previously identified the LRP1-binding peptide KS-487 (Biochem Biophys Rep 2022, 32:101367). Consequently, the following steps were undertaken: Structural analysis of the LRP1 and KS-487 complex using molecular dynamics simulations. Designing nanoparticles that display KS-487 on their surface based on the analyzed structure. Confirming the transfer of KS-487-displaying nanoparticles to the brain *via* subcutaneous injection using bioimaging experiments. Preparing peptide formulations containing KS-133 encapsulated within KS-487-displaying nanoparticles and testing their effects in animal models. These results demonstrated that nanoparticles carrying both KS-133 and KS-487 effectively delivered KS-133 to the brain and restored cognitive dysfunction in animal models to healthy levels (JACS Au 2024, 4:2811-2817). This peptide formulation employs a completely novel mechanism, VIPR2 inhibition, distinct from existing drugs, and is anticipated to become a new drug addressing the unmet medical need of cognitive dysfunction in schizophrenia.





Targeted disease : Schizophrenia (approx. 24 million people worldwide)
Patent information : Application submitted
Characteristics of the technology : mid-size molecular drug, a bicyclic peptide, nanoparticles conjugated with brain-targeting peptides
We are seeking for : Collaboration, license-out, and/or support for transfer to investigator-initiated clinical trial(s)

Development of therapeutic strategy for mosquito-borne diseases by targeting mosquito saliva

Principal Investigator

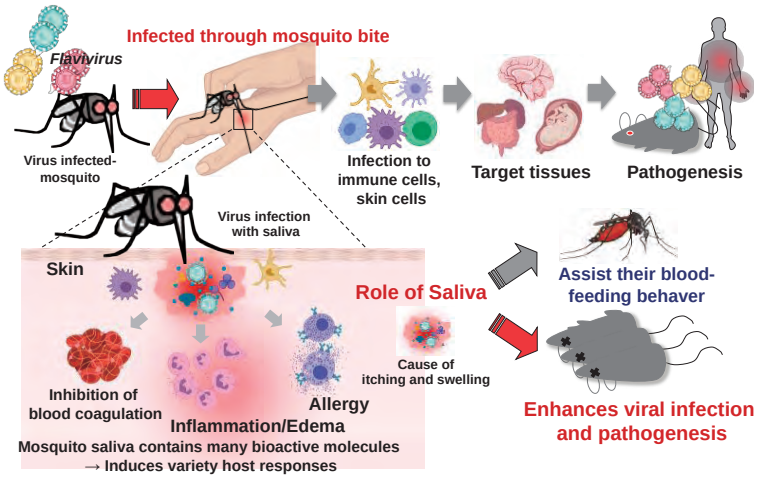
Department of Microbiology, Graduate School of Medicine, Juntendo University

Assistant professor Tatsuya SUZUKI

Project Outline

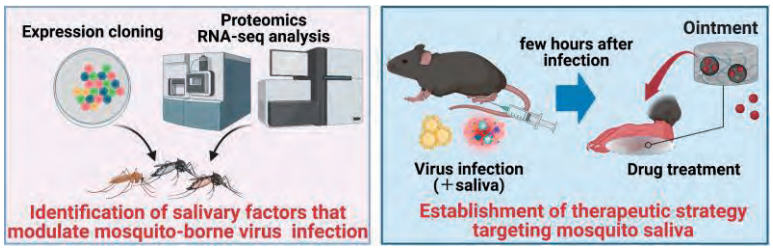
Mosquito saliva is potential therapeutic target for mosquito-borne diseases

- Mosquito-borne viruses such as Dengue virus or Zika virus are injected human with mosquito saliva during blood feeding.
- It has been shown that infection through mosquito bites or injection with **mosquito saliva** enhanced disease severity in several mosquito-borne viruses.
- We found **that targeting for mosquito saliva inhibit viral propagation and pathogenicity in vivo.**
  (Suzuki. et al, Cell Reports, 2025 Sep 23;44 (9):116210)



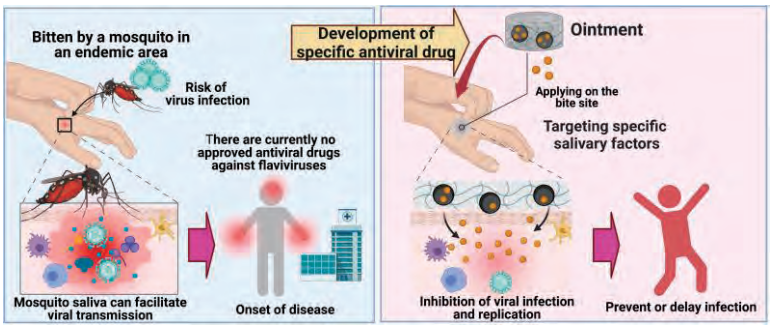
Target of project / Significance

- Drug-resistant virus is less likely to emerge.
- Novel study to develop the antiviral drug through **identification of new salivary factor** that modulate virus infection and pathogenicity.



Aim of this study / In terms of Social impact

- There are no currently available antiviral drug against flaviviruses.
- Our aim is development of specific antiviral drug for targeting mosquito saliva.
- It can be **applied to the study of other mosquito-borne diseases**.



Target diseases: Mosquito-borne flavivirus diseases (Dengue fever, Zika fever)
Patents: Not applied
Characteristics: New therapeutic approach to target mosquito saliva

Development of a novel antibacterial that targets a molecular chaperone

Principal Investigator	Faculty of Engineering, Tottori University
	Professor Tomohiro MIZOBATA

Project Outline

1. Antibiotics are an important and necessary tool in the fight against bacterial infections, and the discovery and development of potent antibiotics have contributed greatly to the quality of life in modern society. Antibiotic resistance, and especially the accelerating emergence of bacterial strains that are immune to multiple antibiotics, threatens our society. However, present efforts to develop a novel, truly innovative antibiotic, in particular an antibiotic that targets Gram-negative bacteria, fall short of the level needed to combat this problem (Right).

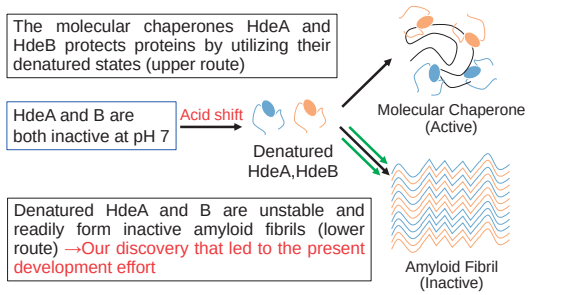
Background; The Emergence of Antimicrobial Resistance (AMR)

"WHO PRIORITY PATHOGENS LIST FOR R&D OF NEW ANTIBIOTICS (2024)"

Critical	*Acinetobacter baumannii* carbapenem resistant *Enterobactenales* carbapenem, cephalosporin(3rd gen) resistant *Mycobacterium tuberculosis* rifampicin resistant
High	*Salmonella enterica* Typhi fluoroquinolone resistant *Shigella spp.* fluoroquinolone resistant *Enterococcus faecium* vancomycin resistant *Pseudomonas aeruginosa* carbapenem resistant non-typhoidal *Salmonella* fluoroquinolone resistant *Neisseria gonorrhoeae* cephalosporin (3rd gen), fluoroquinolone resistant *Staphylococcus aureus* meticillin resistant
Medium	Group A *streptococci* macrolide resistant *Streptococcus pneumoniae* macrolide resistant *Haemophilus influenzae* ampicillin resistant group B *streptococci* penicillin resistant

An urgent need for novel antimicrobials that target Gram-negative bacteria

Concept: The search for a novel antibacterial that targets a molecular chaperone



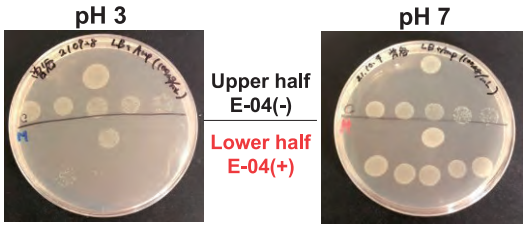
Compounds that promote HdeA/B fibril formation will render bacteria sensitive to acidic conditions
→The search for a novel antibacterial that targets molecular chaperones by promoting their fibrillation

2. The *E. coli* molecular chaperones HdeA and HdeB protect the bacterium from strongly acidic conditions by binding to and stabilizing protein clients from irreversible denaturation and inactivation. Paradoxically, HdeA and HdeB achieves this by utilizing their own acid-denatured structures to recognize and bind clients. We discovered that in this denatured state, both chaperones readily form insoluble fibrils that lead to inactivation (Left).

The present developmental effort searches for compounds that promote this fibrillation and lead to inactivation of HdeA and HdeB, which would render *E.coli* sensitive to acidic conditions.

3. A preliminary search led to the identification of a candidate compound (compound E-04, Right) that promoted the fibrillation of HdeA. Interestingly, E-04 sensitized model *E. coli* cells to transient acid treatment. Curiously, adding E-04 to normal (pH 7) cultures resulted in negligible effect.

Interpreting this result as a proof that validates our concept of using HdeA as target and promotion of fibrillation as mechanism of action of a novel antibacterial, we are presently trying to improve on the initial E-04 candidate for antibacterial potency.



Antibacterial effect by sensitization to low pH | **E-04 is ineffective at pH 7 (specific targeting of HdeA)**

(x10 serial dilution spot assays)

Target: Enterohemorrhagic Escherichia coli ; EHEC
Patent submission process: In preparation
Novelty of technology: An eventual development of a novel antibacterial that acts on molecular chaperones as unique target and inactivation through fibrillation as unique mechanism of action
Factors to accelerate development: Finding suitable partners to test candidate compounds in a clinical setting

Development of SE36-cVLP Malaria Vaccine

Principal Investigator

Laboratory of Malaria Vaccine Development,
Research Institute for Microbial Diseases,The University of Osaka

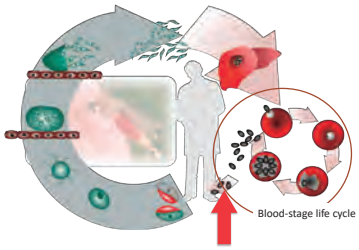
Special Appointed Professor Toshihiro HORII

Project Outline

The BK-SE36 malaria vaccine, which combines SE36 recombinant protein with aluminum hydroxide gel (AHG), demonstrated a 72% protective efficacy in clinical trials in Uganda. Furthermore, studies indicated that increasing vaccine-induced antibody titers could potentially enhance efficacy. Thus, to boost antibody titers, the nucleic acid adjuvant CpG-ODN (K3) was added to the BK-SE36 malaria vaccine. Phase Ib clinical evaluation of NPC-SE36/CpG vaccine commenced in Burkina Faso in May 2018, with final observations completed in April 2020. However, the conventional manufacturing process proved too costly for widespread use in African countries and was limited in annual production capacity. As a result, the formulation was modified to SE36-cVLP. SE36-cVLP exhibits several-fold higher antigenicity than SE36/CpG and can be manufactured at a fraction of the cost. Currently, GMP manufacturing is underway to conduct a Phase I/IIa controlled human malaria infection (CHMI) study at the University of Tübingen.

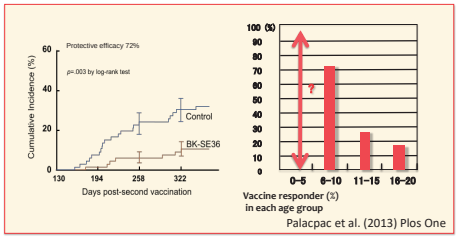
Malaria kills 0.6 million people

Life cycle of P. falciparum



Anti SE36 antibody attacks merozoite of the parasite

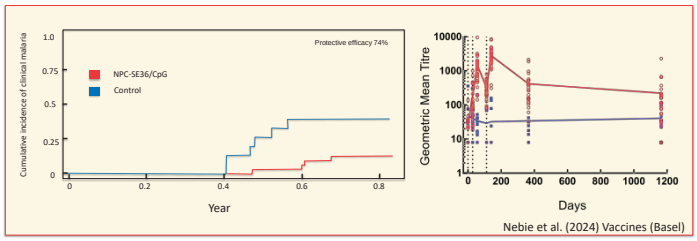
The results of phase Ib clinical trial and follow-up research in Uganda



Palacpac et al. (2013) Plos One

The figure on the left shows the follow-up results from the Phase Ib trial of BK-SE36/AHG vaccine in Uganda. The data suggests that vaccine responsiveness is more prevalent in younger age groups, while repeated infections with age may lead to development of immune tolerance. Consequently, a higher proportion of vaccine responders is anticipated among children aged 0–5 years, who are identified by the WHO as the primary target population for malaria vaccination.

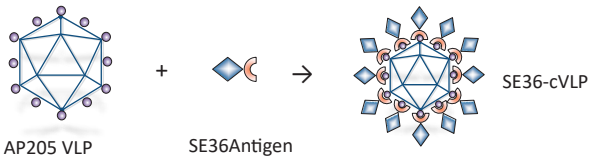
Protective efficacy of BK-SE36/CpG in Phase Ib clinical trial and changes in vaccine-induced antibody titers over time



Nebie et al. (2024) Vaccines (Basel)

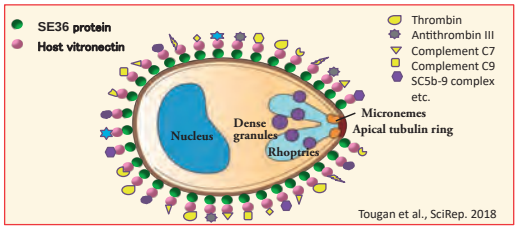
A Phase Ib safety study of BK-SE36/CpG was conducted in Burkina Faso with no serious vaccine-related adverse events reported. Malaria incidence was also measured for one year following vaccination, with a protective efficacy of 74% (p=0.035). Furthermore, a three-year follow-up assessment of vaccine-induced antibody titers revealed that high antibody titers were maintained even three years after vaccination.

Development of a malaria vaccine using a new formulation combining phage capsid and SE36



The clinical trials conducted in Africa demonstrated that SE36 is an excellent candidate for a malaria vaccine. However, the conventional manufacturing method is prohibitively expensive for widespread use in Africa, and is limited in annual production capacity. To address these challenges, the formulation was redesigned as SE36-cVLP, which combines the SE36 protein and the capsid of the *E. coli* RNA phage. SE36 protein is efficiently produced in another bacterial expression system. SE36-cVLP exhibits several-fold higher antigenicity than SE36/CpG and can be manufactured at a fraction of the cost. GMP manufacturing is currently underway to be able to conduct a CHMI study at the University of Tübingen.

Biological function of SE36 protein



Tougan et al., SciRep. 2018

SE36 hijacks host proteins and molecularly camouflages the surface of merozoites to avoid attack by the immune system. It also induces immune tolerance to SE36 by tightly binding to host vitronectin. In endemic areas, antibody responses against SE36 are low due to immune tolerance. The lack of selective pressure from host immunity is thought to be the reason for the low level of SE36 genetic polymorphism.

Target disease: Malaria
Patent information: Patent pending.
Technology features: A novel malaria vaccine, SE36-cVLP, combining the malaria *Plasmodium* antigen polypeptide SE36 with cVLP.
Marketability: Falciparum malaria is an infectious disease that infects 200-300 million people annually and kills more than 600,000 people, mainly infants under the age of 5 (WHO Report 2024). The development of a highly effective vaccine is expected as a drastic measure.
Development challenges: Obtaining funding to conduct large-scale clinical trials in endemic areas.

Development of L862, an Innovative Pulmonary Hypertension Treatment Targeting TRPC3/6

Principal Investigator

1. The University of Osaka, Pharmaceutical Sciences
2. Shinshu University School of Medicine

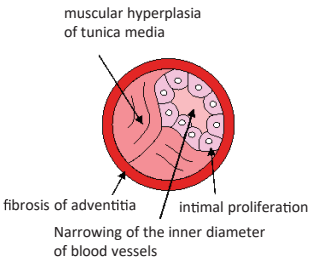
Associate Professor Ryu NAGATA[1]　Professor Koichiro KUWAHARA[2]

Project Outline

Pulmonary arterial hypertension (PAH, designated as an intractable disease)

• It is a condition in which the pulmonary arteries become abnormally narrowed and stiffened, resulting in increased pulmonary artery pressure. Symptoms such as shortness of breath and dyspnea appear with light movements.
• The number of patients in Japan is approximately 4,200 (FY 2020) and increasing every year. The global market size is projected to be USD 9.34 billion by 2034 (Research and Markets).
• The prognosis of PAH associated with systemic sclerosis is particularly poor, and unmet medical needs are still high.
• PAH is caused by pulmonary artery remodeling (intimal proliferation, muscular hyperplasia of tunica media, and fibrosis of adventitia), and existing oral vasodilator drugs are not effective in treating PAH associated with advanced lesions, venous disease, and collagen diseases such as systemic sclerosis.
→ Oral drugs that can directly intervene in remodeling are needed.

Vascular remodeling In PAH patients



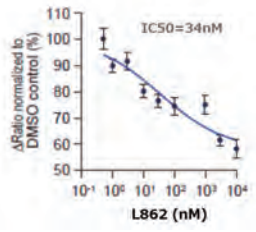
About TRP (Transient Arterial Potential) C3/6

• TRP channels are membrane proteins that exist on lipid membranes and form a superfamily of 28 types.
• They form tetramers and function as non-selective cation channels by permeating Na and Ca ions.
• It acts as a sensor to detect various extracellular signals.
• Various evidences that TRPC3/6 is involved in PAH and remodeling (Kuwahara et.al. JCI 2006; 116: 3114, etc.).
→ TRPC3/6 inhibitors may be therapeutic agents directly involved in PAH remodeling.

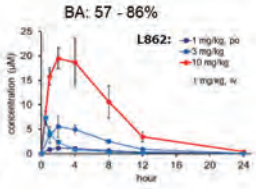
L862, Novel TRPC3/6 inhibitor

- L862 inhibits TRPC3/C6 channels at low concentrations and exhibits high selectivity for other proteins.
- L862 shows excellent physicochemical properties, and PK/safety profiles, with no manufacturing concerns.
- The substance patent application (WO2019208812) has been granted in JP, US, EP, and CN.
- Use Patent applications for heart failure, acute kidney injury, and so on containing L862 were filed.
- At a PMDA face-to-face consultation, we received confirmation that the nonclinical studies submitted for the physician-initiated Phase 1 clinical trial were adequate and that the proposed Phase 1 clinical trial protocol was acceptable.

Inhibition of TRPC6

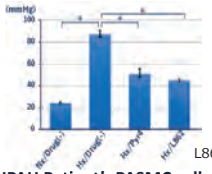


PK Profiles in Rats

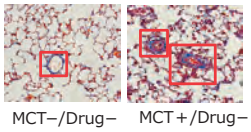


Effects of L862 on PAH model rats and patient-derived pulmonary arterial smooth muscle cells

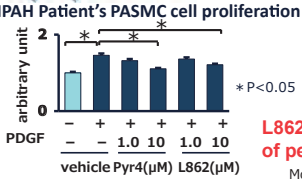
Monocrotaline induced PAH model Rats
systolic pulmonary arterial pressure

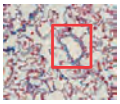


Monocrotaline-induced PH rats (Masson-Trichrome Staining)



IPAH Patient's PASMC cell proliferation





L862 administration suppressed fibrosis of perivascular tissues in the PH model.
Moriuchi, Kuwahara et al. in preparation 2021

L862 improves pulmonary hypertension in various established animal models of PAH.

Target disease: Pulmonary arterial hypertension
Current status: GLP-preclinical studies have been completed and Execution of a P1 clinical trial is under preparation.
Description of technology: Oral small molecule therapeutic agent for PAH based on a novel mechanism of action
Contact for inquiries regarding joint research and licensing: Department of Medical Innovation, The University of Osaka Hospital, Ms. Sasajima, Email: michiyo.sasajima@dmi.med.osaka-u.ac.jp

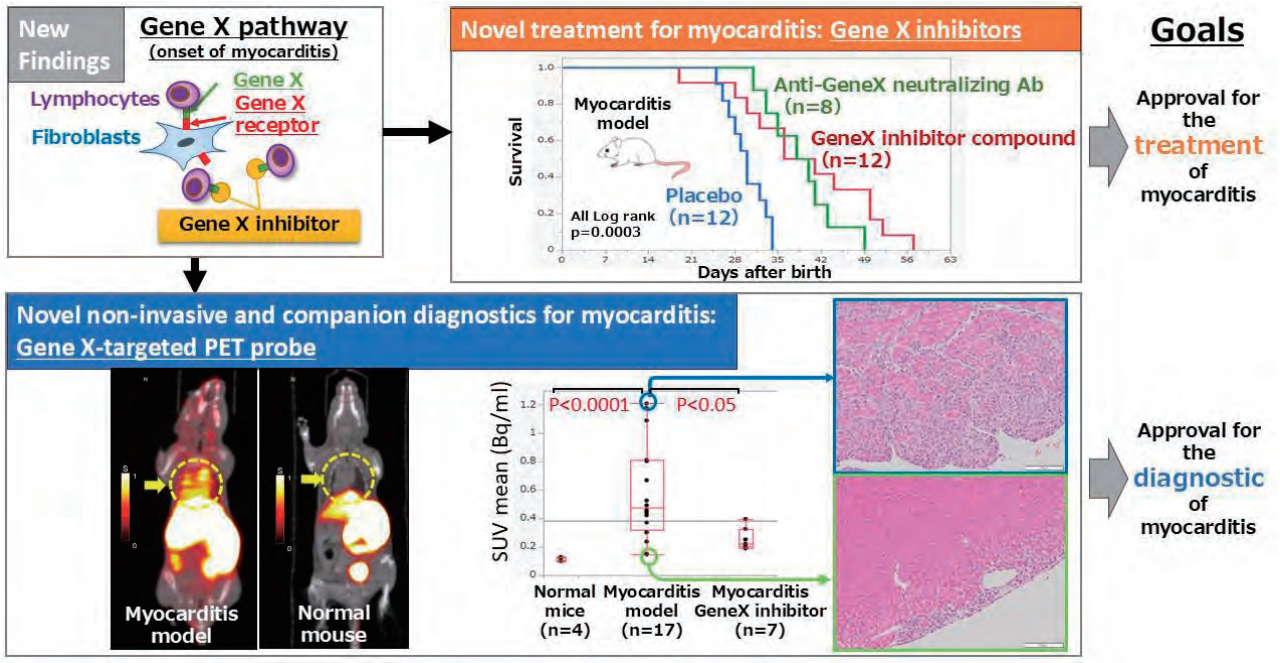
Development of novel companion PET diagnostics and therapeutic agents for myocarditis

Principal Investigator	Department of Medical Biochemistry, Graduate School of Medicine, The University of Osaka
	Associate Professor Ken MATSUOKA

Project Outline

Myocarditis is a fatal disease with currently no effective treatments. In recent years, myocarditis has been accompanied with severe infections including Covid-19, mRNA vaccines, and immune checkpoint inhibitors, which are frequently used in the cancer field. Therefore, there is an extremely high need for the development of effective diagnostic and therapeutic methods for myocarditis.

In the previous study, we have clarified that activated lymphocytes expressing Gene X are involved in the onset of myocarditis, and that Gene X inhibitors improve the prognosis of myocarditis models. Furthermore, we have created a novel PET probe by labeling the Gene X inhibitor with the radioactive C11 nuclide, and successfully detected Gene X-positive lymphocytes infiltrating the myocardium in a myocarditis model by PET/CT. In addition, Gene X inhibitors were more effective in the myocarditis model with high accumulation of the PET probe. From the above, this PET probe is not only a non-invasive diagnostic agent for myocarditis that replaces the conventional highly invasive myocardial biopsy, but also a companion diagnostic agent for Gene X inhibitors. Therefore, it is expected that the combination of these two seeds will significantly improve the prognosis of myocarditis. We are now looking for companies that will cooperate with us to obtain clinical proof of concept for this PET formulation and Gene X inhibitors.



Target disease: Myocarditis (2,200 people/year in Japan, 1.8 million people/year worldwide)

Patent information: Substance patent, application patent

Features: Combination of companion PET diagnostic and therapeutic drug can significantly improve prognosis

Issues: Need company support to obtain clinical POC

Desired company collaboration: Support for clinical trials and licensing out

Development of Therapeutic Agents for Intractable Neurological Diseases Using Novel GAPDH Aggregation Inhibitors

Principal Investigator	Osaka Metropolitan University
	Associate professor Hidemitsu NAKAJIMA

Project Outline

GAPDH Aggregation Inhibitor for the Treatment of Intractable Neuropathy

We are seeking companies to develop it further through licensing.

Potential preventive/therapeutic agent for neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Huntington's disease, ALS, MSA and stroke

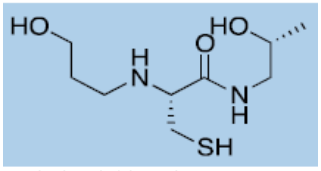
◆Background

In most neurodegenerative disorders, it is well-established that disease-specific proteins aggregate to form amyloids, which subsequently induce neuronal cell death and neuroinflammation. Additionally, various researches have reported that aggregates of the multifunctional protein glyceraldehyde-3-phosphate dehydrogenase (GAPDH) frequently deposit within these pathological lesions. Based on these findings we have proposed the "common cross-seeding hypothesis," which suggests that GAPDH aggregates function as auniversal seeding core-a common seed-that initiates the aggregation and amyloid formation of diverse disease-specific proteins.

◆Description

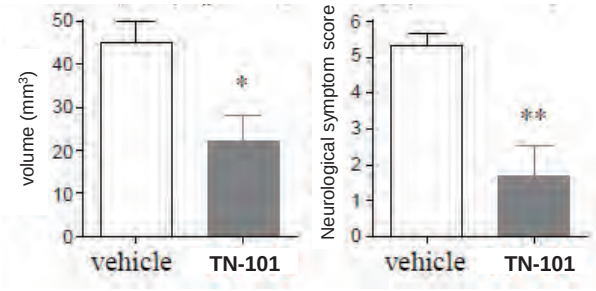
The research group developed a novel compound ***TN-101*** that targets GAPDH aggregation to prevent, treat and improve cranial neuropathy such as Alzheimer's disease, Parkinson's disease, Huntington's disease, ALS, MSA and stroke.

TN-101



IC50 = 0.90 ± 0.11 μM
Amphiphile: cLogP = -1.25
BA≒25% (30 mg/kg, p.o.)
MW = 237

◆In-vivo evaluations of TN-101



Cerebral protective effect of TN-101 in stroke model of mice

TN-101 was administrated to ischemic model mice intraventricularly. At 24 hours post-administration, the infarction volume decreased and neurological symptoms improved. These results show that inhibiting GAPDH aggregation can effectively prevent, treat, or improve neurological symptoms caused by blood flow disorders such as stroke.

Indication : Neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Huntington's disease ALS, MSA and stroke.
Patent : JP6838743B2 , Non-peptidic GAPDH aggregation inhibitor
Modality : New Chemical Entity
We are seeking companies to develop it further through licensing.

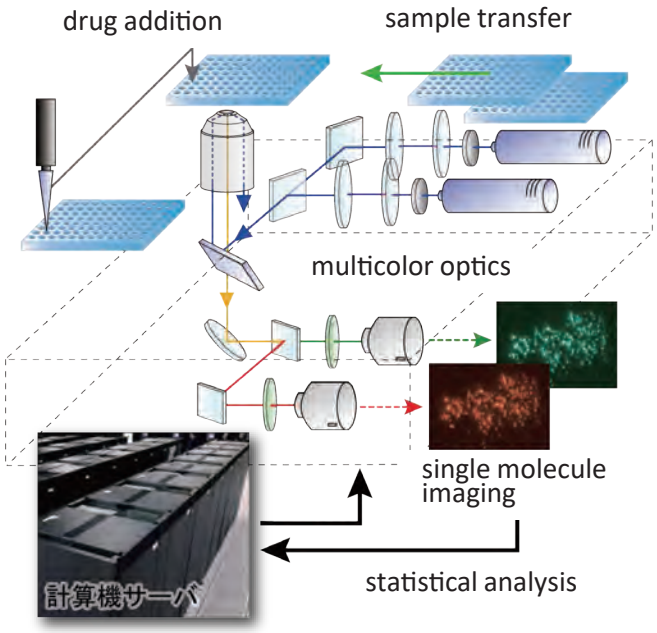
Development of single-molecule imaging-based screening technology for drug discovery

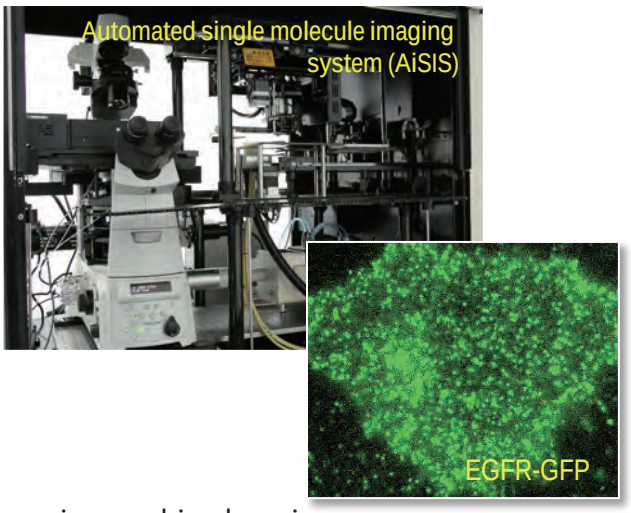
Principal Investigator	Graduate School of Frontier Biosciences, The University of Osaka
	Professor Masahiro UEDA

Project Outline

Single-molecule imaging-based screening for drug discovery
- Novel platform technology -

Single molecule imaging analysis enables us to visualize biomolecules functioning in cells, and to obtain quantitative values related to the diffusion and oligomerization of membrane proteins. We have developed a fully automated single molecule imaging system (AiSIS) and have realized large-scale analysis in living cells (right figure). By applying this method to epidermal growth factor receptor (EGFR), which is the cause of various cancers, we are establishing it as a novel basic technology for drug discovery. Since this approach can be applied to molecular species without enzymatic activity and orphan receptors, it has the potential to realize drug screening for target molecules to which existing methods are difficult to be applied.





Core Technologies
Machine learning (AI) and robotics-assisted automated imaging analysis

- Automatic cell recognition and observation by using machine learning
- Analysis of diffusion and oligomer formation of 8,000 cells per day
- Detection of drug-induced changes in molecular dynamics
- Automated single molecule imaging analysis of various receptors

Yasui et al., ***Nature Commun.*** 9: 3061 (2018)
Watanabe et al., ***Nature Commun.*** 15:8975(2024)

Target diseases: Lung cancer, colorectal cancer, brain and central nervous system cancer, pancreatic cancer, etc
Patent information: Patent 6952300, Patent 7226825, Patent Application 2023-31358, US Patent 11002728、US Patent 11567293B2
Characteristics of technology: Drug screening by visualizing single-molecules functioning in cells
Marketability, challenges in development: Development of drug candidates after single molecule screening

Discovering Peptide-based Therapeutics for Neuropathic Pain

Principal Investigator	Department of Biomedical Engineering Osaka Institute of Technology
	Professor Emiko OKUDA-ASHITAKA

Project Outline

Neuropathic pain associated with nerve damage, diabetes, herpes zoster, and cancer is a chronic intractable pain that does not respond significantly to non-steroidal anti-inflammatory drugs or opioid analgesics. We have previously discovered that nocistatin (NST) inhibits allodynia, which is the pain to the touch seen in neuropathic pain, when administered intrathecally. Based on peptides derived from NST (NST-P), we are developing orally administrable analgesics with minimal side effects. This study will optimize the structure of NST-P as a lead compound, identify the target molecule of the peptide, and elucidate its mechanism of action.

Intraventricular and intrathecal administration of NST inhibits pain

NST is a peptide derived from the same precursor protein as the opioid peptide nociception/orphan FQ (N/OFQ) (Fig. 1).
Intraventricular (icv) and intrathecal (it) administration of NST inhibits a wide variety of pain (Fig. 2).

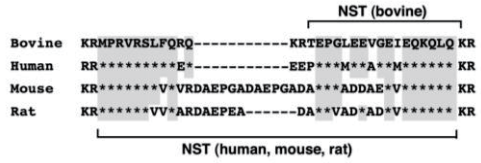


Fig.1 Amino acid sequence of NST

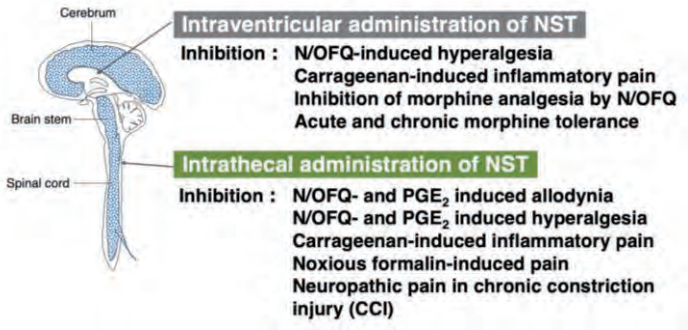


Fig.2 Inhibition of pain by NST

Japanese Unexamined Patent Publication H11-021298, 2001-354695
Nature 392:286-9, 1998; *Curr Pharm Des* 21:868-84,2015

NST-derived peptides (NST-P) inhibit diabetic neuropathic pain

A mouse model of diabetes mellitus was prepared by the administration of streptozotocin (STZ). At 1-3 weeks after STZ administration, pain threshold was lowered by pain analysis using the von Frey test, and onset of pain was observed. Intrathecal and orally administration of NST-P to mice after STZ demonstrated the inhibition of pain (Fig. 3).

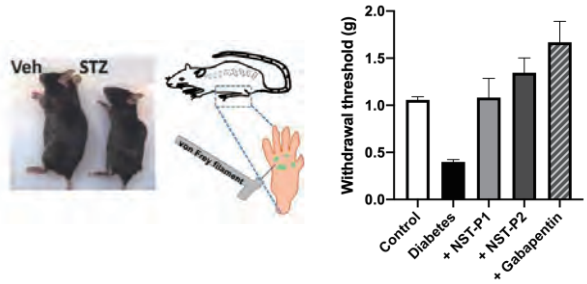


Fig. 3 Effect of NST-P on pain in a diabetic mice model

Target Disease : Neuropathic pain　Patent Information : Japanese Patent Application
Technical Features : Peptide based analgesic
Marketability : 6,000,000 individuals in Japan, approximately 6.9%-10% of the world population
Issues in Development : Mechanism of pain regulated by nocistatin-derived peptides,
Optimization of these peptides
Desired nature of corporate collaboration : Joint Research

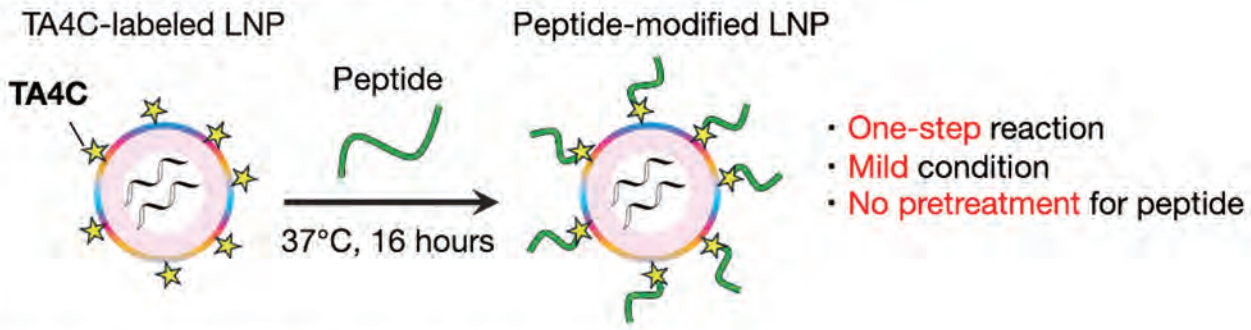
Tissue targeting of lipid nanoparticles by N-terminal modification of peptides

Principal Investigator	Faculty of Environmental Earth Science, Hokkaido University
	Professor Akira ONODA

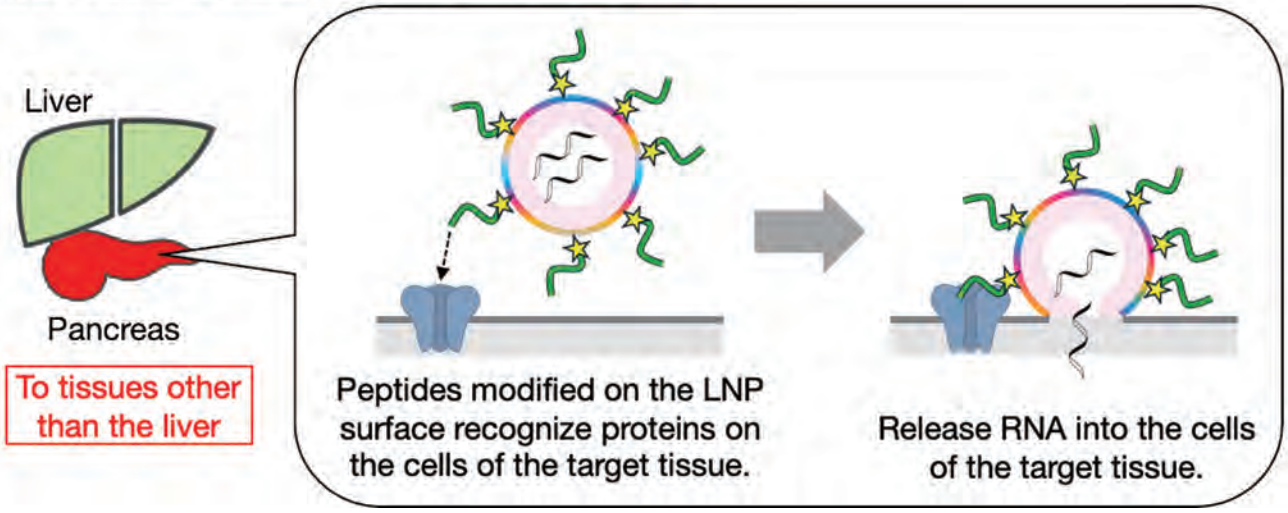
Project Outline

Lipid nanoparticles (LNPs) are attracting attention as carriers for nucleic acid medicine and has been used as COVID-19 vaccines in clinical application. However, the tissue targeting of LNPs is limited to the liver. Our technology will enable to control the tissue targeting of LNPs by surface modification of LNP with peptides using a site-specific modification reagent, "**1*H*-1,2,3-triazole-4-carbaldehyde (TA4C)**". **TA4C** developed in our group is a reagent that efficiently modifies N-terminus of a peptide in one-step at 37°C. Targeting using **TA4C** has a potential to be be applied to a broad spectrum of diseases due to its simple reaction process and compatibility with various peptides.

(1) Scheme of peptide-modified LNP synthesis



(2) Tissue targeting of peptide-modified LNP



Target disease: Genetic disease (ex. hereditary pancreatitis)
Patent information: JP Patent Application No. 2024-172588
Features: Tissue targeting of nucleic acid drugs by LNP surface modification. Site-specific modification of peptide in one-step.
Corporate collaboration: Collaborative research in non-clinical and clinical trials, licensing, and licensing out

Development of repair therapy for skin barrier function by product lipids of novel lipase

Principal Investigator

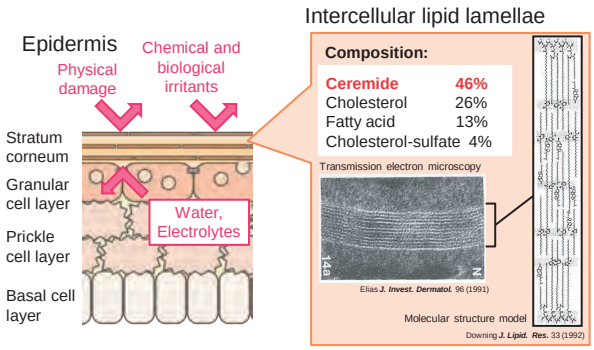
Department of Bio-system Pharmacology,
Graduate School of medicine, The University of Osaka

Associate Professor Ryuichi OHGAKI

Project Outline

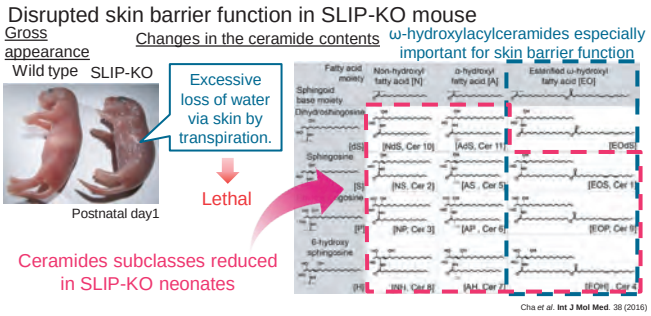
Skin barrier function and ceramides

Intercellular space of stratum corneum, which locates at the outermost layer of the epidermis in skin, is filled with lamellar structures of lipids mainly composed of ceramides. This intercellular lipid lamellae is essential for the "Skin barrier function" to protect our body from physical damage, chemical and biological irritation, and dissipation of water and electrolytes.



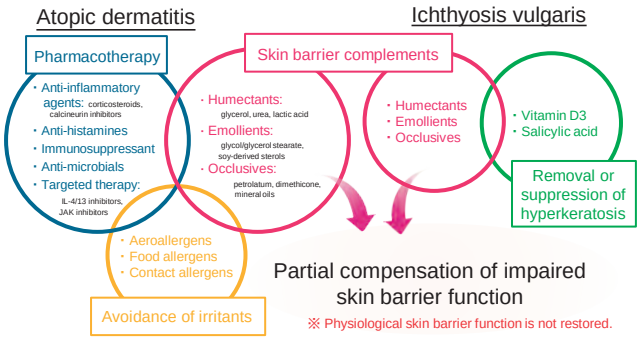
Novel lipase-like protein SLIP, an essential factor for skin barrier function

Gene knockout of SLIP (Skin-specific lipase-like protein), a novel lipase specifically expressed in epidermis, causes disruption of the skin barrier function and death shortly after birth due to excessive water evaporation in mouse. In the stratum corneum of SLIP-KO mice, the lipid lamellar structure becomes unclear, and the permeability of water and macromolecules is enhanced. Ceramides in a wide range of subclasses are reduced considerably.



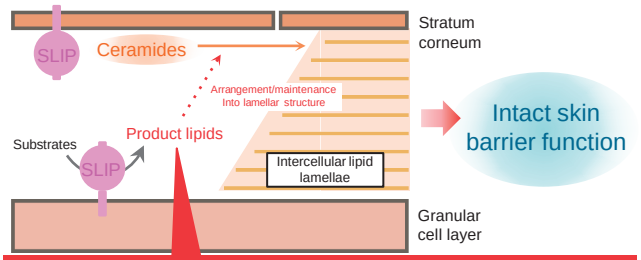
Current therapeutic approaches to pathologically impaired skin barrier function

In diseases such as atopic dermatitis and ichthyosis, the skin barrier function is disrupted due to abnormalities in the homeostasis of ceramides in epidermis. Topical agents containing humectants, emollients, and occlusives are widely used to compensate for the impaired skin barrier function. However, these treatments do not restore the physiological skin barrier function.



Drug discovery for novel skin barrier repair therapy

SLIP is a putative transmembrane protein presenting its lipase domain extracellularly in cell layers including stratum corneum. We are aiming to identify product lipid molecules of SLIP, which are expected to have a function of arranging or maintaining ceramides in the lamellar structure, and to develop a novel repair therapy for skin barrier function.



Product lipids of SLIP are expected to restore the pathologically disrupted skin barrier function in atopic dermatitis and ichthyosis by recovery of the ceramide homeostasis in intercellular lipid lamellae.

Target diseases: Impaired skin barrier function (Atopic dermatitis, ichthyosis vulgaris, etc.)
Patent information: Not applied
Technical features: Unique treatment that restores the physiological skin barrier function
Marketability: Atopic dermatitis – prevalence rate is up to a few percent of the population in worldwide
Ichthyosis vulgaris – prevalence rate is 1 patient in 250 to 300 person.
Challenges in development: Cost for identification of product lipids, Acquisition of non-clinical POC in disease models
Proposal for collaboration: Joint research and development-lipidomics analysis, disease models

Establishment of a new strategy for the treatment of functional restoration in skeletal muscle injury by tissue engineering using osteopontinederived SVVYGLR peptide

Principal Investigator

Department of Oral and Maxillofacial Surgery,
Graduate School of Dentistry, The University of Osaka

Professor Susumu TANAKA

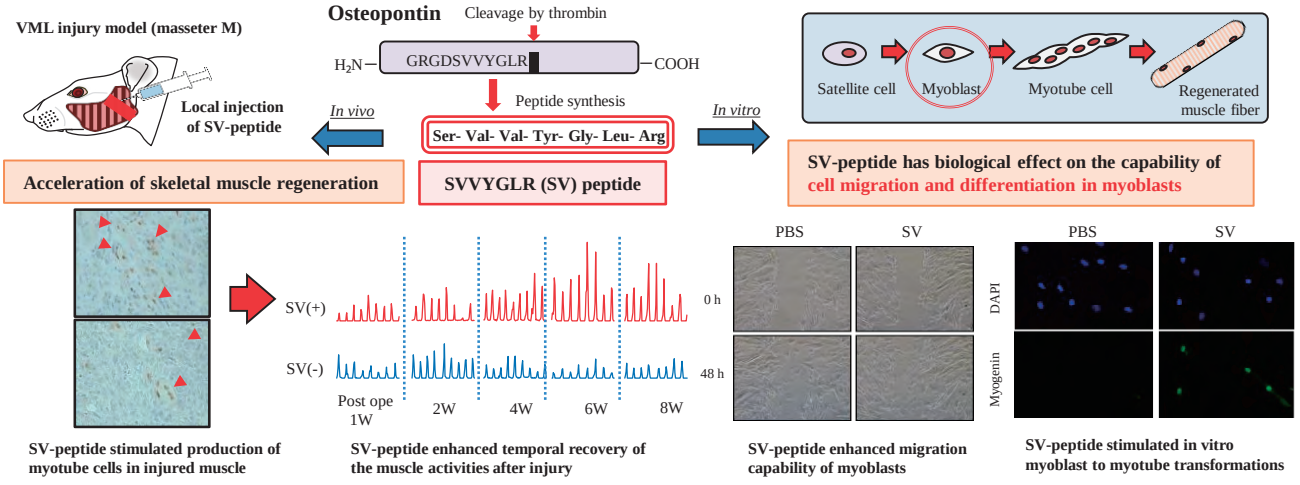
Project Outline

Skeletal muscle dysfunction with serious damages caused by injury or surgery, and congenital diseases with deformed or poorly developed muscular tissue such as cleft palate, conventional treatments including plastic surgery occasionally fail to obtain an adequate functional recovery. SVVYGLR (SV), 7-amino-acid sequence derived from osteopontin (SV peptide) has previously demonstrated strong angiogenic activity, enhancement of the synthesis of collagen type III in myocardial fibrosis and capability for improvement of cardiac function through the differentiation of fibroblasts to myofibroblasts. This peptide was also revealed to be easily degraded by peptidase and show less adverse effects, indicating high biocompatibility. Like myocardium, skeletal muscle is striated, but it is voluntary, composed of multi-nucleated muscle fibers regenerated by tissue-specific muscle stem cells called satellite cells which proliferate and differentiate to form mature myoblasts.

Given the potent role of SV peptide on the repair of injured skeletal muscles like myocardium, it might also contribute to functional restoration after the injury. Our preliminary study using rat volumetric muscle loss (VML) injury model in masseter muscles demonstrated that local injection of SV peptide immediately after the injury increased EMG activities recorded from injured muscles and suppressed fibrosis by the generation of scar tissues compared with injection of PBS or inactive form of SV. In addition, cultured human skeletal muscle precursor cells containing SV-peptide promoted the migration and differentiation of myoblasts.

Development roadmap

	2025	2026	2027	2028	2029	2030
GMP peptide synthesis	Estimation of efficacy Safety evaluation and pharmacokinetics Manufacturing process, quality control					
Non-clinical	Basic research (biological and physiological) Animal testing ADME discovery screening research (pharmacodynamics, pharmacokinetics, toxicity test)					
Phase I			Preparation of protocol, clinical study			
Phase II						
Phase III						
NDA						
Approval						



SV-peptide stimulated production of myotube cells in injured muscle

SV-peptide enhanced temporal recovery of the muscle activities after injury

SV-peptide enhanced migration capability of myoblasts

SV-peptide stimulated in vitro myoblast to myotube transformations

Target diseases in this project: Skeletal muscle injuries with irreversible motor dysfunction in oral and maxillofacial surgery, trauma, and congenital abnormalities including orofacial clefts such as cleft lip and palate. Title of the Invention: Restorative materials for skeletal muscle injury, Patent No. JP 6912117, US 11,077,167 B2 2017-229688. Aim of this project is to identify and develop a new novel peptide therapeutics with small molecule suited for functional regeneration in skeletal muscle injuries.

A new anti-inflammatory drug that utilizes the active site of an endogenous NFkB direct inhibitory protein

Principal Investigator	Graduate School of Frontier Biosciences, The University of Osaka
	Specially Appointed Associate Professor Kazuki OKAMOTO

Project Outline

【Unmet Medical Needs】

1. In severe or fulminant cases, there is no effective drug other than steroid anti-inflammatory drugs (SAIDs).
2. SAIDs have a strong anti-inflammatory effect by directly inhibiting NFκB, however, long-term administrations of SAIDs cause serious side-effects and susceptibility to infection. Also, the emergence of steroid-resistance makes it difficult to continue treatment.
3. An NFκB inhibitor that has the strong anti-inflammatory action as SAIDs together with the high safety is highly recommended, but has not yet been launched.

【Superiority of this new drug seed against SAIDs】

① The investigator found a new intrinsic NFκB inhibitor (MTI-II, Fig. 1).
② The active domain (6A) in MTI-II with cell permeable peptide (CPP; 8R) shows an strong anti-inflammatory action.
③ As 6A-8R directly inhibits the transcriptional activity of NFκB, it has as strong action as SAIDs.
④ As it has few side-effects (Table 1), it can be used for long-term therapy for fulminant cases.
⑤ As it inhibits NFκB by a different pathway from SAIDs, it will overcome the steroid-resistance.
⑥ Table 2 shows the applications of 6A-8R with confirmed therapeutic efficacy in animal models.

【How easy this peptide drug (6A-8R) can be used.】

A) It is easily soluble in saline/TBS/PBS/water and can be administered locally in small volumes at high concentrations (1 g/mL). No viscosity was observed even at a concentration of 1 g/mL.
B) It does not denature, inactivate, or decompose even when heated in aqueous solution (100°C, 5 minutes), or under acidic conditions (approx. pH 2) or alkaline conditions (approx. pH 11).
C) It can be administered topically because it does not denature or become inactive when mixed with an ointment base. Its effectiveness has been confirmed in an experimental atopic dermatitis model.
D) It is not antigenic. (Confirmed by the IEDB (Immune Epitope Database) Analysis Resource.)
E) It can be embedded in enteric-coated tablets, allowing localized delivery to the small intestine, and can also be used as an oral medication.
F) It can be synthesized in accordance with GMP standards.

Fig 1. Intrinsic NFκB Inhibitor, MTI-Ⅱ

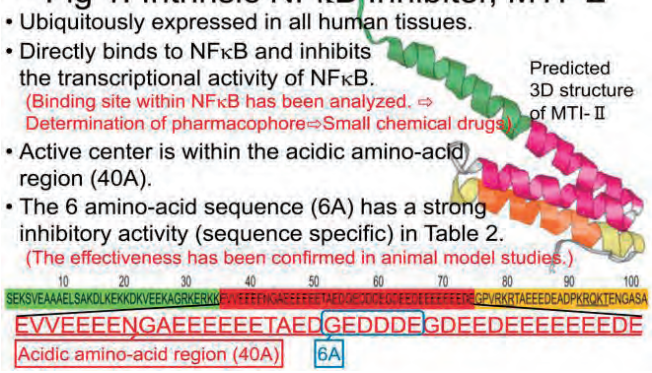


Table 1. Animal POC of MTI Anti-Inflammatory Drugs

Animal Tests	Routes	MTI Anti-Inflammatory Drug	Dose	Control
Carrageenan-induced foot edema	intra-peritoneal	MTI-Ⅱ with CPP* (14.17 kDa) *cell permeable peptide	0.4 μmol/ injection	Indomethacin 1.1 μmol/ injection
Croton oil-induced conjunctival inflammation	binocularly instilled	MTI-Ⅱ with CPP (14.17 kDa)	14 nmol/ drop	Dexamethasone 13 nmol/ drop
	binocularly instilled	6A with CPP 6A-8R (1928 Da)	330 nmol/ drop	Dexamethasone 13 nmol/ drop
Mite antigens induced atopic dermatitis	mixed with ointment base and applied	40A with CPP 40A-8R (5.88 kDa)	170 nmol/ cm^2 (without skin atrophy)	Betamethasone (140 nmol /cm^2) Show severe skin atrophy.
Collagen-induced arthritis	intra-peritoneal (The 28 days consecutive dosage)	40A with CPP 40A-8R (5.88 kDa)	0.6 μmol/ injection	

Do not show the side effects of SAIDs.
No toxicity after repeated injection.

1. No swelling, hypertrophy or atrophy is observed in the internal organs.
2. No bleeding, erosion, nor ulcer was found in the gastrointestinal tract.
3. Blood biochemical test showed no significant difference from NC group → No increase in blood glucose level.
4. White blood cell count and fraction showed not significantly different from NC group → No decrease in neutrophil migration ability.

Table 2. Applications of MTI anti-inflammatory drug (6A-8R) with confirmed therapeutic efficacy in animal model.
Results of joint study with the clinical departments of Osaka University School of Medicine (ophthalmology, orthopedics).

1. Therapeutic agent for Uveitis without glaucoma (safety tested).
2. Therapeutic agent for Rheumatoid arthritis that does not induce osteoporosis (no changes in osteoblasts and osteoclasts).
3. Therapeutic agent for Osteoporosis.

The connections with other clinical departments are possible.

Call for Collaborations : Arrangement of non-clinical and clinical tests of 6A-8R.

Target diseases: osteoarthritis, rheumatism, uveitis, endometriosis, preterm birth and target diseases of SAIDs.

Patents: Patent No.6830651, Patent No. US7,932,226 B2, Patent No.4874798.

Characteristics: An anti-inflammatory drug which has the same actions (NFκB inhibition) as SAIDs with few side-effects has not yet been developed. Using endogenous NFκB inhibitor, we have developed a new drug.

Market Superiority: This drug will replace SAIDs, and help many patients suffering from side effects of SAIDs.

Desired Collaboration: Arrangement of non-clinical and clinical tests for 6A-8R. Synthesis of new chemicals.

Development of a new disinfection device using Pernitric acid solution

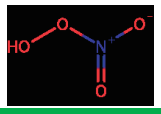
Principal Investigator

Division of Sustainable Energy and Environmental Engineering, Graduate School of Engineering, The University of Osaka

Associate Professor Katsuhisa KITANO

Project Outline

Sterilization by Peroxynitric acid (PNA)



Name	Peroxynitric acid (PNA)
Formula	HNO_4 ($HOONO_2$)
CAS number	26404-66-0

It has been known to exist, but has no applications due to its instability.

There has never been a paper or patent on the use of PNA for sterilization, making it the world's first and only technology [1].

Patent

Sterilization method, preparation for sterilization, and device for producing bactericidal liquid

Patented in Japan, US, UK, Germany, Italy, France, Spain

[1] S. Ikawa, A. Tani, Y. Nakashima, K. Kitano, Journal of Physics D: Applied Physics, 405401(2016).

Chemical synthesis

$$HNO_2 + H_2O_2 \rightarrow \underset{\text{peroxynitrite}}{HOONO} + H_2O$$

$$HOONO + H_2O_2 \rightarrow \underset{\text{PNA}}{HOONO_2} + H_2O$$

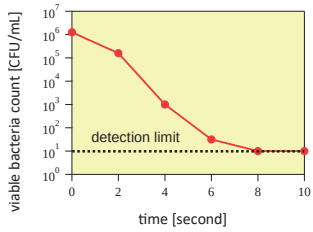
PNA synthesizer

[2] F. Raschig, Angewandte Chemie, 17, 1419 (1904).

Many types pf synthesizer can be provided ※~1M PNA

Sterilization of spore

6.5mM PNA



The D value (time to reduce the bacteria count by one digit) is 1.1 seconds, which is the highest level in the world.

Concentration of PNA

There is a need for disinfectants to be used at lower concentrations than can be harmful. Hydrogen peroxide at 3% is used as oxydol in disinfectants, but at concentrations on the order of 10% it can cause chemical burns, and at concentrations on the order of 90% there is a risk of explosion.

	PNA conc.	equivalent H_2O_2 conc.
undiluted solution	1,000 mM	10,000 %
Medical device sterilization	~10 mM	100 %
Disinfection	~2 mM	20 %

For fungicides, the ratio of fungicidal power to toxicity is important.

Safety studies with animals

	Acute oral toxicity test	Skin irritation test
animal	rat	rabbit
guideline	OECD TG420	OECD TG404
photo		

Sterilization level of disinfection can be applied to living organisms without any problem with 100 mM PNA (1,000% H_2O_2 equivalent).

Material compatibility test

Endurance testing with various materials
Sterilization, washing and drying process ~1000 times

No damage to SUS, O-rings, medical device parts, etc.

Comparison with other bactericides

using spore solution

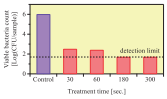
	PNA 1M $HOONO_2$	Oxydol 3% H_2O_2	Antiformin 6% NaClO	Peracetic acid 6% CH_3COO_2H
relative bactericidal activity	3300	1	9.6	400
cost [JPY/L]	1100	1200	28000	27000
cost [JPY/L/bactericidal activity]	0.33	1200	2900	68

PNA solution is odorless.

Unprecedentedly high sterilizing power (equivalent to 10,000% H_2O_2) at low cost

Disinfection of a skin contamination model (pig skin)

Sterilization of vegetative cells (*Staphylococcus aureus*) was simple. Spray jet of PNA solution was applied to pig skin contaminated with spores (*Bacillus subtilis*).



The evaluation criteria for disinfectant efficacy are ~2LogR

The world's first successful sterilization of spores on skin contamination models to the detection limit using disinfectants at concentrations that have been confirmed safe in animal studies

The world's first disinfectant, PNA has an excellent ratio of safety and disinfecting power, and can be applied to various fields from biological disinfection to medical equipment sterilization. The basic patent has been granted in Japan and overseas. Currently, we are building a consortium for research and development of PNA application (http://www.ppl.eng.osaka-u.ac.jp/pna/), in which several companies are participating, and we are looking for new companies to join us.

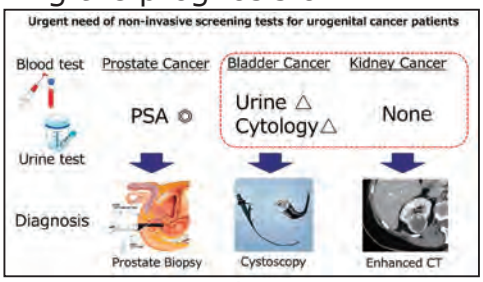
Novel diagnostic marker to differentiate urogenital carcinoma by chiral amino acids in body fluids

Principal Investigator	Department of Urology Graduate School of Medicine, The University of Osaka
	Associate Professor (Lecturer) Atsunari KAWASHIMA

Project Outline

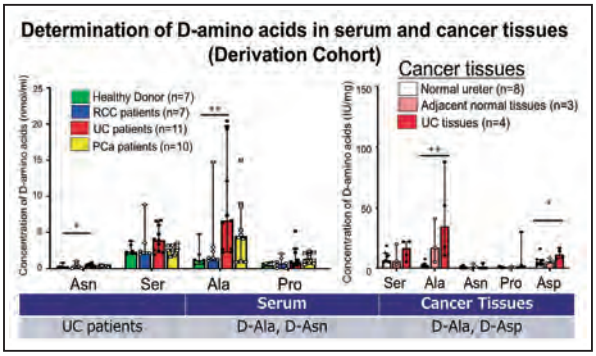
● Importance of differential diagnosis for patients with urogenital cancers including urothelial carcinoma

Early detection and early treatment are key to improving the prognosis of patients with urogenital cancers which have been on the rise in recent years due to the aging society. However, for urothelial carcinoma and renal cell carcinoma, there is no simple and highly diagnostic blood. We have been investigating whether D-amino acids, which are mirror images of L-amino acids and have been thought to have no bioactivity in vivo in humans, could be a novel diagnostic marker for urogenital carcinoma.



【D-amino acids are highly expressed in cancer tissues and blood.】

D-alanine and D-asparagine were highly expressed in the serum of urothelial carcinoma patients, while D-alanine and D-aspartic acid were highly expressed in cancer tissues, respectively. D-alanine and D-aspartic acid were shown to have positive effects on cancer cells by increasing their proliferative, invasive, and migratory capacities against cancer cell lines.



【D-Amino Acids as Potential Tumor Diagnostic Agents】

The results showed that the three independent cohorts of 357 samples had high diagnostic performance in common (left figure). In addition, after comparing the results with urine samples and examining the possibility of differential diagnosis with renal cell carcinoma, we have succeeded in developing a diagnostic agent using blood D-amino acids to differentiate urogenital cancer, and have applied for a patent for this development. (Patent Application No. 2023-036041).

Diagnostic ability of urothelial carcinoma patients using serum D-Asparagine

	Derivation Cohort (n=35)	Validation Cohort 1 (n=254)	Validation Cohort 2 (n=69)
Urothelial carcinoma	n=11	n=92	n=21
Diagnostic Ability (AUC)	0.784	0.851	0.853
Sensitivity	90.9%	78.4%	89.5%
Specificity	66.7%	79.3%	68.0%
Youden's index	0.5758	0.5774	0.5747
Urine Cytology			
Sensitivity	-----	-----	50%
Specificity	-----	-----	100%

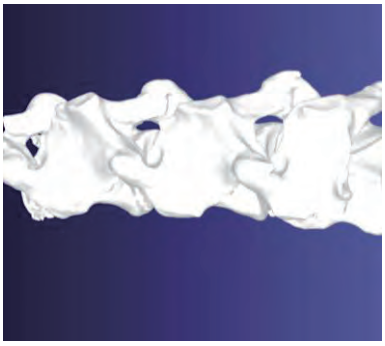
Target disease: Urothelial carcinoma, renal cell carcinoma
Patent information: Patent application 2023-036041
Characteristics of the technology: Novel blood-based urogenital carcinoma differential diagnostic agent
Marketability, challenges in development: Market development through multicenter collaborative research
Desired corporate collaboration: Licensing out

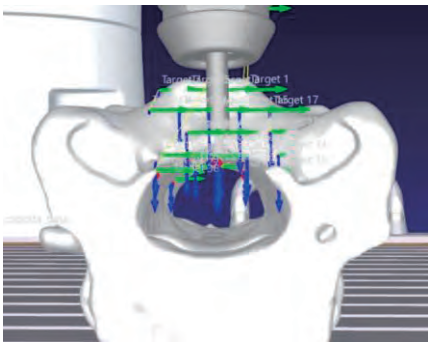
Development of a robot arm for bone processing

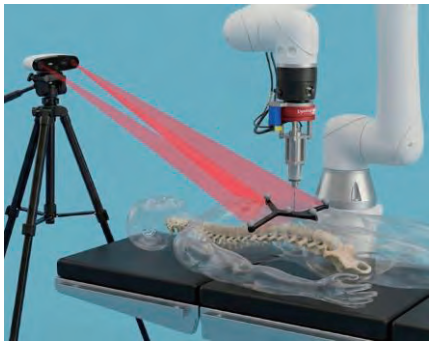
Principal Investigator	Department of Orthopaedic Surgery, Graduate School of Medicine, The University of Osaka
	Associate Professor (Lecturer) Takahito FUJIMORI

Project Outline

Bone drilling, cutting, and resection are fundamental yet highly complex procedures in spinal surgery, carrying significant risks of damage to surrounding nerves and blood vessels. In recent years, advancements in robotic technology have been increasingly recognized for their ability to improve accuracy and safety compared to manual techniques. Driven by the global adoption of robotic surgery and expanding insurance coverage, the demand for surgical assistant robots is projected to continue growing.







3D Modeling from CT Images → **Pre-operative Simulation** → **AutomatedExecution** via NDI tracking and ROS2 control

This project involves the development of an AI control system that automates bone processing procedures, utilizing a general-purpose industrial robotic arm as the base platform.

[Effectiveness] Achieving Safe and Rapid Bone Resection and Standardization of Surgical Techniques

[Principle] The AI system analyzes time-series data from force sensors and motor voltage to infer bone cutting status (e.g., cortical bone breakthrough) in real-time. Based on these predictions, the Robot Operating System 2 (ROS 2) integrates with the NDI Lyra tracking system to provide millisecond-level feedback control, ensuring precise execution according to the pre-operative plan.

Target : lumbar spinal canal stenosis, cervical myelopathy, osteoarthritis, limb fractures

Patent information: Domestic application filed

Technical features: AI-based integrated processing of information from various sensors

Desired type of corporate collaboration: collaboration with companies that have obtained Type 1 manufacturing and sales licenses

Raman spectroscopic tissue detection for minimally-invasive and precise medicine

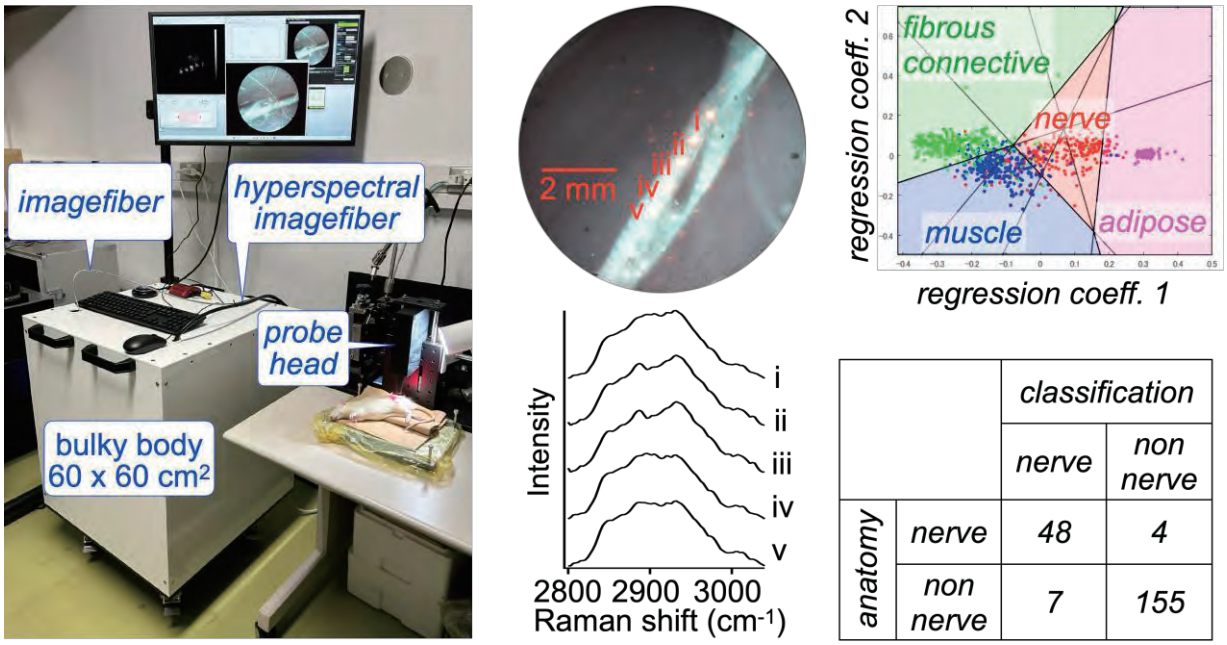
Principal Investigator	Institute for Open and Transdisciplinary Research Initiatives, The University of Osaka
	Associate Professor Yasuaki KUMAMOTO

Project Outline

Raman spectroscopy enables discrimination of cellular and tissue states or types without any sample preprocessing, simply by irradiating the target with laser light and analyzing the resulting Raman-scattered photons. However, Raman signals are inherently weak, and spatially resolved measurements require long acquisition times, which has hindered clinical application. In this study, we aim to develop a spectroscopic analysis method that allows rapid Raman mapping of biological tissues. Unlike conventional Raman mapping techniques, the proposed method measures the entire target region simultaneously. Because illumination is confined strictly to the region of interest, unnecessary light exposure to surrounding areas is avoided, thereby reducing photodamage and preventing degradation of measurement accuracy.

Building on this methodology, our goal is to realize a medical device that can prevent inadvertent injury to critical tissues and incomplete resection of pathological tissues during surgery, while also shortening the operation time. This will contribute to addressing several clinical challenges, including improving postoperative quality of life for patients and reducing the mental and physical burden on surgeons. As an initial application, we are pursuing intraoperative detection of peripheral nerves—structures that are difficult to identify visually—and are evaluating nerve-detection performance using live rat and canine models as well as human clinical specimens.

Currently, the project is in the basic research to preclinical testing phase. Two patent applications have been filed: one for the Raman mapping method and apparatus (filed domestically in January 2022; US/EU national phase entered in July 2024), and another for the portable probe implementation (filed domestically in July 2023; PCT filed in June 2024).



		classification	
		nerve	non nerve
anatomy	nerve	48	4
	non nerve	7	155

Figure. Peripheral nerve discrimination (right) achieved by simultaneous multipoint Raman spectroscopy (center) using the developed device (left).

Development of highly efficient automatic bone marrow stem cell separate system for treatment of stroke patients

Principal Investigator

Department of Regenerative Medicine Research, Institute of Biomedical Research and Innovation, Foundation for Biomedical Research and Innovation at Kobe

Professor Akihiko TAGUCHI

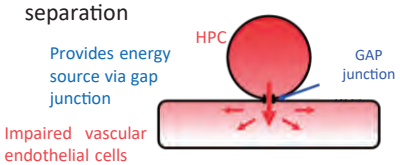
Project Outline

This research aims to “develop an automated stem cell separation device and disposable separation kit” and to “promote economical regenerative medicine through hematopoietic stem cell (HPC) transplantation therapy for cerebral infarction worldwide”. Mononuclear cells containing HPCs have been shown to be effective against cerebral infarction, but until now the therapeutic mechanism was unknown and essential protocols for cell preparation were vague. Our identification of the therapeutic mechanism and inhibitors has enabled us to begin development of a highly effective and low cost cell separation system.

Treatment mechanisms and inhibitors

mechanism

- ✓ Simple cell-cell interaction
- ✓ No need for cell culture and complex separation



Kikuchi-Taura et al, stroke 2020.

inhibitors

Comparison of HPCs injected into stroke patients

Cannot be removed with existing equipment

clot-derived degenerated cells

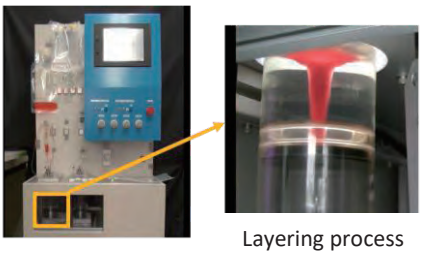
Okinaka et al, stroke 2019.

Current status of cell preparation

Manual separation in CPC

- ✓ High cost
- ✓ Skilled person required

System Development Progress



Layering process

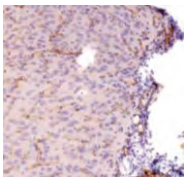
Automated preclinical evaluation device and disposable kit completed

Saino et al, Tissue Eng Part C Methods 2025.

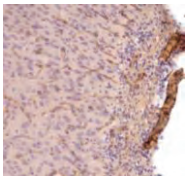
Effect of isolated cells by system

Regeneration of vascular endothelial cells around cerebral infarction

Cerebral infarction model mouse
Brain tissue staining
(CD31 = vascular endothelial cells)



control



Treatment with isolated cells by system

In the course of our research, we have found that this system has the potential to be used in the treatment not only of cerebral infarction but also of all diseases targeted by regenerative medicine using HSCs. We hope to spread this system widely throughout the world as a system that can be used in the treatment of many diseases.

Joint companies：JTEC CORPORATION
Technology：Applicable for various diseases, including dementia, targeted by HSC transplantation therapy.
Patent information：Japanese Patent Application No. 2024-117408, International Application No. PCT/JP2025/025125
We hope to collaborate with medical device manufacturers or companies aiming to industrialize regenerative medicine.
We are considering collaboration on clinical research on HSC transplantation to various disease.

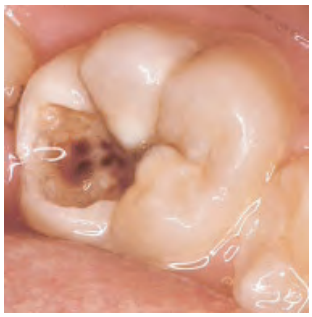
Development of “peptide” pulp capping agent promoting wound healing process of pulp tissue

Principal Investigator	The University of Osaka Dental Hospital
	Associate Professor (Lecturer) Yusuke TAKAHASHI

Project Outline

Dental caries is still spread world wide and pulp tissue is often removed when becoming severe. Once pulp tissue is lost, longevity of the tooth must be shorter. To conserve this tissue, pulp capping procedure is performed and the current success rate is around 60% using conventional materials which were not developed upon the mechanism of wound healing process of pulp.

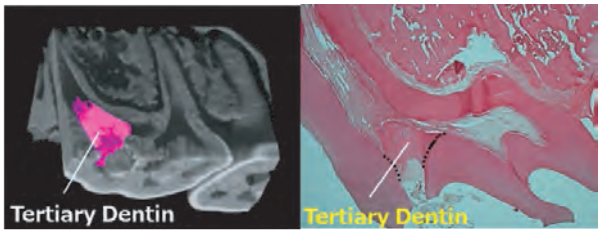
We have performed our research to investigate the pulpal wound healing process and we could identify a critical protein which promoted pulpal repair. In this project, we focus to develop a “peptide” structured pulp capping materials based on the functional domain from the above mentioned protein to enable higher success rate of pulp capping procedure.



40% of Japanese people have untreated caries.

Currently used materials（CaOH, MTA…）
：As source of Ca, P

- Expect wound healing by inducing inflammatory reaction
- Around 60% success rate
- Tertiary dentin formation (Thin, w/defect)



Formation of high quality tertiary dentin after pulp capping with Protein S100A7
(Left: micro CT image, Right: HE staining image)

Current pulp capping material have limitations

Currently used pulp capping materials consist of inorganic substances (eg. Ca, P) and success rate of pulp capping procedure is around 60%. Protein S100A7 which we discovered induced tertiary dentin with higher volume and better quality. Peptide structure derived from this protein can show much higher success rate with safer and cheaper compared with the recombinant proteins. This peptide enables to develop a novel biological evidence based pulp capping agent.

Newly developed peptide based materials
：Wound healing effect of pulp tissue

- Focused on wound healing process of pulp tissue
- Application of materials to promote pulpal repair
- Tertiary dentin formation (Thick, w/o defect)
- Lead to higher success rate than current materials

Peptide materials based on the wound healing process enable higher success rate of pulp capping

This project aims to develop a novel biological pulp capping agent which can be a next generation Mineral Trioxide Aggregate (MTA) and other calcium silicate cements. We have finished to determine a basic structure of the critical peptide and already applied a patent, now searching for an optimal structure of this peptide. We would like to find a company to collaborate with us to develop this agent.

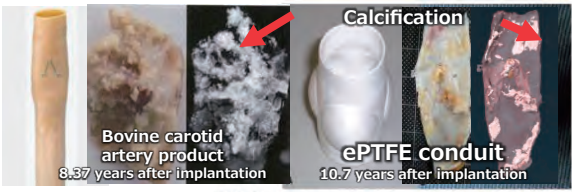
Development of a valved extracardiac conduit using *in situ* tissue restoration

Principal Investigator	Osaka Medical and Pharmaceutical University, Department of Thoracic and Cardiovascular Surgery
	Professor Shintaro NEMOTO

Project Outline

1. Purpose/Background

Currently available valved extracardiac conduits, which are used to reconstruct the continuity between the right ventricle and pulmonary artery in pediatric congenital heart surgery, often result in valve dysfunction and conduit stenosis due to material deterioration (calcification, etc.) or excessive growth of pseudointima. Approximately half of the cases require reoperation for replacement of the deteriorated conduit within 5 to 7 years after surgery. This poses a significant physical and financial burden to patients and their families. In order to solve these problems and reduce the risk of reoperation, this research project will apply our own self-tissue-assembly technology to develop a new valved conduit that maintains its function over a long period of time.



2. Advantages over existing products

We will apply our own technology in a previous research and development of *SYNFOLIUM*®, a hybrid patch for congenital cardiovascular surgery that obtained manufacturing and sales approval in Japan. It has the characteristic that the biodegradable part is gradually replaced by autologous tissue with excellent resistance to deterioration. By adding technical improvements to adapt this patch material to the valve leaflets and outer tube (conduit), we can expect to see a product based on a new concept that solves the problems of existing products.

Time-lapse histological observation of self-organization of *SYNFOLIUM*® after implantation in canine aorta

Nearest goals and project challenges

1. Most recent goals

While experimental evaluation systems, i.e. *in vitro* durability and *in vivo* biological reaction testing, were established in the preceding AMED/ACT-MS research, the physical properties of the valve leaflet and conduit remained to be improved. Regarding optimization, technical solutions are currently being implemented using the AMED/Medical-Engineering Collaborative Innovation Promotion Project. The goal is to establish product specifications within two years, and ultimately finalize a GLP-compliant non-clinical test package through RS strategy consultation with PMDA.

2. Project challenges

Optimizing coating valve leaflet and reinforcement of conduit, confirmation of non-clinical packaging in regulatory process

Target diseases: Congenital heart disease, in which a valved conduit is used to repair, ie, Tetralogy of Fallot, Double outlet right ventricle, Transposition of the great arteries (type III), Corrected transposition of great arteries, and Persistent truncus arteriosus.
Patent information: WO2017/122795 (10 transition countries, domestic patent 6310167), patent 6537656
Partner companies: Teijin Co., Ltd., Fukui Tateami Co., Ltd.

Tumor diagnosis technology using AI analysis of the light spectrum of cytological specimens

Principal Investigator	Medilux Research Center, Nara Institute of Science and Technology (NAIST)
	Professor Yoichiroh HOSOKAWA

Project Outline

A major method of pathological diagnosis is to distinguish tumor cells under an optical microscope. The bottleneck is that even skilled pathologists sometimes have difficulty distinguishing between tumor cells and normal cells. In recent years, artificial intelligence (AI) analysis has attracted attention to solve this problem. The machine learning analysis is about to be applied to the optical microscope images of the pathological specimens.

In the optical microscope, the differences between tumor cells and normal cells are observed in the morphology of cells and intracellular organelles at the micrometer scale. In addition to the microscale changes, the tumor disrupts fine structures of the cytoskeleton and intracellular organelles, including protein denaturation, at the sub-micrometer scale (nanoscale). The light scattering spectrum includes the nanoscale information, which expects to improve the accuracy of the pathological diagnosis. However, the spectral shape is known to be broad and featureless (Fig. 1) due to the highly causal relationship between the light scattering spectrum and the nanoscale structure.

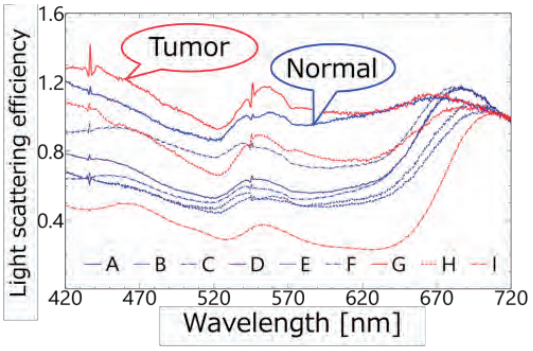


Fig. 1 Light scattering spectra of tumor and normal cells.

For the spectral analysis, we applied Principal Component Analysis (PCA), which is the basis of machine learning analysis. Although the spectral shape had no feature in the difference between tumor cells and normal cells, we found that some of the PCA scores had obvious differences (Fig. 2). We used these PCA scores as training data to discriminate cells and showed that it was possible to discriminate tumor cells with over 95% accuracy.

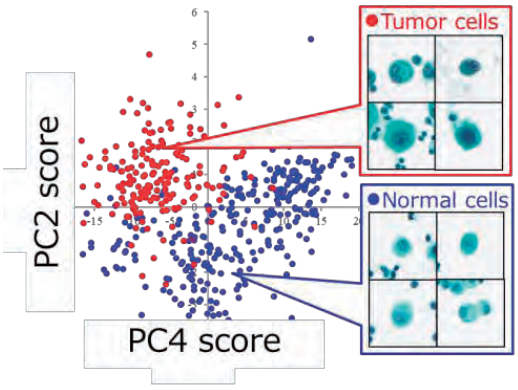


Fig. 2 Scatter plots of the second (PC2) and fourth (PC4) principal components. Each red and blue circle was calculated from light scattering spectra of tumor and normal cells.

Target: Tumor diagnosis

Patent: PTC/JP2024/027247 (JPA No. 2023-125651)

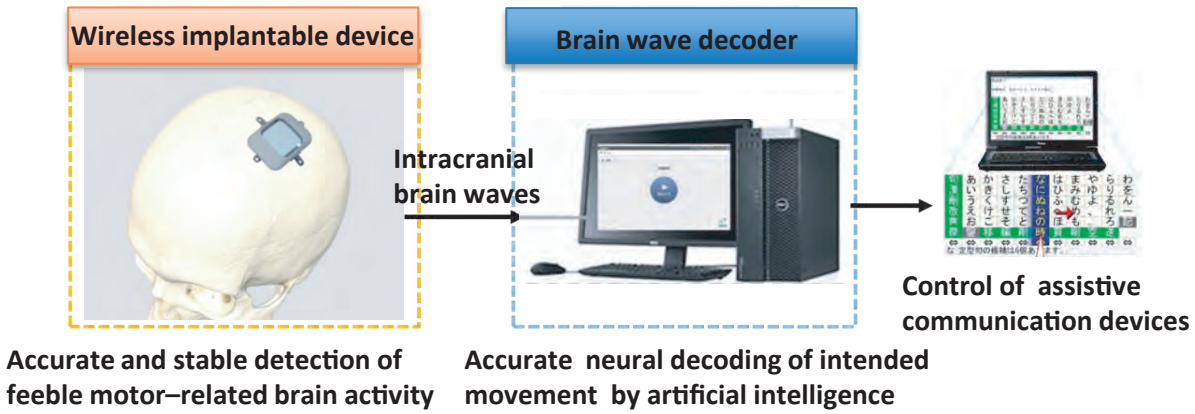
Technical features: Light scattering spectrum was used to distinguish between cell types.

Marketability: This technology is effective as an aid to pathological diagnosis. The challenge is to make accurate training data to realize automatic pathological diagnosis.

Restoration of Motor and Communication by Wireless Implantable Brain Machine Interfaces

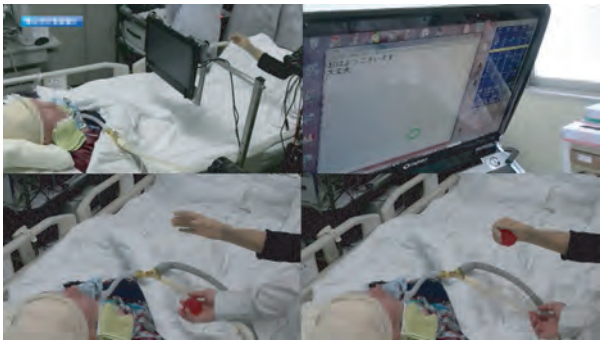
Principal Investigator	Department of Neurological Diagnosis and Restoration, Graduate School of Medicine, The University of Osaka
	Specially Appointed Professor Masayuki HIRATA

Project Outline



A brain-machine interface (BMI) is a technology used to read the contents of motions and communication from brain signals and to control robot arms and communication devices. This is expected as a technology to restore the impaired functions of disable people. In this project, we aim to perform a clinical trial of an implantable BMI device that records accurate brain waves using brain surface electrodes and to license it to a medical company.

In our previous clinical research using wired BMI system, a severely disabled patient with ALS successfully controlled a robot hand. We also developed an implantable wireless device, and completed non-clinical tests. We aim to start a pivotal clinical trial of the implantable wireless device in 2026.



We have developed the implantable device collaborating with Nihon Kohden Corporation and Murata Manufacturing Corporation. We established a start-up company, JiMED Co.Ltd. and now proceed technological transfer, aiming to obtain medical approval and to commercialize the device .

Target diseases：Amyotrophic lateral sclerosis , muscular dystrophy , spinal cord injury
Patents：patented 5, published 1, applied 7, ; PCT 2, USA 4, EU 2, Japan 5
Technologically appealing points：innovative implantable device, Japan quality, high entry barrier, high added value, sustainable profitablity

Human Gastric Tissue Epithelial Stem Cell Organoid Expansion Culture Technology

Principal Investigator	Graduate School of Science and Technology, Nara Institute of Science and Technology (NAIST)
	Professor Akira KURISAKI, Assistant Professor Hitomi TAKADA

Project Outline

When the stomach is entirely removed due to gastric cancer, the decrease in gastric endocrine function and intrinsic factor leads to megaloblastic anemia, along with digestive and absorption disorders and weight loss. Many patients develop post-gastrectomy syndrome. After gastrectomy, the stomach is reconstructed using part of the small intestine to temporarily store food, but no method has been developed to restore the stomach's functions.

We previously succeeded in creating a mini functional stomach tissue from mouse embryonic stem (ES) cells for the first time in the world[1]. Additionally, we developed a method for propagating mouse gastric epithelial stem cells[2],[3]. Building on these achievements, we are currently developing a method to propagate human gastric epithelial stem cells with the ability to differentiate into various functional gastric cell types for stomach tissue regeneration.

1.Nat Cell Biol . 2015, 17(8):984-993. 2.Nat Commun. 2023, 14(1):3750. 3. Japanese Patent Application No. 2023-99622

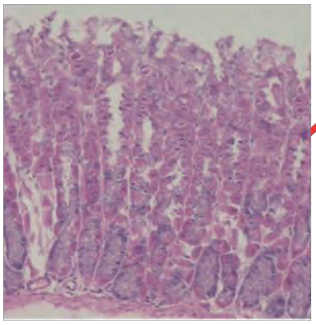


Fig. 1 Gastric tissue

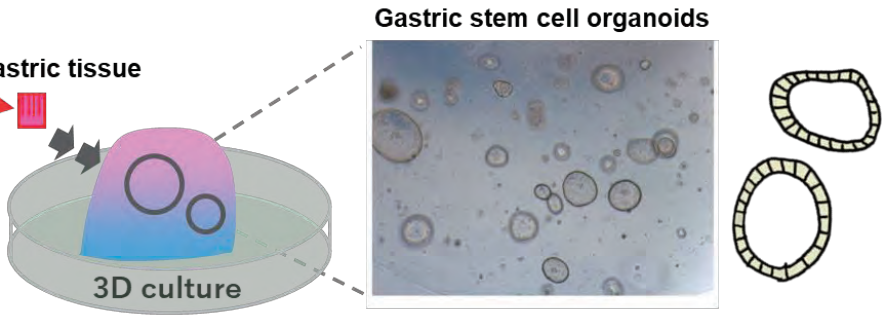


Fig. 2 Proliferating gastric stem cell organoids in 3D culture

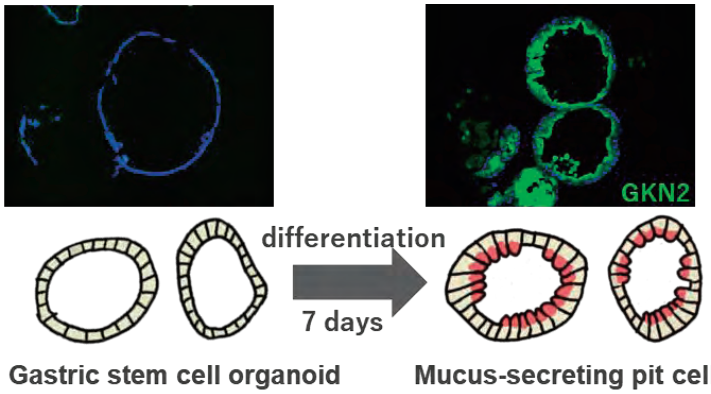


Fig. 3 Mucus-secreting pit cells differentiated from gastric stem cells

Technologies under development

- Method for propagating human gastric stem cells
- Culture media for differentiating human functional gastric cells:
  - Gastric acid-secreting cells
  - Digestive enzyme-secreting cells
  - Gastric mucus-secreting cells

Target Disease: Gastric Cancer.
Japanese Patent application: No. 2023-99622
Technical Features: Propagation technology for human gastric epithelial stem cell organoids capable of differentiating into various functional gastric cells. Growth media and differentiation media for human gastric organoids.
- **Market Potential:** In Japan, over 100,000 people are diagnosed gastric cancer and 10-20% of them undergo total gastrectomy.
- **Challenges:** Development of efficient and scalable production systems for stem cell-derived functional gastric cells.
- **Desired Corporate Collaboration: Collaboration Model:** Joint research and development, followed by licensing-out.

Development of a Novel Culture Container Enabling Simplified Mass Production of Cells

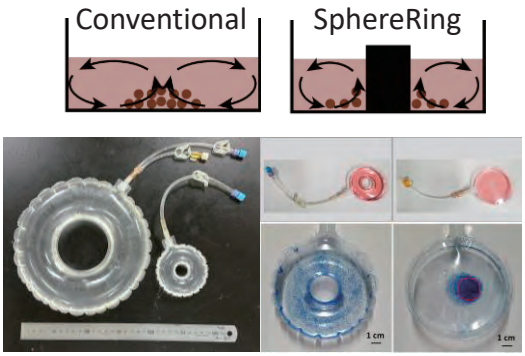
Principal Investigator	Akita University, Department of Materials Science, Applied Chemistry Course
	Associate Professor Ikki HORIGUCHI

Project Outline

○Concept of the project

In therapies utilizing cells or cell-derived products, there is a need to develop methods for obtaining the effective number of cells.

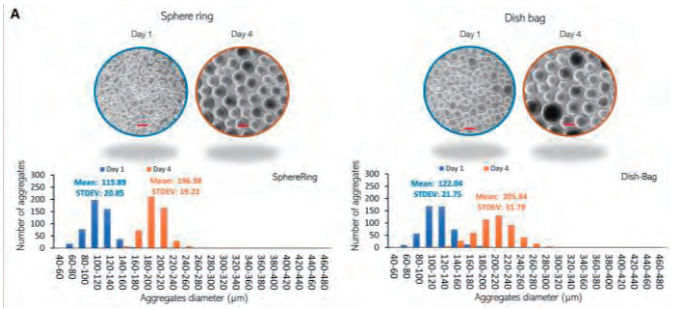
This project is developing a novel closed-system culture vessel for vortex shaking culture, widely used in laboratory basic research. This vessel enables uniform stirring of cell suspensions with low shear stress. Conventional vessels caused cells to concentrate in one area due to flow toward the center of the vessel bottom. By eliminating the central region, this new vessel successfully improves dispersion.



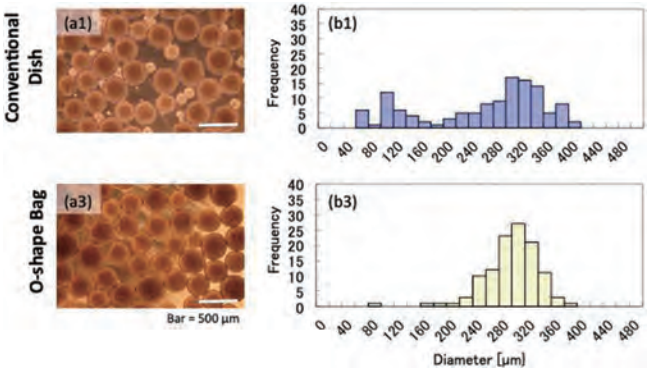
○Application of the product

In developing this product, we obtained aggregates with more uniform particle sizes than conventional culture vessels in suspension cultures of human fetal kidney cell line HEK293, which exhibits aggregation properties, and human iPS cells, which hold promise for regenerative medicine applications. Furthermore, we are advancing studies in suspension culture of mesenchymal stem cells and adipose-derived stem cells. For adipose-derived stem cells, the results have been published in a paper. We are now working on scale-up and SOP design, aiming to establish this as a treatment method and cell preparation method for knee osteoarthritis.

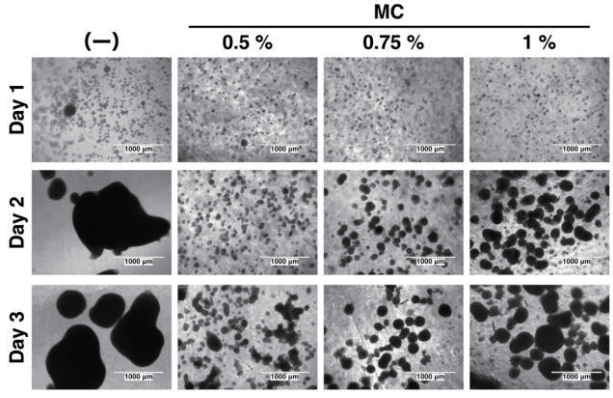
● human iPS cells[2]



● HEK293 cells[1]



● human ADSC[3]



Ref.1: Ikki Horiguchi, Ikumi Suzuki, Takashi Morimura, Yasuyuki Sakai, *J Vis Exp*, e57922, 2019.
Ref.2: Fuad Gandhi Torizal, Seong Min Kim, *et. al.*, *J. Tissue Eng. Regen. Med.*, 2022, 16(3), 254-266.
Ref.3: Takuya Sakamoto, Hiroto Koma, Ayane Kuwano, *et. al.*, *Biochem. Eng. J.*, 2026, 225, 109929

Patent: JP6814380B2, Method for producing cell spheroids.
Feature: A closed-cell manufacturing system that can be implemented simply with low initial investment, structurally stable and advantageous for transportation.

Repair of incurable meniscal injuries using an aligned electrospun nanofibrous scaffold

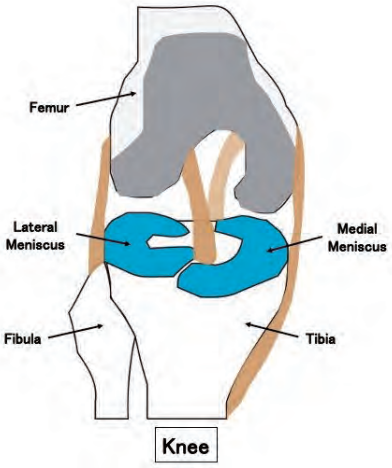
Principal Investigator

Department of Orthopaedic Surgery,
Graduate School of Medicine, The University of Osaka

Guest Professor Kazunori SHIMOMURA

Project Outline

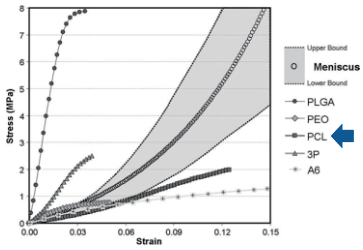
The meniscus plays important roles in the knee joint. Meniscal tears are the most common injury in the knee regardless of age and effective treatments remain challenging. Part of this challenge is due to the meniscus having limited healing potential, owing to its hypocellularity, hypovascularity as well as its complex structure. It is recognized that damaged menisci lose function in the absence of adequate treatment and such knees are at high risk of development of osteoarthritis. However, there have been no established, effective treatments for meniscal tears. As a result, meniscectomy has been commonly advocated for such injuries. Recently, we reported the feasibility of mesenchymal stem cell-seeded electrospun nanofibrous scaffolds to repair the incurable damaged meniscus along with the prevention of subsequent cartilage degeneration using a rabbit model. Thus, the aim of this project is to develop a new meniscal repair technique using our novel tissue engineering method.



Electrospun nanofibrous scaffold

- **Aligned fiber**
- **Biocompatibility**
- **Slow bioabsorbability**
- **High tensile strength**

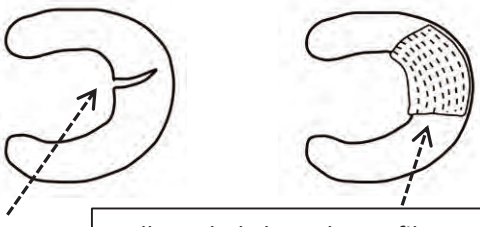
SEM image of poly(ε-caprolactone) (PCL)-based electrospun scaffold



Similar tensile strength w/ meniscus

Target

- **Meniscal tear:**
  Meniscal surgeries performed in Japan (2007–2014): 83,105 cases
  (Rate of meniscectomy: 83.4%)
- **Knee osteoarthritis:**
  Estimated number of patients in Japan: 25 million



Meniscal tear

Cell-seeded aligned nanofibrous scaffold
- Reinforcement for meniscal injured site
- Enhancement of meniscal repair

References

Mauck R, Tissue Eng Part B 2009.
Shimomura K, Tissue Eng Part A 2015.
Shimomura K, Biomaterials 2019

The preclinical POC study aim to be completed until March 2027.

Study aiming to produce human iPSC-derived cell formulation for metabolic hepatic disorder

Principal Investigator

Department of iPS Stem Cell Regenerative Medicine, Kansai Medical University

Associate Professor (Lecturer) Yasumasa SHIROUZU

Project Outline

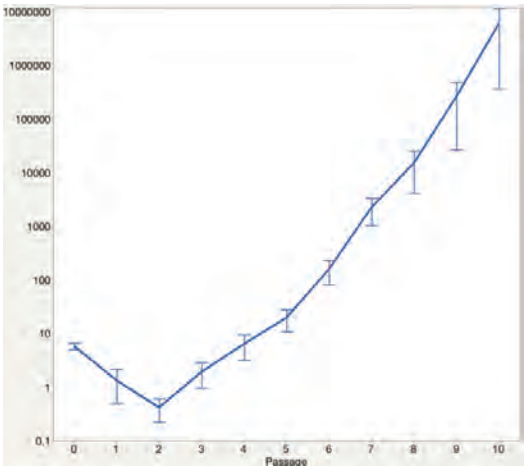
Urea cycle disorder exhibits the symptoms of hyperammonemia caused by the inborn error of the metabolic enzyme of urea cycle. Severe cases show the short-term poor prognosis, while non-severe cases may also show the irreversible nerve system damage. The prevalence is considered to be 1: 8,000–44,000 live births (Morioka D et al, Liver Transpl 2005; 11: 1332). Living donor liver transplantation (LDLT) is a complicated treatment for infants less than 6 Kg who have smaller abdominal cavity, and the earlier introduction of LDLT is supposed difficult although it is only a curative therapy in Japan (Shirouzu Y et al, Liver Transpl 2006; 12: 1224).

Meanwhile, cell transplantation using hepatocytes from deceased donor livers or hepatocytes differentiated from embryonic stem cells (ESC) and induced pluripotent stem cells (iPSC) is regarded as minimally invasive treatment by intraportal administration (Figure 1). Even new born babies can undergo the hepatocyte transplantation therapy via the umbilical vein, and it brings about the revision of hepatic metabolic disorders. However, it remains only a temporal or adjunctive treatment before liver transplantation suggesting the importance of hepatic stem cells as transplanted cells don't work for a long time (Iansante V et al, Pediatr Res 2018; 83: 232).

Figure 1 The comparison with the existing treatments

	Liver transplantation	Hepatocyte transplantation	iPSC-derived hepatic stem cell-like cell transplantation
Problems about donors	Yes	Yes (Quality is usually poor)	No
Cryopreservation	No	Yes	Yes
Inclusion of stem cells	Yes	No	Yes
Treatment invasion	Highly	Minimally	Minimally
Effectiveness	Permanent	Short-term	Long-term ?
Technical difficulty	Yes→Not applicable to new born babies	No→Applicable to new born babies	

Figure 2. Growth curve of iPSC-derived hepatic stem cell-like cells



We successfully developed iPSC-derived hepatic stem cell-like cells which can be proliferated under chemically defined condition and maintained for a long time (Figure 2, 3). They can self-renew as the hepatic progenitors and are differentiated into matured hepatocytes by the alteration of the medium composition (Figure 4). Cryopreserving them as the products make the emergent transplantation feasible because the infants suffering from the severe hepatic metabolic disorders require the immediate revision. Transplantation experiments are currently being prepared aiming to find the proof of concept.

Figure 3. Immunostaining of iPSC-derived hepatic stem cell-like cells after 146-day culture

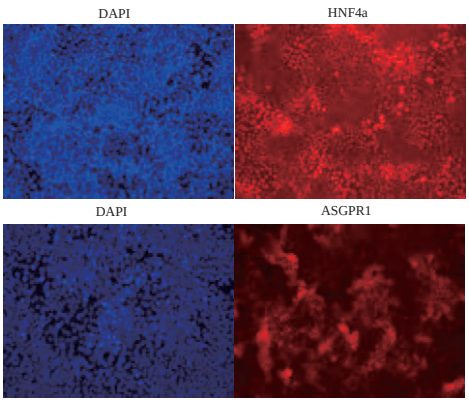
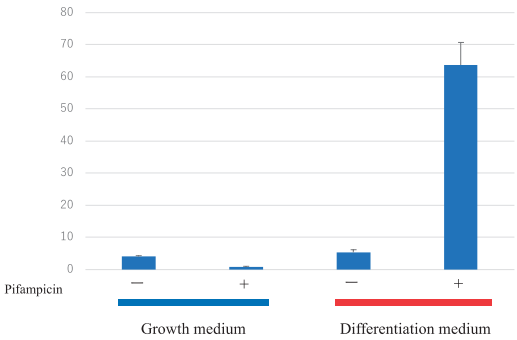


Figure 4. CYP3A4 mRNA expression after repeated passages



iPSC-derived hepatic stem cell-like cells expressed CYP3A4 mRNA following 48-hour Rifampicin treatment not in growth medium but in differentiation medium.

Object : Congenital metabolic hepatic disorder
Patent : No
Characteristics : iPSC-derived hepatic progenitors that are expandable with neither serum nor purification
Development subject : Difficulties of clinical trials for a scarcity of patients

Development of oncolytic adenovirus agents composed of human adenovirus type 35

Principal Investigator	Graduate School of Pharmaceutical Sciences, The University of Osaka
	Professor Hiroyuki MIZUGUCHI

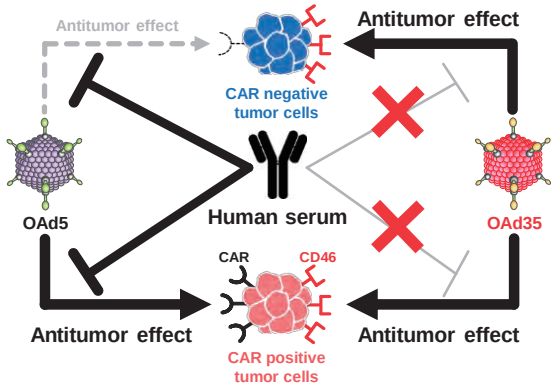
Project Outline

[Abstract]

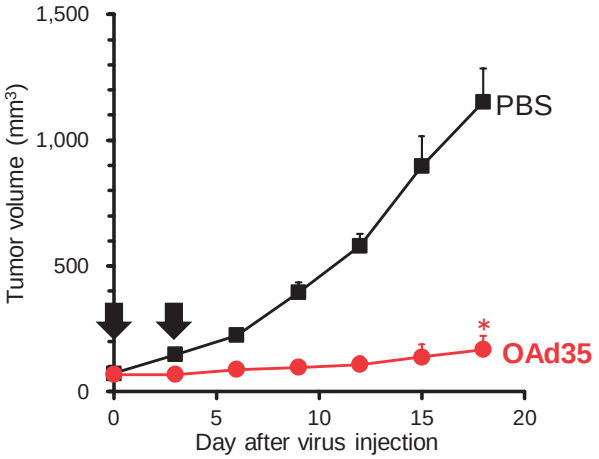
Oncolytic viruses, which can specifically replicate in and kill tumor cells without apparent toxicity to normal cells, are attracting much attention as a novel cancer therapeutic agent. Among various types of oncolytic viruses, the oncolytic adenoviruses (OAds) are one of the most promising. Almost all Oads are composed of human adenovirus (Ad) serotype 5 (Ad5), which belongs to species C. However, the OAds composed of Ad5 (OAd5) has two major drawbacks. OAd5 recognizes coxsackievirus-adenovirus receptor (CAR) as an infection receptor. CAR expression is often reduced on malignant tumor cells, leading to inefficient infection with OAd5. In addition, more than 80% of adults have neutralizing antibodies against Ad5 due to natural infection with Ad5 during childhood. In order to overcome these drawbacks, we developed a novel OAd fully composed of human Ad serotype 35 (Ad35) (OAd35), which belongs to species B2. Ad35 recognizes human CD46 as an infection receptor. CD46, which is a complement regulatory protein, is ubiquitously expressed on all human cells except erythrocytes. Moreover, CD46 is often upregulated on malignant tumor cells. In addition, 20% or fewer adults have neutralizing antibodies against Ad35. OAd35 efficiently killed not only CAR-positive but also CAR-negative tumor cells. Anti-Ad5 serum did not inhibit the OAd35-mediated tumor cell killing. Intratumoral administration of OAd35 resulted in significant growth suppression of the subcutaneous CAR-positive and CAR-negative tumors.

[Significance of the research and Future perspective]

OAd35 become a promising alternative oncolytic virus, especially for tumors resistant to a conventional oncolytic Ad.



Characteristics of OAd35



Intratumoral administration of OAd35 significantly suppressed tumor growth

Target disease.：Cancer
Patent information：Patent No. JP7508109, Application No. JP2023-138116, PCT/JP2024/28319, Application No. JP2025-027505
Reference papers：Mol. Ther. Oncolytics. 2021, 20, 399-409. doi: 10.1016/j.omto.2021.01.015
J. ImmunoTher. Cancer, 2025, 13, e006558. doi: 10.1136/jitc-2022-006558.
https://doi.org/10.1101/2022.12.09.519732.
Subject for development：Preclinical studies in clinically relevant models (currently in progress)
Details of desired corporate collaboration：General research support for clinical application

Development of gene therapy for arrhythmogenic right ventricular cardiomyopathy

Principal Investigator

Department of Cardiovascular Medicine
The University of Osaka Graduate School of Medicine

Associate Professor/Lecturer Shuichiro HIGO

Project Outline

【Background of the Study】

Severe heart failure at a young age refractory to standard therapy is an unmet medical need in cardiovascular medicine. Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a rare disease caused by genetic variants in genes encoding components of the cardiac intercalated disc. Patients with ARVC exhibit progressive contractile dysfunction in both right and left ventricles and fatal arrhythmias. Among the causative genes for ARVC, desmoglein-2 (*DSG2*) is known to be the most common in Japan. We identified desmoglein-2-deficient cardiomyopathy due to genetic variants in a patient with severe heart failure and demonstrated the therapeutic concept of *DSG2* gene replacement using adeno-associated virus (AAV) vectors in iPSC-derived cardiomyocytes (iPSC-CMs) (*Hum Mol Genet. 2021 Jul 9;30(15):1384-1397*). Furthermore, we found that impaired intercalated disc structure due to pathogenic *DSG2* gene variants is concealed not only in dilated cardiomyopathy but also in various forms of refractory heart failure (*Hum Genome Var. 2024 Dec 20;11(1):47*, *The 89th Annual Scientific Meeting of the JCS*). Although the incidence of ARVC is estimated to be approximately 1 in 5,000 individuals, our genetic analysis data suggest that *DSG2*-related intercalated disc dysfunction may be concealed in a large population of refractory heart failure. We found that desmoglein-2 expression in cardiac tissues was decreased in cases with *DSG2* variants, indicating the necessity of developing gene therapy to restore *DSG2* in the heart.

【Current Progress】

Building upon our established research and development platform utilizing iPS cells (*Stem Cell Reports, 2022. 17(2): 337-351; Circ Genom Precis Med. 2022 Jul 12; JACC Basic Transl Sci, Feb 08, 2023*), we are advancing our studies from both basic and clinical perspectives. Our efforts include the construction of a case registry, the establishment of human iPSC-CM disease models from patients with ARVC, and the development of a mouse model that recapitulates desmoglein-2-deficient cardiomyopathy. Furthermore, we are employing AAV vector for cardiac gene therapy equipped with a heart failure-responsive enhancer, developed by Associate Professor Ken Matsuoka (the Department of Medical Chemistry, Osaka University Graduate School of Medicine). This vector enables robust, cardiac-specific expression even at low doses of AAV, offering the potential for high efficacy and safety.

【Our Aim】

At the University of Osaka Hospital, many patients with severe refractory heart failure receive medical therapy. Our goal is to deliver precise and safe medical therapy based on basic research to these patients. The development of AAV-based gene therapy requires extensive infrastructure, advanced technologies, and robust industry-academia collaboration. We seek partnerships with companies that share our vision for advancing medical therapy. For more details about our research, please refer to the link (→).

Target Disease: Arrhythmogenic right ventricular cardiomyopathy caused by DSG2 gene variants
Patent Information: Patent Application No. 2022-508325; Patent granted on November 18, 2025
Technical Features: A gene therapy vector targeting arrhythmogenic right ventricular cardiomyopathy caused by *DSG2* gene variants
Market Potential and Development Challenges: We aim to develop therapeutic agents targeting gene variants specific to Japanese and East Asian populations
Desired Industry Collaboration: Joint research, GMP manufacturing of AAV gene therapy drugs, and out-licensing

Development of Liver Assist Device Using Hypoimmunogenic Hepatocyte System

Principal Investigator	Graduate School of Medicine, The University of Osaka
	Professor Takanori TAKEBE

Project Outline

Acute-on-chronic Liver Failure (ACLF) is a disease in which a patient with cirrhosis or other chronic liver failure develops due to some trigger such as infection, gastrointestinal hemorrhage, or heavy alcohol consumption, leading to a precipitous state of liver dysfunction within 28 days. ACLF is characterized by systemic inflammatory response syndrome (SIRS) and multiple organ failure and is a critical disease with a mortality rate of over 80% for ACLF Grade 3, the most severe form. However, there exists no effective treatment other than liver transplantation at present, and many patients' lives cannot be saved.

In this project, we are developing an extracorporeal circulatory system (UTOpiASystem) for liver function assistance by incorporating liver organoids (iHLC: induced Hepatocyte-Like Cells) derived from Low immunogenic induced pluripotent stem cells (iPSCs) into the system for such serious liver diseases, based on the liver organoid technology obtained in our previous research (Figure 1). The UTOpiAsystem is a unique extracorporeal circulation system that consists of a granulocyte and monocyte adsorption apheresis (GMA) column, which traps neutrophils and inflammatory cytokines released in excess due to inflammation, and an iHLCcolumn, which is capable of supplementing proteins secreted by the liver and removing toxins such as ammonia and bilirubin. Successful development of this product would provide a new treatment option other than liver transplantation for patients with severe liver failure.

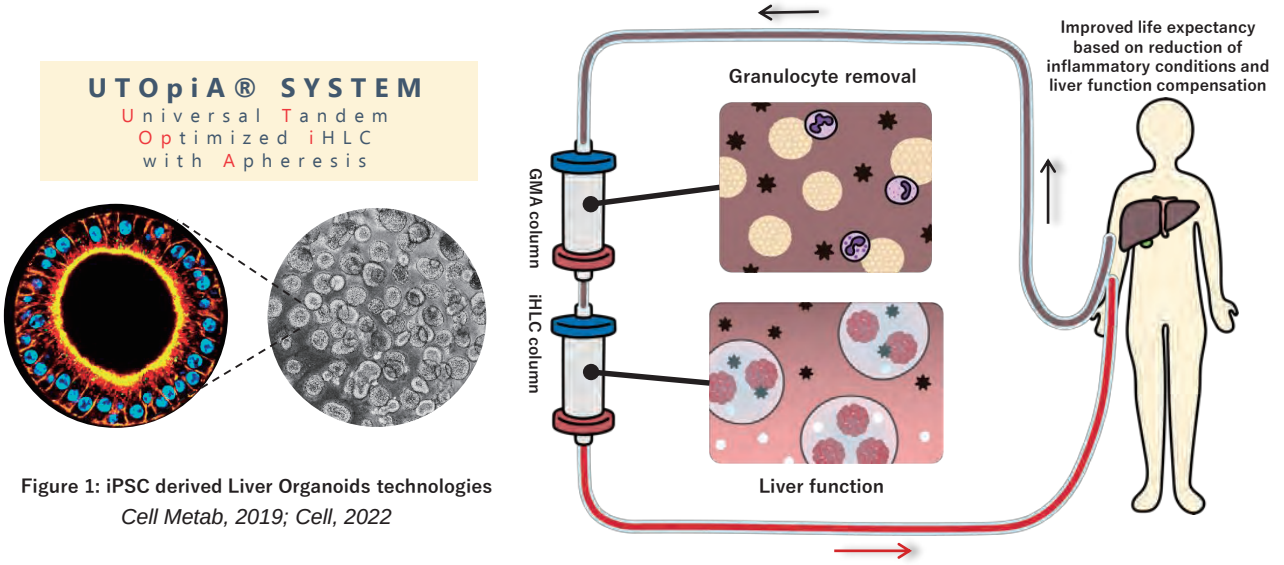


Figure 1: iPSC derived Liver Organoids technologies
Cell Metab, 2019; Cell, 2022

【Results of research to date and future plans for development】

When ACLF model rats were treated with UTOpiAfor 2 hours, a significant improvement in survival rate was observed compared to the group that was not treated with UTOpiAor the group that was treated with each column alone. We are currently working to scale up the manufacturing process of liver organoids for clinical application and to establish a technology to produce columns of a size that can be used for patients. After establishing the manufacturing method and conducting non-clinical safety studies, we aim to begin clinical studies to confirm safety and tolerability within two to three years.

Target disease: ACLF, Acute Liver Failure, Post Hepatectomy Liver Failure, Severe Alcoholic Hepatitis
Patent information: PCT filed
Technology features: Non-clinical POC obtained using ACLF model rats
Markets and challenges in development: Large market expected due to the global increase in liver failure patients. Scale-up of manufacturing is the challenge.
Desired corporate collaboration: Joint research with Yokohama City University Venture KanzoBiomedicines, Inc.

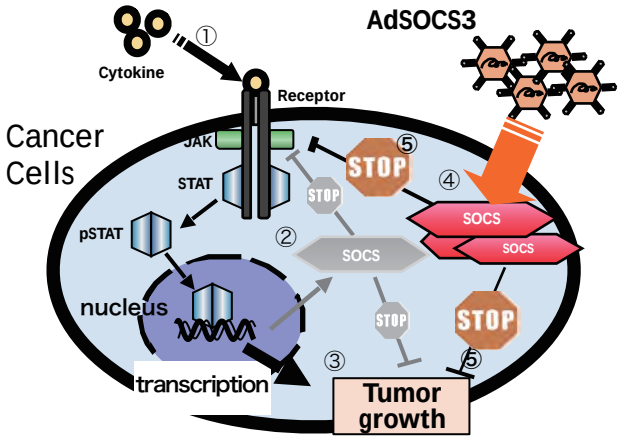
Development of novel treatment for malignant pleural mesothelioma using viral vector
(Investigator-initiated clinical trial of gene therapy using AdSOCS3 for malignant pleural mesothelioma)

Principal Investigator	Institute for Biomedical Sciences, Division of Drug Discovery and Medical Device Development, Iwate Medical University
	Professor Tetsuji NAKA

Project Outline

Malignant pleural mesothelioma is a cancer with a poor prognosis caused by exposure to asbestos. In Japan, asbestos was used until the mid-1980s, and due to the inhalation of dust generated during the disposal of debris from the Great Hanshin-Awaji Earthquake and the Great East Japan Earthquake, it is estimated that the number of patients with malignant pleural mesothelioma will increase until after 2030, and the development of new treatment methods is required. AdSOCS3 is a new gene therapy that incorporates a suppressor of cytokine signaling-3 (SOCS-3) into an adenoviral vector. AdSOCS3 showed high antitumor effect in malignant pleural mesothelioma cell line and mouse model of malignant mesothelioma. So far, we have completed GMP-compliant manufacturing and non-clinical testing (quality testing, GLP testing) of AdSOCS3. In this project, we will conduct an investigator-initiated clinical trial to evaluate the safety and efficacy of AdSOCS3.

Action mechanism of gene therapy with AdSOCS3

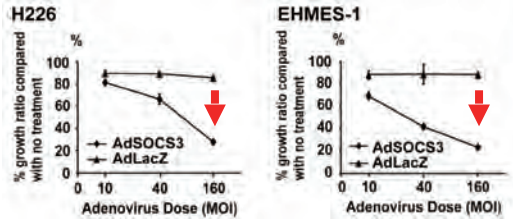


Excessive cytokine stimulation leads to abnormal cell proliferation and canceration. SOCS is a JAK/STAT signal inhibitory molecule (②) induced by cytokine stimulation (①). In malignant pleural mesothelioma, the endogenous SOCS gene is inactivated, resulting in enhanced cancer growth signals (③).

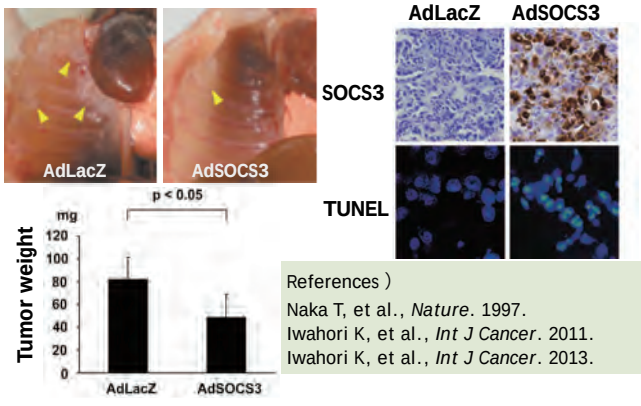
By overexpressing SOCS3 in cells (④), AdSOCS3 exerts a strong inhibition on cytokine signals, resulting in the arrest of cancer growth signals (⑤).

Antitumor effect of AdSOCS3 on malignant pleural mesothelioma

AdSOCS3 exerts antitumor effects in vitro against malignant pleural mesothelioma cell lines.



Administration of AdSOCS3 to mice model transplanted with malignant pleural mesothelioma in thoracic cavity promotes apoptosis of mesothelioma cells and reduces tumor weight.



References)
Naka T, et al., *Nature*. 1997.
Iwahori K, et al., *Int J Cancer*. 2011.
Iwahori K, et al., *Int J Cancer*. 2013.

Target disease: Malignant pleural mesothelioma
Patent information: Patent application 2008-301919
Technology features: Gene therapy using adenoviral vectors (regenerative medicine products)
Marketability and development issues: The number of Malignant mesothelioma patients will peak around 3,000 per year around 2030, but no effective treatment has been developed yet and development of novel therapeutic drug is awaited.
Corporate collaboration: Takara Bio Co., Ltd. (manufacturer of investigational drug), Mitsubishi Tanabe Pharma Corporation (licensing-out after completion of phase I trial), ONSSI Co., Ltd. (venture company launched by R&D representatives)

Development of a novel treatment for pediatric craniofacial deformity using human reconstructed elastic cartilage

Principal Investigator

Division of Regenerative Medicine,
Institute of Medical Science, University of Tokyo

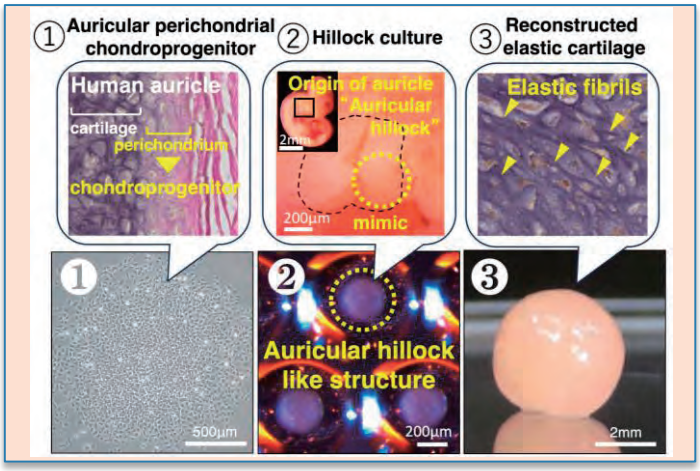
Professor Hideki TANIGUCHI

Project Outline

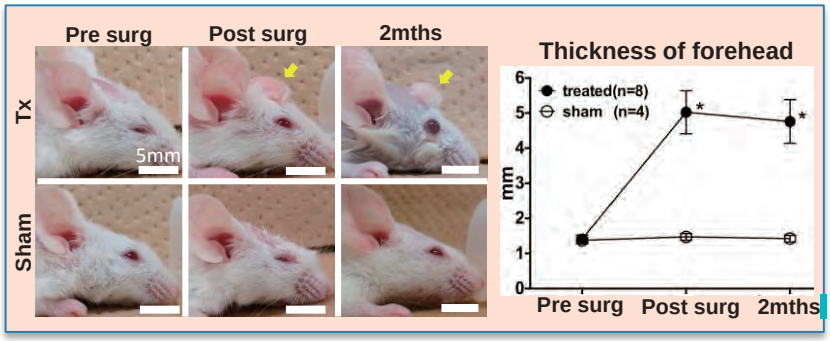
Pediatric craniofacial deformities caused by congenital malformations and traffic trauma are not only cosmetic problems, but also cause serious adverse effects on children's mental development and may lead to school refusal. Establishing a minimally invasive, morphologically stable treatment for pediatric craniofacial deformity is required.

Previously, we have succeeded in developing the world's first method of isolating and culturing human cartilage progenitor cells with the ability to differentiate into elastic cartilage (Fig①).[1] Using these unique cells, a novel three-dimensional rotational culture method was developed to create a scaffold-free human elastic cartilage reconstruction.[2] Furthermore, by discovering that chondrogenesis to be promoted by mimicking the auricular development in a morphological manner, we established a novel “hillock culture” method that can promote chondrogenesis efficiently (Fig②).[3] Utilizing these new technologies, we have developed the world's first in vitro scaffold-free human reconstructed elastic cartilage (Fig③).[3]

Reconstructed elastic cartilage first in vitro



Effect of reconstructed elastic cartilage in vivo



Owing to the sufficient maturation in vitro, our novel scaffold-free reconstructed elastic cartilage shows high morphological stability even after transplantation (left figs), which cannot be seen in the existing methods.[3]

In this project, we aim to obtain the clinical POC of this novel treatment by carrying out a clinical trial.

1 : Kobayashi, …Taniguchi. Reconstruction of human elastic cartilage by a CD44+ CD90+ stem cell in the ear perichondrium. *Proc Natl Acad Sci U S A*. 2011

2 : Enomura,…, Taniguchi. Development of a method for Scaffold-Free Elastic Cartilage Creation. *Int J Mol Sci.* 2020

3 : Oba, …,Taniguchi. In Vitro Elastic Cartilage Reconstruction Using human Auricular Perichondrial Chondroprogenitor Cell-Derived Micro 3D Spheroids. *J Tissue Eng*. 2022

Target disease : Pediatric craniofacial deformity

Patent information : Patent application no. 2021-141210; PCT/JP2022/25582

Cooperate collaboration : Japan Tissue Engineering Co., Ltd, JTEC Corporation Co., Ltd

Joint research : Yokohama City University, Kanagawa Children's Medical Center

Prognosis biomarkers that can discriminate early-stage pancreatic cancer patients with worse prognosis prior to surgery

Principal Investigator

Department of Gastroenterology and Hepatology,
Kochi Medical School, Kochi University

Associate Professor Keisuke TANIUCHI

Project Outline

(Abstract)

- Pancreatic cancer is one of the most aggressive tumors, and the prognosis is poor, with 1- and 5-year survival rates of only 20% and 6%, respectively.
- The UICC TNM staging system for pancreatic cancer is a useful predictor of postoperative prognosis.
- More reliable prognostic predictors that can discriminate pancreatic cancer patients into two prognosis groups (longer disease-free survival and/or better pancreatic cancer-related survival vs. shorter disease-free survival and/or poor pancreatic cancer -related survival) are necessary for clinical decision-making.
- The combination of Protein-A with Protein-B accurately predicted the postoperative outcomes of pancreatic cancer patients, and they were superior compared to the TNM staging system (Figure described below).
- There are no reliable biomarkers to gauge the response to neoadjuvant therapy prior to the initiation of the therapy. A retrospective clinical study (UMIN000032835) showed that overexpression of Protein-A and Protein-B in 25 preoperative biopsy pancreatic cancer tissue samples was correlated with postoperative survival (P=0.04).

(On going)

- Antibodies against Protein-A and Protein-B have been generated in July 2021.
- We are trying to commercialize an immunohistochemical staining kit.
- We are trying to develop an artificial intelligence system that can automatically evaluate the immunostaining scores of Protein-A and Protein-B.
- A prospective clinical study (UMIN000034022) has been conducted to determine if immunohistochemical scores of Protein-A and Protein-B can be used as reliable biomarker of the response to neoadjuvant therapies prior to their initiation.

Multivariate analysis using the Cox proportional hazards regression model

	HR (95% CI)	P
UICC Stage		
0, IA, IB	0.25 (0.09-0.70)	0.009
IIA, IIB	Reference	
III, IV	3.05 (1.25-7.42)	0.014
ARHGEF4 expression	2.52 (1.28-5.00)	0.007
ARHGEF4 expression and intrapancreatic nerve invasion	2.97 (1.36-6.49)	0.006
ARHGEF4 and ITGB1 expression	0.22 (0.08-0.59)	0.003
Protein-A and Protein-B expression	6.27 (2.58-15.2)	< 0.001
Protein-A and Protein-C expression	3.93 (1.74-8.91)	0.001

The language of red gerberas is
“Positivity,” “Endless Challenge,”
and “Passion.”

Nurtured with care in the palm is
a small research seed
that leads to the future.

As it gradually sprouts and
continues to bloom,
the flower symbolizes
the driving force behind
continuously improving health
—the Engine of Improving Health.

When people’s passions
become the power and
continue to take on challenges,
great flowers will eventually bloom
that will support society.

Maya

大阪大学医学部附属病院　未来医療開発部

〒565-0871　大阪府吹田市山田丘2-2

Department of Medical Inovation, The University of Osaka Hospital

2-2 Yamadaoka, Suita, Osaka 565-0871, Japan

TEL:+81-06-6210-8289　FAX:+81-06-6210-8301

E-mail: mirai@hp-mctr.med.osaka-u.ac.jp

URL: http://www.dmi.med.osaka-u.ac.jp/dmi/index.html